ISSN 0120-9957
ISSN 2500-7440 (Online)
DOI: https://doi.org/10.22516/issn.2500-7440

RCG Revista Colombiana de Gastroenterología

Volume 39 - Number 2
April - June 2024

www.revistagastrocol.com
www.gastrocol.com · www.scielo.org.co





Editorial

Artificial intelligence: the future made reality

Original articles

Automatic Auditing System for Endoscopic Exploration of the Stomach with Artificial Intelligence-Gastro UNAL: Gastroendoscopy UNit for Automatic Labeling

Experience in Peroral Endoscopic Myotomy in a Center in Bogotá, Colombia, Between 2018 and 2022

Stent Duodenal in Malignant Obstruction of the Gastric Outflow Tract in a Reference Center in Cundinamarca: Case Series

Baveno VII Criteria for the Exclusion of Esophageal Varices in a Peruvian Population: Cross-Sectional Study

Beyond the Gut: Extraintestinal Manifestations of Inflammatory Bowel Disease in Children and Adolescents

Review articles

Research and Publish. 2. Answering the Question: Study Design

Pyloric EndoFlip and Its Clinical Use in Gastroparesis

Disorders of Gut-Brain Interaction (Functional Gastrointestinal Disorders): Neuromodulators in Clinical Practice (Part I)

Case reports

Extensive Pancreatic Necrosis, Successful Management with Percutaneous Endoscopic Necrosectomy

New Technique for Buried Bumper Syndrome Resolution

Gastric Polyposis in Familial Adenomatous Polyposis: A Case Report. An Approach for the Endoscopist

Spontaneous Pneumoperitoneum: A Pathology Not Always Surgical. Presentation of Two Documented Cases in Patients in Association with SARS-CoV-2 Infection

Primary Congenital Intestinal Lymphangiectasia: A Case Report

Celiac Disease, A Silent Enemy: A Case Report

Metastasis of Lung Cancer in the Pancreas, Diagnosis Using Endoscopic Ultrasound: A Case Report

ASOCIACION COLOMBIANA DE GASTROENTEROLOGIA
1947

Volume 39 No. 2 | April - June 2024

Contents

RCG Revista Colombiana de Gastroenterología

Editorial

Artificial intelligence: the future made reality 131
David B. Páramo-Hernández, Ricardo A. Cepeda-Vásquez.

Original articles

Automatic Auditing System for Endoscopic Exploration of the Stomach with Artificial Intelligence-Gastro UNAL: Gastroendoscopy UNit for Automatic Labeling 133
Martín Gómez, Diego Bravo, Josué Ruano, María Jaramillo, Fabio A. González, Eduardo Romero.

Experience in Peroral Endoscopic Myotomy in a Center in Bogotá, Colombia, Between 2018 and 2022 146
Tatiana Barragán-Briceño, Paola González-A., Carlos Fuentes-D., Jesús Rodríguez-F., María Camila Gómez-Ayala.

Stent Duodenal in Malignant Obstruction of the Gastric Outflow Tract in a Reference Center in Cundinamarca: Case Series 153
Margarita Gutiérrez, Martín Garzón-Olarte, Andrea Gómez, Juan Carlos Marulanda, Natan Hormaza-Arteaga, Katherine Marrugo, Juan Carlos Molano, Laura Moya, Christian Labrador, Mario Rey-Tovar.

Baveno VII Criteria for the Exclusion of Esophageal Varices in a Peruvian Population: Cross-Sectional Study 158
Celide Campoverde-Cueva, Williams Celedonio-Campos, Brayan Campos-Salazar, Rommel Zambrano-Huailla, Karla Alejandra Vizcarra-Zevallos, Jorge Garavito-Rentería.

Beyond the Gut: Extraintestinal Manifestations of Inflammatory Bowel Disease in Children and Adolescents 166
Angie Vanessa Vergara-Espitia, Diana Victoria Mora-Quintero, José Antonio de la Hoz-Valle, Ana María Castañeda-Figueroa, Fernando Quintero-Sarmiento.

Review articles

Research and Publish. 2. Answering the Question: Study Design 176
Margarita Rey-Rubiano.

Pyloric EndoFlip and Its Clinical Use in Gastroparesis **179**
Albis Cecilia Hani de Ardila, Aldair Chaar, Juan Hernández, Raúl Cañadas, María del Carmen Figueredo.

Disorders of Gut-Brain Interaction (Functional Gastrointestinal Disorders): Neuromodulators in Clinical Practice (Part I) **187**
Luis Fernando Pineda-Ovalle, David Benigno Páramo-Hernández, Laura Marcela Moya-Valenzuela, Alejandro Concha-Mejía, Juan David Páramo-Díaz.

Case report

Extensive Pancreatic Necrosis, Successful Management with Percutaneous Endoscopic Necrosectomy **194**
Daniela Giraldo-Campillo, Juliana Lucía Molina-Valencia, Juan Camilo Ricaurte-Ciro, Carlos Andrés Delgado-López.

New Technique for Buried Bumper Syndrome Resolution **199**
Marisol Vázquez-Zeas, Pablo Sempértegui-Cárdenas, Miurkis Endis-Miranda, Lenin Quezada-Méndez, Mauricio Siavichay-Romero, Faviola Rodríguez-Cárdenas.

Gastric Polyposis in Familial Adenomatous Polyposis: A Case Report. An Approach for the Endoscopist **205**
Maykel Alain Padilla-Ruiz, Gustavo Ariza-Cotes.

Spontaneous Pneumoperitoneum: A Pathology Not Always Surgical. Presentation of Two Documented Cases in Patients in Association with SARS-CoV-2 Infection **211**
Gustavo Aguirre, Cristian Torres, Nicolás Arredondo, Andrés Falla.

Primary Congenital Intestinal Lymphangiectasia: A Case Report **219**
Tatiana Díaz-Gómez, Pablo Sempértegui-Cárdenas, Ana Tinoco-Ochoa.

Celiac Disease, A Silent Enemy: A Case Report **224**
Diana Carolina Urbano-Albán, Bairon Díaz-Idrobo, Rosales Sebastián Hooker-Herrera, Julio César Hooker-Mosquera.

Metastasis of Lung Cancer in the Pancreas, Diagnosis Using Endoscopic Ultrasound: A Case Report **230**
Estefanía García, Edgar Julián Ferreira, Germán Tovar-Fierro, Diana Gaona.

Cover: *Upper gastrointestinal endoscopy showing extensive diffuse gastric polyposis*
Article: Gastric Polyposis in Familial Adenomatous Polyposis: A Case Report. An Approach for the Endoscopist
Courtesy by: Maykel Alain Padilla-Ruiz, Gustavo Ariza-Cotes.

https://doi.org/10.22516/25007440.1236

Editorial

Artificial intelligence: the future made reality

David B. Páramo-Hernández,[1*] Ricardo A. Cepeda-Vásquez.[2]

OPEN ACCESS

Citation:
Páramo-Hernández DB, Cepeda-Vásquez RA. Artificial intelligence: the future made reality. Revista. colomb. Gastroenterol. 2024;39(1):131-132. https://doi.org/10.22516/25007440.1236

[1] Editor and Director, Revista Colombiana de Gastroenterología. Gastroenterologist, GutMédica, Hospital Santa Clara. Bogotá, Colombia.
[2] Surgeon, Subspecialist in Gastroenterology and Digestive Endoscopy, Instituto de Enfermedades Digestivas. Bogotá, Colombia.

***Correspondence:** David B. Páramo-Hernández. paramo.david@gmail.com

Received: 13/06/2024
Accepted: 14/06/2024

CC BY NC ND

The significant advancements in artificial intelligence (AI) in recent years have established it as a crucial innovation in medicine and gastroenterology, with the potential to transform medical practice[1]. AI's remarkable capability to analyze complex algorithms and develop self-learning technologies—incorporating new concepts similarly to human learning—can enhance diagnostic accuracy, streamline management flowcharts, stratify risks, and optimize treatments, thereby facilitating personalized and efficient care[1]. One of the most promising applications of AI in gastroenterology and digestive endoscopy is its immense ability to analyze endoscopic images with speed and precision.

Initial applications included computer-aided diagnosis (CAD) for the detection, differentiation, and characterization of neoplastic and non-neoplastic polyps[2]. A randomized controlled trial involving 1058 patients demonstrated a significant increase in adenoma detection rates with the use of CAD compared to standard colonoscopy (29% vs. 20%, $p < 0.001$), with higher detection rates of diminutive adenomas (185 vs. 102, $p < 0.001$) and hyperplastic polyps (114 vs. 52, $p < 0.001$). There was no statistical difference in the detection of larger adenomas[2]. Local experiences, such as those of Dr. Gómez and colleagues published in our journal[3], contribute to understanding how AI techniques can improve the accuracy of endoscopic image interpretation, which often suffers from significant interobserver variability, as also noted in a previous issue[4].

In this one, we publish the article by Dr. Martín Gómez and colleagues[5], winner of the ACADI 2023 National Research Award in Gastroenterology. This article exemplifies how AI can contribute to the quality audit of upper digestive tract endoscopy through an AI-based endoscopic exploration protocol of the stomach. This protocol allowed the identification of gastric areas, achieving a sensitivity of 85.5% and a specificity of 98.8% in interpreting the 13 specific areas described. These results demonstrate AI's potential effectiveness as a valuable tool for assisting endoscopists in performing a thorough and meticulous examination of the entire stomach.

The development of AI systems that can assist endoscopists in real-time during procedures can provide instant analyses of endoscopic images, highlight areas of interest, and suggest differential diagnoses. By integrating AI into clinical practice, endoscopists can improve their efficiency and accuracy, leading to better patient outcomes[6,7].

High-quality datasets and robust algorithms are indispensable for this integration. This necessitates close collaboration among physicians, researchers, and IT experts. However, AI algorithms and their applications require further studies and validation. Additionally, more clinical data are needed to demonstrate their efficacy, value, and impact on patient

care and outcomes. Finally, cost-effective AI models and products must be developed to enable physicians, clinics, and hospitals to incorporate AI into daily clinical use.

We must view the use of AI as a tool to further improve clinical outcomes for patients with gastrointestinal diseases while also considering the risks of its potential misuse[7].

REFERENCES

1. Kaul V, Enslin S, Gross SA. History of artificial intelligence in medicine. Gastrointest Endosc. 2020;92(4):807-812. https://doi.org/10.1016/j.gie.2020.06.040
2. Wang P, Berzin TM, Glissen Brown JR, Bharadwaj S, Becq A, Xiao X, et al. Real-time automatic detection system increases colonoscopic polyp and adenoma detection rates: a prospective randomised controlled study. Gut. 2019;68(10):1813-1819. https://doi.org/10.1136/gutjnl-2018-317500
3. Gómez Zuleta MA, Cano Rosales DF, Bravo Higuera DF, Ruano Balseca JA, Romero Castro E. Detección automática de pólipos colorrectales con técnicas de inteligencia artificial. Rev. colomb. Gastroenterol. 2021;36(1):7-17. https://doi.org/10.22516/25007440.471
4. Cepeda Vásquez RA. Inteligencia artificial en la detección de pólipos colónicos: qué dicen los estudios. Rev. colomb. Gastroenterol. 2021;36(1):2-6. https://doi.org/10.22516/25007440.726
5. Gómez M, Bravo D, Ruano J, Jaramillo M, González F, Romero E. Sistema de auditoría automática para la exploración endoscópica del estómago con Inteligencia Artificial – Gastro UNAL: Gastroendoscopy UNit for Automatic Labeling. Rev. colomb. Gastroenterol. 2024;39(2):133-145. https://doi.org/10.22516/25007440.1163
6. Okagawa Y, Abe S, Yamada M, Oda I, Saito Y. Artificial Intelligence in Endoscopy. Dig Dis Sci. 2022;67(5):1553-1572. https://doi.org/10.1007/s10620-021-07086-z
7. Ali H, Muzammil MA, Dahiya DS, Ali F, Yasin S, Hanif W, et al. Artificial intelligence in gastrointestinal endoscopy: a comprehensive review. Ann Gastroenterol. 2024;37(2):133-141. https://doi.org/10.20524/aog.2024.0861

https://doi.org/10.22516/25007440.1163

Original article

Automatic Auditing System for Endoscopic Exploration of the Stomach with Artificial Intelligence-Gastro UNAL: Gastroendoscopy UNit for Automatic Labeling

Martín Gómez,[1*] Diego Bravo,[2] Josué Ruano,[3] María Jaramillo,[2] Fabio A. González,[4] Eduardo Romero.[5]

OPEN ACCESS

Citation:
Gómez M, Bravo D, Ruano J, Jaramillo M, González F, Romero E. Automatic Auditing System for Endoscopic Exploration of the Stomach with Artificial Intelligence-Gastro UNAL: Gastroendoscopy UNit for Automatic Labeling. Revista. colomb. Gastroenterol. 2024;39(2):133-145. https://doi.org/10.22516/25007440.1163

[1] Internist and Gastroenterologist, Hospital Universitario Nacional de Colombia. Associate Professor of Internal Medicine, Director of the Gastroenterology Unit, Universidad Nacional de Colombia. Bogotá, Colombia.
[2] Ph.D. Student in Electrical Engineering, Research Group: Computer Imaging and Medical Applications Laboratory (CIM@LAB), Universidad Nacional de Colombia. Bogotá, Colombia.
[3] Ph.D. Student in Systems and Computing Engineering, Research Group: Computer Imaging and Medical Applications Laboratory (CIM@LAB), Universidad Nacional de Colombia. Bogotá, Colombia.
[4] Ph.D. in Computer Science. Director of the Research Group: Machine Learning, Perception, and Discovery (MINDLAB). Full Professor, Department of Systems and Industrial Engineering, Universidad Nacional de Colombia. Bogotá, Colombia. Bogotá, Colombia.
[5] Ph.D. in Biomedical Sciences, Director of the Master's Program in Biomedical Engineering, Director of the Research Group: Computer Imaging and Medical Applications Laboratory (CIM@LAB). Professor, Medical School, Universidad Nacional de Colombia. Bogotá, Colombia.

***Correspondence:** Martín Gómez.
martinalonsogomezz@gmail.com

Received: 19/12/2023
Accepted: 10/04/2024

Abstract

Introduction: Upper endoscopy is the standard method for diagnosing early-stage gastric cancer. However, according to estimates, up to 20% of tumors are not detected, and their accuracy may be affected by the variability in their performance. In Colombia, most diagnoses take place in advanced stages, which aggravates the problem. Protocols have been proposed to ensure the complete observation of areas prone to premalignant lesions to address variability. **Objective:** To build and validate an automatic audit system for endoscopies using artificial intelligence techniques. **Methodology:** In this study, 96 patients from a teaching hospital underwent video-documented endoscopies, spanning 22 stations rearranged to minimize overlaps and improve the identification of 13 key gastric regions. An advanced convolutional network was used to process the images, extracting visual characteristics, which facilitated the training of artificial intelligence in the classification of these areas. **Results:** the model, called Gastro UNAL, was trained and validated with images of 67 patients (70% of cases) and tested with 29 different patients (30% of cases), which reached an average sensitivity of 85,5% and a specificity of 98,8% in detecting the 13 gastric regions. **Conclusions:** The effectiveness of the model suggests its potential to ensure the quality and accuracy of endoscopies. This approach could confirm the regions evaluated, alerting less experienced or trained endoscopists about blind spots in the examinations, thus, increasing the quality of these procedures.

Keywords

Esophagogastroduodenoscopy, artificial intelligence, diagnostic blind spots, neural network.

INTRODUCTION

Gastric cancer (GC) is a significant public health concern. Globally, nearly one million new cases of GC were diagnosed in 2022, making it the fifth most common cause of cancer-related deaths, with 660,175 fatalities recorded in the same period[(1)]. In Colombia, according to GLOBOCAN 2022, there were an estimated 8938 new cases of GC, representing the fourth most frequent cancer (7.6%) and the leading cause of cancer mortality, with 6901 deaths (12.2%)[(1)]. This places the average mortality rate for GC in Colombia at approximately 11.5 per 100,000 inhabitants, with even higher rates in the Andean region[(2,3)]. The high incidence and the fact that most cases are detected at advanced stages make GC a critical public health issue.

Endoscopic technology has advanced significantly in recent decades and is now widely used for the diagnosis of early gastric cancer (EGC)[4]. Esophagogastroduodenoscopy (EGD), or upper gastrointestinal endoscopy, is the preferred procedure for examining the stomach for premalignant lesions or cancer. However, it has been reported that between 11% and 20% of EGC cases are not diagnosed during an EGD[5]. This high error rate is primarily due to human factors that can affect the efficacy of endoscopy in the early detection of gastric lesions[6].

These factors include the presence of mucus and saliva on the gastric mucosa, conducting the examination too quickly, and inadequate training of the endoscopist, who may not evaluate all areas of the stomach, leaving some blind spots[7]. Therefore, avoiding blind spots is a fundamental prerequisite for the efficacy of endoscopy in detecting early-stage gastric cancer[8,9]. In general, it is very challenging for a trainee physician to acquire the necessary skills to maneuver the endoscopic device and interpret the observed anatomy; this training requires hundreds of supervised procedures[10]. In this context, various gastroenterology associations worldwide have developed protocols to improve the efficiency and quality of the procedure[11-13]. Systematic photography of specific anatomical areas of the stomach is recommended as a quality indicator for endoscopic procedures by the British Society of Gastroenterology (BSG)[14] and the European Society of Gastrointestinal Endoscopy (ESGE)[15]. They recommend acquiring images in eight specific locations within the stomach. The ESGE suggests an image capture rate (photodocumentation) of over 90% of all anatomical markers as an indicator of a complete examination. Meanwhile, the Japan Gastroenterological Endoscopy Society (JGES) implemented a more extensive systematic screening protocol of the stomach (SSS)[16], initially described by Professor Kenshi Yao, consisting of a series of 22 endoscopic photographs capturing four areas that cover 100% of the gastric surface: the gastric antrum, distal body, middle, and upper part of the gastric body[8].

Recently, the World Endoscopy Organization (WEO) provided practical guidelines for professionals to conduct comprehensive photodocumentation of endoscopic procedures. This document detailed 28 distinct endoluminal areas, covering the entire inner lining of the upper gastrointestinal tract, from the hypopharynx to the second portion of the duodenum[17]. Our study focuses on the gastric cavity; therefore, we used Dr. Yao's guidelines as a reference for our research.

Despite the high agreement among experts, these protocols have not been widely disseminated, and many endoscopists neither visually document nor likely observe these regions[15]. This situation poses a challenge to ensuring a thorough inspection of the stomach, which could partly explain the difference in early-stage tumor detection rates between Japan and Colombia. In Japan, approximately 70% of cases are detected at this curable stage. In contrast, in Colombia, this percentage is minimally representative, as over 90% of diagnosed cases are in advanced stages, when the disease is potentially fatal[19-23]. Therefore, it would be desirable for endoscopists to practice a systematic inspection of the stomach, documenting these 22 specific areas to eliminate blind spots or unevaluated regions. However, to validate that this is routinely done, a monitoring system would be useful to verify the evaluation of all areas or alert the endoscopist about regions that may have been missed during the examination.

In this context, integrating computational methods into medical practice can provide substantial support to gastroenterologists, enabling them to routinely perform comprehensive and high-quality endoscopies. These methods can act as a second reader for the anatomical regions that need analysis by the specialist. This second reader could identify areas that have not been examined, have been incompletely evaluated, or are blind spots in the entire gastric cavity, potentially reducing the omission of precancerous and malignant lesions. By verifying whether all anatomical landmarks in Dr. Yao's protocol have been inspected, the computational approach can play an essential role. If the system detects an incomplete examination, it can function as an alert, notifying the specialist that a specific anatomical region has yet to be evaluated. This is crucial, as early-stage gastric cancer can go unnoticed, often presenting as small or subtle lesions that could be overlooked if a specific area is not thoroughly examined.

MATERIALS AND METHODS

This study explores the automatic classification of different regions of the stomach that must be reviewed during endoscopic procedures using deep learning image classification methods. **Figure 1** shows the layout of the regions of interest in the stomach, accompanied by sample images, and illustrates the proposed methodology. The strategy used is transfer learning, which leverages a deep learning model previously trained with millions of natural images to capture low-level visual features (e.g., edges), adapt the model's high-level features to endoscopic images, and use them as input for a classification module.

The first stage of the process, feature extraction, involves a Convolutional Neural Network (CNN) that has been pre-trained on a large dataset of natural images. The second stage, classification, involves a set of dense layers trained using the specific image set for the problem. The model's output is a softmax layer with 13 neurons corresponding

to the 13 different classes of stomach regions, assigning a probability to each class and highlighting the highest as the definitive classification for the region in question. For the feature extraction stage, a state-of-the-art CNN architecture, such as ConvNext Tiny[24], was used. This architecture was selected for its superior performance in a previous study compared to 22 other evaluated networks[25].

Acquisition and Preprocessing Protocol

Esophagogastroduodenoscopy and image capture are performed by a highly experienced gastroenterologist with over 20 years of practice in endoscopy and a history of over 50,000 procedures. This specialist works at Hospital Universitario Nacional de Colombia and follows the systematic endoscopy protocol developed by Dr. K. Yao[8]. The process unfolds as follows: when a patient is scheduled for an upper digestive endoscopy, they sign informed consent forms for the procedure, sedation, research protocol, and image capture before entering the room. They are then given a preparation consisting of 10 mL of a solution containing 400 mg of N-acetylcysteine and 200 mg of simethicone approximately half an hour before the procedure. The patient is instructed to lie in the left lateral decubitus position for 5 minutes, followed by a wait of 20 to 30 minutes before entering the procedure room. In the room, a cannula is placed in the patient's right arm, and a certified anesthesiologist administers intravenous sedation with propofol. Once the patient is sedated, an Olympus series 190 endoscope is introduced.

Upon entering the gastric cavity, the endoscope performs aspiration of residues from the gastric contents, distends the cavity, and proceeds to locate itself in the duodenum. After inspecting the duodenum, the pylorus is identified, and the endoscope is withdrawn 5 cm to begin photodocumentation of the antrum. This process starts from the greater cur-

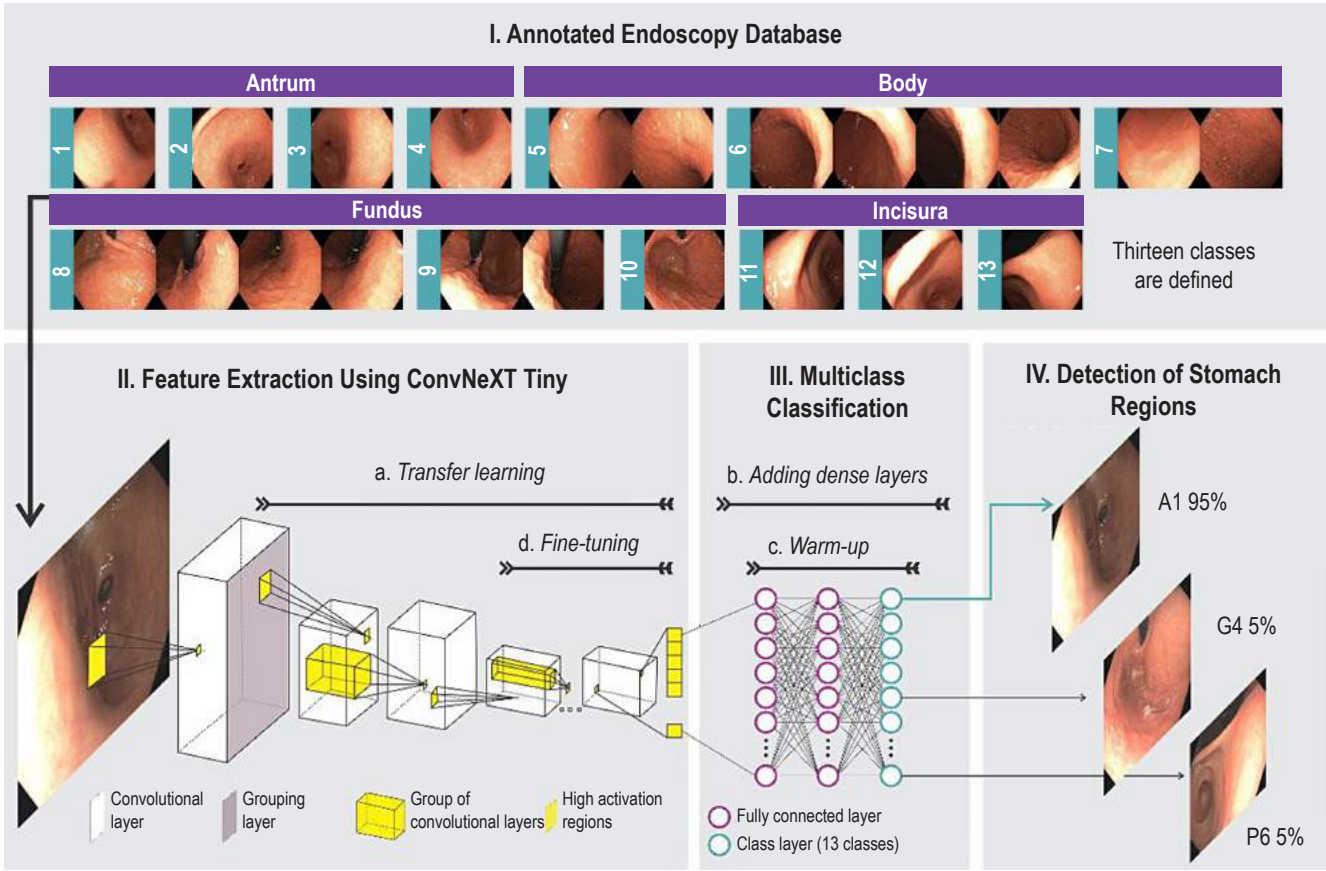


Figure 1. Flow of the proposed method to automatically identify 13 gastric regions. In (**I**), the endoscopic image database is consolidated and categorized into anatomical regions, divided into training, validation, and test partitions. In (**II**), each training frame feeds a convolutional neural network-based model. This model (**II-a**) is pre-trained with millions of natural images. In (**III-b**), a densely connected layer is added to the neural network, and (**III-c**) it is pre-trained. In (**II-d**), neuron layers responsible for information extraction are unfrozen to learn contextual relationships. The trained network is evaluated in (**IV**) to classify each frame into one of the 13 regions of the stomach. Source: Author's own research.

vature and proceeds clockwise, capturing four overlapping photos as follows: greater curvature (photo 1-G1); anterior wall (photo 2-A1); lesser curvature (photo 3-L1); and posterior wall (photo 4-P1). The endoscope is then withdrawn 15 cm and positioned in the distal gastric body, where photos are taken in the same clockwise manner: greater curvature (photo 5-G2); anterior wall (photo 6-A2); lesser curvature (photo 7-L2); and posterior wall (photo 8-P2). Next, the endoscope is withdrawn an additional 15 cm and positioned in the upper-middle gastric body to continue the recording in a clockwise direction: greater curvature (photo 9-G3); anterior wall (photo 10-A3); lesser curvature (photo 11-L3); and posterior wall (photo 12-P3). Subsequently, the gastroscope is advanced to the corpoantral junction, where retroflexion is performed to visualize the cardia and gastric fundus. From this position, photodocumentation continues as follows: greater curvature (photo 13-G4); anterior wall (photo 14-A4); lesser curvature (photo 15-L3); and posterior wall (photo 16-P4). With the endoscope in retroversion, it is advanced along the lesser curvature by 5 cm to fully visualize it and obtain the following three photos: anterior wall (photo 17-A5); lesser curvature (photo 18-L5); and posterior wall (photo 19-P5). Finally, the tip of the endoscope is positioned at the incisura and visualized in its entirety to obtain the last set of photos: anterior wall (photo 20-A6); lesser curvature (photo 21-L6); and posterior wall (photo 22-P6). The results of this documentation are presented in **Figure 2**.

After capturing images of the 22 regions and completing the process of assigning labels in an information system, the creation of the artificial intelligence model, named GastroUNAL in honor of our university, begins. We observed that some areas are anatomically very similar and often overlap, making differentiation difficult. Therefore, in colla-

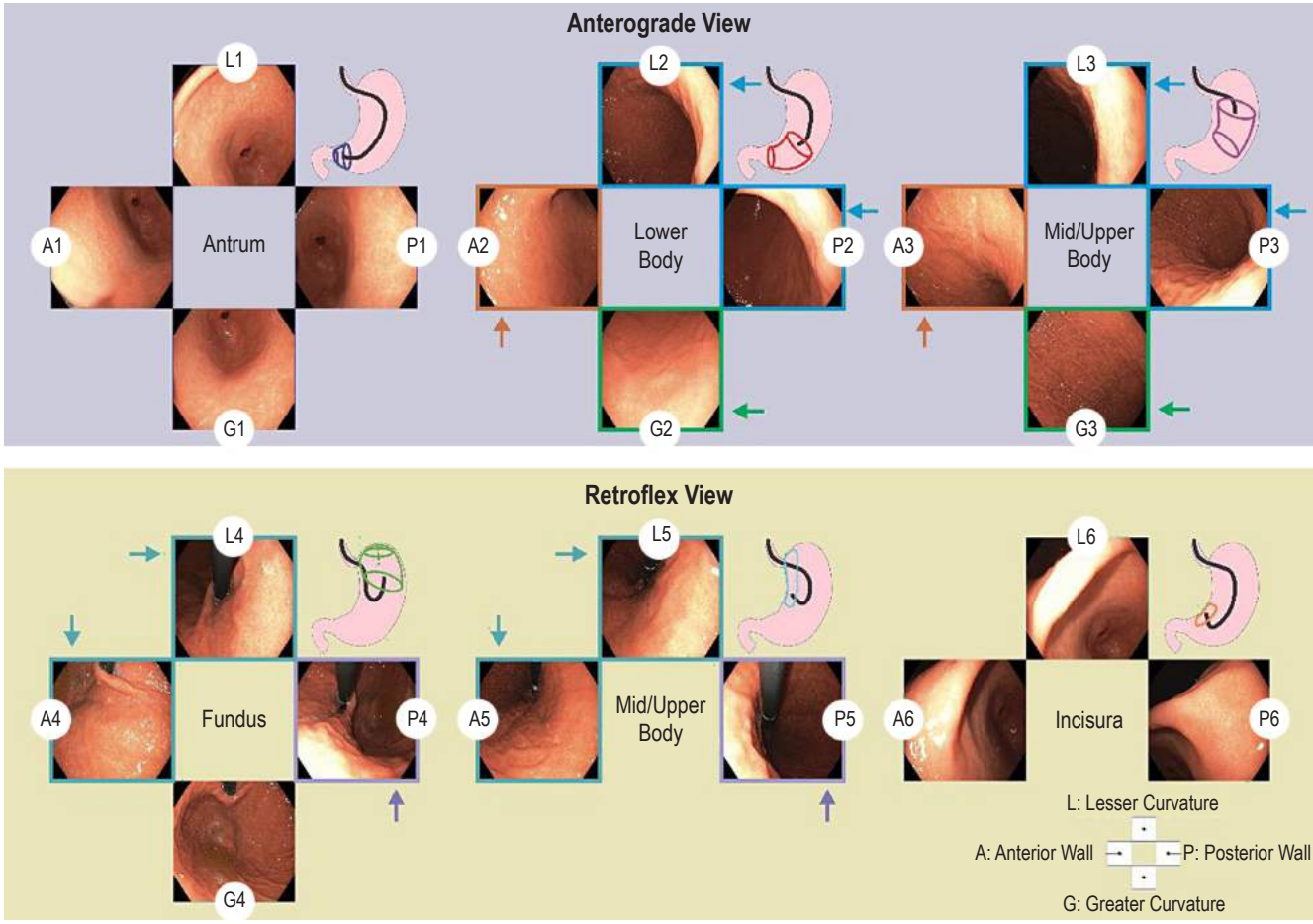


Figure 2. Protocol for photographic documentation of the stomach, which begins as soon as the endoscope is inserted into the gastric antrum. Using the anterograde view, endoscopic photographs are taken of four quadrants of the gastric antrum, lower, middle, and upper body. Then, using the retroflex view, endoscopic photographs are taken of four quadrants of the cardia fundus and three quadrants of the upper middle body and gastric incisura. In total, the SSS series comprises 22 endoscopic photographs. The arrows represent the unification of labels to obtain 13 categories. A: anterior wall; G: greater curvature; L: lesser curvature; P: posterior wall; Q: quadrant. Source: Author's own research.

boration with the team, we decided to regroup the 22 zones into 13 by merging those that inspect similar areas. The grouped regions are described as follows:

- Lower body region in L2 and P2, and upper middle region in L3 and P3
- Lower body region in A2 and upper middle region in A3
- Lower body region in G2 and upper middle region in G3
- In retroflex view, cardia fundus region in L4, A4, and upper middle region in L5, A5
- In retroflex view, cardia fundus region in P4 and upper middle region in P5

Case Collection and Region Labeling System

The storage, organization, and labeling of endoscopic videos and images corresponding to the 22 regions of the stomach were carried out using a prototype information system developed specifically for this study. The system was designed based on the functional requirements gathered with the guidance of two gastroenterologists. These requirements encompass the clinical information needed to document an endoscopy study, the strategies for visualizing endoscopic videos and images, and the tools necessary for labeling these videos and images. The non-functional requirements were established collaboratively with a team of three engineers experienced in clinical prototypes. They focused on scalability, security, interoperability, and usability to ensure stable operation and secure handling of sensitive data. This system was developed using the Django web development framework in conjunction with the PostgreSQL database management system. This combination provides a secure and reliable environment for capturing sensitive information, such as clinical data. Django incorporates advanced security strategies for transmitting data via the web, which PostgreSQL then encrypts and stores. According to the requirements, the system includes the following modules:

- Authentication: Controls user registration and access.
- Patient Management: Allows users to view, create, and edit information of patients involved in the study.
- Endoscopic Procedure Management: Assigns one or more procedures to a specific patient, capturing the associated clinical information, the video of the procedure, and the informed consent.
- Procedure Visualization and Labeling: The system displays the video of a procedure in a web player (**Figure 3-I**) along with the specific frame sequence for the current moment of the video (**Figure 3-II**). When the user, in this case, a gastroenterologist, identifies one of the 22 gastric regions while viewing the video, they can select and label an image or a sequence of images representing that region (**Figure 3-III**).

Architecture of the Convolutional Neural Network for Describing Endoscopic Images

A Convolutional Neural Network (CNN) constructs a hierarchical representation of distinctive gastric patterns based on appearance—such as color and texture—and anatomical structures from various perspectives, including gastric folds, the lower esophageal sphincter, pylorus, and incisura, among others. A CNN is organized as a set of neurons grouped into layers, which are sequentially connected from input to output, as illustrated in **Figure 1** (**II-III**). The initial stages of these layers take an image as input and decompose it into primitives, which are extracted by applying convolutions or sets of filters designed to capture local patterns. This initial transformation of the image is processed sequentially through consecutive layers of additional convolutions, progressively selecting relevant information. Throughout this process, layers are commonly introduced to reduce dimensionality or group information, along with other layers that normalize the output of each neuron using activation functions to mitigate signal attenuation from sequential processing. This relatively simple process is repeated layer by layer, transforming the image into increasingly complex, non-linear patterns with fewer statistical dependencies.

The architecture of the network is defined by the number of filters, layers, and neurons, which in turn determine the number of parameters in the model, typically in the order of millions. For this study, we selected the ConvNext Tiny architecture[24], a convolutional neural network that learns spatial relationships at different scales while maintaining the simplicity and efficiency of traditional convolutional networks. The ConvNeXt architecture consists of a sequence of blocks called Inverted Bottleneck Blocks. Each block includes the following components: depthwise separable convolution, self-attention mechanism, traditional convolution, layer normalization, and GeLU (Gaussian Error Linear Units) activation. This architecture incorporates direct connections between non-contiguous layers, known as residual blocks, which help mitigate the gradient attenuation problem. The model's architecture comprises 27 million parameters, of which 11,000 correspond to the fully connected layers of the neural network, with the remainder assigned to the weights of the convolutional layers.

Classification of Endoscopic Images Using Transfer Learning

The performance of a convolutional neural network (CNN) in classification tasks significantly depends on the volume of data used; training it with a small dataset is ineffective. This study implemented transfer learning on the ConvNeXt

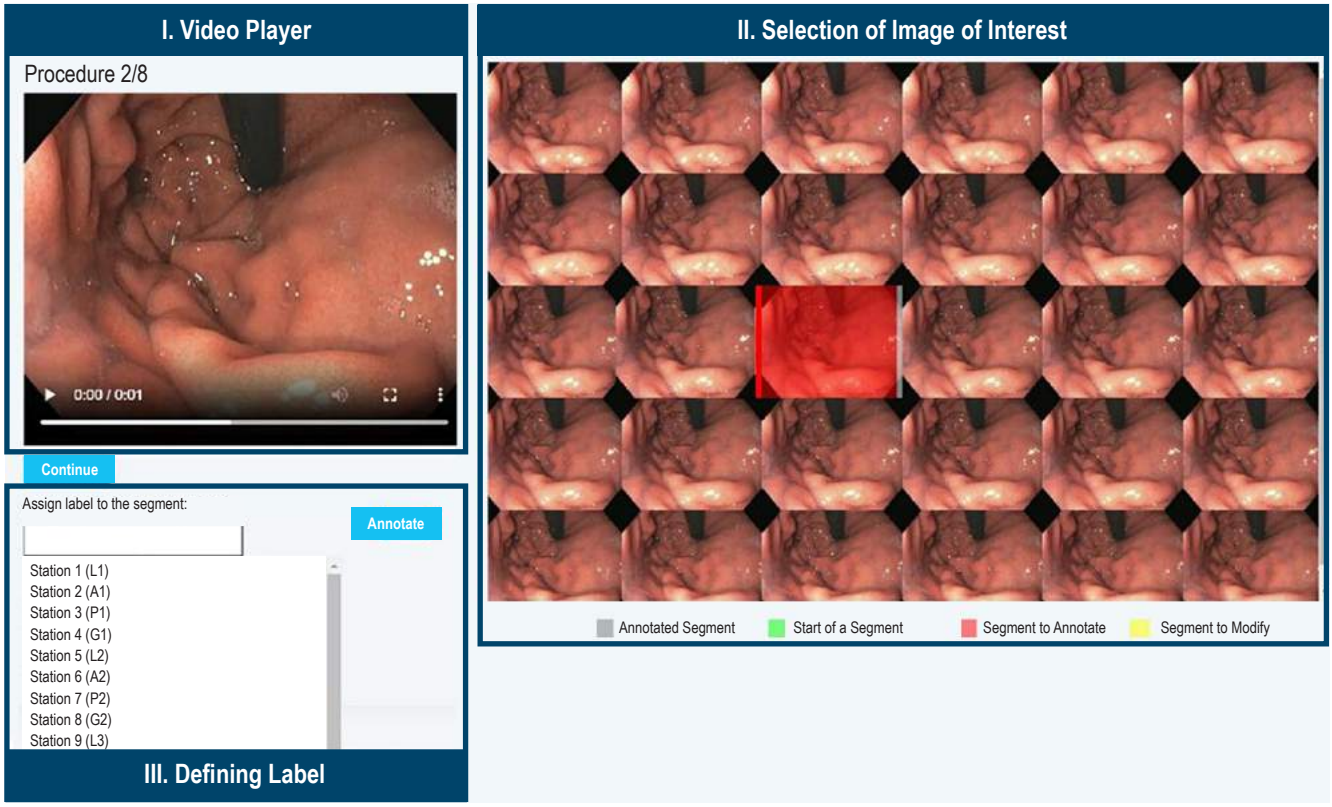


Figure 3. Anatomical Region Labeling System. The video of the procedure is displayed alongside the images associated with the current moment of the video, allowing the annotation of the image that best represents the region. Once the image is selected, it is marked in red, and an option to assign a label to the image is enabled. Source: Author's own research.

architecture, utilizing the extensive ImageNet database as the initial information source, which includes more than 14 million natural images distributed across nearly 20,000 categories. The ConvNeXt has been rigorously trained and validated with these images, leveraging the large volume of examples in ImageNet[26,27]. Similar to how the human visual system constructs a representation of the world using visual primitives up to the primary cortex[28-30], and learns specific domain associations in higher regions, these networks capture the informative units of an image. This learned information can then be adapted for this specific problem. This process, known as transfer learning, involves using the weights of filters learned from millions of natural image examples while adapting some layers, usually the last ones, to learn from upper gastrointestinal endoscopy images. This training consists of three stages:

- Frozen convolutional layers: These are layers whose parameters are not updated with endoscopic images.
- Unfrozen layers: These layers have their parameters adjusted by training the network with endoscopic images (fine-tuning), resulting in a feature vector output.
- Classification layers: These fully connected layers are trained for the specific classification problem presented in this study (**Figure 1**). The number of neurons in the output layer is determined by the number of classes. This final layer also provides a confidence score, indicating the probability that an image belongs to a specific class (**Figure 1-IV**). The learning process of the network is iterative and adaptive, using a relatively low learning rate over several iterations (epochs). In each epoch, data batches are trained until all samples in the training set have been processed. The number of epochs is determined by the complexity of the classification problem. Finally, the training concludes when the classification error on the validation data is below a specified threshold.

Databases

The database comprises 96 patient cases who underwent EGD procedures. From the white-light videos recorded, 2054 images were obtained, with their anatomical locations established as one of the 22 possible regions in the

Kenshi Yao protocol (see the Label column in **Table 1**)[8], later unified into 13 regions. These annotations were made by consensus among the group of residents and the head of gastroenterology, who has over 20 years of experience at Hospital Universitario Nacional. Each frame was captured with a spatial resolution of 1350 x 1080 pixels. This study was conducted in accordance with the principles of the Declaration of Helsinki and received approval from the Ethics Committee of Hospital Universitario Nacional de Colombia (approval number CEI-2019-06-10). A detailed description of the database is presented in **Table 1**.

ETHICAL CONSIDERATIONS

This study was conducted in accordance with Resolution 008430 of 1993, which establishes the scientific, technical, and administrative standards for research involving humans, as specified in Article 11. This project is classified as minimal-risk research since it only involves the use of digital images generated from anonymized endoscopic videos. Therefore, there is no way to identify the subjects included in the study.

Study participants provided informed consent, clarifying that the information obtained during their medical care could be used for educational and research purposes. This agreement ensures that such data, including anonymized images and videos, will be handled with the highest standards of confidentiality, security, and custody, in compliance with applicable regulations for this type of research.

RESULTS

This section evaluates the performance of the proposed methodology by comparing the predictions of a convolutional neural network with the annotations made by a highly qualified expert. The following details the experimental setup and the quantitative validation scheme applied to the proposed approach.

Experimental Setup

Our study involved 96 patients with an average age of 62 ± 15.5 years. Among these participants, 50.6% were women and 49.4% were men. The developed model was evaluated using a 70-30 split scheme: 70% of the cases for training and validation (67 cases, 1383 images) and the remaining 30% for testing (29 cases, 671 images). Cross-entropy with class weights was used as the loss function to balance

Table 1. Distribution of the EGD Database in Images for the Validation Scheme

Name	Label*	Training (n = 58)	Validation (n = 9)	Test (n = 29)	Total (n = 96)
Antrum A1	1	48	7	29	84
Antrum L1	2	48	5	37	90
Antrum P1	3	45	7	30	82
Antrum G1	4	56	7	33	96
Body A2-3	5	114	18	58	190
Body L2-3, P2-3	6	223	39	121	383
Body G2-3	7	114	19	58	191
Cardia–Fundus A4-5, L4-5	8	231	38	120	389
Cardia–Fundus P4-5	9	106	18	58	182
Cardia–Fundus G4	10	54	8	33	95
Incisura A6	11	46	12	31	89
Incisura L6	12	56	10	34	100
Incisura P6	13	44	10	29	83

n: number of patients. *Label: corresponds to the station or grouping. Labels 1-7 are for anterograde view, and labels 8-13 are for retroflex view. Source: Author's own research.

the number of samples relative to the predominant class (**Table 1**). This unequal proportion was maintained in the test dataset.

The CNN was trained in two stages: a pre-training of the classification layers (warm-up) with a constant learning rate over 10 epochs, and fine-tuning of the last 20% of layers over 100 epochs with an early stopping criterion of 15 epochs without an increase in the macro F1-score metric. The details of the CNN and training configuration are as follows:

- Pretrained weights: ImageNet
- Optimizer: Adam
- Loss function: cross-entropy
- Dense layers: one dense layer followed by a batch normalization layer, a dropout layer, and finally two dense layers with 13 categories

The warm-up and fine-tuning stages were included in a hyperparameter optimization with 200 trials, monitoring the F1 metric to find the optimal batch size, initial learning rate, and learning rate schedule (gamma and step size). The values during the optimization were as follows:

- Learning rate for pre-training: 0.001 with gamma: 0.1
- Range of hyperparameter values during optimization: batch size (8-128), gamma (0.1-0.5), step size (5-10), and learning rate ($1e^{-3}$ to $1e^{-5}$)

After the optimization process, the hyperparameters that maximized the F1 score were found in validation trial 132/200, with a batch size of 8, a learning rate of 0.00071, a step size of 7, and a gamma of 0.30 for the learning rate schedule.

Quantitative Evaluation

The convolutional neural network (CNN) is designed to estimate one of 13 possible anatomical locations for each image, as illustrated in **Figure 4**. These categories correspond to different anatomical regions: the antrum (4 classes), the gastric body (3 classes), the cardia fundus (3 classes), and the incisura (3 classes). The network's performance is evaluated by comparing its predictions with expert annotations using a confusion matrix that records true positives (TP), true negatives (TN), false positives (FP), and false negatives (FN). Specific metrics for each class, as well as an overall average of these metrics, are calculated from this matrix, as presented in **Table 2**. The results demonstrate that the proposed method effectively classifies the 13 classes, achieving an average accuracy of 86%.

Given that the primary objective of this study is the detection of anatomical regions, it is important to highlight that the method achieves the highest F1 score (94.1%) for the cardia region A4-5, L4-5 in the retroflex view (**Figure 4**). In contrast, the class with the lowest F1 score is the gastric body

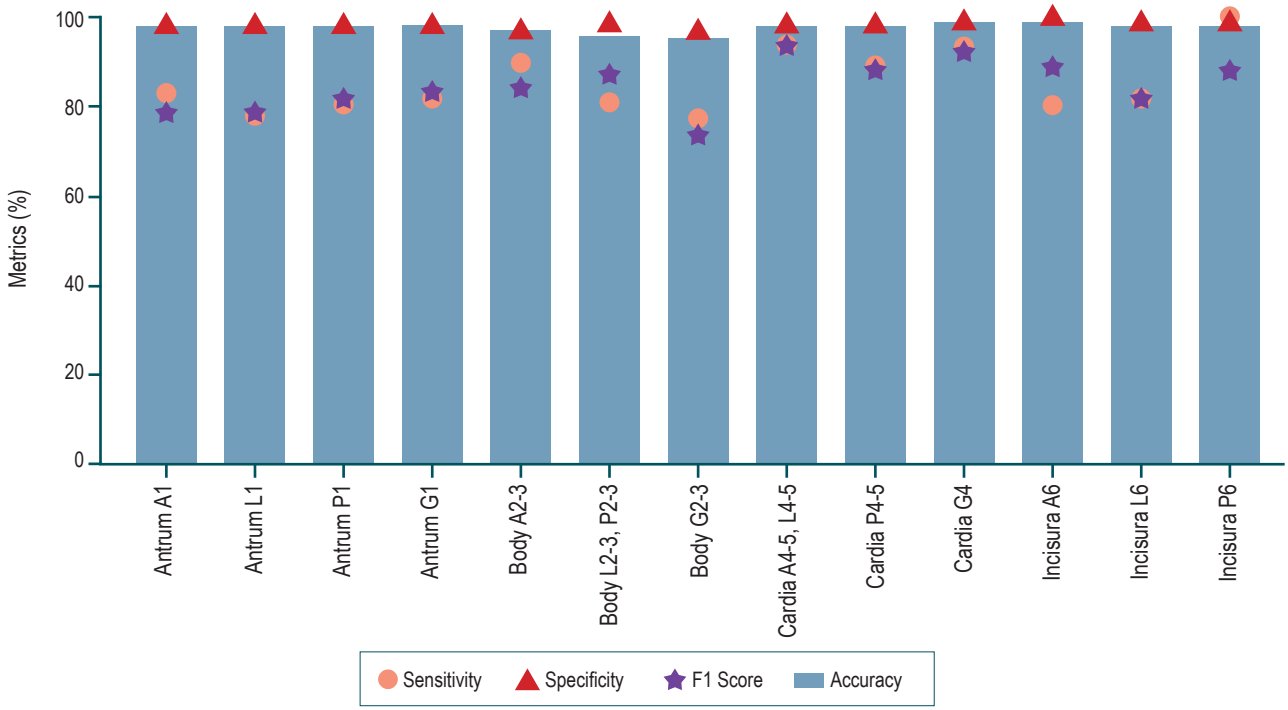


Figure 4. Sensitivity, specificity, and accuracy metrics of the CNN for classifying stomach regions in EGD images into 13 locations. Source: Author's own research.

G2-3, with 73.7% (**Figure 4**). This is likely due to the fact that, in some cases, the gastric tissue does not present a distinctive pattern that allows for precise region localization, a limitation that could be mitigated with a larger training dataset. Nonetheless, it is important to emphasize that the proposed method demonstrates a strong capability to handle the high variability of the various anatomical structures and views.

Table 2. Results for the Proposed Configuration

Metric (%)	13 Stations
Accuracy	85.99
Specificity	98.82
Macro Sensitivity	85.53
Macro Precision	84.73
Macro F1	84.86
Weighted Sensitivity	85.99
Weighted Precision	86.64
Weighted F1	86.07

Source: Author's own research.

Qualitative Evaluation

Using Grad-CAM (Gradient-Weighted Class Activation Mapping), we identified the areas in the images that the network considers most representative for distinguishing between different anatomical regions. **Figure 5** illustrates the evaluation of a test case involving the 13 classes.

For the regions of the antrum (A1, L1, P1, and G1), it is observed that the pattern of the pyloric sphincter location is crucial. For the gastric body regions, the network uses the quadrant of the gastric wall. Regarding the cardia fundus, the positioning and location of the endoscope determine the class structure. Finally, for the incisura (A6, L6, and P6), capturing the anterior, middle, and posterior portions is crucial for accurate identification.

DISCUSSION

Upper gastrointestinal endoscopy, also known as esophagogastroduodenoscopy (EGD), is the preferred method for diagnosing gastric cancer and premalignant lesions. Identifying and monitoring these lesions is crucial to prevent this serious disease, necessitating high-quality endoscopic procedures. EGD is also used as a screening tool for early diagnosis of upper gastrointestinal cancer in high-risk areas[18]. In a study by Hamashima, Chisato, and colleagues[31], the impact of endoscopic screening on reducing gastric cancer mortality was evaluated. The results indicated that gastric cancer mortality was significantly lower in the endoscopic screening group compared to the radiographic screening and photofluorography groups. The study concluded that endoscopic screening for gastric cancer is associated with a notable 57% reduction in mortality from this disease, highlighting its effectiveness in early detection and treatment.

In clinical practice, a systematic approach by a gastroenterologist during endoscopy minimizes the likelihood of missing areas or having blind spots. However, there is generally no record of how a specialist performed the procedure, whether a minimum number of regions were observed, or the duration of observation for each region. Consequently, photodocumentation has become an important aspect of the EGD report. A recent study found a positive correlation between the number of endoscopic images and the detection rate of clinically significant gastric lesions ($p < 0.001$). In the clinical setting, a trained endoscopist can perform systematic and efficient photodocumentation, but this requires proper endoluminal orientation through extensive prior training and a clean mucosa to ensure optimal visualization. Inadequate mucosal cleaning can impact the quality and integrity of the procedure. Successful photographic documentation also demands adequate insufflation and equipment control. Additionally, patient movement and anatomical variability can influence this documentation. Finally, a significant barrier is the storage and analysis of images, which remains a common disadvantage of current endoscopic equipment[17].

Currently, well-designed studies are needed to examine the relationship between the number of images, a specific photodocumentation protocol, and the neoplasm detection rate during EGD[32]. However, an Asian consensus on standards in upper gastrointestinal endoscopy suggests that methodical observation of the upper gastrointestinal tract can improve the detection of superficial neoplasms by minimizing unvisualized areas. Additionally, the expert panel concluded that current evidence supports the use of simethicone to enhance visual clarity during the examination[33].

In this context, a second reader (artificial intelligence) should not only recognize the gastric anatomical regions of interest but also ensure they are observed for a minimum duration. Thorough inspection of the entire gastric cavity is a crucial step in the systematic search for early gastric cancer. Consequently, there is a global interest in applying artificial intelligence in this area, and some researchers have classified frames using convolutional neural network (CNN) architectures[34]. For example, Takiyama and colleagues[35] used a GoogleNet architecture to accurately recognize four anatomical locations (larynx, esophagus, stomach, and

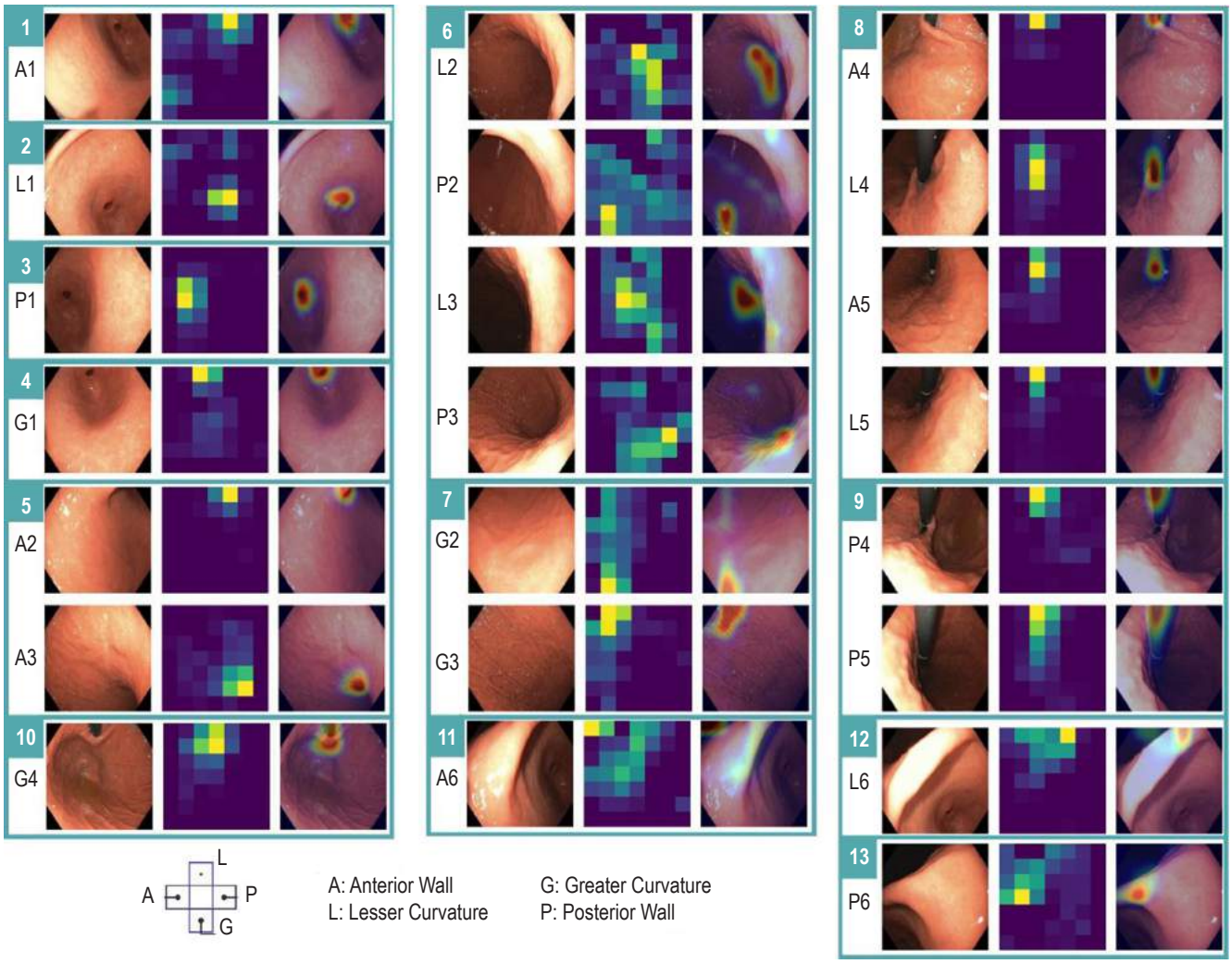


Figure 5. Analysis of a convolutional neural network in a test case. The sequence includes an endoscopic image, a heatmap visualizing the importance of the areas of the image in the network's prediction, and the superposition of this heatmap on the endoscopic image to highlight the relevant zones. In this case, 13 regions (marked with a green rectangle) were identified with a prediction confidence above 95%, matching the labels assigned by an expert. Within the rectangle, A1-P6 corresponds to the region grouping mechanism. A: anterior; G: greater curvature; L: lesser curvature; P: posterior. Source: Author's own research.

duodenum), as well as three specific sub-classifications for stomach images. Wu and colleagues[36] employed a VGG-16 network to classify gastric locations into 10 categories and then refined the classification into 26 anatomical parts (22 for the stomach, 2 for the esophagus, and 2 for the duodenum). Additionally, Chang and colleagues[37] trained a ResNeSt architecture to classify EGD images into eight anatomical locations, with an additional location specifically for the pharynx. However, most proposed architectures have a large number of parameters, making real-time task resolution challenging, thus necessitating the training of smaller architectures. In a previous study[25], the performance of 22 architectures was compared to identify six anatomical regions of the stomach, including state-of-the-art architectures, and the best performance was obtained with ConvNext Tiny. This network has around 27 million parameters, which would allow its implementation in a clinical setting.

In the present study, we developed an automated auditing system for the endoscopic exploration protocol of the stomach using artificial intelligence, enabling the identification of gastric areas. We achieved a macro sensitivity of 85.5% in interpreting the 13 specific areas previously described. These results demonstrate the potential effec-

tiveness of artificial intelligence as a valuable tool to assist endoscopists in conducting thorough and meticulous examinations of the entire stomach.

Various experts and organizations have proposed guidelines regarding the number of images that should be captured during an EGD. An appropriate number of images encourages endoscopists to perform the procedure with greater attention, and this information can be used to train, validate, and improve the performance of artificial intelligence strategies. This factor is essential to overcome the challenge of effectively addressing this clinical problem with AI technology.

One of the major limitations of this type of study is the lack of a common validation framework, a frequent issue in the analysis of endoscopic images, which has limited the comparison between existing approaches. It is difficult to determine which of these methods could have a real advantage in clinical use.

In summary, this proposal presents a computerized quality monitoring system that identifies 13 anatomical gastric regions (covering the entire gastric cavity) using a convolutional neural network. The performance of this methodology could be improved and applied to more anatomical regions with an increase in annotated cases. This system is expected to become a valuable tool for the recognition of stomach regions, alerting to incomplete explorations of the gastrointestinal tract and, consequently, ensuring the quality of the procedure. Additional studies are currently being conducted to further validate and enhance the effectiveness of this system.

Finally, this pioneering study, which to our knowledge is the first in Latin America, can guide future research on the application of automatic classification to the 22 gastric regions recommended by K. Yao[8] or other upper endoscopy photodocumentation protocols as presented in other studies[14,15,17].

Acknowledgments

This work was partially supported by the project coded 110192092354 and titled "Early Detection Program for Premalignant Lesions and Gastric Cancer in Urban, Rural, and Dispersed Areas of the Department of Nariño", from call 920 of 2022 by the Ministry of Science.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global Cancer Observatory: Cancer Today [Internet]. Lyon, France: International Agency for Research on Cancer; 2024 [consultado el 1 de abril de 2024]. Disponible en: https://gco.iarc.who.int/today, accessed [01 04 2024].
2. Oliveros-Wilches R, Grillo-Ardila CF, Vallejo-Ortega M, Gil-Parada F, Cardona-Tobón M, Páramo-Hernández D, et al. Guía de práctica clínica para la prevención primaria y secundaria y diagnóstico temprano de cáncer gástrico. Rev Colomb Cancerol. 2022;26(1):39-96. https://doi.org/10.35509/01239015.754
3. Oliveros R, Navarrera LF. Diagnóstico, estadificación y tratamiento del cáncer gástrico en Colombia desde 2004 a 2008 (REGATE -Colombia). Rev Colomb Gastroenterol. 2012;27(4):269-74.
4. Pasechnikov V, Chukov S, Fedorov E, Kikuste I, Leja M. Gastric cancer: Prevention, screening and early diagnosis. World J Gastroenterol WJG. 2014;20(38):13842-62. https://doi.org/10.3748/wjg.v20.i38.13842
5. Kaise M. Advanced endoscopic imaging for early gastric cancer. Best Pract Res Clin Gastroenterol. 2015;29(4):575-87. https://doi.org/10.1016/j.bpg.2015.05.010
6. Pimenta-Melo AR, Monteiro-Soares M, Libânio D, Dinis-Ribeiro M. Missing rate for gastric cancer during upper gastrointestinal endoscopy: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. 2016;28(9):1041-9. https://doi.org/10.1097/MEG.0000000000000657
7. Lee SH, Park YK, Cho SM, Kang JK, Lee DJ. Technical skills and training of upper gastrointestinal endoscopy for new beginners. World J Gastroenterol WJG. 2015;21(3):759-85. https://doi.org/10.3748/wjg.v21.i3.759
8. Yao K. The endoscopic diagnosis of early gastric cancer. Ann Gastroenterol Q Publ Hell Soc Gastroenterol. 2013;26(1):11.
9. Yao K, Uedo N, Muto M, Ishikawa H. Development of an e-learning system for teaching endoscopists how to diagnose early gastric cancer: basic principles for improving early detection. Gastric Cancer. 2017;20(Suppl 1):28-38. https://doi.org/10.1007/s10120-016-0680-7
10. Kim JS, Kim BW. Training in Endoscopy: Esophagogastroduodenoscopy. Clin Endosc. 2017;50(4):318-21. https://doi.org/10.5946/ce.2017.096
11. Eisen GM, Baron TH, Dominitz JA, Faigel DO, Goldstein JL, Johanson JF, et al. Methods of granting hospital privileges to perform gastrointestinal endoscopy. Gastrointest Endosc. 2002;55(7):780-3. https://doi.org/10.1016/S0016-5107(02)70403-3

12. Farthing MJ, Walt RP, Allan RN, Swan CH, Gilmore IT, Mallinson CN, et al. A national training programme for gastroenterology and hepatology. Gut. 1996;38(3):459-70. https://doi.org/10.1136/gut.38.3.459
13. Beattie AD, Greff M, Lamy V, Mallinson CN. The European Diploma of Gastroenterology: progress towards harmonization of standards. Eur J Gastroenterol Hepatol. 1996;8(4):403-6. https://doi.org/10.1097/00042737-199604000-00021
14. Beg S, Ragunath K, Wyman A, Banks M, Trudgill N, Pritchard DM, et al. Quality standards in upper gastrointestinal endoscopy: a position statement of the British Society of Gastroenterology (BSG) and Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland (AUGIS). Gut. 2017;66(11):1886-99. https://doi.org/10.1136/gutjnl-2017-314109
15. Bisschops R, Areia M, Coron E, Dobru D, Kaskas B, Kuvaev R, et al. Performance measures for upper gastrointestinal endoscopy: A European Society of Gastrointestinal Endoscopy quality improvement initiative. United Eur Gastroenterol J. 2016;4(5):629-56. https://doi.org/10.1177/2050640616664843
16. Yao K, Uedo N, Kamada T, Hirasawa T, Nagahama T, Yoshinaga S, et al. Guidelines for endoscopic diagnosis of early gastric cancer. Dig Endosc Off J Jpn Gastroenterol Endosc Soc. 2020;32(5):663-98. https://doi.org/10.1111/den.13684
17. Emura F, Sharma P, Arantes V, Cerisoli C, Parra-Blanco A, Sumiyama K, et al. Principles and practice to facilitate complete photodocumentation of the upper gastrointestinal tract: World Endoscopy Organization position statement. Dig Endosc. 2020;32(2):168-79. https://doi.org/10.1111/den.13530
18. Kim GH, Bang SJ, Ende AR, Hwang JH. Is screening and surveillance for early detection of gastric cancer needed in Korean Americans? Korean J Intern Med. 2015;30(6):747-58. https://doi.org/10.3904/kjim.2015.30.6.747
19. Asaka M, Mabe K. Strategies for eliminating death from gastric cancer in Japan. Proc Jpn Acad Ser B Phys Biol Sci. 2014;90(7):251-8. https://doi.org/10.2183/pjab.90.251
20. Hamashima C, Systematic Review Group and Guideline Development Group for Gastric Cancer Screening Guidelines. Update version of the Japanese Guidelines for Gastric Cancer Screening. Jpn J Clin Oncol. 2018;48(7):673-83. https://doi.org/10.1093/jjco/hyy077
21. Yashima K, Shabana M, Kurumi H, Kawaguchi K, Isomoto H. Gastric Cancer Screening in Japan: A Narrative Review. J Clin Med. 2022;11(15):4337. https://doi.org/10.3390/jcm11154337
22. Goss PE, Lee BL, Badovinac-Crnjevic T, Strasser-Weippl K, Chavarri-Guerra Y, St Louis J, et al. Planning cancer control in Latin America and the Caribbean. Lancet Oncol. 2013;14(5):391-436. https://doi.org/10.1016/S1470-2045(13)70048-2
23. Bravo LE, Hernández Vargas JA, Collazos P, García LS, Valbuena AM, Acuña L. Survival in stomach cancer: analysis of a national cancer information system and a population-based cancer registry in Colombia. Colomb Médica CM. 2023;53(4):e2025126. https://doi.org/10.25100/cm.v53i4.5126
24. Liu Z, Mao H, Wu CY, Feichtenhofer C, Darrell T, Xie S. A ConvNet for the 2020s [Internet]. arXiv; 2022 [consultado el 15 de septiembre de 2023]. Disponible en: http://arxiv.org/abs/2201.03545. https://doi.org/10.1109/CVPR52688.2022.01167
25. Bravo D, Ruano J, Jaramillo M, Gallego D, Gómez M, González FA, et al. Automatic Classification of Esophagogastroduodenoscopy Sub-Anatomical Regions. En: 2023 IEEE 20th International Symposium on Biomedical Imaging (ISBI). 2023. p. 1-5. https://doi.org/10.1109/ISBI53787.2023.10230483
26. Deng J, Dong W, Socher R, Li LJ, Li K, Fei-Fei L. ImageNet: A large-scale hierarchical image database. En: 2009 IEEE Conference on Computer Vision and Pattern Recognition. 2009. p. 248-55. https://doi.org/10.1109/CVPR.2009.5206848
27. Russakovsky O, Deng J, Su H, Krause J, Satheesh S, Ma S, et al. ImageNet Large Scale Visual Recognition Challenge [Internet]. arXiv; 2015 [consultado el 15 de septiembre de 2023]. Disponible en: http://arxiv.org/abs/1409.0575
28. Serre T, Kreiman G, Kouh M, Cadieu C, Knoblich U, Poggio T. A quantitative theory of immediate visual recognition. Prog Brain Res. 2007;165:33-56. https://doi.org/10.1016/S0079-6123(06)65004-8
29. Lee H, Ekanadham C, Ng A. Sparse deep belief net model for visual area V2 [Internet]. Advances in Neural Information Processing Systems; 2007 [consultado el 24 de septiembre de 2023]. Disponible en: https://papers.nips.cc/paper_files/paper/2007/file/4daa3db355ef2b0e64b472968cb70f0d-Paper.pdf
30. Glorot X, Bordes A, Bengio Y. Deep Sparse Rectifier Neural Networks. International Conference on Artificial Intelligence and Statistics; 2011 [consultado el 24 de septiembre de 2023]. Disponible en: https://www.semanticscholar.org/paper/Deep-Sparse-Rectifier-Neural-Networks-Glorot-Bordes/67107f78a84bdb2411053cb54e94fa226eea6d8e
31. Hamashima C, Ogoshi K, Narisawa R, Kishi T, Kato T, Fujita K, et al. Impact of endoscopic screening on mortality reduction from gastric cancer. World J Gastroenterol WJG. 2015;21(8):2460-6. https://doi.org/10.3748/wjg.v21.i8.2460
32. Kim SY, Park JM. Quality indicators in esophagogastroduodenoscopy. Clin Endosc. 2022;55(3):319-31. https://doi.org/10.5946/ce.2022.094
33. Chiu PWY, Uedo N, Singh R, Gotoda T, Ng EKW, Yao K, et al. An Asian consensus on standards of diagnostic upper endoscopy for neoplasia. Gut. 2019;68(2):186-97. https://doi.org/10.1136/gutjnl-2018-317111
34. Renna F, Martins M, Neto A, Cunha A, Libânio D, Dinis-Ribeiro M, et al. Artificial Intelligence for Upper

Gastrointestinal Endoscopy: A Roadmap from Technology Development to Clinical Practice. Diagn Basel Switz. 2022;12(5):1278. https://doi.org/10.3390/diagnostics12051278
35. Takiyama H, Ozawa T, Ishihara S, Fujishiro M, Shichijo S, Nomura S, et al. Automatic anatomical classification of esophagogastroduodenoscopy images using deep convolutional neural networks. Sci Rep. 2018;8(1):7497. https://doi.org/10.1038/s41598-018-25842-6
36. Wu L, Zhou W, Wan X, Zhang J, Shen L, Hu S, et al. A deep neural network improves endoscopic detection of early gastric cancer without blind spots. Endoscopy. 2019;51(6):522-31. https://doi.org/10.1055/a-0855-3532
37. Chang YY, Li PC, Chang RF, Yao CD, Chen YY, Chang WY, et al. Deep learning-based endoscopic anatomy classification: an accelerated approach for data preparation and model validation. Surg Endosc. 2022;36(6):3811-21. https://doi.org/10.1007/s00464-021-08698-2

https://doi.org/10.22516/25007440.1134

Original article

Experience in Peroral Endoscopic Myotomy in a Center in Bogotá, Colombia, Between 2018 and 2022

Tatiana Barragán-Briceño,[1*] Paola González-A.,[1] Carlos Fuentes-D.,[2] Jesús Rodríguez-F.,[3] María Camila Gómez-Ayala.[4]

OPEN ACCESS

Citation:
Barragán-Briceño T, González P, Fuentes C, Rodríguez J, Gómez-Ayala MC. Experience in Peroral Endoscopic Myotomy in a Center in Bogotá, Colombia, Between 2018 and 2022. Revista. colomb. Gastroenterol. 2024;39(2):146-152.
https://doi.org/10.22516/25007440.1134

[1] Department of General Surgery, Universidad Militar Nueva Granada. Bogotá, Colombia.
[2] Department of Gastroenterology and Digestive Endoscopy, Clínica Universitaria Colombia. Bogotá, Colombia.
[3] Department of Gastroenterology and Digestive Endoscopy, Clínica Shaio. Bogotá, Colombia.
[4] Department of Clinical Epidemiology and Biostatistics, Pontificia Universidad Javeriana. Bogotá, Colombia.

***Correspondence:** Tatiana Barragán-Briceño.
tatianabarraganb@hotmail.com

Received: 03/08/2023
Accepted: 15/01/2024

CC BY NC ND

Abstract

Background: Achalasia is a low-incidence disease, but it significantly affects the life quality of patients. Before 2010, peroral endoscopic myotomy (POEM) was the preferred course of treatment. However, due to its effectiveness and safety, POEM has been widely used since then. **Objective:** To describe the results of the largest cohort of patients with achalasia–treated with endoscopic surgery–with the poem technique to date in Colombia. **Methods:** Observational cohort study that included patients treated with peroral endoscopic myotomy in the city of Bogota, Colombia, between 2018 and 2022. Information from medical records was collected and analyzed retrospectively, with subsequent telephone follow-up prospectively. The presurgical and follow-up Eckardt scale was used to establish clinical success. **Results:** Between 2018 and 2022, 31 patients were intervened, 61% of which were men. The mean age was 47 years. Technical and clinical success was obtained in 97% of cases, with an Eckardt score less than or equal to three, in 93%, at two months of follow-up. Forty-five percent of the procedures were outpatient. The complication rate was 10%. **Conclusion:** Our study shows that peroral endoscopic myotomy for achalasia management is an effective, low complication rate, and safe technique to perform on an outpatient basis.

Keywords

Achalasia of the esophagus, myotomy, endoscopy, Colombia.

INTRODUCTION

Achalasia is a chronic disorder of esophageal motility caused by inflammation and cellular degeneration of the myenteric plexus. This condition leads to decreased relaxation of the lower esophageal sphincter and altered esophageal peristalsis, resulting in symptoms such as dysphagia, the primary symptom of this disease, as well as regurgitation, chest pain, and heartburn[1,2]. Due to the non-specific nature of these symptoms, achalasia is often detected late[3]. Diagnosis is based on the results of a series of studies, including upper gastrointestinal endoscopy (UGIE), timed barium esophagogram, and high-resolution manometry, the latter being the gold standard[4].

High-resolution manometry allows for the visualization and evaluation of esophageal pressure topography through 36 pressure sensors spaced along a transnasal catheter[1]. The diagnosis is confirmed when there is a lack of relaxation at the gastroesophageal junction, indicated by an integrated relaxation pressure (IRP) in the supine position exceeding 15 mm Hg, and absence of peristalsis in all swallows. According to manometric findings, the Chicago

© 2024 Asociación Colombiana de Gastroenterología

Classification Version 4.0 subdivides achalasia into three types based on pressurization patterns, which aids in guiding treatment and determining prognosis[1,4].

Once the diagnosis is confirmed, the severity of the disease is assessed using the Eckardt score, which allows for monitoring and evaluating the therapeutic response and the effectiveness of the medical-surgical management applied. This tool consists of four components: dysphagia, chest pain, regurgitation, and weight loss. Each component is assigned a score from 0 to 3 based on the patient's self-reported response, resulting in a total score ranging from 0 to 12 points. A score of three or less is considered remission of the disease[5,6].

Current treatments focus on symptomatic management. Available options include pharmacological, endoscopic, and surgical methods, such as oral medications, botulinum toxin, pneumatic dilation, Heller myotomy, and peroral endoscopic myotomy (POEM)[4,5,7].

Pharmacotherapy includes calcium channel blockers, which have short-term effectiveness, reducing lower esophageal sphincter pressure in 13% to 65% of patients. However, the short duration of action of these medications (30 to 120 minutes) requires multiple daily doses, which can lead to side effects and poor treatment adherence[6]. Botulinum toxin injected at the esophagogastric junction provides 50% symptom relief in approximately 80% of patients for up to six months, with progressive reduction in relief month by month[6]. Pneumatic dilation is an effective but not definitive alternative, requiring multiple sessions every 4 to 6 weeks. Symptomatic improvement is observed in 66% to 88% of patients after one year, but this decreases from 25% to 29% after 10 years[1]. Finally, surgical management remains one of the most effective treatments for achalasia. The original Heller myotomy was the preferred surgery for many years, but with the advent of minimally invasive techniques, laparoscopic myotomy with partial fundoplication has become the current surgical method of choice. This procedure is efficient, with a success rate of up to 89%, clinical improvement in 87% of patients at 40 months follow-up, less morbidity, better pain control, and faster recovery[1,4].

With the development of POEM in 2010, following the advent of natural orifice transluminal endoscopic surgery (NOTES) in the mid-2000s, a new alternative for the treatment of achalasia was introduced. This procedure is considered safe, with success rates comparable to or even surpassing those of laparoscopic myotomy, and it has a low complication rate[1,3,8,9].

In Latin America, this technique is still in its developmental stages, and there is limited literature describing the experience and effectiveness of the procedure among various groups. Consequently, the aim of this study was to describe the outcomes of the largest cohort to date in Colombia of patients diagnosed with achalasia and treated with POEM in Bogotá.

MATERIALS AND METHODS

An observational cohort study was conducted. The study included patients over fifteen years of age with a diagnosis of achalasia confirmed by high-resolution manometry, who were treated with POEM at a quaternary care hospital in Bogotá, Colombia, between January 2018 and May 2022 by a group of three endoscopic surgeons. Patients with incomplete medical records or a concurrent diagnosis of gastroesophageal malignancy were excluded. Once patients meeting the selection criteria were identified, they were contacted by phone to invite them to participate in the study and, if they agreed, to complete the informed consent process via telephone.

Surgical Technique

Prior to the procedure, patients were instructed to follow a full liquid diet for two days and a clear liquid diet for one day. After verifying informed consent, the procedure was carried out in the operating room under general anesthesia, following the technique described by Inoue and colleagues[10], as outlined below.

With the patient in the left lateral decubitus position, the esophagus was thoroughly irrigated with sterile water using a conventional gastroscope fitted with a plastic cap. A submucosal injection was performed on the posterior wall with a mixture of hypertonic saline, gentamicin, and methylene blue. The injection site depended on the type of achalasia, the characteristics of the esophagus, and the presence or absence of prior interventions. Subsequently, the mucosa was incised with a hybrid knife endoscopic scalpel to enter the submucosal space and begin tunnel dissection. This was done by applying the previously described mixture with electrofulguration using the scalpel in aerosol function for coagulation up to 2 cm distal to the esophagogastric junction, respecting the perforating vessels. The myotomy was performed 2 cm distal to the initial mucosal incision, cutting the muscle fibers of the esophagus up to 2 cm distal to the cardia, while preserving the longitudinal fibers. Hemostasis of the dissection bed was achieved, followed by another irrigation, and the mucosal incision was closed with metal clips. At the end of the procedure, the presence of capnoperitoneum was clinically evaluated, and if present, decompression was performed with a single puncture using a 14-gauge needle in the left flank.

The patients were transferred to recovery and subsequently discharged with instructions to follow a full liq-

uid diet for three days and then transition to a soft diet. Analgesic management was indicated with nonsteroidal anti-inflammatory drugs (NSAIDs) for one week and a proton pump inhibitor for two months. The first follow-up was conducted eight days postoperatively, during which the Eckardt score was applied again, followed by another evaluation at three months with a new UGIE to assess esophagitis and a timed barium esophagogram.

Data Collection and Outcome Measurement

Sociodemographic and clinical data were retrospectively collected from medical records, including information on the diagnosis and procedure. Technical success was defined as the completion of the surgery. Additionally, immediate postoperative complications, hospital stay duration, and the Eckardt score at two months postoperatively were recorded. Data extraction was performed independently by two researchers in chronological order, and the database was subsequently reviewed by a third researcher.

Prospectively, the Eckardt score was applied at six and twelve months post-intervention, with clinical success defined as a score of three or less. Additionally, the results of UGIE at six months post-surgery and the need for proton pump inhibitors (PPIs) in relation to gastroesophageal reflux symptoms or endoscopic findings of esophagitis were evaluated.

Statistical Analysis

A descriptive analysis of the results was performed. For qualitative variables, summary measures such as ratios and percentages, as well as relative and absolute frequencies, were used as appropriate. For quantitative variables, measures of central tendency and dispersion were used.

Ethical Considerations

This project was presented to and approved by the Ethics Committee of Hospital Militar Central de Bogotá.

RESULTS

Thirty-five patients over the age of fifteen diagnosed with achalasia and managed with POEM were identified. Four were excluded due to incomplete medical records at the start of the study.

General Characteristics

Among the 31 patients included in the cohort, 61% (19) were men and 39% (12) were women. The average age was 47 years, with a range between 15 and 87 years, and 10% (3) of the patients were over 65 years old. Associated comorbidities were identified in 26% (8) of the patients.

Diagnosis and Procedure Characteristics

All 31 patients had a manometric diagnosis of achalasia with the following distribution: type I: 23% (7 patients), type II: 61% (19 patients), and type III: 16% (5 patients). The median pre-surgical Eckardt score was 8 (interquartile range [IQR]: 6-8), with a range between 4 and 12. Additionally, 32% (10) of the patients had received prior treatment for achalasia, with the most common being Heller myotomy with fundoplication, accounting for 13% (4) of the patients.

Regarding the procedure characteristics, the average duration was 80 minutes, with a range between 80 and 120 minutes. The myotomy length ranged from 4 to 20 cm, with an average of 11 cm, and closure was achieved with clips in all cases. 45% (14) of the patients were tended to on an outpatient basis, 35% (11) had a hospital stay of 24 hours, and the remaining 20% (6) had a stay ranging from 48 hours to one week. Among the patients with hospitalizations longer than 24 hours, the increased stay was due to one case of pneumonia, one case of pneumothorax that resolved with medical management, and one case of major bleeding that required the suspension of the procedure and subsequent transfusion support. This last case was considered the only instance of therapeutic failure in our study.

Overall, the complication rate was 10% (3 patients). Additionally, 26% (8) of the patients experienced capnoperitoneum, clinically diagnosed during the procedure by subcutaneous emphysema in the chest, which was managed with drainage by puncture; this event was not considered a complication but an adverse event, as none of the cases required hospitalization or additional studies. There were no cases of mortality during the study.

The sociodemographic characteristics, comorbidities, and preoperative variables, including the type of achalasia and the preoperative Eckardt score of the patients, are summarized in **Table 1**.

Follow-Up

Follow-up was conducted using the Eckardt score at two, six, and twelve months, focusing only on cases of technical success, which included 30 patients. The results are presented in **Table 2**. There was one failed case involving a patient with a prior diagnosis of megaesophagus and type III achalasia, who had also undergone open myotomy over ten years ago. The tortuosity and dilation of the esophagus, along with anatomical changes due to the previous surgery,

led to significant bleeding that necessitated stopping the procedure. Consequently, this case was excluded from the analysis of the results presented below.

Table 1. Sociodemographic and Preoperative Characteristics of Patients

Characteristics of Patients		n = 31 (%)
Age (mean + SD)		47.2 + 15.6
Sex	Men	19 (61.2)
	Women	12 (38.7)
Comorbidities	Diabetes mellitus	1 (3.2)
	Hypertension (HTN)	3 (9.7)
	Hypothyroidism	2 (6.5)
	Obesity	2 (6.5)
BMI (mean + SD)		24.8 + 5.5
Type of achalasia	Type I	7 (22.6)
	Type II	19 (61.3)
	Type III	5 (16.1)
Previous treatment	Laparoscopic Heller myotomy	4 (12.9)
	Open myotomy	2 (6.5)
	Pneumatic dilations	2 (6.5)
	Medical management	1 (3.2)
Pre-POEM Eckardt score; mean ± SD		7.5 (2.1)

SD: standard deviation; HTN: hypertension; BMI: body mass index; POEM: peroral endoscopic myotomy. Source: Author's own research.

Table 2. Summary Measures for Pre- and Post-Surgical Eckardt Score

Evaluation Timepoint	Median	IQR	Range	n
Pre-surgical	8	6-8	4-11	30
2 months	0	0-1	0-5	30
6 months	1	1-2	0-7	29
12 months	1	1-3	0-7	21

IQR: interquartile range. Source: Author's own research.

97% (30) of the patients completed follow-up at two and six months, while the twelve-month follow-up rate was 71% (22 patients). At two months postoperatively, the reported clinical success rate was 93% (28/30), and this figure remained consistent at six months (28/30). At twelve months postoperatively, the clinical success rate slightly decreased to 91% (20/22). Three cases required additional management with pneumatic dilation due to persistent symptoms following POEM.

When evaluating clinical success at each follow-up point according to the type of achalasia, it was found that the prevalence of success was higher at all time points for patients with types II and III achalasia. These results are detailed in **Table 3**.

Table 3. Prevalence of Clinical Success by Achalasia Type at Each Follow-Up Point

Achalasia Type	Clinical Success	No Clinical Success	Total	Prevalence of Success
Follow-up at 2 months				
I	6	1	7	0,86
II	18	1	19	0,95
III	4	0	4	1,00
Total	28	2	30	
Follow-up at 6 months				
I	7	0	7	1,00
II	17	2	19	0,89
III	4	0	4	1,00
Total	28	2	30	
Follow-up at 12 months				
I	4	1	5	0,8
II	12	1	13	0,92
III	4	0	4	1,00
Total	20	2	22	

Source: Author's own research.

At the time of discharge, all patients were prescribed PPI and underwent follow-up UGIE at two months postoperatively. In 26% of cases (8 patients), erosive esophagitis of varying severity, as per the Los Angeles classification, was observed, with grade A being the most prevalent. These results are detailed in **Table 4**. Of the 30 patients who were followed up, 43% (13 patients) required an extended duration of PPI therapy due to symptoms associated with gastroesophageal reflux disease (GERD).

DISCUSSION

Since the advent of POEM, numerous studies have assessed its effectiveness and safety globally. In Colombia, the number of achalasia cases treated with POEM is increasing; however, to date, only a small series of cases, published four years

Table 4. Classification According to UGIE

Measure	n = 8 (%)
Post-POEM Esophagitis According to UGIE	
- Los Ángeles A	3 (9,7)
- Los Ángeles B	3 (9,7)
- Los Ángeles C	2 (6,4)
- Los Ángeles D	0

UGIE: upper gastrointestinal endoscopy; POEM: peroral endoscopic myotomy. Source: Author's own research.

ago by Rodríguez and colleagues[11], is available. This study represents the largest series of cases reported in Colombia.

Compared to global statistics on achalasia, which typically show a 1:1 ratio between men and women and a bimodal age distribution with peaks between 20-40 years and 50-70 years[4,5], our study found a slightly higher prevalence in males with a ratio of 1:0.6 and a mean age of 47 years. The most common type of achalasia was type II (61%), which is similar to the findings of Kahaleh and colleagues, Zhou and colleagues[1,5], and Hernández-Mondragón and colleagues[6], who reported frequencies of 66% and 52%, respectively.

Our successful outcomes are comparable to those reported in other Latin American studies. In a 2021 multicenter study that included 125 patients, Kahaleh and colleagues[12] reported a technical success rate of 93.5% and a clinical success rate of 88.8%, with an average follow-up of 16 months and a complication rate of 21.6%. Similarly, in a retrospective analysis of 15 patients in 2017, Mejía and colleagues[13] achieved 100% technical and clinical success with follow-up ranging from 1 to 15 months. Ramírez and colleagues[14], who published their results the same year, described a technical success rate of 100% and a clinical success rate of 88.6% in 35 patients, with an average follow-up of 10 months and a complication rate of 2.8%.

We believe that our success and complication rates are comparable to those of previous studies. The differences observed can be attributed to variable sample sizes and losses during long-term follow-up.

Other studies have evaluated the association between the type of achalasia and clinical success. Andolfi and colleagues[15] conducted a meta-analysis that included 20 studies, reporting clinical success rates of 95%, 97%, and 93% for type I, II, and III achalasia, respectively. They argued that there is no clear relationship between these variables[15]. When evaluating our results, we observed a trend towards better outcomes for patients with type III achalasia at the two and twelve-month follow-ups. However, these findings are limited by the small sample size and losses during follow-up, which prevent drawing definitive conclusions regarding this association.

Traditionally, this procedure is performed on an inpatient basis with a hospital stay ranging from 2.8 days in the Chilean group[13], 3 days in the Mexican group [12], and 1.3 days in the Argentinian group[14]. In our study, 45% of cases were managed on an outpatient basis, suggesting that POEM for achalasia can be performed on a scheduled outpatient basis in selected cases and in centers with the necessary experience and infrastructure for managing complex gastrointestinal pathology.

One of the few aspects where POEM has not yet proven its superiority over Heller myotomy is in postoperative GERD. In our study, 42% (7) of patients required extended PPI consumption for more than two months due to persistent GERD symptoms. However, only 26% (11) of patients presented postoperative esophagitis as evidenced by follow-up UGIE at two months. Some studies report a prevalence of GERD in up to 50% of cases[14], but these figures vary considerably depending on the method of diagnosis and follow-up. For example, in the study by Hernández and colleagues[16], 17% had clinical manifestations, 15% had some degree of esophagitis on UGIE, and 37% had a positive pHmetry, confirming reflux disease one month after surgery.

Although our results are comparable to those of Hernández and fall below the described incidence of post-POEM GERD in the literature, it is important to consider that these studies evaluated GERD using pHmetry associated with UGIE. The absence of these diagnostic tests in our follow-up may have led to an underestimation of GERD presence, indicating that incorporating these methods could enhance future study results in Colombia.

We acknowledge the study's limitations and primarily aim to describe our experience; we believe our results are valuable and comparable with the Latin American literature, contributing important information to the national literature to encourage further research in this area.

Future research, preferably prospective and multicentric, should ideally include timed esophagogram evaluations, pHmetry, and manometry at six months for an objective assessment of the results. This approach would enable comparisons with the Eckardt score before and after the intervention.

CONCLUSION

Our results indicate that POEM is a procedure with low morbidity and mortality, achieving high technical and clinical success rates in both the short and medium term. Additionally, in selected cases, it could be performed on

an outpatient basis with standardized protocols. The outcomes observed are comparable with those from other specialized centers in Latin America.

This study, the largest published in Colombia to date, demonstrates that POEM is an effective technique with low morbidity and mortality. This underscores the importance of training and improving techniques in endoscopic surgery for managing gastrointestinal tract pathologies. It also opens opportunities for new studies with larger sample sizes and longer follow-up periods to analyze long-term outcomes.

Author Contributions

Tatiana Barragán, MD: conception of the idea, study design, data collection and analysis, writing, and final approval of the article. Paola González-A., MD: conception of the idea, study design, data collection and analysis, writing, and final approval of the article. Carlos Fuentes-D., MD: conception of the idea, data analysis, critical review, and final approval of the article. Jesús Rodríguez-F., MD: conception of the idea, critical review, and final approval of the article. María Camila Gómez-Ayala, MD, MSc: conception of the idea, study design, data analysis, writing, critical review, and final approval of the article.

Conflict of Interest

The authors declare no potential conflicts of interest with the publication of this article.

REFERENCES

1. Zhou MJ, Kamal A, Freedberg DE, Markowitz D, Clarke JO, Jodorkovsky D. Type II Achalasia Is Increasing in Prevalence. Digestive Diseases and Sciences. 2021;66(10):3490-4. https://doi.org/10.1007/s10620-020-06668-7
2. Kumbhari V, Tieu A, Onimaru M, el Zein M, Teitelbaum E, Ujiki M, et al. Peroral endoscopic myotomy (POEM) vs laparoscopic Heller myotomy (LHM) for the treatment of Type III achalasia in 75 patients: a multicenter comparative study. Endoscopy International Open. 2015;3(03):E195-201. https://doi.org/10.1055/s-0034-1391668
3. Mandavdhare HS, M PK, Shukla J, Kumar A, Sharma V. Role of Peroral Endoscopic Myotomy in Advanced Achalasia Cardia With Sigmoid and/or Megaesophagus: A Systematic Review and Metanalysis. J Neurogastroenterol Motil. 2022;28(1):15-27. https://doi.org/10.5056/jnm21122
4. Dirks RC, Kohn GP, Slater B, Whiteside J, Rodriguez NA, Docimo S, et al. Is peroral endoscopic myotomy (POEM) more effective than pneumatic dilation and Heller myotomy? A systematic review and meta-analysis. Surg Endosc. 2021;35(5):1949-1962. https://doi.org/10.1007/s00464-021-08353-w
5. Kahaleh M, Xu MM, Zamarripa F, Martínez G, Arantes VN, Rodriguez FC, et al. POEM in Latin America: The Rise of a New Standard. J Clin Gastroenterol. 2019;53(8):e352-e355. https://doi.org/10.1097/MCG.0000000000001161
6. Hernández-Mondragón OV, Solórzano-Pineda OM, González-Martínez MA, Blancas-Valencia JM, Caballero-Luengas C. Miotomía endoscópica peroral para el tratamiento de acalasia y otros trastornos motores del esófago. Resultados a corto y mediano plazo en un centro de referencia en México. Rev Gastroenterol Méx. 2019;84(1):1-10. https://doi.org/10.1016/j.rgmx.2017.09.001
7. Kahrilas PJ, Katzka D, Richter JE. Clinical Practice Update: The Use of Per-Oral Endoscopic Myotomy in Achalasia: Expert Review and Best Practice Advice From the AGA Institute. Gastroenterology. 2017;153(5):1205-1211. https://doi.org/10.1053/j.gastro.2017.10.001
8. Gu L, Ouyang Z, Lv L, Liang C, Zhu H, Liu D. Safety and efficacy of peroral endoscopic myotomy with standard myotomy versus short myotomy for treatment-naïve patients with type II achalasia: a prospective randomized trial. Gastrointest Endosc. 2021;93(6):1304-1312. https://doi.org/10.1016/j.gie.2020.10.006
9. de Moura ETH, Jukemura J, Ribeiro IB, Farias GFA, de Almeida Delgado AA, Coutinho LMA, et al. Peroral endoscopic myotomy *vs* laparoscopic myotomy and partial fundoplication for esophageal achalasia: A single-center randomized controlled trial. World J Gastroenterol. 2022;28(33):4875-4889. https://doi.org/10.3748/wjg.v28.i33.4875
10. Inoue H, Minami H, Kobayashi Y, Sato Y, Kaga M, Suzuki M, et al. Peroral endoscopic myotomy (POEM) for esophageal achalasia. Endoscopy. 2010;42(4):265-71. https://doi.org/10.1055/s-0029-1244080
11. Rodríguez-Fajardo JA, Mantilla-Gaviria HJ, Pineda-Ovalle LF, Jalal-Espitia AA, Escobar-Cruz HJ, Arbelaez-Méndez VH, et al. Miotomía endoscópica por vía oral (POEM) para el tratamiento de acalasia: nuestras primeras experiencias. Rev Colomb Gastroenterol. 2018;33(3):228-34. https://doi.org/10.22516/25007440.197
12. Kahaleh M, Tyberg A, Suresh S, Lambroza A, Casas FR, Rey M, et al. The learning curve for peroral endoscopic myotomy in Latin America: A slide to the right? Clin Endosc. 2021;54(5):701-5. https://doi.org/10.5946/ce.2020.290
13. Mejía R, Donoso A, Manríquez E, Sáez J, Crovari F, Gabrielli M, et al. Miotomía endoscópica por vía oral (POEM) para el tratamiento de la acalasia. Experiencia

clínica inicial y resultados a corto plazo. Rev Chil Cirugía. 2017;69(5):429-34. https://doi.org/10.1016/j.rchic.2017.03.004
14. Ramírez M, Zubieta C, Ciotola F, Amenabar A, Badaloni A, Nachman F, et al. Per oral endoscopic myotomy vs. laparoscopic Heller myotomy, does gastric extension length matter? Surg Endosc. 2018;32(1):282-288. https://doi.org/10.1007/s00464-017-5675-x
15. Andolfi C, Fisichella PM. Meta-analysis of clinical outcome after treatment for achalasia based on manometric subtypes. Br J Surg. 2019;106(4):332-341. https://doi.org/10.1002/bjs.11049
16. Hernández Mondragón OV, González Martinez MA, Blancas Valencia JM, Hernandez Reyes ML, Solórzano Pineda OM, Blanco Velasco G. Long-term quality of life after peroral endoscopic myotomy remains compromised in patients with achalasia type III. Endoscopy. 2017;49(12):1209-1218. https://doi.org/10.1055/s-0043-117401

https://doi.org/10.22516/25007440.1054

Original article

Stent Duodenal in Malignant Obstruction of the Gastric Outflow Tract in a Reference Center in Cundinamarca: Case Series

Margarita Gutiérrez,[1] Martín Garzón-Olarte,[2*] Andrea Gómez,[2] Juan Carlos Marulanda,[2] Natan Hormaza-Arteaga,[2] Katherine Marrugo,[2] Juan Carlos Molano,[2] Laura Moya,[2] Christian Labrador,[2] Mario Rey-Tovar.[2]

OPEN ACCESS

Citation:
Gutiérrez M, Garzón-Olarte M, Gómez A, Marulanda JC, Hormaza-Arteaga N, Marrugo K, Molano JC, Moya L, Labrador C, Rey-Tovar M. Stent Duodenal in Malignant Obstruction of the Gastric Outflow Tract in a Reference Center in Cundinamarca: Case Series. Revista. colomb. Gastroenterol. 2024;39(2):153-157. https://doi.org/10.22516/25007440.1054

[1] Second-Year Fellow in Gastroenterology and Digestive Endoscopy, Universidad del Rosario. Bogotá, Colombia.
[2] Gastroenterology and Digestive Endoscopy Unit, Hospital Universitario de la Samaritana. Bogotá, Colombia.

***Correspondence:** Martín Garzón-Olarte.
martingarzon@gmail.com

Received: 23/03/2023
Accepted: 09/02/2024

Abstract

Objective: To describe the experience of the insertion of the duodenal stent in patients with malignant obstruction of the gastric outflow tract in a third-level reference center in Cundinamarca. **Materials and methods:** Observational study, case series. Patients with Malignant gastric outlet obstruction (MGOO) diagnosed between December 2019 and February 2022 underwent the insertion of a self-expanding duodenal metal stent in the Gastroenterology unit of Hospital Universitario de la Samaritana. **Results:** 17 patients were enrolled, 76% of whom were male, with a mean age of 69 years (standard deviation [SD]: 11 years). Histology confirmed gastric adenocarcinoma was found in 82% of the patients, and 41% reported peritoneal carcinomatosis. We achieved total technical success (100%) and clinical success (88%) (15 patients). Regarding the size of the stent used, 35% (6 patients) were 12 cm, 53% (9 patients) were 9 cm, and 12% (2 patients) were 6 cm. Fluoroscopic and endoscopic guidance was used in 88% of cases. Patient survival at follow-up was an average of 84 days (2.8 months; range: 0-414 days) and currently, 1 patient continues in post-insertion surveillance for stent at the time described in the study. **Conclusion:** Duodenal stent is an effective and safe palliative management alternative in patients with MGOO that improves symptoms, particularly, oral tolerance and early hospital discharge in this group of patients (with advanced terminal neoplastic disease in the palliative management phase), reducing the need for surgical management.

Keywords

Gastric outlet obstruction, self-expandable metal stents, palliative care.

INTRODUCTION

Malignant gastric outlet obstruction (MGOO) is defined as mechanical obstruction of the pylorus or duodenum caused by extrinsic compression or infiltration from advanced locoregional neoplasms, which impede oral intake and lead to associated nutritional compromise[(1)]. This condition is due to the narrowing of the gastroduodenal region, delaying the passage of gastric contents from the stomach to the duodenum[(1,2)]. Gastroduodenal outlet tract stenosis is most frequently observed in patients with advanced gastric, duodenal, or pancreatic neoplasms[(1,3)]. This complication significantly affects the quality of life of these patients, which is why current palliative treatment strategies include surgical gastrojejunostomy, ultrasound-guided endoscopic gastroenterostomy, or the insertion of a duodenal stent[(2)]. Given the high surgical risk and short life expectancy of these patients, endoscopic management with duodenal stents has emerged as a non-surgical alternative to improve symptoms and quality of life, and to reduce hospital stays[(2)].

Gastroduodenal stents have been in use since the 1990s to offer a minimally invasive treatment for these cases[(3)]. The

technical effectiveness of stent insertion is approximately 97%, irrespective of the technique used (insertion through the working channel, fluoroscopic guide with endoscopic vision, or endoscopic guidance alone). The low rate of technical failure is primarily due to severe distal obstruction that prevents guide advancement for proper stent positioning[3,4]. Symptom resolution typically occurs around four days post-stent insertion, with improvements in food intake and oral tolerance seen in over 87% of cases. Cases where patients do not exhibit symptomatic improvement are usually due to disease progression or early stent migration[5].

The objective of this case series is to describe the experience of duodenal stent insertion in patients with malignant gastric outlet obstruction at a tertiary reference center in the department of Cundinamarca, Colombia.

MATERIALS AND METHODS

This is an observational study, presented as a case series. Data were collected from 17 patients over 18 years old diagnosed with MGOO between December 2019 and February 2022. These patients underwent duodenal self-expanding metal stent insertion in the gastroenterology unit at Hospital Universitario de la Samaritana.

The WallFlex™ duodenal self-expanding metal stent from Boston Scientific, available in sizes of 6 cm, 9 cm, and 12 cm, was used. The stent size was determined based on the length of the stenosis identified through upper gastrointestinal radiography, contrast-enhanced abdominal computed tomography (CT) scan, or during the endoscopic procedure when equipment passage through the stenosis was possible before stent deployment. Most procedures were performed with fluoroscopic guidance and under sedation managed by an anesthesiologist. The Olympus® EVIS Exera II CV 180 equipment was used.

RESULTS

Of the 17 patients included, 76% were men, with a mean age of 69 years (standard deviation [SD]: 11 years). The indication for duodenal stent insertion was malignant pyloric syndrome with oral intake intolerance in all cases (100%), primarily caused by gastric adenocarcinoma confirmed histologically in 82% (14 patients). In two patients, the obstruction was due to compression and infiltration by pancreatic cancer, and in one patient, there was no histological confirmation, with suspected lymphoproliferative disease. 12% (2 patients) had liver metastasis, and 41% (7 patients) had peritoneal carcinomatosis. The technical success rate was 100%, and clinical success, defined as tolerance to a liquid and soft diet, was 88% (15 patients). Clinical success was not achieved in two cases due to persistent nausea and vomiting caused by peritoneal carcinomatosis and distal obstruction. Regarding the stent sizes used, 35% (6 patients) had a 12 cm stent, 53% (9 patients) had a 9 cm stent, and 12% (2 patients) had a 6 cm stent. Fluoroscopic and endoscopic guidance was used in 88% of the cases, as illustrated in **Figure 1**. The average patient survival during follow-up was 84 days (2.8 months; range: 0-414 days), with one patient still under follow-up after stent insertion within the study period.

In patients with gastric adenocarcinoma, the obstruction was located above the papilla, whereas in others, it was due to infiltration of the duodenal bulb and the second portion. No patient experienced stent migration. Due to the short survival of the patients given their advanced oncological condition, no stent intrusion, migration, or obstruction was observed during follow-up. The clinical success allowed for early hospital discharge with tolerance to oral intake, and patients continued in end-of-life care management.

DISCUSSION

Malignant gastric outlet obstruction (MGOO) is caused by the narrowing of the gastroduodenal region, leading to a delay or failure in the passage of gastric contents from the stomach to the duodenum[1,2]. This condition typically presents with early satiety, weight loss, nausea, vomiting, and abdominal pain[1]. It is commonly found in patients with advanced gastric, duodenal, or pancreatic neoplasms[1,3]. In Colombia, the incidence rate of gastric cancer in 2020 was 12.8 per 100,000 inhabitants for both men and women, with a total of 8214 new cases, accounting for 7.5% of all diagnosed cancers[6]. The prevalence is 4.1%, corresponding to 11,611 cases over the past five years[6]. The mortality rate for the same year was 9.9 per 100,000 inhabitants, with 6451 deaths from this pathology, making it the third leading cause of cancer-related death[6].

Among the complications of gastric cancer, MGOO occurs in 20% of cases, significantly limiting curative treatment options[7]. MGOO manifests with symptoms such as nausea, difficult-to-manage vomiting, dehydration, abdominal pain, and malnutrition[8]. Other causes of gastric outlet obstruction include pancreatic neoplasms and, less frequently, duodenal or ampullary neoplasms, cholangiocarcinoma, lymphoma, or adenopathies from other neoplasms[9]. As previously noted, this complication severely impacts the quality of life of these patients. Current palliative treatment strategies include surgical gastrojejunostomy, ultrasound-guided endoscopic gastroenterostomy with LAMS (lumen-apposing metal stents), or the insertion of a duodenal stent[2].

The practice of inserting gastroduodenal stents for malignant pathology has demonstrated similar outcomes regar-

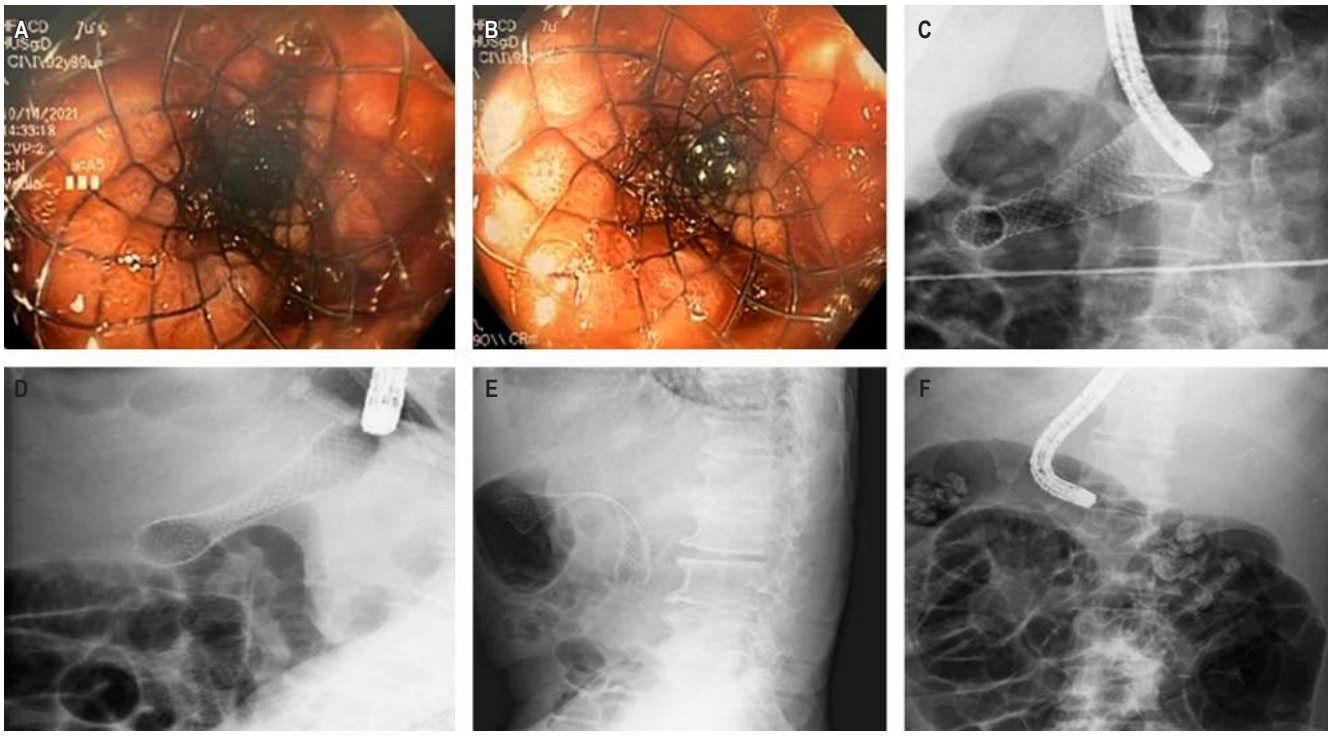


Figure 1. A and **B.** Endoscopic images from two cases showing the proximal cup of the deployed stent in the stenosis area. **C**, **D**, **E**, and **F.** Fluoroscopic images showing stent positioning in cases with different stent sizes. Source: Author's File.

ding success rates, adverse events, and improvements in symptoms and quality of life among experienced groups from Europe, Australia, Japan, and the United States[10-13]. It has been considered a feasible and safe procedure for managing malignant gastric outlet obstruction. In Colombia, studies have been published comparing duodenal stent insertion with gastrojejunostomy. Castaño and colleagues described a study with 70 patients, which found that the insertion of self-expanding metal stents resulted in better outcomes than surgery in terms of hospital stay duration, oral intake tolerance, and lower morbidity[14]. Another study conducted in Colombia by Vargas Rubio and colleagues with 31 patients with distal gastric cancer who underwent duodenal stent insertion showed similar results in effectiveness and symptom improvement compared to international studies[15].

When comparing the results from our patients with those described in the literature, the average age of our patients is similar to that reported by JP Ratone and colleagues[11]. Unlike reports from France and Spain, where the primary cause of MGOO is pancreatic cancer[10,11], in our study, as well as in the studies by Castaño and colleagues[14] and Vargas and colleagues[15], the primary cancer causing MGOO is gastric adenocarcinoma.

The technical success rate of stent placement in our study was 100%, comparable to what is reported in the literature, as was the clinical success rate, defined as tolerance to oral intake, which was 88% in our patients[3,5]. In the study by Vargas and colleagues[15], patient survival was 91 days, with similar findings in European case reports[10,11]. In our study, survival was slightly lower, which may be related to the tumor stage at diagnosis and the characteristics of the patients at our hospital. As a reference center for the department, we serve a population from distant rural areas with significant barriers to healthcare access, which may explain the late diagnosis and advanced disease stage at the time of diagnosis in our patients.

Regarding severe complications associated with the procedure, bleeding and perforation occur in about 1% of cases. Other non-severe complications include stent obstruction, abdominal pain, fever, vomiting, and stent migration[5]. No other complications were observed in our series. As noted earlier, patients without clinical success had distal obstruction of the stent due to peritoneal carcinomatosis.

In the palliation of malignant gastroduodenal obstruction, several studies have compared the efficacy of metallic gastroduodenal stents and lumen-apposing metal stents

released with ultrasound to the standard treatment of surgical gastrojejunostomy.

A study by Jeurnink and colleagues compared self-expanding metal stents with gastrojejunostomy for palliation of malignant gastroduodenal obstruction. The results indicated that self-expanding metal stents could be an effective alternative for palliation in these cases, while surgery is reserved for patients with a longer expected survival (more than six months)[16].

Nagaraja and colleagues conducted a meta-analysis comparing surgical gastrojejunostomy and endoscopic stenting for the palliation of malignant gastric outlet obstruction. The results suggest that stent placement is associated with better short-term outcomes, making duodenal stenting a safe means of palliating malignant stomach obstruction[17].

We do not have the availability or experience with the use of lumen-apposing metal stents for managing malignant gastric outlet obstruction at our institution.

CONCLUSIONS

Duodenal stenting is an effective and safe palliative management alternative for patients with MGOO, improving quality of life, tolerance to oral intake, and allowing for early hospital discharge, thereby reducing costs for the healthcare system and patients in managing this disease.

REFERENCES

1. Jue TL, Storm AC, Naveed M, Fishman DS, Qumseya BJ, McRee AJ, et al. ASGE guideline on the role of endoscopy in the management of benign and malignant gastroduodenal obstruction. Gastrointest Endosc. 2021;93(2):309-322.e4. https://doi.org/10.1016/j.gie.2020.07.063
2. Troncone E, Fugazza A, Cappello A, Del Vecchio Blanco G, Monteleone G, Repici A, et al. Malignant gastric outlet obstruction: Which is the best therapeutic option? World J Gastroenterol. 2020;26(16):1847-60. https://doi.org/10.3748/wjg.v26.i16.1847
3. Ding NS, Alexander S, Swan MP, Hair C, Wilson P, Clarebrough E, et al. Gastroduodenal outlet obstruction and palliative self-expandable metal stenting: A dual-centre experience. J Oncol. 2013;2013:167851. https://doi.org/10.1155/2013/167851
4. Reijm AN, Zellenrath PA, Van Der Bogt RD, Van Driel LMJW, Siersema PD, Bruno MJ, et al. Self-expandable duodenal metal stent placement for the palliation of gastric outlet obstruction over the past 20 years. Endoscopy. 2022;54(12):1139-46. https://doi.org/10.1055/a-1838-5642
5. Dormann AJ, Meisner S, Verin N, Wenk Lang A. Self-expanding metal stents for gastroduodenal malignancies: Systematic review of their clinical effectiveness. Endoscopy. 2004;36(6):543-50. https://doi.org/10.1055/s-2004-814434
6. Globocan, WHO. Estimated age-standardized incidence and mortality rates (World) in 2020, Colombia, both sexes, all ages [Internet]. Globocan, WHO; 2020 [15 de junio de 2022]. Disponible en: https://gco.iarc.who.int/media/globocan/factsheets/populations/170-colombia-fact-sheet.pdf
7. Tang SJ. Endoscopic stent placement for gastric outlet obstruction. Video J Encycl GI Endosc. 2013;1(1):133-6. https://doi.org/10.1016/S2212-0971(13)70057-8
8. Adler DG. Should Patients With Malignant Gastric Outlet Obstruction Receive Stents or Surgery? Clin Gastroenterol Hepatol. 2019;17(7):1242-4. https://doi.org/10.1016/j.cgh.2018.11.049
9. Chelsey C Ciambella, Rachel E Beard TJM. Current role of palliative interventions in advanced pancreatic cancer. World J Gastrointest Surg. 2018;10(7):75-83. https://doi.org/10.4240/wjgs.v10.i7.75
10. Alcalá-González LG, Masachs-Perecaula M, Dot Bach J, Abu-Suboh-Abadia M, Armengol Bertroli J, Pascasio-Hernández MJ, et al. Endoscopic stenting for gastroduodenal outlet obstruction of a malignant origin, real life experience in a single center. Rev Esp Enfermedades Dig. 2020;112(9):712-5. https://doi.org/10.17235/reed.2020.6600/2019
11. Ratone JP, Caillol F, Zemmour C, Bories E, Pesenti C, Lestelle V, et al. Outcomes of duodenal stenting: Experience in a French tertiary center with 220 cases. Dig Liver Dis. 2020;52(1):51-6. https://doi.org/10.1016/j.dld.2019.06.025
12. Van Halsema EE, Rauws EAJ, Fockens P, Van Hooft JE. Self-expandable metal stents for malignant gastric outlet obstruction: A pooled analysis of prospective literature. World J Gastroenterol. 2015;21(43):12468-81. https://doi.org/10.3748/wjg.v21.i43.12468
13. Miwa H, Sugimori K, Kaneko T, Ishii T, Iwase S, Irie K, et al. Clinical outcome of a highly flexible duodenal stent for gastric outlet obstruction: A multicenter prospective study. JGH Open. 2020;4(4):729-35. https://doi.org/10.1002/jgh3.12326
14. Castaño R, Álvarez O, Ruiz M, Juliao F, Cárdenas A, Sanín E, et al. Comparación entre la gastroyeyunostomía y el stent metálico autoexpandible para la paliación de la obstrucción maligna gastroduodenal. Rev Colomb Gastroenterol. 2006;21(1):11-8.

15. Vargas Rubio RD, Ovalle Hernández AF, Ursida Serrano V, Torres Arciniegas SC, Hani de Ardila AC. Experiencia con los stents metálicos autoexpandibles para el manejo de cáncer gástrico distal. Rev Gastroenterol Peru. 2018;38(4):331-9.
16. Jeurnink SM, Van Eijck CH, Steyerberg EW, Kuipers EJ, Siersema PD. Stent versus gastrojejunostomy for the palliation of gastric outlet obstruction: a systematic review. BMC Gastroenterol. 2007;7:18. https://doi.org/10.1186/1471-230X-7-18
17. Nagaraja V, Eslick GD, Cox MR. Endoscopic stenting versus operative gastrojejunostomy for malignant gastric outlet obstruction-a systematic review and meta-analysis of randomized and non-randomized trials. J Gastrointest Oncol. 2014;5(2):92-8. https://doi.org/10.3978/j.issn.2078-6891.2014.016

https://doi.org/10.22516/25007440.1156

Original article

Baveno VII Criteria for the Exclusion of Esophageal Varices in a Peruvian Population: Cross-Sectional Study

Celide Campoverde-Cueva,[1] Williams Celedonio-Campos,[2] Brayan Campos-Salazar,[3] Rommel Zambrano-Huailla,[2] Karla Alejandra Vizcarra-Zevallos,[1*] Jorge Garavito-Rentería.[2]

OPEN ACCESS

Citation:
Campoverde-Cueva C, Celedonio-Campos W, Campos-Salazar B, Zambrano-Huailla R, Vizcarra-Zevallos KA, Garavito-Rentería J. Baveno VII Criteria for the Exclusion of Esophageal Varices in a Peruvian Population: Cross-Sectional Study. Revista. colomb. Gastroenterol. 2024;39(2):158-165. https://doi.org/10.22516/25007440.1156

[1] Professional School of Human Medicine, Universidad Privada San Juan Bautista. Lima, Peru.
[2] Liver Unit, Gastroenterology Service, Hospital Nacional Arzobispo Loayza. Lima, Peru.
[3] Department of Neurobiology, Duke University, North Carolina, United States.

***Correspondence:** Karla Alejandra Vizcarra-Zevallos.
karla.vizcarra@upsjb.edu.pe

Received: 13/12/2023
Accepted: 03/04/2024

Abstract

Introduction: Esophageal varices represent one of the main complications in patients with liver cirrhosis. The main objective was to determine the diagnostic performance of the new Baveno VII criteria to exclude the presence of esophageal varices in compensated advanced chronic liver disease (cACLD), in an independent Peruvian population. **Materials and methods:** A cross-sectional study, including patients with cACLD, upper digestive endoscopy, and transient hepatic elastography from January 2017 to December 2019. **Results:** The mean age was 59.4 (12.9) years, while the mean measurement of liver stiffness was 27.21 (14.6) kPa. The prevalence of esophageal varices was 85.6%; non-alcoholic fatty liver disease (NAFLD) (63.6%) was the most prevalent etiology, followed by viral hepatitis (14.4%). For esophageal varices exclusion, Baveno VII criteria for all etiologies demonstrated adequate sensitivity and negative predictive value (sensitivity: 96.7%; 95% confidence interval [CI]: 92.3%-98.8%; negative predictive value: 76.9%, 95% CI: 56.4% -91%). However, better diagnostic performance was found when applying the Baveno VII criteria without considering NAFLD patients (sensitivity: 98.4%, 95% CI: 79.2% -99.2%; negative predictive value: 90.9%, 95% CI: 79.2% -99.2%). This would prevent 14% of endoscopic studies with a 9% risk of failing to detect esophageal varices. **Conclusions:** The Baveno VII criteria present good diagnostic performance for the exclusion of esophageal varices, especially in patients with cACLD without NAFLD, in an independent Peruvian population.

Keywords

Esophageal varices, gastrointestinal endoscopy, liver cirrhosis, portal hypertension.

INTRODUCTION

Latin America has one of the highest prevalences of mortality associated with liver disease[1]. However, there is limited epidemiological information specific to our context[2]. In Peru, chronic liver disease imposes a considerable economic burden on the healthcare system[3,4].

Gastrointestinal bleeding is one of the most frequent complications (39.4%) of compensated advanced chronic liver disease (cACLD). Approximately half of the patients with liver cirrhosis develop esophageal varices, and this percentage can reach 40% in those with a recent diagnosis[5,6].

The prognosis of chronic liver disease depends on the degree of portal vein pressure increase. Clinically significant portal hypertension (CSPH) is diagnosed with values above 10 mm Hg measured by the hepatic venous pressure gradient (HVPG)[7-9]. CSPH is associated with the development of complications related to cirrhosis, such as esophageal varices (EV), ascites, and hepatic encephalopathy[10,11]. Additionally, upper gastrointestinal endoscopy

© 2024 Asociación Colombiana de Gastroenterología

(EGD) is a direct method to detect varices and assess the risk of bleeding. However, the invasive nature of HVPG and EGD limits their routine use[12].

Various non-invasive diagnostic methods have been proposed to monitor the progression of hepatic fibrosis, with transient liver elastography being one of them[13-19]. The latest update of the Baveno criteria recommends using non-invasive methods to identify advanced chronic liver disease and the presence of clinically significant portal hypertension. Therefore, this study aims to evaluate the diagnostic performance of the new Baveno criteria (liver stiffness less than 15 kPa and platelet count greater than 150×10^9/L) [20] to exclude the presence of esophageal varices in an independent sample of the Peruvian population with cACLD.

MATERIALS AND METHODS

Study Design

This study is a retrospective, cross-sectional analysis of patients with compensated advanced chronic liver disease who were treated in the gastroenterology service at Hospital Nacional Arzobispo Loayza in Lima, Peru.

Study Population

The study included 209 patients with liver cirrhosis who underwent endoscopic and elastographic evaluations between January 2017 and December 2019. Based on etiology, they were classified into four groups: metabolic dysfunction-associated steatotic liver disease (MASLD), alcoholic liver disease (ALD), viral liver disease (chronic hepatitis B and C infections), and autoimmune liver disease (primary biliary cholangitis, autoimmune hepatitis, and primary sclerosing cholangitis).

The diagnosis of MASLD was based on ultrasonographic evidence of fatty liver along with the presence of one or more of the following criteria: abdominal circumference (≥90 cm for men and ≥80 cm for women), overweight or obesity, diabetes *mellitus*, or evidence of metabolic risk factors (blood pressure ≥ 130/85 mmHg, triglycerides ≥ 1.70 mmol/L, HDL-C < 40 mg/dL for men and < 50 mg/dL for women, HOMA-IR ≥ 2.5)[21]. Alcohol intake was considered the primary cause if no other underlying reason was identified. The diagnoses of viral hepatitis were confirmed by detecting positive viral markers for hepatitis B and C infections. Autoimmune liver diseases were diagnosed based on positive antibody tests, imaging studies, and liver biopsies when necessary. The diagnosis of cACLD was established through clinical data, radiological findings, or liver biopsy.

Inclusion criteria for patients were those who had undergone upper gastrointestinal endoscopy and liver elastography within three months of biochemical studies. Exclusion criteria included patients with secondary prophylaxis for esophageal variceal bleeding, post-transplant patients, pregnant women, and patients with heart failure.

Data Collection

The following variables were collected: age, sex, platelet count, international normalized ratio (INR), creatinine, albumin, total and fractionated bilirubin, Child-Pugh score, and MELD-Na score.

Endoscopic Evaluations

Endoscopic evaluations were performed under the supervision of two well-trained endoscopists. Esophageal varices were classified into two categories: low risk, defined by a diameter less than 5 mm and absence of red signs, and high risk, characterized by a diameter greater than 5 mm with or without red signs[22].

Measurement of Liver Stiffness

Liver stiffness was measured using transient liver elastography (FibroScan® model 502, Echosens, Paris, France), conducted by trained hepatologists. Measurement quality was ensured with at least ten measurements, a success rate of ≥ 60%, and an interquartile range (IQR/M) ≤ 30%. M or XL probes were used as necessary.

Statistical Analysis

Statistical analysis was conducted using RStudio v.1.1.463. Quantitative variables were presented as means and standard deviations, while qualitative variables were expressed as absolute values and proportions. The Kolmogorov-Smirnov or Shapiro-Wilk test was used to verify the normal distribution of the data. Kruskal-Wallis or ANOVA tests were used for numerical data, while the chi-square test was employed for categorical variables. Diagnostic performance was assessed through sensitivity, specificity, negative predictive value, positive predictive value, percentage of missed esophageal varices, and percentage of upper gastrointestinal endoscopies avoided. Statistical significance was set at a p-value < 0.05.

Ethical Considerations

This study adhered to ethical research guidelines and was approved by the ethics and research committee of Hospital Nacional Arzobispo Loayza in Lima, Peru, under protocol number 170302020.

RESULTS

Clinical Profile of Patients with Esophageal Varices

The average age of the patients was 59 years, with 57.4% of the study population being female. The most common etiology of cACLD was MASLD (63.6%), followed by viral hepatitis (14.4%). A total of 179 patients presented with esophageal varices (85.6%), with the majority classified as high risk (63.1% compared to 36.9%). **Table 1** summarizes the clinical and biochemical findings.

Patients with low-risk esophageal varices showed significantly lower elastography measurements (27.1 ± 9.8 kPa compared to 32.1 ± 15.1 kPa, $p < 0.0001$). Significant differences were also observed between the groups in terms of platelet count, bilirubin, albumin, and INR values.

Diagnostic Performance of Transient Liver Elastography and Platelet Count for the Exclusion of Esophageal Varices

The Baveno VII criteria demonstrated high diagnostic accuracy for ruling out esophageal varices with a cut-off point of < 15 kPa, showing a sensitivity of 96.7% and a negative predictive value of 76.9% (**Table 2**).

In the sub-analysis of patients with cACLD excluding those with MASLD, the diagnostic performance for ruling out esophageal varices improved, with a sensitivity of 98.4% and a negative predictive value of 90.9% (**Table 3**).

Table 1. Characterization of Clinical and Biochemical Parameters Among Different Groups*

Parameter	All (n = 209)	No Varices (n = 30)	Varices (n = 179)		*p*-Value
			Low Risk (n = 66)	High Risk (n = 113)	
Age (years)	59.44 ± 12.9	64.5 ± 11.4	59.6 ± 11.8	57.9 ± 13.7	0.0815
Female. n (%)	120 (57.4)	24 (80)	44 (67)	52 (46)	0.0007
Etiology. n (%)					
MASLD	133 (63.6)	17 (57)	41 (62)	75 (66)	0.0022
Viral	30 (14.4)	4 (13)	11 (17)	15 (13)	
Autoinmune	25 (12)	9 (30)	10 (15)	6 (5)	
ALD	21 (10)	-	4 (6)	17 (15)	
Platelets (x 10^9 cells/L)	148.3 ± 75.2	206.4 ± 87.1	149.9 ± 74.7	131.9 ± 64.1	<0.0001
Bilirubin (mg/dL)	1.7 ± 2.4	1.1 ± 0.9	1.5 ± 1.7	2.1 ± 2.9	0.0003
Albumin (g/dL)	3.78 ± 0.6	4.2 ± 0.5	4 ± 0.6	3.5 ± 0.6	<0.0001
Creatinine (mg/dL)	0.83 ± 0.8	1.2 ± 2.01	0.8 ± 0.3	0.7 ± 0.2	0.5027
INR	1.2 ± 0.2	1.1 ± 0.3	1.2 ± 0.3	1.3 ± 0.2	<0.0001
MELD-Na	11.7 ± 4.5	10.7 ± 4.1	10.9 ± 4.7	12.44 ± 4.4	0.0067
Child-Pugh. n (%)					
≤ 6 points	108 (51.7)	28 (93)	47 (71)	33 (29)	<0.0001
≥ 7 points	101 (48.3)	2 (7)	19 (29)	80 (71)	
LSM. kPa (mean)	27.21 ± 14.6	9.3 ± 1.6	27.1 ± 9.8	32.1 ± 15.1	<0.0001

*Numerical variables were compared using the Kruskal-Wallis test; categorical variables were compared using the chi-square test. INR: international normalized ratio; MELD: model for end-stage liver disease; LSM: liver stiffness measurement. Author's own research.

Table 2. Sensitivity and Negative Predictive Value of Liver Stiffness Measurement and Platelet Count for Excluding Esophageal Varices Across All Etiologies

LSM Cut-Off Points	Varices	No Varices	Sensitivity (95% CI)	NPV (95% CI)
<15 kPa	13	30	92.7 (87.9-96.1)	69.8 (53.9-82.8)
<15 kPa + ≥150 x 10^9/L platelets	6	20	96.7 (92.3-98.8)	76.9 (56.4-91)

CI: confidence interval; kPa: kilopascals; LSM: liver stiffness measurement; NPV: negative predictive value. Author's own research.

Table 3. Sensitivity and Negative Predictive Value of Liver Stiffness Measurement and Platelet Count for Excluding Esophageal Varices in Patients Without MASLD

LSM Cut-Off Points	Varices	No Varices	Sensitivity (95% CI)	NPV (95% CI)
<15 kPa	4	13	93.6 (84.3-98.2)	76.5 (50.1-93.2)
<15 kPa + ≥150 x 10^9/L platelets	1	10	98.4 (97.3-99.9)	90.9 (58.7-99.8)

CI: confidence interval; kPa: kilopascals; LSM: liver stiffness measurement; NPV: negative predictive value. Author's own research.

In terms of optimizing patient selection for ruling out esophageal varices, our study found that the use of gastrointestinal endoscopies in the overall population could be reduced upper by 12%, though with the risk of missing 23% of patients with esophageal varices. However, when excluding patients with MASLD from the analysis, the reduction in upper gastrointestinal endoscopies increased to 14%, with a lower risk of missing esophageal varices (9%) (**Figure 1**).

DISCUSSION

This study aimed to evaluate the effectiveness of the new Baveno VII criteria for excluding esophageal varices in patients with compensated liver cirrhosis. Our findings indicate a higher prevalence of esophageal varices compared to previous studies[23-25]. To avoid invasive diagnostics and reduce the number of endoscopic procedures, we applied the Baveno VII criteria (liver stiffness less than 15 kPa and platelet count greater than 150 × 10^9/L) for the exclusion of esophageal varices in our population. Our results demonstrate that the new Baveno criteria exhibit good diagnostic performance for excluding esophageal varices in patients without MASLD (sensitivity: 98.4%, negative predictive value: 90.9%). Additionally, applying these criteria could reduce upper gastrointestinal endoscopies by 14% with a low probability of missing esophageal varices (9%).

The high percentage of esophageal varices (85.6%) in our study may be attributed to the predominance of MASLD (63.6%) as the most prevalent etiology, aligning with demographic changes observed in our region[26]. Patients with MASLD are more likely to develop clinically significant portal hypertension, even in the early stages of hepatic fibrosis, compared to other etiologies[27,28].

The improvement in both sensitivity and negative predictive value may be attributed to the evaluation of patients with MASLD, which reduces the diagnostic accuracy of transient liver elastography. MASLD is defined by the presence of hepatic steatosis (demonstrated by imaging or liver histology) and metabolic risk factors[21]. Hepatic steatosis can alter the liver's viscoelastic properties[29]. Additionally, previous studies have not found a direct relationship between the degree of fibrosis and portal pressure measurements in patients with MASLD[27,30], suggesting the presence of subclinical portal hypertension in early and extensive stages of fibrosis[31]. From a technical standpoint, vibration-controlled transient elastography has limitations in its reliability for certain patients, particularly those with obesity, due to the greater distance between the skin and the liver caused by adipose tissue[13,32,33]. Pons and colleagues[13] found that patients with non-alcoholic steatohepatitis (NASH) and liver stiffness values similar to those in our population had a lower incidence of clinically significant portal hypertension. Including body mass index in the analysis could improve the non-invasive diagnosis of clinically significant portal hypertension, as proposed by the Anticipate study[34]. Therefore, hepatic steatosis and patients' physical characteristics can influence the accuracy of liver stiffness measurements.

As previous studies have highlighted, the etiology of advanced chronic liver disease can negatively impact the

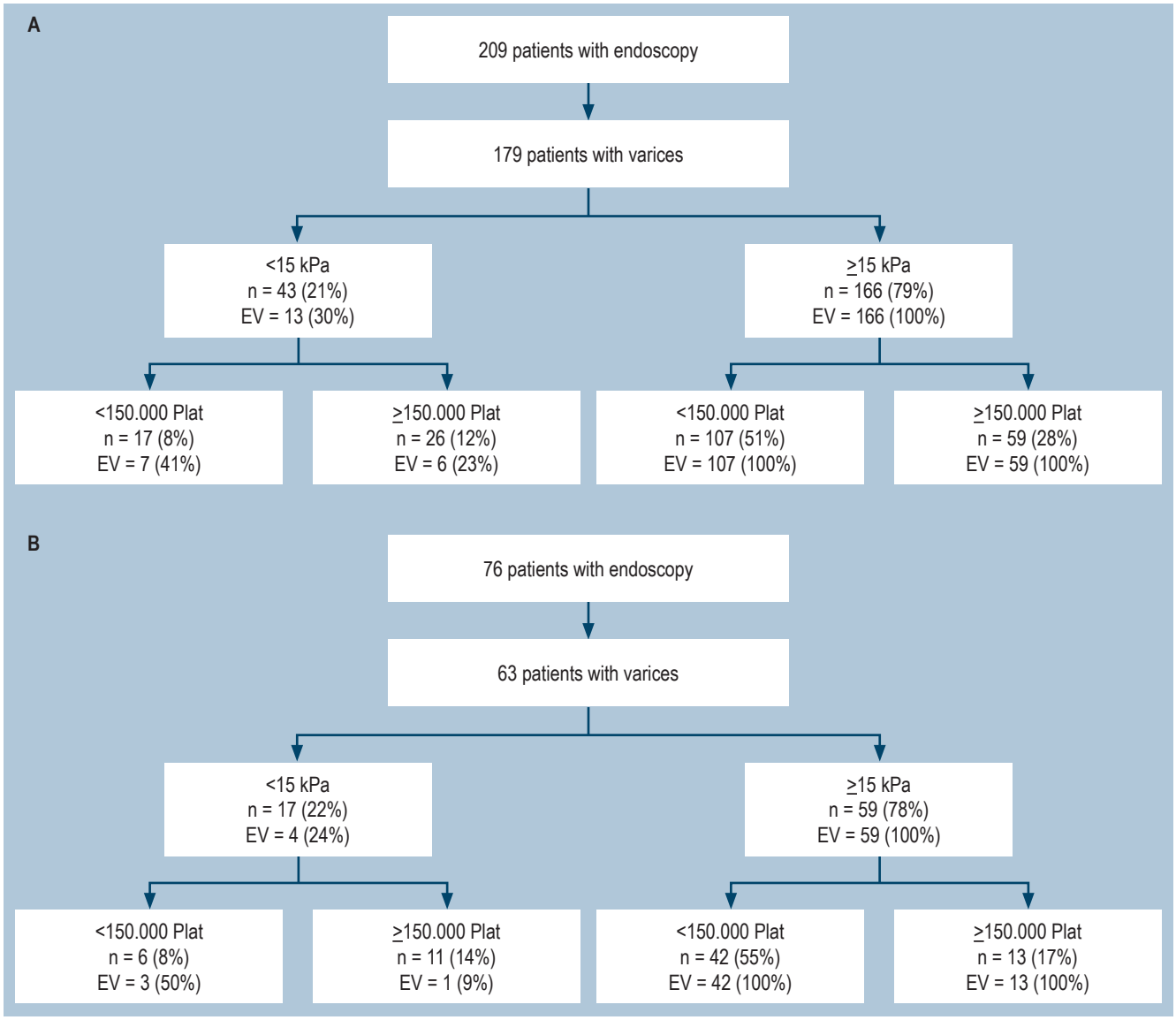


Figure 1. Performance Characteristics of the Baveno VII Criteria Across All Etiologies (**A**) and Excluding MASLD (**B**). Plat: platelets; EV: esophageal varices. Author's own research.

diagnostic performance of liver elastography for excluding esophageal varices[21-23]. In this independent sample of the Peruvian population, the Baveno VII criteria demonstrated good efficacy in reducing the need for endoscopic studies, with a decreased rate of missed esophageal varices in patients with cACLD without MASLD. This suggests that implementing these criteria is beneficial in daily clinical practice.

This is the first Peruvian study to apply the new Baveno consensus criteria for excluding the presence of esophageal varices in patients with liver cirrhosis who have no history of decompensation due to gastrointestinal bleeding. While endoscopic evaluation remains mandatory for patients with liver cirrhosis, the availability of liver elastography in some centers allows for the application of the Baveno criteria to avoid unnecessary upper gastrointestinal endoscopies. Our findings align with previous studies indicating that the diagnostic performance of transient liver elastography for excluding esophageal varices is reduced in patients with MASLD[35-37].

There are several limitations to this study. First, the sample size was small, necessitating a larger prospective study. Second, the cross-sectional design limits our ability to establish a causal relationship between different etiologies and diagnostic performance. Third, since the study was

conducted at a single center, the conclusions are restricted to our study population. Lastly, interobserver variability in liver stiffness measurements can impact results; however, all procedures were performed by two hepatologists who adhered to the same protocol and validity criteria for transient liver elastography measurements.

CONCLUSION

The new Baveno criteria have proven useful in preventing unnecessary upper gastrointestinal endoscopies, thus reducing the risk of missing esophageal varices in patients with cACLD without MASLD in an independent Peruvian population. Future large-scale prospective studies are recommended to validate and expand these results.

Author Contributions

CCC, RZH, AZ, and JGR contributed to the conceptualization and methodology of the study. RHZ, JGR, CCC, and WCC conducted the investigation. BCS, RZH, CCC, WCC, and AZ built the database and performed the statistical analysis. AZ, RZH, and BCS validated the study results. AZ and JGR managed the research project, and AZ provided administrative support. All authors were involved in drafting and approving the manuscript.

Funding Sources

This research received financial support from Universidad Privada San Juan Bautista SAC (PI0032).

Conflict of Interest

The authors declare no conflicts of interest related to this study.

Acknowledgments

None.

REFERENCES

1. Asrani SK, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. J Hepatol. 2019;70(1):151-171. https://doi.org/10.1016/j.jhep.2018.09.014
2. Mokdad AA, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, et al. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. BMC Med. 2014;12:145. https://doi.org/10.1186/s12916-014-0145-y
3. Malpica-Castillo A, Ticse R, Salazar-Quiñones M, Cheng-Zárate L, Valenzuela-Granados V, Huerta-Mercado TJ. Mortalidad y readmisión en pacientes cirróticos hospitalizados en un hospital general de Lima, Perú. Rev Gastroenterol Perú. 2013;33(4):301-305.
4. Bustíos C, Dávalos M, Román R, Zumaeta E. Características Epidemiológicas y Clínicas de la Cirrosis Hepática en la Unidad de Hígado del HNERM Es-Salud. Rev Gastroenterol Perú. 2007;27(3):238-245.
5. Garcia-Tsao G, Bosch J. Management of Varices and Variceal Hemorrhage in Cirrhosis. N Engl J Med. 2010;362(9):823-32. https://doi.org/10.1056/NEJMra0901512
6. Bosch J, Abraldes JG, Berzigotti A, Garcia-Pagan JC. Portal hypertension and gastrointestinal bleeding. Semin Liver Dis. 2008;28(1):3-25. https://doi.org/10.1055/s-2008-1040318
7. Mauro E, Gadano A. What's new in portal hypertension? Liver Int. 2020;40 Suppl 1:122-127. https://doi.org/10.1111/liv.14366
8. Bochnakova T. Hepatic Venous Pressure Gradient. Clin Liver Dis (Hoboken). 2021;17(3):144-148. https://doi.org/10.1002/cld.1031
9. Sauerbruch T, Schierwagen R, Trebicka J. Managing portal hypertension in patients with liver cirrhosis. F1000Res. 2018;7:F1000 Faculty Rev-533. https://doi.org/10.12688/f1000research.13943.1
10. Ripoll C. Hepatic Venous Pressure Gradient and Outcomes in Cirrhosis. J Clin Gastroenterol. 2007;41(3):S330-5. https://doi.org/10.1097/MCG.0b013e318150d0f4
11. D'Amico G, Pasta L, Morabito A, D'Amico M, Caltagirone M, Malizia G, et al. Competing risks and prognostic stages of cirrhosis: a 25-year inception cohort study of 494 patients. Aliment Pharmacol Ther. 2014;39(10):1180-93. https://doi.org/10.1111/apt.12721
12. Friedrich-Rust M, Poynard T, Castera L. Critical comparison of elastography methods to assess chronic liver disease. Nat Rev Gastroenterol Hepatol. 2016;13(7):402-11. https://doi.org/10.1038/nrgastro.2016.86
13. Pons M, Augustin S, Scheiner B, Guillaume M, Rosselli M, Rodrigues SG, et al. Noninvasive Diagnosis of Portal Hypertension in Patients With Compensated Advanced Chronic Liver Disease. Am J Gastroenterol. 2021;116(4):723-732. https://doi.org/10.14309/ajg.0000000000000994
14. Buechter M, Kahraman A, Manka P, Gerken G, Jochum C, Canbay A, et al. Spleen and Liver Stiffness Is Positively Correlated with the Risk of Esophageal Variceal Bleeding.

Digestion. 2016;94(3):138-144. https://doi.org/10.1159/000450704
15. Llop E, Berzigotti A, Reig M, Erice E, Reverter E, Seijo S, et al. Assessment of portal hypertension by transient elastography in patients with compensated cirrhosis and potentially resectable liver tumors. J Hepatol. 2012;56(1):103-8. https://doi.org/10.1016/j.jhep.2011.06.027
16. Sporea I, Rațiu I, Sirli R, Popescu A, Bota S. Value of transient elastography for the prediction of variceal bleeding. World J Gastroenterol. 2011;17(17):2206-10. https://doi.org/10.3748/wjg.v17.i17.2206
17. Kazemi F, Kettaneh A, N'kontchou G, Pinto E, Ganne-Carrie N, Trinchet JC, et al. Liver stiffness measurement selects patients with cirrhosis at risk of bearing large oesophageal varices. J Hepatol. 2006;45(2):230-5. https://doi.org/10.1016/j.jhep.2006.04.006
18. Stenberg Ribeiro M, Hagström H, Stål P, Ajne G. Transient liver elastography in normal pregnancy - a longitudinal cohort study. Scand J Gastroenterol. 2019;54(6):761-765. https://doi.org/10.1080/00365521.2019.1629007
19. Hu Z, Li Y, Li C, Huang C, Ou Z, Guo J, et al. Using Ultrasonic Transient Elastometry (FibroScan) to Predict Esophageal Varices in Patients with Viral Liver Cirrhosis. Ultrasound Med Biol. 2015;41(6):1530-7. https://doi.org/10.1016/j.ultrasmedbio.2015.02.005
20. de Franchis R, Bosch J, Garcia-Tsao G, Reiberger T, Ripoll C; Baveno VII Faculty. Baveno VII - Renewing consensus in portal hypertension. J Hepatol. 2022;76(4):959-974. https://doi.org/10.1016/j.jhep.2021.12.022
21. Eslam M, Sanyal AJ, George J, International Consensus Panel. MAFLD: A Consensus-Driven Proposed Nomenclature for Metabolic Associated Fatty Liver Disease. Gastroenterology. 2020;158(7):1999-2014.e1. https://doi.org/10.1053/j.gastro.2019.11.312
22. Garcia-Tsao G, Sanyal AJ, Grace ND, Carey WD; Practice Guidelines Committee of American Association for Study of Liver Diseases; Practice Parameters Committee of American College of Gastroenterology. Prevention and management of gastroesophageal varices and variceal hemorrhage in cirrhosis. Am J Gastroenterol. 2007;102(9):2086-102. https://doi.org/10.1111/j.1572-0241.2007.01481.x
23. Montes Ramirez ML, Pascual-Pareja JF, Sánchez-Conde M, Bernardino De la Serna JI, Zamora Vargas FX, Miralles P, et al. Transient elastography to rule out esophageal varices and portal hypertensive gastropathy in HIV-infected individuals with liver cirrhosis. Aids. 2012;26(14):1807–12. https://doi.org/10.1097/QAD.0b013e3283573267
24. Gaete MI, Díaz LA, Arenas A, González K, Cattaneo M, Fuster F, et al. Baveno VI and Expanded Baveno VI criteria successfully predicts the absence of high-risk gastro-oesophageal varices in a Chilean cohort. Liver Int. 2020;40(6):1427–34. https://doi.org/10.1111/liv.14373
25. Augustin S, Pons M, Maurice JB, Bureau C, Stefanescu H, Ney M, et al. Expanding the Baveno VI criteria for the screening of varices in patients with compensated advanced chronic liver disease. Hepatology. 2017;66(6):1980-8. https://doi.org/10.1002/hep.29363
26. Pinto Marques Souza de Oliveira C, Pinchemel Cotrim H, Arrese M. Nonalcoholic Fatty Liver Disease Risk Factors in Latin American Populations: Current Scenario and Perspectives. Clin Liver Dis (Hoboken). 2019;13(2):39-42. https://doi.org/10.1002/cld.759
27. Ferrusquía-Acosta J, Bassegoda O, Turco L, Reverter E, Pellone M, Bianchini M, et al. Agreement between wedged hepatic venous pressure and portal pressure in non-alcoholic steatohepatitis-related cirrhosis. J Hepatol. 2021;74(4):811–8. https://doi.org/10.1016/j.jhep.2020.10.003
28. Bassegoda O, Olivas P, Turco L, Mandorfer M, Serra-Burriel M, Tellez L, et al. Decompensation in Advanced Nonalcoholic Fatty Liver Disease May Occur at Lower Hepatic Venous Pressure Gradient Levels Than in Patients With Viral Disease. Clin Gastroenterol Hepatol. 2022;20(10):2276-2286.e6. https://doi.org/10.1016/j.cgh.2021.10.023
29. Tapper EB, Loomba R. Noninvasive imaging biomarker assessment of liver fibrosis by elastography in NAFLD. Nat Rev Gastroenterol Hepatol. 2018;15(5):274-82. https://doi.org/10.1038/nrgastro.2018.10
30. Sourianarayanane A, Talluri J, Humar A, McCullough AJ. Stage of fibrosis and portal pressure correlation in nonalcoholic steatohepatitis. Eur J Gastroenterol Hepatol. 2017;29(5):516–23. https://doi.org/10.1097/MEG.0000000000000825
31. Baffy G, Bosch J. Overlooked subclinical portal hypertension in non-cirrhotic NAFLD: Is it real and how to measure it? J Hepatol. 2022;76(2):458-463. https://doi.org/10.1016/j.jhep.2021.09.029
32. Petta S, Maida M, Macaluso FS, Di Marco V, Cammà C, Cabibi D, et al. The severity of steatosis influences liver stiffness measurement in patients with nonalcoholic fatty liver disease. Hepatology. 2015;62(4):1101-10. https://doi.org/10.1002/hep.27844
33. Caussy C, Chen J, Alquiraish MH, Cepin S, Nguyen P, Hernandez C, et al. Association Between Obesity and Discordance in Fibrosis Stage Determination by Magnetic Resonance vs Transient Elastography in Patients with Nonalcoholic Liver Disease. Clin Gastroenterol Hepatol. 2018;16(12):1974-1982.e7. https://doi.org/10.1016/j.cgh.2017.10.037
34. Abraldes JG, Bureau C, Stefanescu H, Augustin S, Ney M, Blasco H, et al. Noninvasive tools and risk of clinically significant portal hypertension and varices in compensated cirrhosis: The "Anticipate" study. Hepatology. 2016;64(6):2173-2184. https://doi.org/10.1002/hep.28824
35. Galizzi HO, Couto CA, Taranto DOL, Araújo SIO, Vilela EG. Accuracy of non-invasive methods/models for predicting esophageal varices in patients with compensated advanced chronic liver disease secondary to nonalcoholic

fatty liver disease. Ann Hepatol. 2021;20:100229. https://doi.org/10.1016/j.aohep.2020.07.003
36. Petta S, Wong VWS, Cammà C, Hiriart JB, Wong GL, Marra F, et al. Improved noninvasive prediction of liver fibrosis by liver stiffness measurement in patients with nonalcoholic fatty liver disease accounting for controlled attenuation parameter values. Hepatology. 2017;65(4):1145–55. https://doi.org/10.1002/hep.28843
37. Zhou JH, Cai JJ, She ZG, Li HL. Noninvasive evaluation of nonalcoholic fatty liver disease: Current evidence and practice. World J Gastroenterol. 2019;25(11):1307-1326. https://doi.org/10.3748/wjg.v25.i11.1307

https://doi.org/10.22516/25007440.1168

Original article

Beyond the Gut: Extraintestinal Manifestations of Inflammatory Bowel Disease in Children and Adolescents

Angie Vanessa Vergara-Espitia,[1*] Diana Victoria Mora-Quintero,[2] José Antonio de la Hoz-Valle,[3] Ana María Castañeda-Figueroa,[4] Fernando Sarmiento-Quintero.[5]

OPEN ACCESS

Citation:
Vergara-Espitia AV, Mora-Quintero DV, de la Hoz-Valle JA, Castañeda-Figueroa AM, Sarmiento-Quintero F. Beyond the Gut: Extraintestinal Manifestations of Inflammatory Bowel Disease in Children and Adolescents. Revista. colomb. Gastroenterol. 2024;39(2):166-175.
https://doi.org/10.22516/25007440.1168

[1] Fellow in Pediatric Gastroenterology, Universidad El Bosque. Pediatrician, Universidad Nacional de Colombia. Specialist in Epidemiology, Universidad de Los Andes. Bogotá, Colombia.
[2] Pediatric Gastroenterologist, Universidad El Bosque. Leader of the Pediatric Gastroenterology Service, Fundación Hospital Pediátrico La Misericordia (HOMI). Bogotá, Colombia.
[3] Medical Epidemiologist, Universidad El Bosque. Head of Clinical Studies, Fundación Santa Fe de Bogotá. PhD Candidate in Biomedical Sciences, Universidad del Rosario. Bogotá, Colombia.
[4] Pediatrician, Fundación Hospital Pediátrico La Misericordia (HOMI). Epidemiologist, Universidad Nacional de Colombia. Bogotá, Colombia.
[5] Pediatric Gastroenterologist and Nutritionist, INTA, Universidad de Chile. Full Professor Emeritus of Pediatrics, Universidad Nacional de Colombia. Leader of the research group recognized by MinCiencias "Gastroenterology, Hepatology, and Nutrition in Pediatrics". Former President of COLGAHNP. Former Coordinator of Nutrition, LASPGHAN. Bogotá, Colombia.

***Correspondence:** Angie Vanessa Vergara-Espitia.
vvergarae@unbosque.edu.co

Received: 13/01/2024
Accepted: 23/04/2024

Abstract

Background: Extraintestinal manifestations (EIM) are common in children and adults and their presence is associated with a higher severity of inflammatory bowel disease (IBD). In pediatrics, studies are scarce in Latin America and do not exist in Colombia. **Objective:** To describe the prevalence of EIM in children with IBD and the associated demographic, clinical, and biochemical characteristics. **Methodology:** Retrospective study of patients diagnosed with pediatric-onset IBD between 2007 and 2022 treated at an institution in Bogotá. A descriptive analysis was performed and in the groups with and without EIM clinical and biochemical variables were compared using Fisher's exact test, Student's T, and Mann-Whitney's U. **Results:** Of 71 confirmed cases, 45% had typical ulcerative colitis, 27% Crohn's disease, 7% atypical ulcerative colitis, 1.4% colonic Crohn's, and 20% unclassifiable IBD. Thirteen patients (18%) had at least one EIM, and mucocutaneous was the most frequent (58%). The time from symptoms onset to diagnosis was higher in the EIM group (13.2 years vs. 10.2 years; p = 0.02). Nocturnal diarrhea, hyporexia, and weight loss were more frequent in children with EIM. The EIM group showed lower hemoglobin levels, and higher globular sedimentation rate, and received biologics more frequently (38% vs. 23%, p = 0.2). **Conclusions:** The frequency of MEI in this series is similar to that reported in the literature; its presence is associated with higher disease severity, higher frequency of biological use, and longer time IBD diagnosis.

Keywords

Inflammatory bowel disease, arthritis, uveitis, erythema nodosum, hepatitis, pyoderma, pediatrics.

INTRODUCTION

Inflammatory bowel disease (IBD) is a condition of unknown etiology that includes Crohn's disease (CD), ulcerative colitis (UC), and inflammatory bowel disease unclassified (IBDU) in adults. In children, it also encompasses atypical ulcerative colitis (AUC) and colonic Crohn's disease (CCD)[1,2]. IBD can manifest at any age, and its incidence is rising across all age groups[3,4]. The pathogenesis involves polygenic and epigenetic factors and is characterized by chronic inflammation of the gastrointestinal tract[2,5].

The presentation, progression, behavior, and prognosis of pediatric-onset inflammatory bowel disease (PIBD) differ

© 2024 Asociación Colombiana de Gastroenterología

significantly from adult-onset IBD. The reclassification by the Porto Group since 2011 has established criteria that are highly informative for understanding PIBD. These criteria aim to guide classification for accurate diagnosis in children and adolescents by defining phenotypes based on clinical, endoscopic, histopathological, and radiological differences. The result is the PIBD-classes, which divides PIBD into five phenotypes: typical ulcerative colitis (TUC), atypical ulcerative colitis (AUC), Crohn's disease (CD), colonic Crohn's disease (CCD), and inflammatory bowel disease unclassified (IBDU)[1,2].

Although the intestine is the primary target, other organs can be affected. In adults, 50% develop at least one extra-intestinal manifestation (EIM) during the course of the disease, and EIMs can precede intestinal symptoms in 16% to 25% of cases[6-9]. In Colombia, a prevalence of 23.3% has been reported in adults, with joint involvement being the most frequent, as noted in other series[6,10]. Most EIMs occur in parallel with bowel disease activity and are more common in CD, especially in CCD patients[11,12].

Patients with PIBD experience significantly more EIMs both at diagnosis and during follow-up[13,14]. In pediatrics, the prevalence of EIMs at diagnosis ranges from 6% to 29%[15]. In a cohort of 1649 patients, the cumulative incidence was 9% at one year, 19% at five years, and 29% at fifteen years post-diagnosis[16]. EIMs usually present in children older than six years and, like in adults, are more frequently associated with CD (61%) than with UC (29%) [12,16,17], with 4% to 25% possibly preceding intestinal involvement[11,12,15].

When PIBD is accompanied by EIMs, it follows a more aggressive clinical course in terms of progression and extent, necessitating increased use of corticosteroids, immunosuppressants, biological therapies[14], and surgery, particularly in UC[13]. Increased EIM activity is associated with a higher relapse rate in CD[15].

The pathophysiology of EIMs is not fully understood. Possible contributing factors include genetic predisposition, changes in the intestinal microbiome, and alterations in the immune response from the intestine to other organs, affecting leukocyte circulation[12,18]. Based on these factors, EIMs can be classified as *classic* when the inflammatory process occurs in distant sites (musculoskeletal, mucocutaneous, ocular, and hepatobiliary), *associated* when they occur with other immunologically mediated diseases (multiple sclerosis, myocarditis, psoriasis, systemic lupus erythematosus), and as *complications* in the case of anemia and malnutrition, as manifestations of systemic inflammation[18-21].

Classic EIMs most frequently affect the joints, skin, and eyes but can also involve other organs such as the liver, lungs, and pancreas[18]. A common misconception is that successful therapy of intestinal inflammation is sufficient to satisfactorily treat EIMs[22]; generally, peripheral spondyloarthropathy, oral ulcers, episcleritis, and erythema nodosum may improve with standard treatment of intestinal inflammation, but uveitis, ankylosing spondylitis, and primary sclerosing cholangitis (PSC) progress independently of disease flares[12].

In children, EIMs primarily affect the joints and skin[13,14], and less frequently the eyes and liver, significantly impacting and worsening quality of life[15]. Although their improvement or resolution is part of the general management of PIBD, their presence should always be considered when deciding on therapy for managing intestinal inflammation[8,12].

In this context, it is essential to understand the clinical, evolutionary, and prognostic characteristics of EIMs in the pediatric population, as well as their prevalence, to estimate their impact and thus offer a comprehensive approach in the therapy and follow-up of patients with PIBD.

MATERIALS AND METHODS

Study Type

A descriptive cross-sectional study was conducted through a retrospective review of medical records from 2007 to 2022. The manuscript was prepared according to the STROBE guidelines[23].

Study Population

The study population consisted of pediatric patients with a confirmed diagnosis of IBD treated at the Fundación Hospital Pediátrico La Misericordia (HOMI), a high-complexity hospital and national referral center for pediatric gastrointestinal diseases located in Bogotá, Colombia (**Figure 1**).

Sample Selection and Size

Sampling was carried out using a non-probabilistic, sequential method. Due to the descriptive nature of the study, no formal sample size calculation was performed. All patients who met the inclusion criteria during the study period were included.

Diagnostic Criteria

The diagnosis of PIBD was made according to the recommendations of the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) established in 2014 through the Porto criteria and PIBD-classes. These criteria integrate the majority of evidence on recommended diagnostic methods and provide an initial

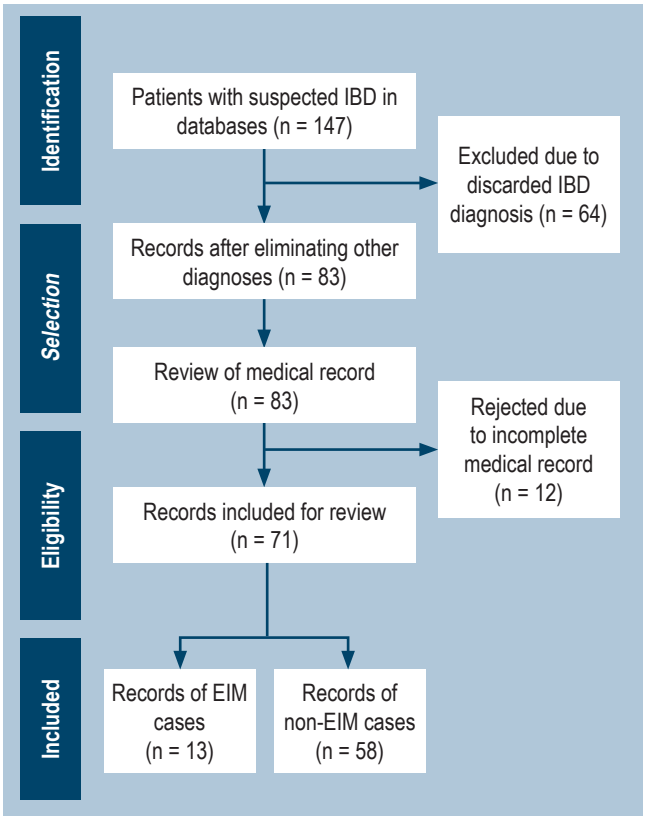


Figure 1. Flowchart of Record Eligibility. IBD: inflammatory bowel disease; EIM: extraintestinal manifestations. Author's file.

approach for the practical classification of the five disease phenotypes[1]. This classification allows for a more precise diagnosis, appropriate therapeutic decisions, and prediction of disease progression and prognosis.

The diagnosis of EIMs was based on the medical evaluation by the pediatric gastroenterology team through physical examination and interdisciplinary clinical criteria recorded in the medical record. The classic EIMs analyzed included spondyloarthropathies (peripheral and axial), uveitis, pyoderma gangrenosum, erythema nodosum, aphthous stomatitis, skin tags (anal folds), psoriasis, and sclerosing cholangitis.

Anemia, malnutrition, and growth failure were considered complications and therefore were not included. Nutritional diagnosis was conducted using the current criteria of the World Health Organization (WHO), endorsed by the Ministry of Health and Social Protection of Colombia[24]. Anemia was defined according to WHO criteria (hemoglobin < 11 g/dL for children)[18].

EIMs affecting the musculoskeletal system, particularly the joints, were grouped under the term *spondyloarthropathies*, using the diagnostic criteria developed by the Assessment in SpondyloArthritis International Society (ASAS), which distinguish between peripheral and axial manifestations; both can occur in PIBD patients, with special considerations for application to the pediatric population[25,26].

Mucocutaneous involvement was classified into four groups:

- Reactive: when they share the immunopathogenic mechanism but not the histopathological characteristics (erythema nodosum, pyoderma gangrenosum, Sweet syndrome, oral lesions).
- Specific: when the histopathological characteristics are similar but present outside the gastrointestinal tract, as in metastatic Crohn's disease[27].
- Treatment-associated: psoriasiform lesions, skin infections, and eczema are manifestations secondary to treatment complications, adverse or paradoxical reactions to medications used: thiopurines, sulfasalazine, methotrexate, and especially anti-tumor necrosis factor (anti-TNF)[28].
- Nonspecific: these lesions can be diverse, and their diagnosis is based on clinical characteristics and the exclusion of other dermatological disorders[18,29].

All EIMs were diagnosed by the corresponding expert pediatricians in dermatology, rheumatology, ophthalmology, and hepatology.

To control for potential information and recall biases when retrospectively applying the PIBD-classes criteria in reclassifying PIBD, the following strategies were employed:

- Integration into REDCap of the "IBD Classes (Catherine McEwasan Foundation)" application.
- Verification and clarification of inconsistent data.
- Review of data entry values for variables.
- Simple imputation of missing data when required.
- Confirmation of the appropriate phenotypic classification of patients by one of the investigators, who had prior training in its application.

Data Collection

Medical records of patients who met the diagnostic criteria for PIBD and EIM at the time of disease diagnosis were reviewed. Data collection was carried out through retrospective review of medical records, with variables recorded using a data collection form created in REDCap®, which was later exported to the statistical software STATA 18.0®.

Statistical Analysis

Descriptive statistics determined the frequency and percentages of categorical variables. For continuous variables, central tendency measures were determined according to

their distribution (mean with standard deviation [SD], median with interquartile range [IQR]). The association between EIMs and demographic, clinical, and biochemical characteristics was evaluated using Fisher's F for qualitative variables; for quantitative variables, the Mann-Whitney U test and Student's T test were used according to the nature of the data distribution. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

This study was approved by the ethics committee of Fundación Hospital Pediátrico La Misericordia (HOMI). Data were extracted from medical records, so there was no interaction with participants, and informed consent was not required.

Data were collected using an MS Excel format. No individual data or information that could identify any patient or their family were disclosed, in accordance with the Statutory Law on Data Protection.

RESULTS

Demographic Features

Over a 15-year period, 71 cases of PIBD were confirmed, of which 18% (13/71) presented EIMs during the course of the disease. Among these, 62% (8/13) were male. The median age at diagnosis for the entire group was 11.4 years (IQR = 7.4-17.6). **Table 1** summarizes the demographic characteristics of patients in the EIM and non-EIM groups.

Clinical Features

The time from the onset of symptoms to diagnosis was longer in the group with EIMs (13.2 years versus 10.2 years; p = 0.02). Four patients had a personal history of autoimmune disease (two with arthritis and two with autoimmune hepatitis), while another four reported a history of psychiatric illness; among the latter, three had depression and one had attention deficit hyperactivity disorder. Regarding family history, four patients had a first-degree relative with IBD, and none belonged to the group with EIMs. **Table 2** shows the most frequently reported symptoms and signs in the group with EIMs.

Nutritional Status

Of the 71 patients, 42% (28) exhibited short stature or were at risk of short stature, 43% (29) were malnourished, and 10% (6) were overweight or obese. No significant differences were found between the groups analyzed with or without EIM.

Table 1. Demographic Characteristics of Patients with PIBD

	Does Patient Have EIM?		Total	*p*-Value
	With EIM	Without EIM		
Time in years	n =13 (18%)	n = 58 (82%)	n = 71 (100%)	
- Age at symptom onset	9.9 (SD: 6.1)	9.07 (SD: 4.8)	10.2 (IQR: 4.7-9.25)	0.4
- Age at PIBD diagnosis	13.2 (SD: 3.5)	10.2 (SD: 4.4)	11.4 (IQR: 7.4-17.6)	**0.02***
Sex			Total: 71 (100%)	
- Female	5 (38%)	27 (47%)	32 (45%)	0.4+
- Male	8 (62%)	31 (53%)	39 (55%)	
Origin			Total: 58 (100%)	
- Urban	8 (80%)	43 (89%)	51 (88%)	0.3
- Rural	2 (20%)	5 (10%)	7 (12%)	
Affiliation regime			Total: 71 (100%)	
- Contribution-based	11 (85%)	40 (69%)	51 (72%)	0.6
- Subsidized	2 (15%)	13 (22%)	15 (21%)	
- Private	0	5 (9%)	5 (7%)	

+Fisher's exact test. * Mann-Whitney U test. Author's own research.

Table 2. Clinical Characteristics at Diagnosis

	Does Patient Have EIM?		Total = 71 (100%)	*p*-Value
	Yeas = 13 (18%)	No = 58 (82%)		
Symptom				
- Rectal bleeding	10 (77%)	48 (83%)	58 (82%)	0.4
- Diarrhea	12 (92%)	41 (71%)	53 (75%)	0.9
- Abdominal pain	6 (46%)	36 (62%)	42 (59%)	0.2
- Weight loss	9 (69%)	19 (33%)	28 (39%)	**0.02**⁺
- Disruption of activities	6 (46%)	11 (19%)	17 (24%)	0.05
- Hyporexia	6 (46%)	8 (14%)	14 (20%)	**0.02**⁺
- Nocturnal diarrhea	7 (54%)	5 (9%)	12 (17%)	**0.001**⁺
- Vomiting	1 (8%)	4 (7%)	5 (7%)	0.6
- Fever in the last three days	1 (8%)	4 (7%)	5 (7%)	0.6
Physical Exam				
- Pallor	8 (62%)	13 (22%)	21 (30%)	**0.009**⁺
- Perianal fissures	4 (31%)	1 (2%)	5 (7%)	**0.003**⁺
- Fistulas	2 (15%)	1 (2%)	3 (4%)	0.08
- Perianal abscess	1 (8%)	1 (2%)	2 (3%)	0.3
- Jaundice	1 (8%)	0	1 (1.4%)	0.2
Time to Diagnosis				
- Average time between symptom onset and diagnosis	3.2 (SD: 3.4)	1.1 (SD: 1.4)	1.5 (SD: 2.1)	**0.02***

⁺Fisher's exact test. * Mann-Whitney U test. Author's own research.

Extraintestinal Manifestations

Among the 13 patients with EIMs, 54% (7/13) had one manifestation and 46% had two or more. These were more frequent in women (p = 0.08) (**Table 3**) and predominantly mucocutaneous, followed by musculoskeletal involvement. The frequency distribution of EIMs in the entire sample is presented in **Figure 2**.

Table 4 shows the distribution of EIMs according to phenotype.

Paraclinical Tests

Among the 71 patients, half were anemic. The hemoglobin levels were significantly lower in the group with EIMs (9.8 [SD: 2.7] vs. 12.3 [SD: 2.8] g/dL; p = 0.004). Albumin levels were also lower in this group, and they exhibited higher erythrocyte sedimentation rates (ESR: 36.4 [SD: 12.3] vs. 22 [SD: 17.3] mm/h, p = 0.02) and higher platelet counts (**Figure 3**). Calprotectin levels were reported in 21 patients, with 17 of them showing positive results (> 250 µg/g).

Treatment

Induction treatment with biological therapy was more common in the EIM group compared to the non-EIM group (38% vs. 23%). Four of the 71 patients required surgical intervention as part of their treatment, including two colectomies with ileostomy, one drainage of an intra-abdominal abscess, and one exploratory laparotomy. None of these four patients were in the EIM group.

DISCUSSION

This study examined the prevalence of EIMs in the largest cohort of patients with PIBD over a 15-year period in Colombia. The findings reveal that EIMs are common, with

Table 3. Types of EIMs

Type	Frequency
Articular (spondyloarthropathy)	8 (33%)
- Axial (ankylosing spondylitis)	1 (4%)
- Peripheral	7 (29%)
Mucocutaneous	14 (58%)
- Aphthous stomatitis	3 (12.5%)
- Erythema nodosum	4 (16.6%)
- Pyoderma gangrenosum	3 (12.5%)
- Psoriasis	1 (4%)
- Skin-tag	4 (16.6%)
Hepatic	1 (4%)
- Sclerosing cholangitis	1
Ophthalmologic	1 (4%)
- Uveitis	1

Author's own research.

Table 4. Distribution of EIMs According to PIBD Phenotype

Type of EIM	TUC (n = 10)	AUC (n = 0)	IBDU (n = 3)	CCD (n = 0)	CD (n = 12)
Articular					
- Axial: sacroiliitis	1	0	0	0	0
- Peripheral	4	0	1	0	2
Cutaneous					
- Aphthous stomatitis	1	0	0	0	2
- Erythema nodosum	0	0	1	0	3
- Pyoderma gangrenosum	1	0	0	0	2
- Psoriasis	1	0	0	0	0
- Skin-tag	1	0	1	0	2
Hepatic					
- Sclerosing cholangitis	1	0	0	0	0
Ophthalmologic					
- Uveitis	0	0	0	0	1

Author's own research.

a prevalence of 18% at the time of diagnosis, which aligns with previously reported figures in the literature ranging from 6% to 29%[15]. Additionally, it has been reported that between 4% and 25% of EIMs could precede intestinal involvement[11,12]. Furthermore, the presence of MEIs is associated with greater clinical and paraclinical severity of PIBD.

The prevalence of EIMs in PIBD varies significantly across published studies, likely due to the lack of unified criteria for defining them in pediatrics, as current guidelines are primarily based on adult data[11]. This variability is reflected in studies reporting prevalences as high as 80%, likely an overestimation due to the inclusion of osteopenia and growth retardation, which are now considered complications of PIBD[18]. While the prevalence at diagnosis found in this study is similar to the reports by Jansson and colleagues (14.1%) and Duricova and colleagues (8.9%) [13,15], it is notable that it is slightly higher in the present cohort, possibly due to the interdisciplinary approach.

This study also found that the time between the onset of symptoms and the age at diagnosis of PIBD was significantly longer in cases with EIMs. This delay in definitive diagnosis may suggest that the initial evaluation was directed at other organs or systems rather than the digestive system[7].

EIMs often involve more than one organ or system. In this study, nearly half (6/13) of the patients with EIMs had involvement in multiple organs or systems. In fact, the likelihood of developing an EIM increases as the disease progresses and with the prior presence of an EIM[11]. Over the course of the disease, up to 50% of adult patients with IBD will develop at least one EIM, and this involvement can be a significant source of morbidity and even a risk factor for mortality, especially in cases such as primary sclerosing cholangitis or venous thromboembolic events[18].

In the present cohort, mucocutaneous manifestations were the most common, occurring in 58% of cases. Mucocutaneous involvement has been described in 15%-20% of patients and is often determined by the shared underlying immunopathogenic mechanisms of PIBD[18,29]. In the pediatric population, reports of mucocutaneous involvement are scarce, but this study suggests a higher association with CD, which aligns with existing literature[27]. These manifestations are strongly linked to intestinal inflammatory activity and, in up to 50% of cases, appear simultaneously with the initial gastrointestinal symptoms[29]. Diagnosis is based on clinical characteristics and the exclusion of other dermatological disorders. Given the heterogeneity of lesions, diagnosing these manifestations can pose a challenge for pediatric gastroenterologists, emphasizing the importance of interdisciplinary evalua-

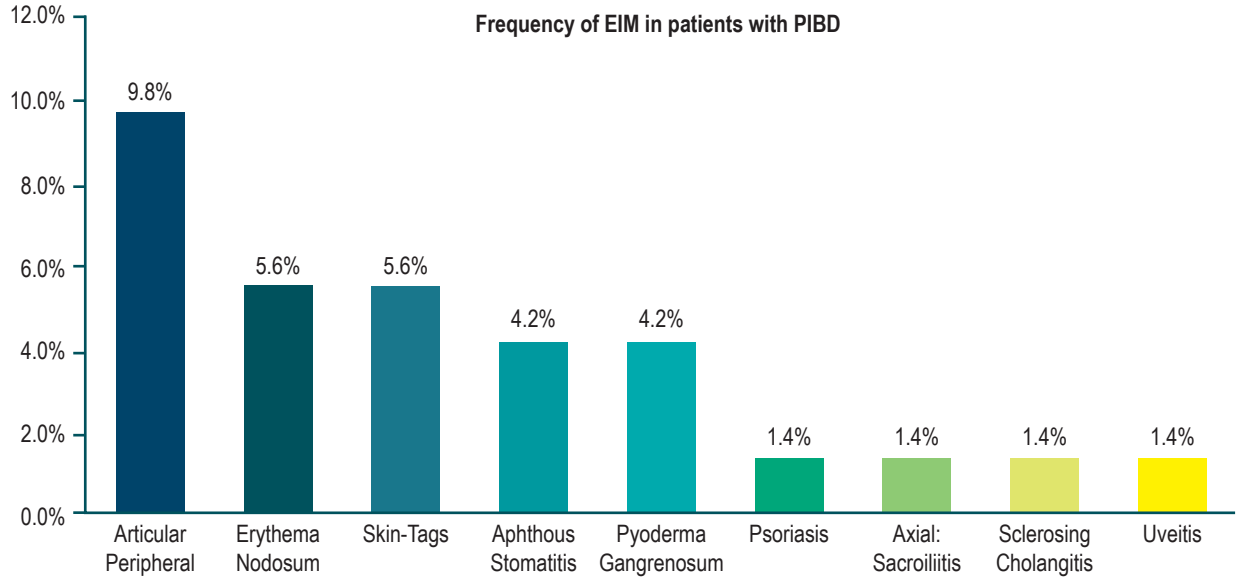


Figure 2. Frequency of EIMs in patients with PIBD. Author's file.

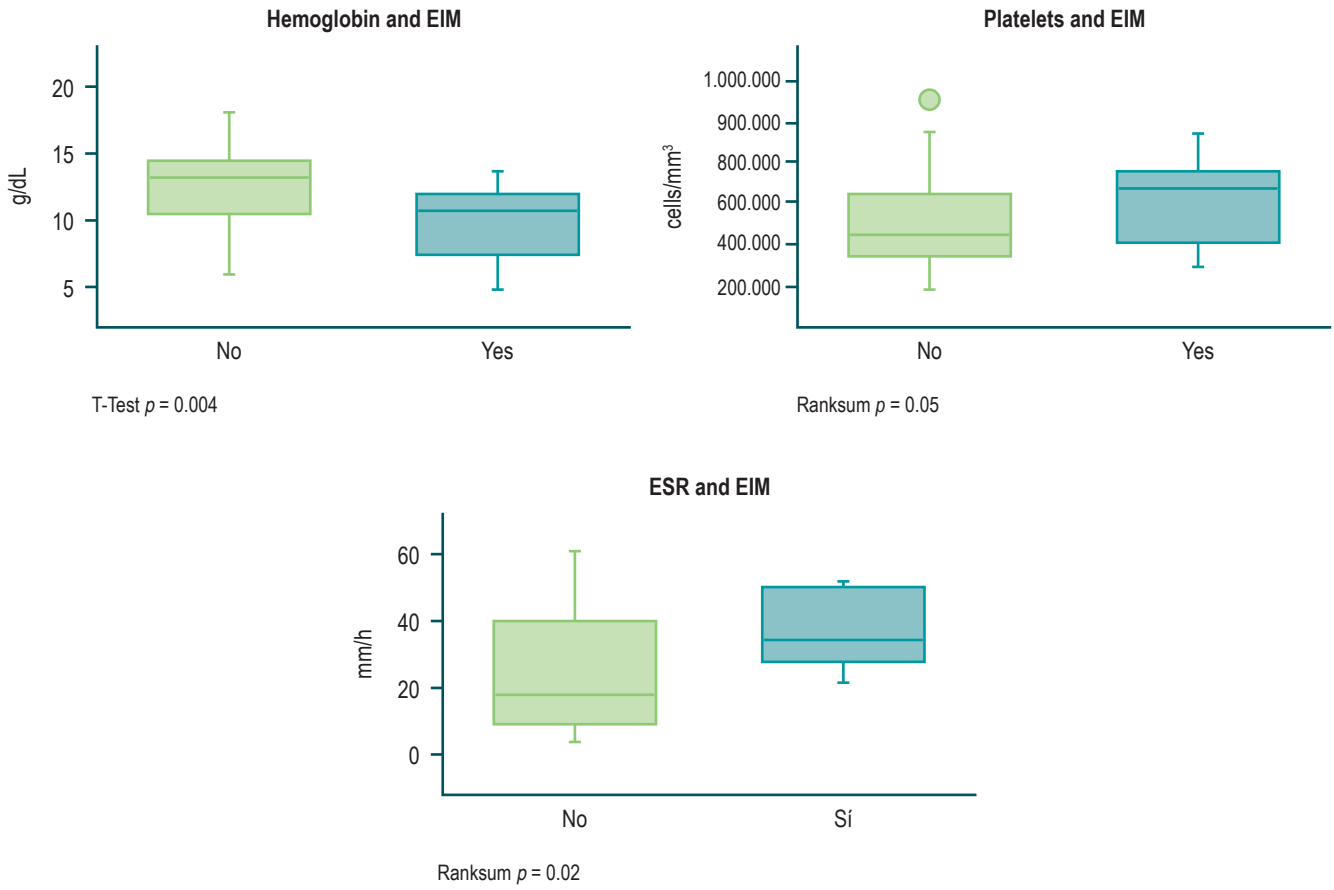


Figure 3. Paraclinical Tests at the Time of Diagnosis in PIBD. Author's file.

tion, including dermatology, and considering the psychological implications and impact on quality of life[18,27].

Musculoskeletal involvement (spondyloarthropathies) was the second most frequent EIM in this cohort. The association between IBD and axial or peripheral spondyloarthropathy indicates a common inflammatory pathway; genomic studies have identified shared loci that increase the risk of these diseases, involving the interleukin (IL)-12/23 signaling pathways[18]. Recent systematic reviews in adults have described peripheral joint involvement as the most frequent manifestation, with a prevalence of 13%, similar to data reported in adults in Colombia[6,30]. In this study, the prevalence is 33%, which is consistent with other reports, although the prevalence reported in pediatrics varies between 2% and 35%, highlighting a lack of standardized definitions and criteria[31].

The most frequently reported signs and symptoms in these 13 patients were nocturnal diarrhea, weight loss, and pallor. Additionally, these patients exhibited significantly lower levels of hemoglobin and albumin, along with elevated ESR. These findings are considered indicators of higher disease activity and greater systemic involvement. This is consistent with multiple studies indicating a more aggressive clinical course in terms of progression and extension when PIBD is associated with EIMs[19], with a higher likelihood of corticosteroid use, immunosuppressive therapy[14], biological therapy, and surgical management, especially in UC[13]. In CD, EIMs are associated with a higher relapse rate[15].

The prevalence of anemia in all PIBD cases was 50%. Although anemia was not considered an EIM, the most recent guidelines from the European Crohn's and Colitis Organisation (ECCO) define it as a complication of the disease[18]. Thus, it is a fundamental aspect to evaluate and treat in patients with IBD, given its negative influence on disease progression[32]. Reports of anemia in adults are highly variable, ranging from 6% to 74%, likely due to the heterogeneity of the patients included in studies[18]. In children, the prevalence of anemia at the time of diagnosis has been described as high as 90%[21,33]. In this cohort, the high prevalence of anemia is particularly relevant due to the potential consequences in children during critical phases of growth and development[32]. Calprotectin levels do not appear to be related to EIMs, and there is no evidence to support its routine use for their identification, as it is a nonspecific marker of inflammation[34].

Among the study's limitations is the risk of information bias due to its retrospective design. Data taken only at the time of diagnosis may lead to an underestimation of cases. Over the 15-year study period, scientific advances may have led to lower initial diagnosis rates.

Regarding the COVID-19 pandemic, which occurred during the study period and caused significant global changes in life and health, its occurrence could not have been anticipated in the study design.

This study's strength lies in being the first in Colombia to describe the frequency of EIMs in PIBD, with an interdisciplinary approach that enabled comprehensive management of these patients at a high-experience center.

CONCLUSIONS

EIMs are common in PIBD and their presence is associated with greater disease severity and progression. This study corroborates this association through the presence of symptoms and certain biochemical markers. However, these findings need to be confirmed in prospective investigations.

The diagnosis of PIBD in patients with EIMs tends to occur at older ages, possibly due to a clinical focus on systems other than the digestive system, representing an opportunity to improve early diagnosis.

In the pediatric context, it is essential to provide an interdisciplinary approach in specialized centers that comprehensively address all aspects related to the diagnosis, treatment, and follow-up of patients with PIBD associated with EIMs, to not overlook the potential impact on disease course, pharmacological treatment decisions, quality of life, and emotional well-being of patients.

Acknowledgments

To the Pediatric Gastroenterology Service of the Fundación Hospital Pediátrico La Misericordia (HOMI).

Funding Sources

The authors disclose that no external funding was received for the drafting of this manuscript.

REFERENCES

1. Levine A, Koletzko S, Turner D, Escher JC, Cucchiara S, De Ridder L, et al. ESPGHAN revised porto criteria for the diagnosis of inflammatory bowel disease in children and adolescents. J Pediatr Gastroenterol Nutr. 2014;58(6):795-806. https://doi.org/10.1097/MPG.0000000000000239
2. Vera-Chamorro JF, Sanchez-Franco C, Vargas-Sandoval M, Mora-Quintero DV, Riveros-López JP, Sarmiento-Quintero

F, et al. Consenso colombiano de la enfermedad inflamatoria intestinal pediátrica. Rev Colomb Gastroenterol. 2023;38(Supl 1):1-72. https://doi.org/10.22516/25007440.943
3. Sýkora J, Pomahačová R, Kreslová M, Cvalínová D, Štych P, Schwarz J. Current global trends in the incidence of pediatric-onset inflammatory bowel disease. World J Gastroenterol. 2018;24(25):2741-63. https://doi.org/10.3748/wjg.v24.i25.2741
4. Larrosa-Haro A, Abundis-Castro L, Contreras MB, Gallo MJ, Peña-Quintana L, Targa Ferreira CH, et al. Epidemiologic trend of pediatric inflammatory bowel disease in Latin America: The Latin American Society for Pediatric Gastroenterology, Hepatology and Nutrition (LASPGHAN) Working Group. Rev Gastroenterol Mex. 2021;86(4):328-34. https://doi.org/10.1016/j.rgmxen.2021.07.004
5. Rubalcava NS, Gadepalli SK. Inflammatory Bowel Disease in Children and Adolescents. Adv Pediatr. 2021;68:121-142. https://doi.org/10.1016/j.yapd.2021.05.005
6. Juliao-Baños F, Arrubla M, Osorio L, Camargo J, Londoño J, Cáceres C, et al. Characterization and prevalence of extraintestinal manifestations in a cohort of patients with inflammatory intestinal disease in Medellin, Colombia. Gastroenterol Hepatol. 2021;44(6):398-404. https://doi.org/10.1016/j.gastre.2020.07.015
7. Vavricka SR, Rogler G, Gantenbein C, Spoerri M, Vavricka MP, Navarini AA, et al. Chronological order of appearance of extraintestinal manifestations relative to the time of IBD diagnosis in the Swiss Inflammatory Bowel Disease Cohort. Inflamm Bowel Dis. 2015;21(8):1794-800. https://doi.org/10.1097/MIB.0000000000000429
8. Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal Manifestations of Inflammatory Bowel Disease. Inflamm Bowel Dis. 2015;21(8):1982-92. https://doi.org/10.1097/MIB.0000000000000392
9. Hedin CRH, Vavricka SR, Stagg AJ, Schoepfer A, Raine T, Puig L, et al. The Pathogenesis of Extraintestinal Manifestations: Implications for IBD Research, Diagnosis, and Therapy. J Crohn's Colitis. 2019;13(5):541-54. https://doi.org/10.1093/ecco-jcc/jjy191
10. Kethu SR. Extraintestinal manifestations of inflammatory bowel diseases. J Clin Gastroenterol. 2006;40(6):467-75. https://doi.org/10.1097/00004836-200607000-00003
11. Harbord M, Annese V, Vavricka SR, Allez M, Acosta MB de, Boberg KM, et al. The first european evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. J Crohn's Colitis. 2016;10(3):239-54. https://doi.org/10.1093/ecco-jcc/jjv213
12. Rogler G, Singh A, Kavanaugh A, Rubin DT. Extraintestinal Manifestations of Inflammatory Bowel Disease: Current Concepts, Treatment, and Implications for Disease Management. Gastroenterology. 2021;161(4):1118-1132. https://doi.org/10.1053/j.gastro.2021.07.042
13. Duricova D, Leroyer A, Savoye G, Sarter H, Pariente B, Aoucheta D, et al. Extra-intestinal Manifestations at Diagnosis in Paediatric- and Elderly-onset Ulcerative Colitis are Associated With a More Severe Disease Outcome: A Population-based Study. J Crohns Colitis. 2017;11(11):1326-1334. https://doi.org/10.1093/ecco-jcc/jjx092
14. Duricova D, Sarter H, Savoye G, Leroyer A, Pariente B, Armengol-Debeir L, et al. Impact of Extra-Intestinal Manifestations at Diagnosis on Disease Outcome in Pediatric- and Elderly-Onset Crohn's Disease: A French Population-Based Study. Inflamm Bowel Dis. 2019;25(2):394-402. https://doi.org/10.1093/ibd/izy254
15. Jansson S, Malham M, Paerregaard A, Jakobsen C, Wewer V. Extraintestinal Manifestations Are Associated With Disease Severity in Pediatric Onset Inflammatory Bowel Disease. J Pediatr Gastroenterol Nutr. 2020;71(1):40-5. https://doi.org/10.1097/MPG.0000000000002707
16. Jose FA, Garnett EA, Vittinghoff E, Ferry GD, Winter HS, Baldassana RN, et al. Development of extraintestinal manifestations in pediatric patients with inflammatory bowel disease. Inflamm Bowel Dis. 2009;15(1):63-8. https://doi.org/10.1002/ibd.20604
17. Nóbrega VG, Silva IN de N, Brito BS, Silva J, da SILVA MCM, Santana GO. The onset of clinical manifestations in inflammatory bowel disease patients. Arq Gastroenterol. 2018;55(3):290-5. https://doi.org/10.1590/s0004-2803.201800000-73
18. Gordon H, Burisch J, Ellul P, Karmiris K, Katsanos K, Allocca M, et al. ECCO Guidelines on Extraintestinal Manifestations in Inflammatory Bowel Disease. J Crohns Colitis. 2024;18(1):1-37. https://doi.org/10.1093/ecco-jcc/jjad108
19. Greuter T, Vavricka SR. Extraintestinal manifestations in inflammatory bowel disease-epidemiology, genetics, and pathogenesis. Expert Rev Gastroenterol Hepatol. 2019;13(4):307-17. https://doi.org/10.1080/17474124.2019.1574569
20. Herzog D, Fournier N, Buehr P, Rueger V, Koller R, Heyland K, et al. Age at disease onset of inflammatory bowel disease is associated with later extraintestinal manifestations and complications. Eur J Gastroenterol Hepatol. 2018;30(6):598-607. https://doi.org/10.1097/MEG.0000000000001072
21. Wiskin AE, Fleming BJ, Wootton SA, Beattie RM. Anaemia and iron deficiency in children with inflammatory bowel disease. J Crohn's Colitis. 2012;6(6):687-91. https://doi.org/10.1016/j.crohns.2011.12.001
22. Jang HJ, Kang B, Choe BH. The difference in extraintestinal manifestations of inflammatory bowel disease for children and adults. Transl Pediatr. 2019;8(1):4-15. https://doi.org/10.21037/tp.2019.01.06
23. Von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)

statement: Guidelines for reporting observational studies. Epidemiology. 2007;18(6):800-4. https://doi.org/10.1097/EDE.0b013e3181577654
24. Ministerio de Salud y Protección Social. Resolución 2465 de 2016, por la cual se adoptan los indicadores antropométricos, patrones de referencia y puntos de corte para la clasificación antropométrica del estado nutricional de niñas, niños y adolescentes menores de 18 años de edad, adultos de 18 a 64 años de edad y gestantes adultas y se dictan otras disposiciones [Internet]. Colombia: Minsalud; 2016 [consultado el 1 de junio de 2023]. Disponible en: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/DE/DIJ/resolucion-2465-2016.pdf
25. Rudwaleit M, Van Der Heijde D, Landewé R, Akkoc N, Brandt J, Chou CT, et al. The Assessment of SpondyloArthritis international Society classification criteria for peripheral spondyloarthritis and for spondyloarthritis in general. Ann Rheum Dis. 2011;70(1):25-31. https://doi.org/10.1136/ard.2010.133645
26. Burgos-Vargas R. The assessment of the spondyloarthritis international society concept and criteria for the classification of axial spondyloarthritis and peripheral spondyloarthritis: A critical appraisal for the pediatric rheumatologist. Pediatr Rheumatol Online J. 2012;10(1):14. https://doi.org/10.1186/1546-0096-10-14
27. Diaconescu S, Strat S, Balan GG, Anton C, Stefanescu G, Ioniuc I, et al. Dermatological manifestations in pediatric inflammatory bowel disease. Medicina (Kaunas). 2020;56(9):425. https://doi.org/10.3390/medicina56090425
28. Sridhar S, Maltz RM, Boyle B, Kim SC. Dermatological Manifestations in Pediatric Patients with Inflammatory Bowel Diseases on Anti-TNF Therapy. Inflamm Bowel Dis. 2018;24(9):2086-92. https://doi.org/10.1093/ibd/izy112
29. Antonelli E, Bassotti G, Tramontana M, Hansel K, Stingeni L, Ardizzone S, et al. Dermatological manifestations in inflammatory bowel diseases. J Clin Med. 2021;10(2):364. https://doi.org/10.3390/jcm10020364
30. Karreman MC, Karreman MC, Luime JJ, Hazes JMW, Weel AEAM, Weel AEAM. The prevalence and incidence of axial and peripheral spondyloarthritis in inflammatory bowel disease: A systematic review and meta-analysis. J Crohn's Colitis. 2017;11(5):631-42. https://doi.org/10.1093/ecco-jcc/jjw199
31. Ali A, Schmidt M, Piskin D, Crowley E, Berard R. Epidemiology of Musculoskeletal Manifestations in Pediatric Inflammatory Bowel Disease: A Systematic Review. ACR Open Rheumatol. 2022;4(6):547-54. https://doi.org/10.1002/acr2.11431
32. Fritz J, Walia C, Elkadri A, Pipkorn R, Dunn RK, Sieracki R, et al. A Systematic Review of Micronutrient Deficiencies in Pediatric Inflammatory Bowel Disease. Inflamm Bowel Dis. 2019;25(3):445-59. https://doi.org/10.1093/ibd/izy271
33. Isa HM, Alahmed FA, Mohamed M, Mohamed A. The Prevalence of Iron and Vitamin D Deficiencies in Pediatric Patients With Inflammatory Bowel Disease in Bahrain. Cureus. 2023;15(4):e37074. https://doi.org/10.7759/cureus.37074
34. Orfei M, Gasparetto M, Hensel KO, Zellweger F, Heuschkel RB, Zilbauer M. Guidance on the interpretation of faecal calprotectin levels in children. PLoS One. 2021;16(2):e0246091. https://doi.org/10.1371/journal.pone.0246091

https://doi.org/10.22516/25007440.1189

Review article

Research and Publish. 2. Answering the Question: Study Design

Margarita Rey-Rubiano.[1*]

OPEN ACCESS

Citation:
Rey-Rubiano M. Research and Publish. 2. Answering the Question: Study Design. Revista. colomb. Gastroenterol. 2024;39(2):176-178. https://doi.org/10.22516/25007440.1189

[1] Gastroenterologist. Assistant Professor, Medical School, Universidad de Los Andes. Institutional Specialist, Gastroenterology and Digestive Endoscopy Section, Hospital Universitario Fundación Santa Fe de Bogotá. Bogotá, Colombia.

***Correspondence:** Margarita Rey-Rubiano.
margaritarey1@hotmail.com

Received: 03/03/2024
Accepted: 17/04/2024

Abstract

Introduction: Study design guides the methodology for obtaining an answer to a research question. Understanding the different types of research, their advantages, and disadvantages will help ensure the validity of our results. **Objective:** To describe experimental and non-experimental research designs, along with their respective advantages and disadvantages, in order to guide researchers in selecting the most appropriate design based on their research question. **Results and Conclusions:** The literature is reviewed to describe the main characteristics, the simplest and most useful classifications for determining the best study design. The study population, internal and external validity of the studies are also determined, in order to understand, based on our research question, the possible extrapolation of our results.

Keywords

Experimental project, reliability and validity, validity of the results, validity of the result, reliability (epidemiology), population groups.

INTRODUCTION

The study design guides the methodology to obtain the answer to the research question. However, as we learned in the previous article on "how to formulate a research question," it is the question itself that determines the appropriate architecture, tactics, and strategy to be used[(1)].

Research study designs can be broadly categorized into two groups: experimental and non-experimental, based on the level of manipulation performed by the researcher on the study population or sample. The sample, as depicted in **Figure 1**, consists of individuals selected (based on inclusion and exclusion criteria) from the accessible population, derived from the target population or characterized by the most important feature of our study (e.g., patients with gastric cancer, inflammatory bowel disease, or gastroesophageal reflux, among others)[(2,3)].

EXPERIMENTAL STUDIES

Experimental studies, also known as *randomized studies*, are characterized by researcher manipulation. This manipulation or intervention (such as medication, a device, or surgical intervention) is referred to as the *independent variable*, while the dependent variable is the final outcome intended to be demonstrated by the intervention (e.g., pain improvement, histological resolution, mortality, survival, among others)[(1,2)]. The aim of these experimental studies is to determine the cause-effect relationship between the intervention (independent variable) and the outcome (depen-

© 2024 Asociación Colombiana de Gastroenterología



Figure 1. Representation of the Population Sample of a Study. Author's File.

dent variable) by comparing it to a randomized control group, thereby minimizing the risk of confounding factors. Within experimental studies, there is a subclass known as *quasi-experimental* studies, where the key difference is that there is intervention or manipulation but no randomization. These studies typically involve a single designated group or comparisons with previous studies or historical cases[1,2].

The advantages of these studies are their simplicity and universal acceptance, their applicability across various fields, the ease of interpreting and analyzing their results, and their usefulness in all phases of studies and in meta-analyses. However, the disadvantages include their susceptibility to confounding factors, significant variability among patients if not properly selected, high cost, the general need for large sample sizes, and the challenge of reproducing results in real-world settings if the study is too controlled[1-3].

OBSERVATIONAL STUDIES

The key characteristic of observational studies is that the researcher does not intervene in the exposure or independent variable. As a result, the relationship with the dependent variable is not controlled and is typically biased by other variables. These studies can be descriptive when there is no comparison group, or analytical when there is a comparison group, allowing for statistical inferences and relationships between exposures or risk factors and the dependent variable or expected outcome[2,3].

Non-Analytical Observational Studies

Classic examples of this type are case reports and case series. These studies are very valuable, as they describe the disease history, clinical presentation, diagnostic approach, and treatment response. They generally involve rare diseases or presentations and sometimes report adverse drug events. These studies help to formulate or create hypotheses related to each case[2,3].

The statistical analysis of these studies is limited, typically determining only symptomatic prevalences. Their advantages include identifying unknown clinical presentations, exploring new treatment possibilities, and generating new hypotheses about disease mechanisms or risk factors. However, their disadvantages are the scarcity of statistical data due to the absence of a control group, lack of efficacy or safety data, inability to determine associations, and high risk of publication bias[1-3].

Analytical Observational Studies

These studies include control groups for comparison and encompass cross-sectional studies, case-control studies, and prospective and retrospective cohort studies.

Cross-Sectional Studies

Cross-sectional studies investigate the characteristics of a sample population at a specific point in time. Patients are randomized based on the development of the disease to determine whether exposure leads to the development of the disease or condition[2,3].

The statistical analysis of these studies is based on odds and prevalence. Their advantage lies in their ability to determine disease prevalence and the measures of associations between exposure and disease[1]. However, in cases of rare or infrequent diseases, the disadvantages include potential overestimation in cases of long-duration diseases or underestimation in short-duration diseases, and the inability to establish causality due to the single-time-point nature of the study[2-4].

Case-Control Studies

In case-control studies, patients or individuals in the case group are identified by the presence of the disease or specific characteristic (dependent variable). Controls are individuals from the same target population who do not have the disease or characteristic, and the researcher retrospectively examines the risk factors possibly related to the development of the disease. Statistical analysis is based on the odds ratio regarding exposure[2,3].

The advantages of case-control studies include their cost-effectiveness in examining multiple risk factors simultaneously relying on a small sample and their suitability for studying rare diseases. However, disadvantages include the potential difficulty in accurately determining cases and controls based on diagnostic criteria (equal risk in the same population)[2-4].

Cohort Studies

In cohort studies, individuals are categorized based on the presence of a risk factor or exposure and are followed over time to determine the development of the disease or characteristic (dependent variable). Participants are divided into two groups—exposed and non-exposed—and are followed in parallel, either prospectively or retrospectively, depending on the study design[2-4].

The statistical analysis in these studies is based on disease risk and frequency. The primary advantage of cohort studies is the ability to directly observe the temporal sequence between exposure and disease development. However, the disadvantages include high cost, long duration, and a significant likelihood of loss to follow-up[2-4].

CONCLUSIONS

To answer a research question, various study designs and research methods are outlined, highlighting their main characteristics and the most practical classifications for determining the best study design. Key aspects of the study population, advantages and disadvantages, and the internal and external validity of the studies are discussed to understand, based on the research question, the potential for extrapolating the results.

REFERENCES

1. Carvalho S, Fregni F. Study population. En: Fregni F, Illigens B (editores). Critical Thinking in clinical research. Nueva York; Oxford University Press: 2018. p. 45-67. https://doi.org/10.1093/med/9780199324491.003.0003
2. Gomez A, Fregni F. Basic Study Desings. En: Fregni F, Illigens B (editores). Critical Thinking in clinical research. Nueva York; Oxford University Press: 2018. p. 68-86. https://doi.org/10.1093/med/9780199324491.003.0004
3. Bosdriesz JR, Stel VS, van Diepen M, Meuleman Y, Dekker FW, Zoccali C, et al. Evidence-based medicine-When observational studies are better than randomized controlled trials. Nephrology (Carlton). 2020;25(10):737-743. https://doi.org/10.1111/nep.13742
4. Hernández V. Estudios epidemiológicos: tipos, diseño e interpretación. Enfermedad Inflamatoria Intestinal Al Día. 2017;16(3):98-105. https://doi.org/10.1016/j.eii.2017.03.001

https://doi.org/10.22516/25007440.1183

Review article

Pyloric EndoFlip and Its Clinical Use in Gastroparesis

Albis Cecilia Hani de Ardila,[1] Aldair Chaar,[2*] Juan Hernández,[3] Raúl Cañadas,[1] María del Carmen Figueredo.[4]

OPEN ACCESS

Citation:
Hani de Ardila AC, Chaar A, Hernández J, Cañadas R, Figueredo MC. Pyloric EndoFlip and Its Clinical Use in Gastroparesis. Revista. colomb. Gastroenterol. 2024;39(2):179-186. https://doi.org/10.22516/25007440.1183

[1] Specialist in Gastroenterology, Hospital Universitario San Ignacio; Full Professor of Gastroenterology, Pontificia Universidad Javeriana. Bogotá, Colombia.
[2] Gastroenterology Fellow, Hospital Universitario San Ignacio; Pontificia Universidad Javeriana. Bogotá, Colombia.
[3] Gastroenterology Intern, Hospital Universitario San Ignacio, Pontificia Universidad Javeriana. Bogotá, Colombia.
[4] Specialist in Gastroenterology, Hospital Universitario San Ignacio; Adjunct Clinical Professor of Gastroenterology, Pontificia Universidad Javeriana. Bogotá, Colombia.

***Correspondence:** Aldair Chaar.
chaarha@javeriana.edu.co

Received: 02/03/2024
Accepted: 28/04/2024

Abstract

Gastroparesis is a chronic disorder of gastric motility that results in marked impairment of quality of life and significant costs to health care systems. Medical therapies are limited in their management, thus, the reason for a growing enthusiasm for pylorus-targeted therapies. The functional luminal imaging probe (FLIP) is a useful diagnostic tool for assessing pylorus characteristics, especially in refractory cases, which could lead to a better management strategy and, in many cases, predict clinical response.

Keywords

Gastroparesis, pylorus, gastric emptying, electrical impedance, EndoFLIP.

INTRODUCTION

Gastroparesis is a chronic motility disorder characterized by poor gastric accommodation, leading to symptoms such as nausea, vomiting, early satiety, abdominal pain, and weight loss. As a *sine qua non* condition, it is essential to rule out mechanical obstruction and confirm delayed gastric emptying[(1)]. The annual cost associated with gastroparesis is approximately $568 million dollars[(2)]. In the United States, the prevalence is 21.5 cases per 100,000 inhabitants, with a higher incidence in females (female-male ratio 3.8:1) and in Caucasians (71.7%), followed by African Americans (15.2%), Hispanics (11.2%), and Asians (1.9%).

Diabetes *mellitus* is the primary cause (57.4%), followed by gastrointestinal surgical procedures, particularly those involving vagotomy (15.0%), medications (11.8%), idiopathic causes (11.3%), and miscellaneous causes (4.5%), which include connective tissue diseases[(3)]. The pathophysiology involves altered gastric motility or increased pyloric pressure. Disruptions in the accommodation of the gastric body and fundus, antral hypomotility, lack of pyloric relaxation, and small intestine dysmotility can result in delayed gastric emptying. Immune-mediated mechanisms likely play a critical role in the pathogenesis. Structural studies have reported lesions in the interstitial cells of Cajal (ICCs), nerves, and gastric smooth muscle

cells, as well as the loss of macrophages with an anti-inflammatory phenotype[4].

Diagnosis is made through solid-phase gastric emptying scintigraphy, which evaluates gastric emptying by ingesting food labeled with a radiotracer (technetium-99m [^{99m}Tc]). Interpretation is based on measuring the percentage and time of emptying (usually over 4 hours) and the percentage of retention of the labeled food. In patients with > 60% retention at 2 hours or > 10% at 4 hours, the study is considered conclusive for gastroparesis[5].

Complementary methods include the breath test, where a substrate (octanoic acid or *Spirulina platensis*) labeled with a stable carbon isotope (^{13}C) is added to a solid food portion. After digestion and absorption in the small intestine, these substrates are metabolized by the liver, exhaled as ^{13}C through the lungs, and quantified by mass spectrometry[4].

FDA-approved wireless motility capsules are sensitive for detecting delays in gastric emptying, though their clinical relevance is still debated. They also allow for the evaluation of abnormal intestinal transit and are valuable for addressing comorbidities such as constipation associated with gastroparesis[4]. Other techniques like magnetic resonance imaging and ultrasound are useful in research; however, their clinical use faces limitations due to factors like cost and equipment availability[6].

Recently, the functional lumen imaging probe (EndoFLIP) has been validated as an attractive tool for measuring parameters in the pylorus, such as pyloric hypertonia, which is one of the potential pathophysiological mechanisms implicated in delayed gastric emptying. Its potential role in this field is being increasingly studied, given its usefulness in identifying the subtype of patients with pyloric dysfunction who could benefit from pylorus-directed therapies (**Figure 1**).

The treatment of gastroparesis involves a combination of pharmacological and non-pharmacological strategies. A fractionated diet (4 to 5 low-fat and low-fiber portions daily) is fundamental[7], followed by the use of prokinetics such as metoclopramide, domperidone, and levosulpiride.

Despite these measures, up to 40% of patients develop refractory gastroparesis[8], which the American Gastroenterological Association (AGA) defines as persistent symptoms despite dietary adjustments and at least four weeks of effective therapy with first-line prokinetics at an optimal dose and with adequate adherence[9].

Alternative therapies have been employed, such as hydraulic balloon pyloric dilation (HBPD), botulinum toxin (BT), laparoscopic pyloromyotomy, and gastric pacemakers, with varying success rates (43% to 77%[10], 83% to 86%[11], and 53.7%, respectively[12]).

Gastric peroral endoscopic myotomy (G-POEM) has emerged as an innovative option with technical and clinical success and a positive impact on quality of life[13]. Despite an adverse event rate of 5%-10%[14], G-POEM shows efficacy similar to laparoscopic pyloroplasty but with shorter procedure times and fewer complications, making it a potentially preferred choice for refractory gastroparesis, especially in those documented with pyloric hypertonia[15].

THE PYLORIC SPHINCTER: A ZONE OF SPECIAL INTEREST IN GASTRIC EMPTYING

The pyloric sphincter is a narrow area of smooth muscle with increased luminal pressure located between the stomach and the duodenum. Its function is regulated by intrinsic innervation from the gastric myenteric plexus and extrinsic innervation through branches of the vagus nerve. Hence, pyloric dysfunction represents a key mechanism in gastroparesis, whose nature can vary depending on the underlying cause[4]. The contractions and relaxations of the pylorus depend on the transmission of nerve signals through the ICCs and the response of smooth muscle cells. There are at least two independently controlled functional areas: the circular muscle near the myenteric plexus, dominated by the propagation of gastric slow waves, resulting in sphincter contractions at the end of each peristaltic movement, and the deeper circular muscle, regulated by motor neurons, where slow waves have no influence. The pylorus has garnered increasing interest because its relaxation in synchrony with motor activity between the antrum and the duodenum facilitates gastric emptying[8].

ENDOFLIP DEVICE AND ITS OPERATIONAL CHARACTERISTICS

EndoFLIP is a widely used diagnostic tool in the esophagus for evaluating the lower esophageal sphincter (LES). It utilizes a catheter with 16 sensors that, when inflated, measures diameter (D), pressure (P), cross-sectional area (CSA), and distensibility index (DI). The DI indicates the sphincter's ability to stretch and is calculated by measuring the CSA at the narrowest point of the sphincter and dividing it by its P. There are two catheter models: EF-325 and EF-322, which differ in length (8 cm and 16 cm respectively) and the distance between their sensors (1 cm and 2 cm respectively). LES measurements have been standardized and are represented through the FLIP 1.0 and FLIP 2.0 modules as a 3D topographic image of the esophagus[16].

Its use at the pyloric level shares similar procedural characteristics. After a minimum fast of six hours for non-clear liquids and two hours for water, the patient should be positioned in the left lateral decubitus position and sedated. A therapeutic endoscope is inserted through the esophagus into the stomach and antrum, where an endoscopic

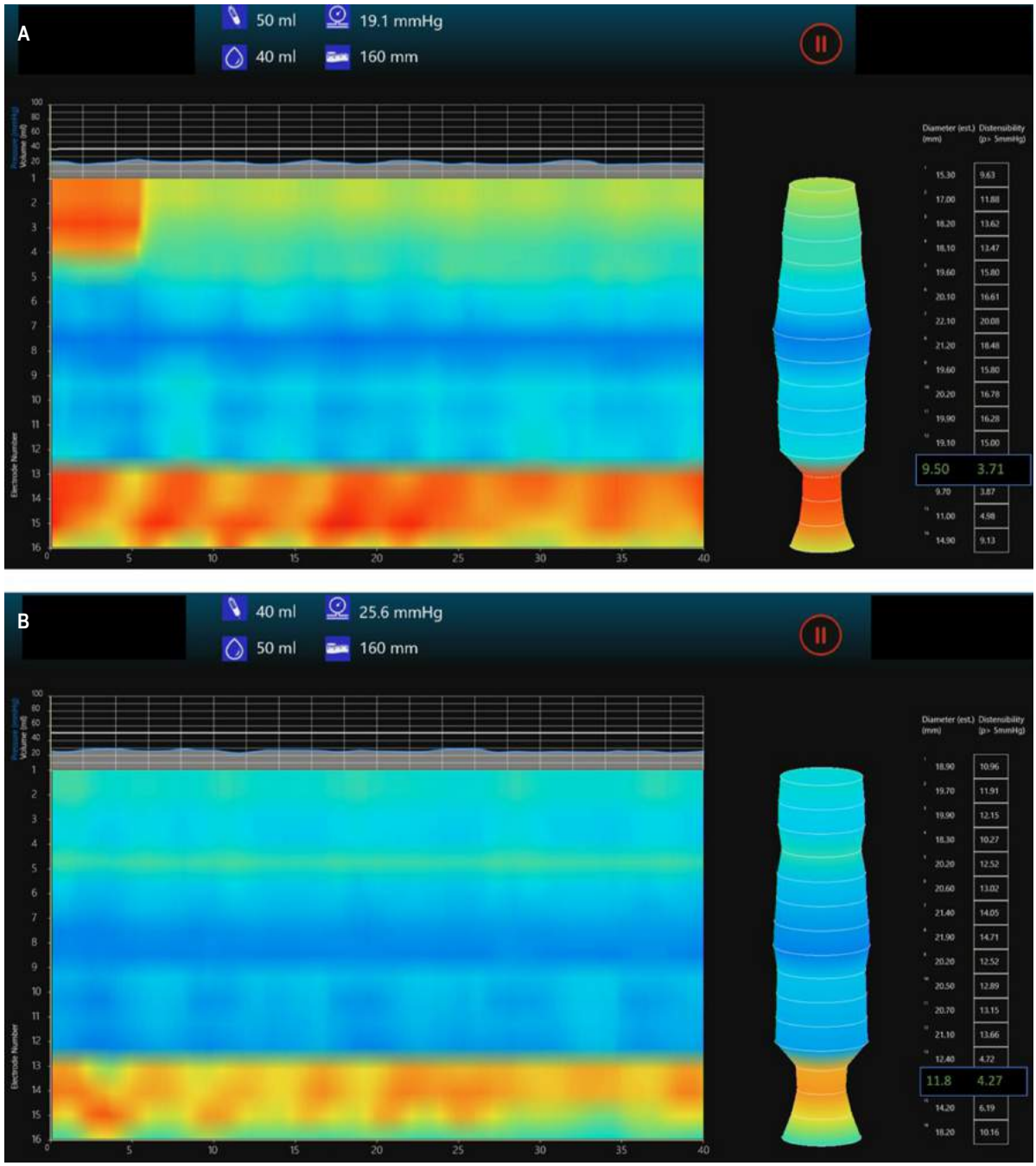


Figure 1. Pyloric EndoFLIP with decreased diameter and pyloric distensibility index in a patient with gastroparesis. Images show (**A**) balloon inflated to 40 mL and (**B**) to 50 mL. Author's file.

examination is performed before crossing the pylorus. Next, the EndoFLIP catheter (ideally the pyloric model EF-325N) is zero-calibrated and lubricated with conductive gel before being inserted through the working channel of the endoscope. Once the catheter is positioned in the pylorus under direct visualization, the balloon is inflated at a rate of 1 mL/s until reaching 40 mL-50 mL (optimal observation of the pyloric contour is obtained at 40 mL). Pressure is then measured for five seconds in mmHg using the pressure transducer located in the probe. For

CSA measurement, conductive liquid is perfused through the infusion port at the proximal end of the probe, obtaining an impedance value by planimetry based on Ohm's law (voltage = current x resistance); the diameter is then derived as the square root of 4 CSA/π. The DI (a measure indicating the ease of structure stretching) is derived from the ratio between the CSA and P at the narrowest point of the sphincter. Elasticity, providing information on the ease of stretching along the entire sphincter, is calculated similarly to the DI but considers the total volume from 1 cm above to 1 cm below the narrowest point of the sphincter. After completing the pyloric measurement, the catheter is withdrawn through the channel, and the upper endoscopic examination is completed with direct visualization of the pylorus and duodenum to rule out lesions caused by previous treatments and the examination itself[17-19]. It should be noted that general anesthesia may cause a slight increase in P and a decrease in pyloric DI, which should be corroborated with prospective trials[20].

PYLORUS MEASUREMENTS

For the accurate interpretation of measurements in the pylorus, it is crucial to consider two aspects. The first aspect is the position of the FLIP catheter balloon in relation to the pylorus. Three positions have been predefined: proximal (with 75% of the balloon in the duodenum and 25% in the antrum), mid (50% in the duodenum and 50% in the antrum), and distal (25% in the duodenum and 75% in the antrum). Yim and colleagues demonstrated that the balloon's position relative to the pylorus results in different measurements of DI, CSA, and P (**Table 1**). Specifically, the measurement of P was significantly higher when most of the balloon was distal to the pylorus and folded in the second part of the duodenum compared to when most of the balloon was in the antrum. The pyloric DI is significantly lower when the balloon is primarily positioned in the duodenum compared to the stomach. These findings may be due to balloon deformation and changes in geometry or spatial arrangement when placed within the duodenum.

The second aspect concerns the geometry of the duodenal bulb. The FLIP catheter runs straight at the level of the LES. However, in the case of the pylorus, where esophageal EndoFLIP catheters are commonly used, the curved geometry of the duodenal bulb causes balloon deformation. Consequently, the sensors do not remain centered, affecting the CSA estimates of the pyloric sphincter through impedance planimetry. Since DI measurements are calculated from CSA, it is not surprising to see alterations in this parameter with different positions[19]. Therefore, it is concluded that positioning the FLIP catheter balloon primarily in the antrum (distal) minimizes deformation, allowing for more reliable measurements.

Table 1. Variation of EndoFLIP Measurements Related to the Balloon Position with Respect to the Pylorus

Measurement	Inflation Volume (mL)	Proximal Position	Mid Position	Distal Position
CSA (mm²)	40	130.1	137.9	115.0
	50	183.0	190.2	185.8
Average pressure (mmHg)	40	15.2	11.6	10.6
	50	28.1	31.5	21.1
Distensibility index (mm²/mm Hg)	40	9.8	13.9	13.1
	50	6.7	9.4	9.6

Adapted from: Yim B and colleagues; J Neurogastroenterol Motil. 2023;29(2):192-99.

Several studies have addressed defining reference values for pyloric EndoFLIP measurements. Gourcerol and colleagues evaluated a cohort of healthy volunteers and found that the average DI was 25.2 ± 2.4 mm^2/mmHg when inflating the EndoFLIP balloon to 40 mL, with no significant variations when measured at 10, 20, and 30 mL consecutively. This study also evaluated a subgroup of patients with gastroparesis of various etiologies (diabetic, idiopathic, and post-fundoplication) and found that the pyloric DI decreased significantly at all evaluated volumes, establishing a normality threshold value greater than 10 mm^2/mmHg.

Zhen and colleagues evaluated another larger cohort of healthy volunteers and found D values of 13.0 ± 2.5, 14.3 ± 1.8, and 17.2 ± 2.0 mm, DI values of 10.9 ± 4.8, 11.3 ± 5.8, and 11.1 ± 4.3 mm^2/mmHg, and P values of 12.5 ± 3.9, 15.8 ± 4.8, and 21.7 ± 5.3 mmHg for distensions of 40, 50, and 60 mL, respectively[22].

Various series have evaluated these measurements in patients with gastroparesis. Jacques and colleagues[23] and Malik and colleagues[24] evaluated patients with diabetic gastroparesis (DG) and idiopathic gastroparesis (IG) and found DI values at 40 mL inflation of 11.7 and 10.0 ± 1.3 mm^2/mmHg, respectively. Although the results obtained in these studies did not define a definitive cutoff point for DI with a high discriminative capacity between healthy and sick subjects, it appears that values below 10 mm^2/mmHg could identify most patients with gastroparesis. The population with values between 10 and 25.2 ± 2.4 mm^2/mmHg

should be characterized in prospective studies, as those with values close to the lower limit could correspond to false negatives.

Desprez and colleagues compared pyloric DI among three groups: healthy volunteers, patients with DGP, and patients with IG. They also examined the clinical characteristics of the diabetic patients in detail. For this study, DI values greater than 10 mm^2/mmHg were considered normal. The results showed that the DI measured with 40 mL inflation was lower in the DGP and IG groups, specifically 10.8 ± 0.9 mm^2/mmHg and 14.8 ± 2.2 mm^2/mmHg, respectively, compared to the healthy volunteer group, which had a DI of 25.2 ± 2.3 mm^2/mmHg ($p < 0.005$). A reduced pyloric DI was observed in 56.5% of the DGP patients, 51.5% of the IG patients, and 10% of the healthy volunteers. No correlation was found between the pyloric sphincter measurements and diabetes-related characteristics, including blood glucose levels, glycated hemoglobin, type of diabetes *mellitus*, neuropathy, or the use of glucagon-like peptide-1 (GLP-1) agonists. Both DI and P of the pyloric sphincter were altered in DGP and IG, while distensibility did not correlate with diabetes parameters[25]. **Table 2** summarizes the different variables measured in these studies.

Based on these findings, subsequent research has focused on determining whether DI measurement could predict the clinical outcomes of therapies specifically targeting the pylorus, such as HBPD, BT, or G-POEM. For HBPD, it has been shown that patients who experience greater symptomatic relief had lower DI values before dilation (7.2 ± 1.0 mm^2/mmHg)[26]. The EsoFLIP (dilation balloon with incorporated EndoFLIP) could be a useful strategy to improve the success rate of this procedure, as it safely allows surpassing the dilation target threshold of 18-20 mm; in selected cases, it achieves residual diameters of up to 30 mm without increasing the complication rate[27].

Regarding the use of BT, DI values less than 8-10 mm^2/mmHg predict a good symptomatic response post-intervention[28]. Saadi and colleagues also demonstrated the utility of EndoFLIP in predicting symptom response. Besides conventional measurements, they evaluated elasticity (very similar to DI, see the Operational Characteristics section). Patients with greater pre-BT elasticity showed marked improvement in nausea ($r = –0.34$, $p = 0.03$) and early satiety ($r = –0.34$, $p = 0.04$) at eight weeks. Interestingly, patients with higher preoperative DI experienced less abdominal pain eight weeks postoperatively, while those with lower DI, CSA, and D had more severe symptoms of nausea and vomiting[18].

Recent studies have focused on evaluating the role of EndoFLIP in the treatment of patients who are candidates for G-POEM. Preoperative data from Jacques and colleagues[23] showed that DI values below 9.2 mm^2/mmHg predict clinical success at three months. Postoperatively, Vosoughi and colleagues demonstrated that CSA measurement appears to be the best predictor of clinical success and increased gastric emptying, with values greater than 154 mm^2 at a distension volume of 40 mL predicting clinical success at one year with a sensitivity and specificity of 71% and 91%, respectively[20]. Additionally, increases greater than 20% in CSA compared to the preoperative value correlate with clinical success[30]. This suggests that EndoFLIP could be used both before and after the proce-

Table 2. Pyloric EndoFLIP Measurements in Healthy and Gastroparesis Patients

Study	Etiology of Gastroparesis	Inflation Volume (mL)	Average Pyloric Diameter (mm)	Distensibility Index (mm^2/mm Hg)	Average Pressure (mmHg)	CSA (mm^2)
Gourcerol, et al.	Healthy patients	40	-	25.2	-	-
Zheng, et al.	Healthy patients	40	13.0 ± 2.5	10.9 ± 3.8	12.5 ± 3.9	138.6 ± 55.4
		50	14.3 ± 1.8	11.3 ± 5.8	15.8 ± 4.8	162.4 ± 39.2
Jacques, et al.	50% diabetic, 20% idiopathic, 25% miscellaneous*, 5% post-surgical	40	13.9	11.7	11.7	152.2
		50	17.3	8.1	28.9	234.5
Malik, et al.	72% idiopathic, 28% diabetic	40	12.2 ± 0.44	10.0 ± 1.3	18 ± 1.23	125.2 ± 9.15
		50	14.1 ± 0.41	6.0 ± 1.3	32.5 ± 1.55	164.7 ± 10.2

*15% secondary to Sjögren's syndrome, 5% to Parkinson's disease, and 5% to systemic sclerosis. Author's own research.

dure to help predict or confirm the efficacy of pyloromyotomy, guiding the procedure similarly to its use for the LES in patients with achalasia.

In Colombia, the limited number of specialized centers in gastrointestinal physiology and the high cost of EndoFLIP technology compared to other diagnostic strategies restrict its reproducibility and negatively impact the characterization and appropriate selection of pylorus-targeted therapies. Overcoming these obstacles could lead to its routine use and inclusion in local guidelines for managing patients with refractory gastroparesis.

CONCLUSION

Pyloric EndoFLIP is an attractive complementary diagnostic tool for the characterization of gastroparesis, especially in cases of refractory gastroparesis, to initial traditional management. Most studies have shown an inverse correlation between pyloric distensibility, gastric emptying, and gastroparesis symptoms. This could allow for the individualization of each case by identifying the characteristics of the pylorus, guiding towards a better management strategy, and, in many cases, predicting clinical response.

Ethical Considerations

This study does not disclose any information that could identify patients, so it did not require informed consent or protocol approval by an institutional ethics committee in accordance with the Declaration of Helsinki and Resolution 008430 of October 4, 1993.

Funding Sources

No sponsorship was received from any of the participating institutions for the preparation of this article.

Conflict of Interests

The authors declare no conflict of interest.

REFERENCES

1. Lacy BE, Wise JL, Cangemi DJ. Gastroparesis: time for a paradigm change. Curr Opin Gastroenterol. 2023;39(6):503-511. https://doi.org/10.1097/MOG.0000000000000978
2. Wadhwa V, Mehta D, Jobanputra Y, Lopez R, Thota PN, Sanaka MR. Healthcare utilization and costs associated with gastroparesis. World J Gastroenterol. 2017;23(24):4428-4436. https://doi.org/10.3748/wjg.v23.i24.4428
3. Ye Y, Yin Y, Huh SY, Almansa C, Bennett D, Camilleri M, et al. Epidemiology, Etiology, and Treatment of Gastroparesis: Real-World Evidence From a Large US National Claims Database. Gastroenterology. 2022;162(1):109-121.e5. https://doi.org/10.1053/j.gastro.2021.09.064
4. Camilleri M, Sanders KM. Gastroparesis. Gastroenterology. 2022 ;162(1):68-87.e1. https://doi.org/10.1053/j.gastro.2021.10.028
5. Mayor V, Aponte D, Prieto R, Orjuela E. Diagnóstico y tratamiento actual de la gastroparesia: una revisión sistemática de la literatura. Rev. colomb. Gastroenterol. 2020;35(4):471-484. https://doi.org/10.22516/25007440.561
6. Grover M, Farrugia G, Stanghellini V. Gastroparesis: a turning point in understanding and treatment. Gut. 2019;68(12):2238-2250. https://doi.org/10.1136/gutjnl-2019-318712
7. Olausson EA, Störsrud S, Grundin H, Isaksson M, Attvall S, Simrén M. A small particle size diet reduces upper gastrointestinal symptoms in patients with diabetic gastroparesis: a randomized controlled trial. Am J Gastroenterol. 2014;109(3):375-385. https://doi.org/10.1038/ajg.2013.453
8. Soliman H, Gourcerol G. Targeting the pylorus in gastroparesis: From physiology to endoscopic pyloromyotomy. Neurogastroenterol Motil. 2023;35(2):e14529. https://doi.org/10.1111/nmo.14529
9. Lacy BE, Tack J, Gyawali CP. AGA Clinical Practice Update on Management of Medically Refractory Gastroparesis: Expert Review. Clin Gastroenterol Hepatol. 2022;20(3):491-500. https://doi.org/10.1016/j.cgh.2021.10.038
10. Bromer MQ, Friedenberg F, Miller LS. Endoscopic pyloric injection of botulinum toxin A for the treatment of refractory gastroparesis. Gastrointest Endosc. 2005;61(7):833-839. https://doi.org/10.1016/S0016-5107(05)00328-7
11. Shada AL, Dunst CM, Pescarus R, Speer EA, Cassera M, Reavis KM, et al. Laparoscopic pyloroplasty is a safe and effective first-line surgical therapy for refractory gastroparesis. Surg Endosc. 2016;30(4):1326-1332. https://doi.org/10.1007/s00464-015-4385-5
12. Shen S, Luo H, Vachaparambil C. Gastric peroral endoscopic pyloromyotomy versus gastric electrical stimulation in the treatment of refractory gastroparesis: a propensity score-matched analysis of long-term outcomes. Endoscopy. 2020;52(5):349-358. https://doi.org/10.1055/a-1111-8566
13. Spadaccini M, Maselli R, Chandrasekar VT, Anderloni A, Carrara S, Galtieri PA, et al. Gastric peroral endoscopic

pyloromyotomy for refractory gastroparesis: a systematic review of early outcomes with pooled analysis. Gastrointest Endosc. 2020;91(4):746-752. https://doi.org/10.1016/j.gie.2019.11.039
14. Mohan BP, Chandan S, Jha LK, Khan SR, Kotagiri R, Kassab LL, et al. Clinical efficacy of gastric per-oral endoscopic myotomy (G-POEM) in the treatment of refractory gastroparesis and predictors of outcomes: a systematic review and meta-analysis using surgical pyloroplasty as a comparator group. Surg Endosc. 2020;34(8):3352-3367. https://doi.org/10.1007/s00464-019-07135-9
15. Vohra I, Gopakumar H, Adler DG. G-POEM for gastroparesis: past, present and future. Curr Opin Gastroenterol. 2023;39(5):390-396. https://doi.org/10.1097/MOG.0000000000000950
16. Hani A, Delgado D, Bejarano J, Meza D, Ramírez R, Pinto M, et al. EndoFLIP: una nueva tecnología. Rev. colomb. Gastroenterol. 2021;36(2):227-240. https://doi.org/10.22516/25007440.741
17. Lorenz F, Brunner S, Berlth F, Dratsch T, Babic B, Fuchs HF, et al. Using an Endoluminal Functional Lumen Imaging Probe (EndoFLIP™) to Compare Pyloric Function in Patients with Gastroparesis to Patients After Esophagectomy. J Gastrointest Surg. 2023;27(4):682-690. https://doi.org/10.1007/s11605-022-05502-x
18. Saadi M, Yu D, Malik Z, Parkman HP, Schey R. Pyloric sphincter characteristics using EndoFLIP® in gastroparesis. Rev Gastroenterol Mex (Engl Ed). 2018;83(4):375-384. English, Spanish. https://doi.org/10.1016/j.rgmx.2018.02.013
19. Yim B, Gregor L, Siwiec RM, Al-Haddad M, Nowak TV, Wo JM. Pyloric Functional Lumen Imaging Probe Measurements Are Dependent on Balloon Position. J Neurogastroenterol Motil. 2023;29(2):192-99. https://doi.org/10.5056/jnm22053
20. Desprez C, Jacques J, Clavier T, Wallenhorst T, Leroi AM, Gourcerol G. Impact of anesthetics on pyloric characteristics measured using the EndoFLIP® system in patients with gastroparesis. Neurogastroenterol Motil. 2023;35(10):e14651. https://doi.org/10.1111/nmo.14651
21. Gourcerol G, Tissier F, Melchior C, Touchais JY, Huet E, Prevost G, et al. Impaired fasting pyloric compliance in gastroparesis and the therapeutic response to pyloric dilatation. Aliment Pharmacol Ther. 2015;41(4):360-367. https://doi.org/10.1111/apt.13053
22. Zheng T, Vosoughi K, Busciglio I, Tebay L, Burton D, Camilleri M. Fasting pyloric diameter and distensibility by functional endoluminal imaging probe in unsedated healthy volunteers. Neurogastroenterol Motil. 2022;34(10):e14386. https://doi.org/10.1111/nmo.14386
23. Jacques J, Pagnon L, Hure F, Legros R, Crepin S, Fauchais AL, et al. Peroral endoscopic pyloromyotomy is efficacious and safe for refractory gastroparesis: prospective trial with assessment of pyloric function. Endoscopy. 2019;51(1):40-49. https://doi.org/10.1055/a-0628-6639
24. Malik Z, Sankineni A, Parkman HP. Assessing pyloric sphincter pathophysiology using EndoFLIP in patients with gastroparesis. Neurogastroenterol Motil. 2015;27(4):524-31. https://doi.org/10.1111/nmo.12522
25. Desprez C, Chambaz M, Melchior C, Basile P, Prevost G, Jacques J, et al. Assessment of pyloric sphincter distensibility and pressure in patients with diabetic gastroparesis. Neurogastroenterol Motil. 2021;33(8):e14064. https://doi.org/10.1111/nmo.14064
26. Jehangir A, Malik Z, Petrov RV, Parkman HP. EndoFLIP and pyloric dilation for gastroparesis symptoms refractory to pyloromyotomy/pyloroplasty. Dig Dis Sci. 2020;66(8):2682-2690. https://doi.org/10.1007/s10620-020-06510-0
27. Murray FR, Schindler V, Hente JM, Fischbach LM, Schnurre L, Deibel A, et al. Pyloric dilation with the esophageal functional lumen imaging probe in gastroparesis improves gastric emptying, pyloric distensibility, and symptoms. Gastrointest Endosc. 2021;94(3):486-494. https://doi.org/10.1016/j.gie.2021.03.022
28. Desprez C, Roman S, Leroi AM, Gourcerol G. The use of impedance planimetry (Endoscopic Functional Lumen Imaging Probe, EndoFLIP®) in the gastrointestinal tract: A systematic review. Neurogastroenterol Motil. 2020;32(9):e13980. https://doi.org/10.1111/nmo.13980
29. Vosoughi K, Ichkhanian Y, Jacques J, Aadam AA, Benias PC, Law R, et al. Role of endoscopic functional luminal imaging probe in predicting the outcome of gastric peroral endoscopic pyloromyotomy (with video). Gastrointest Endosc. 2020;91(6):1289-1299. https://doi.org/10.1016/j.gie.2020.01.044
30. Conchillo JM, Straathof JWA, Mujagic Z, Brouns JH, Bouvy ND, Keszthelyi D, et al. Gastric peroral endoscopic pyloromyotomy for decompensated gastroparesis: comprehensive motility analysis in relation to treatment outcomes. Endosc Int Open. 2021;9(2):E137-E144. https://doi.org/10.1055/a-1311-0859

https://doi.org/10.22516/25007440.1132

Review article

Disorders of Gut-Brain Interaction (Functional Gastrointestinal Disorders): Neuromodulators in Clinical Practice (Part I)

Luis Fernando Pineda-Ovalle,[1*] David Benigno Páramo-Hernández,[2] Laura Marcela Moya-Valenzuela,[3] Alejandro Concha-Mejía,[4] Juan David Páramo-Díaz.[5]

OPEN ACCESS

Citation:
Pineda-Ovalle LF, Páramo-Hernández DB, Moya-Valenzuela LM, Concha-Mejía A, Páramo-Díaz JD. Disorders of Gut-Brain Interaction (Functional Gastrointestinal Disorders): Neuromodulators in Clinical Practice (Part I). Revista. colomb. Gastroenterol. 2024;39(2):187-193. https://doi.org/10.22516/25007440.1132

[1] Specialist in Internal Medicine, Gastroenterology, and Epidemiology. Director of Gut Médica, Instituto de Salud Digestiva. Bogotá, Colombia.
[2] Clinical Gastroenterologist and Epidemiologist, Gut Médica, Instituto de Salud Digestiva. Bogotá, Colombia.
[3] Specialist in Internal Medicine and Gastroenterology. Gastroenterologist, Gut Médica, Instituto de Salud Digestiva. Bogotá, Colombia.
[4] Surgeon; Specialist in Internal Medicine, Gastroenterology, and Epidemiology. Head of Gastroenterology, Clínica del Country. Bogotá, Colombia.
[5] General Psychiatrist. Instructor Professor, Medical School, Pontificia Universidad Javeriana. Bogotá, Colombia.

***Correspondence:** Luis Fernando Pineda-Ovalle. lfpineda@gutmedica.com

Received: 30/08/2023
Accepted: 24/04/2024

Abstract

Introduction: This review article develops the basic principles for the use and action mechanisms of neuromodulators applied in clinical practice and their role in treating different disorders of gutbrain interaction (DGBI), particularly, esophageal disorders in part I. **Materials and methods:** The working group reviewed the most frequent pathologies and medications used according to the most recent literature and presented those with the best clinical evidence in each case. **Results:** Due to the diversity of disorders, types of studies, and therapeutic options, we decided to present the evidence with the best results for each case. We determined the doses used, their results, and the side effects of each one. **Conclusions:** The basic principles of the use and mechanisms of action of the main neuromodulators were reviewed, including their use in this section in the main esophageal gastrointestinal functional disorders. Given that the available evidence is not definitive, more controlled clinical trials are needed for each condition to confirm the effectiveness and safety of neuromodulators.

Keywords

Antidepressants, antipsychotics, central neuromodulators, disorders of gut brain interaction, functional gastrointestinal disorder.

INTRODUCTION

Functional gastrointestinal diseases result from a neurohumoral imbalance of the brain-gut axis caused by various factors: alterations in the microbiome, changes in intestinal permeability, activation of the mucosal immune response, visceral hypersensitivity, and altered central sensory processing, among others [(1)]. These alterations are amplified bidirectionally by emotions, stress, and the patient's psychosocial environment[(2)]. This is the basis of the biopsychosocial model proposed by The Rome Foundation for addressing these disorders. This group also suggests that the traditionally termed *functional gastrointestinal disorders* (FGID) be redefined as disorders of brain-gut interaction (DGBI) to highlight the neurobiological nature of these diseases[(2)]. Consequently, understanding the medications that modulate the brain-gut axis is essential for physicians to treat patients with FGIDs more rationally and effectively. This article aims to review the pharmacological aspects and clinical utility of antidepressant or neuromodulatory medications in FGIDs.

BASIC PRINCIPLES OF USING NEUROMODULATORS IN THE BRAIN-GUT AXIS

The enteric nervous system (ENS) and the central nervous system (CNS) share a common embryonic origin and, consequently, the same neurotransmitters and neuronal receptors. As a result, emotional disorders directly affect gastrointestinal physiology, and gastrointestinal disturbances reciprocally cause dysfunction in the CNS. This bidirectional influence also applies to neuromodulatory medications, which exert pharmacological effects on both the CNS and ENS[1-3].

Antidepressants or neuromodulators act at the postsynaptic level by downregulating and desensitizing the receptors for one or more of the three main monoamines: serotonin (5-HT), norepinephrine (NA), and dopamine (DA)[4]. This mechanism is responsible for pain modulation and also accounts for undesirable side effects such as diarrhea, increased heart rate, and sexual dysfunction[4,5]. These medications influence brain circuits related to pain and emotion processing, producing a direct analgesic effect and altering the patient's experience of symptoms[6,7]. They also act on the posterior horns of the spinal cord, regulating visceral nociceptive sensitivity mediated by opioid, serotonergic, and noradrenergic receptors[8]. Additionally, they provide a direct peripheral visceral analgesic effect that is independent of their antidepressant or anxiolytic actions[8]. Furthermore, there is evidence that neuromodulators induce neuroplasticity changes in the hippocampus and anterior cingulate cortex, regenerating neurons lost due to chronic pain or psychological trauma[9]. Given the stigma and rejection that patients often associate with antidepressants, we recommend that physicians use the term *neuromodulators* instead of *antidepressants* when prescribing these medications. It is important to clearly explain that these medications can alleviate both gastrointestinal and associated psychological symptoms.

BASIC MECHANISM OF ACTION AND CLINICAL USE OF DIFFERENT NEUROMODULATORS

Tricyclic antidepressants (TCAs), such as amitriptyline and imipramine, are noted for their ability to bind to multiple neuronal receptors, including 5-hydroxytryptamine (5-HT), norepinephrine (NA), muscarinic type 1, α1-adrenergic, H1-histaminergic receptors, and sodium channels[4]. Due to this broad receptor affinity, TCAs tend to produce more side effects compared to other classes of neuromodulators. These side effects include xerostomia, constipation, and, at high doses, cardiac arrhythmias. TCAs are particularly valuable for patients with irritable bowel syndrome with diarrhea and for cases of functional dyspepsia, such as epigastric pain syndrome[5]. However, they are not recommended for patients with constipation, as their anticholinergic action can worsen this condition. Using low doses reduces the incidence of undesirable effects, but these agents should still be avoided in patients with left bundle branch block, prolonged QT interval, and elderly patients[4,5].

Selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine, escitalopram, and sertraline, selectively block the presynaptic serotonin transporter (SERT), increasing the availability of this neurotransmitter at the postsynaptic receptors. Although they lack analgesic properties, SSRIs are very useful for addressing symptoms of depression, anxiety, and hypervigilance, which are common in patients with FGIDs[4]. Common side effects include diarrhea, insomnia, night sweats, agitation, headache, weight loss, and sexual dysfunction[5]. SSRIs can also be useful in cases of constipation as they increase gastrointestinal transit.

Serotonin-norepinephrine reuptake inhibitors (SNRIs), such as venlafaxine and duloxetine, share analgesic properties with TCAs but have a lower incidence of side effects due to their reduced affinity for muscarinic and α-adrenergic receptors[4]. SNRIs are useful in treating visceral hypersensitivity associated with various FGIDs and somatic pain syndromes such as fibromyalgia[6]. Side effects, including nausea and sleep disturbances, are infrequent and tend to improve with prolonged use[6].

Tetracyclic antidepressants, such as mirtazapine and trazodone, enhance the neurotransmission of 5-HT and NA by blocking α2-adrenergic autoreceptors[4]. Mirtazapine, as an H1 and 5-HT2C antagonist, is particularly suitable for patients with postprandial distress-type dyspepsia, as it has demonstrated improvements in gastric accommodation and reductions in dysmotility symptoms. These medications are beneficial for FGID patients experiencing appetite loss and weight loss[5].

Other less frequently used antidepressants include azapirones, atypical antipsychotics, and delta ligand agents. Azapirones, such as buspirone and tandospirone, act both centrally and peripherally, affecting areas related to fear and gastrointestinal function, especially in mechanisms of gastric accommodation[4,5]. Atypical antipsychotics, including olanzapine and quetiapine, exhibit diverse pharmacological actions, including anticholinergic properties. They reduce gastric sensitivity in patients with functional dyspepsia, alleviating visceral pain and nausea, and have a lower risk of extrapyramidal side effects compared to typical antipsychotics like haloperidol. Common adverse effects include weight gain, dizziness, and sedation. These medications are useful as adjunctive analgesic therapy, although the formal evidence supporting their application in FGIDs is limited[4,5]. Lastly, delta ligand agents, such as gabapentin and

pregabalin, block the α2δ subunit of presynaptic calcium channels and are effective in managing neuropathic pain and somatic syndromes with central sensitization, such as fibromyalgia. Their primary application in FGIDs is as adjuvant therapy for pain management[7].

UTILITY OF NEUROMODULATORS IN SPECIFIC FUNCTIONAL GASTROINTESTINAL DISORDERS

Functional Heartburn

Patients with functional heartburn are characterized by chronic heartburn with negative diagnostic studies for gastroesophageal reflux disease (GERD) and a lack of response to proton pump inhibitors (PPIs). The most appropriate approach for managing functional heartburn (FH) involves a multi-component strategy that includes lifestyle changes, neuromodulator pharmacotherapy, alternative medicine, and psychotherapy[8]. PPIs are only indicated in cases of functional heartburn that coexist with GERD confirmed by endoscopy or esophageal pH monitoring studies. If GERD is fully ruled out during the diagnostic process and PPIs have not been beneficial in the past, they should be discontinued.

Neuromodulators are the cornerstone of pharmacological treatment in FH as they modify the neurotransmission of different monoamines and reduce esophageal pain, primarily at the central level and, to a lesser extent, at the peripheral level[3,8,9]. Fluoxetine was studied in a group of patients with heartburn refractory to PPIs and normal endoscopy[9]. Sixty patients with abnormal pH monitoring and 84 patients with normal pH monitoring were randomized. Those who received fluoxetine experienced a greater benefit in the percentage of days without heartburn (median: 35.7; interquartile range [IQR]: 21.4-57.1) compared to those who received omeprazole (median: 7.14; IQR: 0-50; $p < 0.001$) or placebo (median: 7.14; IQR: 0-33.6; $p < 0.001$). In the normal pH subgroup, fluoxetine was superior to omeprazole and placebo in terms of the percentage of days without heartburn (median improvement: 57.1; IQR: 35.7-57.1 vs. 13.9; IQR: 0-45.6 and 7.14 vs. 0-23.8; $p < 0.001$), but no significant differences were observed between the medications in the abnormal pH subgroup.

Fluoxetine was only useful in patients with normal pH monitoring. In another controlled clinical trial, imipramine 25 mg daily was compared with placebo in 83 patients with functional heartburn and hypersensitive esophagus over eight weeks[10]. No significant differences were found in heartburn improvement between imipramine and placebo, but there was an improvement in quality of life in the per-protocol analysis ($p = 0.045$). As observed, the evidence supporting the use of neuromodulators in functional heartburn is scarce and limited; however, it is considered the first line of pharmacological treatment due to its regulatory properties of central and peripheral visceral sensitivity. The doses used in the published studies are imipramine 25 mg/day, amitriptyline 25 mg/day, fluoxetine 20 mg/day, tegaserod 6 mg every 12 hours, ranitidine 150 mg/day, and melatonin 6 mg every 12 hours. When using TCAs, they should be administered at bedtime due to their sedative effect, initial doses should be as low as possible, and the increase should be slow and progressive to reduce the occurrence of adverse side effects[3].

Reflux Hypersensitivity

Unlike FH, patients with reflux hypersensitivity (RH) exhibit a relationship between reflux events and symptom generation, even with normal esophageal acid exposure time[11-13]. Consequently, conventional antireflux therapies are generally effective. In a prospective study involving patients with GERD symptoms and normal endoscopy, omeprazole (40 mg/day) improved symptoms in 61% of patients with normal acid exposure and a positive symptom index[14]. Therefore, it is advisable to maximize acid suppression using double doses of PPIs or vonoprazan in patients with confirmed RH[15,16]. Conversely, antisecretory agents should be discontinued in patients with non-acid reflux hypersensitivity identified through pH-impedance monitoring without PPIs[17].

Antireflux surgery has also proven effective in highly selected groups of patients with RH. A controlled study compared Nissen fundoplication with two other intervention groups: PPIs plus desipramine and PPIs plus placebo plus baclofen and desipramine in patients with refractory heartburn and a positive symptom association probability (SAP) during pH-impedance monitoring with PPIs. Nissen fundoplication yielded better outcomes (67%) than the other groups at a one-year follow-up, and the surgical result was not influenced by acid exposure time[18]. In a prospective study, imipramine was compared to placebo in 83 patients with RH and FH[19]. Those who received imipramine did not achieve a higher rate of symptom relief than those who received placebo (37.2% vs. 37.5%, respectively; odds ratio (OR), 0.99; 95% confidence interval (CI), 0.41-2.41). However, treatment with imipramine provided a significant improvement in quality of life in the per-protocol analysis (72 ± 17 vs. 61 ± 19; $p = 0.048$), although the intention-to-treat (ITT) analysis revealed no significant difference (68 ± 19 vs. 61 ± 19; $p = 0.26$). Thus, imipramine may improve the quality of life for RH patients but does not alleviate heartburn. A study conducted in Greece found that citalopram 20 mg was superior to placebo in 75 well-selected patients with a hypersensitive esophagus[20].

At the end of the follow-up period, 38.5% of the citalopram group and 66.7% of the placebo group continued to experience reflux symptoms ($p = 0.021$). Finally, another study mentioned in the previous section found that fluoxetine was superior to omeprazole and placebo in patients with FH or RH[9].

Pharyngeal Globus

Pharyngeal globus (PG) is a somatoform disorder characterized by a sensation of a lump, foreign body, or globus in the upper cervical or pharyngeal region without any structural or functional abnormalities to explain it. After ruling out structural disorders, GERD, and esophageal motor disorders, the initial treatment consists of reassuring the patient, applying non-pharmacological measures, and using neuromodulators. Approximately 50% of patients report symptom improvement when they receive clear information about the benign nature of the condition[21-23]. Non-pharmacological interventions, such as relaxation techniques and hypnotherapy, can also improve symptoms[23]. Physical therapy aimed at improving pharyngolaryngeal tension, administered by speech therapists, has shown satisfactory results in uncontrolled studies[24]. In a randomized controlled trial comparing pantoprazole 40 mg with 25 mg of amitriptyline once a day in patients with PG, the response to amitriptyline was significantly superior to pantoprazole (75% vs. 36%)[25]. Another similar study found that paroxetine provided greater symptomatic relief for PG compared to amitriptyline (44.1% vs. 15.9%; $p = 0.01$) and lansoprazole (64.7% vs. 15.9%; $p = 0.001$)[26]. **Table 1** presents the neuromodulators commonly used in clinical practice for functional esophageal disorders, their dosages, and their main clinical effects.

Non-Cardiogenic Chest Pain

Non-cardiogenic chest pain (NCCP) is a syndrome characterized by chronic retrosternal pain similar to angina but without any underlying heart disease. The causes associated with this syndrome include GERD, esophageal motility disorder (EMD), esophageal hypersensitivity, and psychiatric comorbidities[27,28]. Neuromodulators are considered the cornerstone of treatment for NCCP not related to GERD, regardless of whether EMD is present. When combined with psychological therapy, these medications

Table 1. Recommendations for the Use of Neuromodulators in Functional Esophageal Disorders

Clinical Condition	Neuromodulator	Dosage	Evidence (Reference)	Clinical Effect
Functional heartburn	Fluoxetine	20 mg/day	DBRCT[9]	Improvement in heartburn compared to placebo and omeprazole
	Imipramine	25 mg/night	RCT[10]	Improvement in quality of life compared to placebo
Reflux hypersensitivity	Citalopram or escitalopram	Citalopram 20 mg Escitalopram 10 mg	CCT[19]	Improvement in reflux symptoms compared to placebo
	Imipramine	25 mg/night	CCT[20]	Improvement in quality of life compared to placebo
	Fluoxetine	20 mg/day	CCT[9]	Improvement in reflux symptom quality compared to placebo and omeprazole
Pharyngeal Globus	Amitriptyline	25 mg/night	CCT[24]	Improvement in globus sensation compared to pantoprazole
	Paroxetine	20 mg/day	CCT[25]	Improvement in globus sensation compared to amitriptyline and placebo
NCCP	Imipramine	50 mg/day	DBRCT[29]	Improvement in NCCP frequency by 50% compared to placebo and clonidine
	Paroxetine	10-50 mg/day, mean: 30 mg/day	DBRCT[30]	Improvement in clinical perception
	Trazadone	100-150 mg/day	RCT[28]	Overall symptom improvement compared to placebo

TCAs: tricyclic antidepressants; CM: centrally mediated; NCCP: non-cardiogenic chest pain; CCT: controlled clinical trial; RCT: randomized controlled trial; DBRCT: double-blind randomized controlled trial; SSRIs: selective serotonin reuptake inhibitors; SNRIs: serotonin-norepinephrine reuptake inhibitors; SRMA: systematic review and meta-analysis; IBS: irritable bowel syndrome; CBT: cognitive-behavioral therapy. Adapted from references[9,10,19,20,24,25,29,30].

increase the likelihood of a good short-term response[29]. Imipramine at 50 mg/day for 12 weeks showed a significant reduction in chest pain frequency (50%) compared to clonidine and placebo, although it did not improve quality of life due to the side effects of imipramine compared to placebo[30]. Paroxetine at 5-50 mg/day for 8 weeks and sertraline at 50-200 mg/day for 8 weeks, either alone or in combination with psychotherapy, demonstrated improvement in chest pain scores compared to placebo and also significantly alleviated anxiety symptoms[30]. Trazodone at 100-150 mg/day for 6 weeks was evaluated in a randomized controlled trial and proved effective in treating both functional chest pain and pain related to EMD. Cognitive-behavioral therapy (CBT) and other techniques such as hypnotherapy, biofeedback through breathing exercises, and Joheri window have shown favorable results in reducing pain scales compared to placebo [28,30].

CONCLUSIONS

After reviewing the literature on each DICI, we have selected clinical studies (systematic reviews, controlled clinical trials [CCTs], or the best available evidence in each case) that propose various therapeutic options for pain modulation, as well as obtaining therapeutic benefits from these medications for our patients.

In general, starting with low doses is beneficial, as is the potential to gradually increase the dose and combine certain subgroups of medications or use them simultaneously with psychotherapy targeting gastrointestinal symptoms. However, we emphasize the importance of considering the side effects and interactions of these medications.

There is also a clear need for more CCTs in the future to obtain higher-quality evidence to support the recommendation of these medications in each case.

REFERENCES

1. Drossman DA. Presidential address: Gastrointestinal illness and the biopsychosocial model. Psychosom Med. 1998;60(3):258-67. https://doi.org/10.1097/00006842-199805000-00007
2. Drossman DA. Functional Gastrointestinal Disorders: History, Pathophysiology, Clinical Features and Rome IV. Gastroenterology. 2016;150(6):1262-1279.e2. https://doi.org/10.1053/j.gastro.2016.02.032
3. Drossman DA, Tack J, Ford AC, Szigethy E, Törnblom H, Van Oudenhove L. Neuromodulators for Functional Gastrointestinal Disorders (Disorders of Gut-Brain Interaction): A Rome Foundation Working Team Report. Gastroenterology. 2018;154(4):1140-1171.e1. https://doi.org/10.1053/j.gastro.2017.11.279
4. Elbe D. Stahl's Essential Psychopharmacology: Neuroscientific Basis and Practical Applications, Third Edition. J Can Acad Child Adolesc Psychiatry. 2010;19(3):230.
5. Törnblom H, Drossman DA. Centrally targeted pharmacotherapy for chronic abdominal pain. Neurogastroenterol Motil. 2015;27(4):455-67. https://doi.org/10.1111/nmo.12509
6. Lunn MPT, Hughes RAC, Wiffen PJ. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database Syst Rev. 2014;2014(1):CD007115. https://doi.org/10.1002/14651858.CD007115.pub3
7. Gale JD, Houghton LA. Alpha 2 Delta (α(2)δ) Ligands, Gabapentin and Pregabalin: What is the Evidence for Potential Use of These Ligands in Irritable Bowel Syndrome. Front Pharmacol. 2011;2:28. https://doi.org/10.3389/fphar.2011.00028
8. Aziz Q, Fass R, Gyawali CP, Miwa H, Pandolfino JE, Zerbib F. Functional Esophageal Disorders. Gastroenterology. 2016;150(6):1368-79. https://doi.org/10.1053/j.gastro.2016.02.012
9. Ostovaneh MR, Saeidi B, Hajifathalian K, Farrokhi-Khajeh-Pasha Y, Fotouhi A, Mirbagheri SS, et al. Comparing omeprazole with fluoxetine for treatment of patients with heartburn and normal endoscopy who failed once daily proton pump inhibitors: double-blind placebo-controlled trial. Neurogastroenterol Motil. 2014;26(5):670-8. https://doi.org/10.1111/nmo.12313
10. Limsrivilai J, Charatcharoenwitthaya P, Pausawasdi N, Leelakusolvong S. Imipramine for Treatment of Esophageal Hypersensitivity and Functional Heartburn: A Randomized Placebo-Controlled Trial. Am J Gastroenterol. 2016;111(2):217-24. https://doi.org/10.1038/ajg.2015.413
11. Savarino E, Marabotto E, Zentilin P, Frazzoni M, Sammito G, Bonfanti D, et al. The added value of impedance-pH monitoring to Rome III criteria in distinguishing functional heartburn from non-erosive reflux disease. Dig Liver Dis. 2011;43(7):542-7. https://doi.org/10.1016/j.dld.2011.01.016
12. Savarino E, Zentilin P, Tutuian R, Pohl D, Casa DD, Frazzoni M, et al. The role of nonacid reflux in NERD: lessons learned from impedance-pH monitoring in 150 patients off therapy. Am J Gastroenterol. 2008;103(11):2685-93. https://doi.org/10.1111/j.1572-0241.2008.02119.x
13. Watson RGP, Tham TCK, Johnston BT, McDougall NI. Double blind cross-over placebo controlled study of omeprazole in the treatment of patients with reflux symp-

toms and physiological levels of acid reflux--the "sensitive oesophagus." Gut. 1997;40(5):587-90. https://doi.org/10.1136/gut.40.5.587
14. Zerbib F, Belhocine K, Simon M, Capdepont M, Mion F, Des Varannes SB, et al. Clinical, but not oesophageal pH-impedance, profiles predict response to proton pump inhibitors in gastro-oesophageal reflux disease. Gut. 2012;61(4):501-6. https://doi.org/10.1136/gutjnl-2011-300798
15. Sawada A, Sifrim D, Fujiwara Y. Esophageal Reflux Hypersensitivity: A Comprehensive Review. Gut Liver. 2023;17(6):831-842. https://doi.org/10.5009/gnl220373
16. Hoshikawa Y, Hoshino S, Kawami N, Iwakiri K. Prevalence of behavioral disorders in patients with vonoprazan-refractory reflux symptoms. J Gastroenterol. 2021;56(2):117-124. https://doi.org/10.1007/s00535-020-01751-2
17. Yadlapati R, Gyawali CP, Pandolfino JE, Chang K, Kahrilas PJ, Katz PO, et al. AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review. Clin Gastroenterol Hepatol. 2022;20(5):984-994.e1. https://doi.org/10.1016/j.cgh.2022.01.025
18. Spechler SJ, Hunter JG, Jones KM, Lee R, Smith BR, Mashimo H, et al. Randomized Trial of Medical versus Surgical Treatment for Refractory Heartburn. N Engl J Med. 2019;381(16):1513-23. https://doi.org/10.1056/NEJMoa1811424
19. Limsrivilai J, Charatcharoenwitthaya P, Pausawasdi N, Leelakusolvong S. Imipramine for Treatment of Esophageal Hypersensitivity and Functional Heartburn: A Randomized Placebo-Controlled Trial. Am J Gastroenterol. 2016;111(2):217-24. https://doi.org/10.1038/ajg.2015.413
20. Viazis N, Keyoglou A, Kanellopoulos AK, Karamanolis G, Vlachogiannakos J, Triantafyllou K, et al. Selective serotonin reuptake inhibitors for the treatment of hypersensitive esophagus: a randomized, double-blind, placebo-controlled study. Am J Gastroenterol. 2012;107(11):1662-7. https://doi.org/10.1038/ajg.2011.179
21. Zerbib F, Rommel N, Pandolfino J, Gyawali CP. ESNM/ANMS Review. Diagnosis and management of globus sensation: A clinical challenge. Neurogastroenterol Motil. 2020;32(9):e13850. https://doi.org/10.1111/nmo.13850
22. Brown SR, Schwartz JM, Summergrad P, Jenike MA. Globus hystericus syndrome responsive to antidepressants. Am J Psychiatry. 1986;143(7):917-8. https://doi.org/10.1176/ajp.143.7.917
23. Kiebles JL, Kwiatek MA, Pandolfino JE, Kahrilas PJ, Keefer L. Do patients with globus sensation respond to hypnotically assisted relaxation therapy? A case series report. Dis Esophagus. 2010;23(7):545-53. https://doi.org/10.1111/j.1442-2050.2010.01064.x
24. Khalil HS, Bridger MW, Hilton-Pierce M, Vincent J. The use of speech therapy in the treatment of globus pharyngeus patients. A randomised controlled trial. Rev Laryngol Otol Rhinol (Bord). 2003;124(3):187-90.
25. You LQ, Liu J, Jia L, Jiang SM, Wang GQ. Effect of low-dose amitriptyline on globus pharyngeus and its side effects. World J Gastroenterol. 2013;19(42):7455-60. https://doi.org/10.3748/wjg.v19.i42.7455
26. Zhou WC, Jia L, Chen DY, Liu Y, Liu J, Jiang SM, et al. The effects of paroxetine and amitriptyline on the upper esophageal sphincter (UES) pressure and its natural history in globus pharyngeus. Dig Liver Dis. 2017;49(7):757-763. https://doi.org/10.1016/j.dld.2017.02.008
27. Yamasaki T, Fass R. Reflux Hypersensitivity: A New Functional Esophageal Disorder. J Neurogastroenterol Motil. 2017;23(4):495-503. https://doi.org/10.5056/jnm17097
28. Shibli F, Tawil J, Fass R. Diagnosis and Management of Functional Chest Pain in the Rome IV Era. J Neurogastroenterol Motil. 2019;25(4):487-98. https://doi.org/10.5056/jnm19146
29. George N, Abdallah J, Maradey-Romero C, Gerson L, Fass R. Review article: the current treatment of non-cardiac chest pain. Aliment Pharmacol Ther. 2016;43(2):213-39. https://doi.org/10.1111/apt.13458
30. Nguyen TMT, Eslick GD. Systematic review: The treatment of noncardiac chest pain with antidepressants. Aliment Pharmacol Ther. 2012;35(5):493-500. https://doi.org/10.1111/j.1365-2036.2011.04978.x

https://doi.org/10.22516/25007440.1083

Case report

Extensive Pancreatic Necrosis, Successful Management with Percutaneous Endoscopic Necrosectomy

Daniela Giraldo-Campillo,[1]* Juliana Lucía Molina-Valencia,[2] Juan Camilo Ricaurte-Ciro,[3] Carlos Andrés Delgado-López.[4]

OPEN ACCESS

Citation:
Giraldo-Campillo D, Molina-Valencia JL, Ricaurte-Ciro JC, Delgado-López CA. Extensive Pancreatic Necrosis, Successful Management with Percutaneous Endoscopic Necrosectomy. Revista. colomb. Gastroenterol. 2024;39(2):194-198. https://doi.org/10.22516/25007440.1083

[1] General Surgery Resident, Universidad de Antioquia. Medellín, Colombia.
[2] General Surgery Resident, Universidad de Antioquia. Medellín, Colombia.
[3] Gastroenterologist Internist, Hospital San Vicente Fundación. Medellín, Colombia.
[4] General Surgeon, Pablo Tobón Uribe Hospital. Medellín, Colombia.

***Correspondence:** Daniela Giraldo.
danielagiraldo.9458@gmail.com

Received: 17/05/2023
Accepted: 27/06/2023

Abstract

Percutaneous endoscopic necrosectomy is a procedure indicated for managing extensive pancreatic necrosis. Different endoscopic and surgical alternatives have been described for drainage of peripancreatic collections and debridement of necrosis, and minimally invasive approaches have lower complications and mortality rates. We presented the case of a patient with severe pancreatitis associated with pancreatic necrosis extending to both paracolic gutters, who underwent percutaneous endoscopic necrosectomy, after unsuccessful percutaneous and laparoscopic drainage, and a complete resolution of the clinical picture was achieved.

Management should consider the clinical condition of the patient, the location of the collections, and the time of evolution of the pancreatitis, and thus choose which intervention will be the most effective, considering also the experience of the medical team and the available resources.

Keywords

Acute necrotizing pancreatitis, endoscopy of the digestive system, minimally invasive surgical procedures, persistent infection.

INTRODUCTION

Acute pancreatitis is an inflammatory process with various etiologies; typically, it presents mildly, and recovery does not involve sequelae. However, mortality can reach 40% in severe cases[(1)].

When parenchymal necrosis occurs and collections form, approximately 40% to 63% of patients require different interventions for drainage[(2)].

In recent years, multiple endoscopic and surgical management approaches have been described. The decision to perform these procedures follows a step-up approach, beginning with less invasive methods such as percutaneous or transluminal drains, with surgical necrosectomy as the last option. This strategy aims to minimize surgical trauma, tissue damage, and inflammatory response[(1-3)]. Surgical management is associated with high complication rates, longer hospital stays, and higher mortality compared to minimally invasive endoscopic management[(1)]. Direct endoscopic pancreatic necrosectomy has been described as a minimally invasive procedure for managing walled-off necrosis located near the stomach and duodenum. For collections located laterally, a novel percutaneous procedure has shown good clinical outcomes[(1)].

We present the case of a patient with severe necrotizing acute pancreatitis with extensive collections, in whom per-

© 2024 Asociación Colombiana de Gastroenterología

cutaneous and surgical drainage management failed, but who achieved a favorable clinical response with percutaneous endoscopic necrosectomy.

CASE REPORT

A 33-year-old male patient with a history of obesity was admitted to a secondary-level healthcare institution due to abdominal pain and recurrent vomiting. He was diagnosed with mild biliary-origin pancreatitis and started on medical management. Due to persistent pain, a contrast-enhanced abdominal CT scan was performed, revealing signs of pancreatic necrosis with a collection extending from the pancreas along the left paracolic gutter to the ipsilateral iliac fossa. Multiple percutaneous drainage procedures were performed by interventional radiology. The patient continued to experience abdominal pain, oral intolerance, and signs of systemic inflammatory response; after 20 days, he was transferred to a high-complexity institution.

A new abdominal CT scan (**Figure 1**) showed pancreatic necrotic collections dependent on the tail, with central and left-sided abdominopelvic distribution, and these collections were in contact with the gastric wall.



Figure 1. Contrast-enhanced abdominal CT scan. Coronal section. Percutaneous drains are visible. Author's file.

It was decided to perform laparoscopy for drainage of the collection and pancreatic necrosectomy. During surgery, an inflammatory phlegmon was observed in the upper abdomen with the omentum adhered to the liver and inflammatory thickening between the stomach and transverse colon, a retrogastric peripancreatic collection in the middle and distal thirds of the pancreas, and a frozen abdomen in the left flank. The procedure was suspended, a drain was placed in the cavity, and pancreatic tissue samples were taken. Cultures reported the growth of KPC-producing XDR *Enterobacter cloacae*, so targeted antibiotic therapy with ceftazidime/avibactam and metronidazole was administered concurrently for four weeks.

A follow-up abdominal CT scan revealed the persistence of collections extending into the abdominopelvic cavity with multiple septa and the presence of air inside, which had not decreased in size, with multipurpose catheters located within. Based on the imaging report, it was decided to manage the condition with percutaneous endoscopic necrosectomy.

PERCUTANEOUS ENDOSCOPIC PROCEDURE

The procedure began with the medial pig-tail drain. Contrast medium was advanced, and under fluoroscopy, the drain was confirmed to be in the correct position. A Jagwire metal guidewire was then advanced through the drain, and the catheter was removed. The entry orifice was enlarged with a small 5 mm incision, and a 9 mm Savary bougie was advanced over the guidewire. A fully covered 16 cm esophageal stent was then advanced over the guidewire and deployed (**Figure 2**). A 12-15 mm dilation balloon was used to dilate the stent to 15 mm. An endoscope was then advanced through the stent, revealing a large cavity with necrosis and several drains inside. Using a loop, an endoscopic necrosectomy was performed to remove the abundant necrotic tissue, and the cavity was washed with saline solution. The stent was connected to a collection bag, and the drains were left in place for tidal irrigation (**Figure 3**).

In the third necrosectomy session, a significant reduction in necrotic and purulent content was observed. Consequently, the pancreatic drainage device was removed and a Blake drain was inserted.

The patient showed appropriate clinical progression, with no fever spikes, controlled abdominal pain, and tolerance to oral intake. The patient was discharged with antibiotic management. During the follow-up appointment, it was decided to remove the drains.

DISCUSSION

Pancreatic necrosis develops in approximately 20% to 30% of patients with acute pancreatitis, and in 20% to 40% of these cases, the necrosis becomes infected, significantly increasing mortality to up to 35%[4]. A multidisciplinary approach involving gastroenterologists, surgeons, interventional radiologists, and other specialists is recommended for comprehensive management.

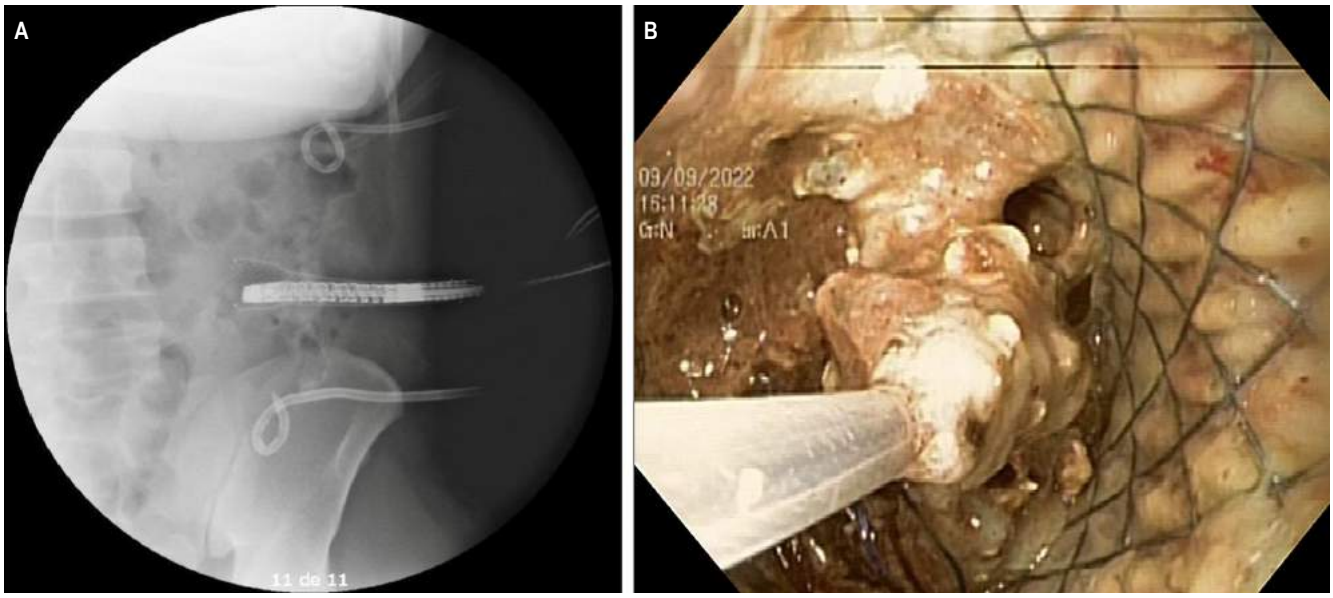


Figure 2. Percutaneous endoscopic necrosectomy. **A.** Placement of the esophageal stent under fluoroscopic guidance. **B.** Percutaneous endoscopic necrosectomy. Author's file.

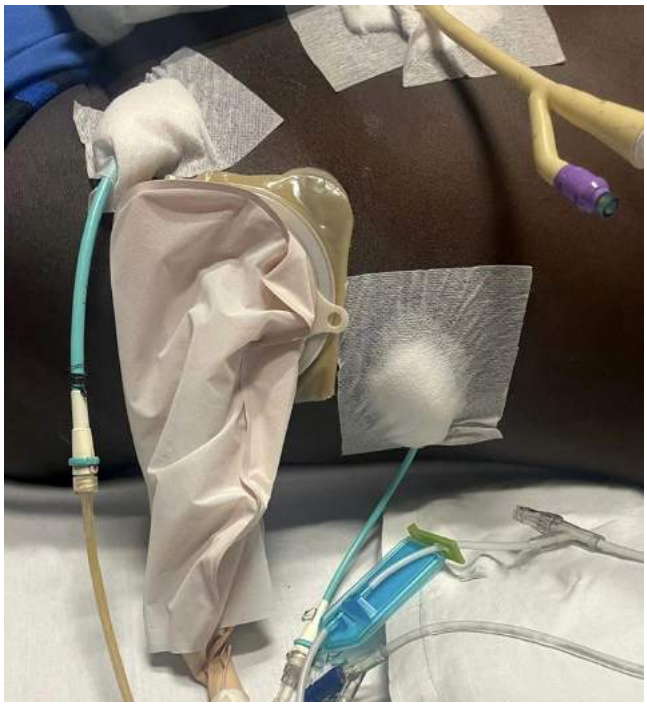


Figure 3. Two pig-tail drains in the left flank, a Foley catheter in the anterior abdominal region, and a working port for percutaneous endoscopic necrosectomy are visible. Author's file.

Timely and effective drainage of infected necrotic tissue is essential for improving outcomes[5]. When there is clinical deterioration or a need for multiple interventions, a follow-up CT scan should be considered for further decision-making[4]. In the presented case, multiple ineffective interventions, undrained collections, and exposure to various antibiotic regimens led to the development of multidrug-resistant bacterial strains, underscoring the importance of effective drainage.

Historically, open surgery with abdominal cavity packing, scheduled laparotomies, and continuous lavage were the standard management approaches, but they carried high mortality rates[2,5]. Over the past two decades, advances in tools and non-invasive techniques have shifted the preference towards minimally invasive approaches for acute necrotizing pancreatitis. The step-up approach has demonstrated better clinical success rates, lower morbidity and mortality, shorter hospital stays, and reduced costs[1,6]. A hybrid approach combining different minimally invasive techniques is also worth considering[7].

The choice of therapeutic modality depends on several factors, including the patient's clinical status, local expertise and resources, anatomical position, content and extent of the collection, timing of presentation, and maturation of

the collection wall. Thus, a single treatment protocol cannot be universally applied[8,9], as each therapeutic modality suits a specific patient group.

In the present case, the transabdominal laparoscopic approach was unsuccessful due to significant inflammatory involvement. As described by De França and colleagues, an alternative is to use laparoscopy as a guide to identify and approach the collection, leaving a working port for the endoscope, and subsequently performing necrosectomy[10].

In the case reported by Lee and colleagues, the patient experienced prolonged hospitalization following initial management with percutaneous drains, without complete resolution of the collections. This led to the decision to perform percutaneous endoscopic necrosectomy, establishing the percutaneous tract under fluoroscopic guidance[11]. In this instance, the fistulous tract was established using a covered esophageal stent.

CONCLUSIONS

A multidisciplinary approach with a step-up strategy, beginning with minimally invasive techniques, is preferred over conventional surgical interventions. Percutaneous endoscopic necrosectomy is a safe and effective procedure, offering lower morbidity and mortality, shorter hospital stays, and reduced costs. It should be considered a viable option in cases of extensive peripancreatic necrosis.

Conflict of Interests

All authors of this manuscript declare no conflict of interest.

Funding Sources

No funding was required for this work.

REFERENCES

1. Goenka MK, Goenka U, Mujoo MdY, Tiwary IK, Mahawar S, Rai VK. Pancreatic Necrosectomy through Sinus Tract Endoscopy. Clin Endosc. 2018;51(3):279-84. https://doi.org/10.5946/ce.2017.066
2. Yang Y, Zhang Y, Wen S, Cui Y. The optimal timing and intervention to reduce mortality for necrotizing pancreatitis: a systematic review and network meta-analysis. World J Emerg Surg. 2023;18(1):9. https://doi.org/10.1186/s13017-023-00479-7
3. Jagielski M, Chwarścianek A, Piątkowski J, Jackowski M. Percutaneous Endoscopic Necrosectomy-A Review of the Literature. J Clin Med. 2022;11(14):3932. https://doi.org/10.3390/jcm11143932
4. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019;14(1):27. https://doi.org/10.1186/s13017-019-0247-0
5. Heckler M, Hackert T, Hu K, Halloran CM, Büchler MW, Neoptolemos JP. Severe acute pancreatitis: surgical indications and treatment. Langenbecks Arch Surg. 2021;406(3):521-35. https://doi.org/10.1007/s00423-020-01944-6
6. Adi J, Dutto C, Victoria R, Torres A, Bussetti B, Gutiérrez M, et al. Necrosectomía endoscópica percutánea en el manejo step-up de walled-off necrosis. Acta Gastroenterol Latinoam. 2020;50(4):459-62. https://doi.org/10.52787/OGFH4481
7. Szakó L, Mátrai P, Hegyi P, Pécsi D, Gyöngyi Z, Csupor D, et al. Endoscopic and surgical drainage for pancreatic fluid collections are better than percutaneous drainage: Meta-analysis. Pancreatology. 2020;20(1):132-41. https://doi.org/10.1016/j.pan.2019.10.006
8. Vyawahare MA, Gulghane S, Titarmare R, Bawankar T, Mudaliar P, Naikwade R, et al. Percutaneous direct endoscopic pancreatic necrosectomy. World J Gastrointest Surg. 2022;14(8):731-42. https://doi.org/10.4240/wjgs.v14.i8.731
9. Xiao NJ, Cui TT, Liu F, Li W. Current status of treatments of pancreatic and peripancreatic collections of acute pancreatitis. World J Gastrointest Surg. 2021;13(7):633-44. https://doi.org/10.4240/wjgs.v13.i7.633
10. de França F, Lopes I, Takada J, Santana N, Antunes R, Kreve F, et al. Necrosectomía endoscópica asistida por laparoscopia: un enfoque efectivo en la necrosis pancreática infectada. Gastroenterol latinoam. 2020;31(3):151-6. https://doi.org/10.46613/gastrolat2020003-05
11. Lee SH, Paik K-H, Kim JC, Park WS. Percutaneous endoscopic necrosectomy in a patient with emphysematous pancreatitis: A case report. Medicine (Baltimore). 2021;100(46):e27905. https://doi.org/10.1097/MD.0000000000027905

https://doi.org/10.22516/25007440.1103

Case report

New Technique for Buried Bumper Syndrome Resolution

Marisol Vázquez-Zeas,[1] Pablo Sempértegui-Cárdenas,[2*] Miurkis Endis-Miranda,[3] Lenin Quezada-Méndez,[4] Mauricio Siavichay-Romero,[5] Faviola Rodríguez-Cárdenas.[6]

OPEN ACCESS

Citation:
Vázquez-Zeas M, Sempértegui-Cárdenas P, Endis-Miranda M, Quezada-Méndez L, Siavichay-Romero M, Rodríguez-Cárdenas F. New Technique for Buried Bumper Syndrome Resolution. Revista. colomb. Gastroenterol. 2024;39(2):199-204. https://doi.org/10.22516/25007440.1103

[1] Physician and Pediatric Specialist. Pediatrician, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[2] Physician, master's in health research, Specialist in Pediatrics, Specialist in Pediatric Gastroenterology and Nutrition. Attending Physician, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[3] Physician, Specialist in Pediatric Surgery. Pediatric Surgeon, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[4] Specialist in Pediatric Surgery, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[5] General Practitioner, Specialist in Pediatric Surgery, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[6] Specialist in Pediatrics, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.

***Correspondence:** Pablo Sempértegui-Cárdenas.
troverospa@gmail.com

Received: 14/07/2023
Accepted: 29/08/2023

Abstract

The buried bumper syndrome (BBS) is a rare complication associated with percutaneous endoscopic gastrostomy (PEG), which undergoes a migration of the internal stop of the tube towards the gastric and abdominal wall and manifests signs of dysfunction of the gastrostomy button. We described three degrees of severity, in which endoscopy is necessary for diagnosis, while treatment depends on the degree of severity. The case of a 4-year-old girl with cerebral palsy who underwent a PEG 1 month earlier and was brought for medical review for a progressive obstruction to the feeding step was presented. An endoscopy was performed in which grade 3 BBS was found 3, which was resolved with an endoscopic technique combined with laparoscopic equipment.

Keywords

Buried bumper syndrome, gastrostomy.

INTRODUCTION

Percutaneous endoscopic gastrostomy is widely used for enteral nutrition in patients who have difficulty feeding orally. Minor complications, which occur in 16.4% to 66.3% of cases, include peristomal infection. Major complications, occurring in 6.1% to 17.5% of cases, include fistula formation and buried bumper syndrome (BBS), which can manifest from weeks to years after the procedure. It is estimated that one in four children will be hospitalized due to complications following PEG placement [1-3].

CLINICAL CASE

A 4-year-old female patient with a history of cerebral palsy and PEG placement one month prior presented with a 24-hour history of feeding difficulties. A thoracoabdominal X-ray confirmed that the tube was in the correct anatomical position (**Figure 1**).

A diagnostic and therapeutic endoscopy was performed under general anesthesia, revealing hemorrhagic mucosal erosions at the junction of the body and gastric antrum over the umbilicated area, with no evidence of the internal



Figure 1. Abdominal X-ray confirming the anatomical position of the tube. Author's file.

bumper of the gastrostomy tube (G-tube), consistent with grade III BBS (**Figure 2**).

Since our institution does not have a modified sphincterotome for BBS (Flamingo Set; Medwork, Hochstadt, Germany) [4] and due to the risks associated with surgical procedures, the following steps were taken under endoscopic guidance:

1. The tube was cut externally, 3 cm from the abdominal wall.
2. A 3 mm laparoscopic grasper forceps (**Figure 3**) was introduced through the tube end to dilate the internal opening.
3. A 5 mm laparoscopic hook forceps (**Figure 4**) was introduced through the channel.
4. The gastric mucosa over the internal bumper area of the gastrostomy was resected radially at the 12, 3, 6, and 9 o'clock positions, with monopolar cauterization (**Figure 5**).
5. The tube was pushed, revealing the internal bumper of the G-tube (**Figure 6**).
6. A biliary guidewire was introduced through the tube.
7. The segment of the G-tube was pushed into the gastric chamber.
8. Using the guidewire, an 18 Fr Mic-Key gastrostomy button was placed.
9. The balloon was inflated, confirming proper placement (**Figure 7**).
10. The internal bumper was removed using a cold polypectomy snare along with the endoscopy equipment, completing the procedure without complications. Feeding was initiated 24 hours later with good tolerance and progress.



Figure 2. Diagnostic endoscopy showing hemorrhagic mucosal erosions at the junction of the body and gastric antrum over the umbilicated area, with no evidence of the internal bumper of the G-tube, consistent with grade III BBS. Author's file.

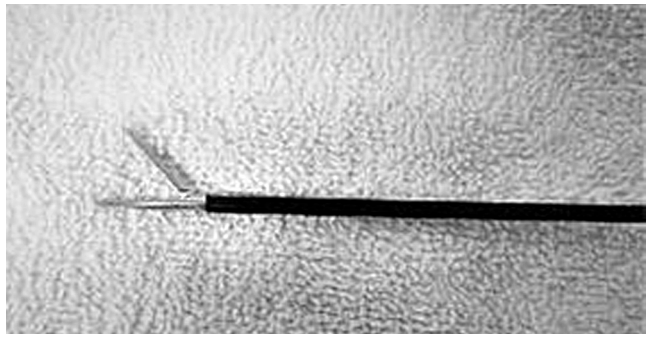


Figure 3. 3 mm laparoscopic grasper forceps. Author's file.

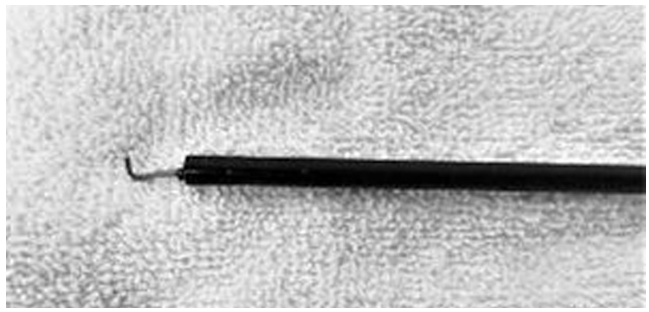


Figure 4. 5 mm laparoscopic hook forceps. Author's file.

DISCUSSION

BBS is a rare complication following PEG, with an incidence of 1.5%. Although it typically occurs later, not before



Figure 5. Radial resection of the gastric mucosa over the internal bumper area of the gastrostomy at the 12, 3, 6, and 9 o'clock positions. Author's file.

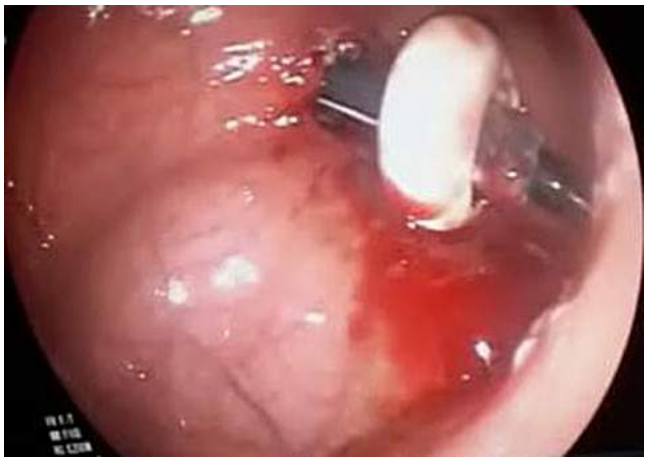


Figure 6. Visualization of the internal bumper of the G-tube after pushing the tube. Author's file.



Figure 7. Inflation of the new balloon confirming proper placement. Author's file.

four months post-procedure, cases have been reported as early as 21 days after PEG placement, similar to the timeframe in our patient[1,2,5].

The internal bumper of the PEG can lodge at any level between the gastric wall and the skin along the initial tract of the G-tube, often due to the external button being too tightly secured to the abdominal wall. This tightness gradually causes the internal bumper to erode the gastric mucosa, leading to the partial or complete migration of the bumper into the gastric wall. This migration results in ischemia, necrosis, and the subsequent formation of granulation tissue, causing the bumper to become embedded in the abdominal wall and completely obstruct the internal lumen of the button. Another mechanism involved is the external traction of the tube, which injures the gastric mucosa [6,7]. Additionally, changes in the physical characteristics of the internal bumper due to gastric secretions can facilitate damage to the gastric tissue and subsequent migration of the bumper[3,5].

The main symptoms are the inability to advance the tube into the gastric lumen, loss of patency, and peristomal leakage[7]. However, this triad is not always present, as the blockage can be intermittent, or there may only be leakage of gastric contents or symptoms of peristomal infection such as edema, erythema, and pain. Difficulty infusing food, requiring increased pressure, or the inability to pass food will present in more advanced stages when the obstruction is complete. In extreme cases, the internal bumper may be palpable under the skin. There may also be a history of significant traction on the gastrostomy button[7,8]. Risk factors include prolonged immobility, traction on the device, lack of preventive maneuvers, and non-cooperative patients or children, which is consistent with the cerebral palsy patient in this case. Regarding the device, important factors include the material, insertion method, the distance between the external button and the skin, and the traction applied during use.

For diagnosis, imaging studies are crucial as they determine the extent of internal bumper migration and the patency of the tract. A computed tomography (CT) scan can reveal a migrated gastrostomy button; with fluoroscopy, if the gastrostomy tract remains open, contrast may reach the gastric cavity, potentially leading to a missed diagnosis. Endoscopic ultrasound (EUS) facilitates locating the internal bumper to determine whether surgical or endoscopic treatment is necessary[4,5]. Panendoscopy is the definitive study to confirm the diagnosis, revealing mucosal ulceration in early stages or granulation tissue covering the internal bumper, with or without a visible residual fistula. It also allows for PEG replacement.

Three degrees of severity have been proposed[9]:

- Grade I: Partial migration Symptoms range from asymptomatic to mild, such as abdominal pain or ostomy infection.
- Grade II: Subtotal migration. Accompanied by tube dysfunction and feeding leakage.
- Grade III: Total migration. Manifests as tube obstruction. Due to the low incidence, treatment is not standardized and depends on the type of device and the depth of internal bumper migration.

In the literature, endoscopy is recommended if the internal bumper is covered by gastric epithelium and has minimally eroded the musculature. A guide or dilator is introduced to push the internal bumper towards the stomach, allowing for standard replacement[2]. If the bumper is completely covered by gastric mucosa, it must be freed with a papillotome and radial cuts to facilitate mobilization and then proceed with the standard replacement. However, if the migration is towards the abdominal wall, a surgical approach is required, either via exploratory laparotomy or laparoscopic surgery[2,6,9]. Costa and colleagues, in a multicenter study, evaluated the safety and effectiveness of a device designed specifically for managing BBS (Flamingo Set; Medwork, Hochstadt, Germany) in a large patient cohort. They reported successful extraction in 96.4% of cases, with a mean procedure time of 22 minutes, an adverse event rate of 12.7% (including bleeding, perforation, gastroesophageal laceration, and sepsis), and an 83% success rate for placing a new device [4]. However, various devices not specifically designed for this purpose have been used successfully, as in the case of our patient, where a combined endoscopic technique with laparoscopic instruments was employed effectively.

To prevent complications following PEG placement, it is crucial to begin at the time of the procedure by correctly positioning the external bumper, leaving at least 1 cm of space from the skin. Once the ostomy has formed and healed, caregivers should be instructed to advance and rotate the tube 360 degrees and ensure the external bumper is correctly positioned (1 cm from the skin). Avoid placing gauze or dressings between the skin and the external bumper, as they increase traction; additionally, ensure that the passage of food is not forced. These care strategies

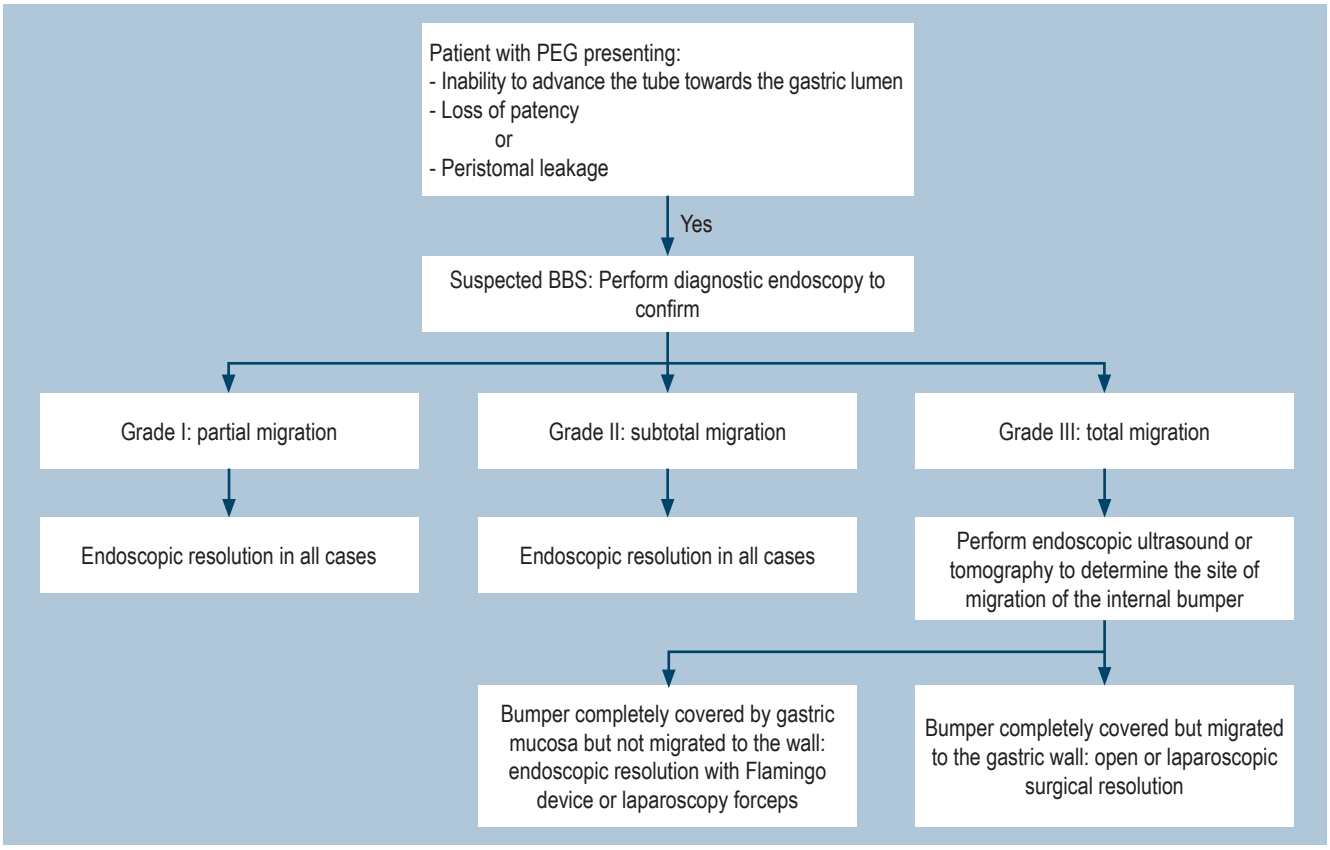


Figure 8. Proposed management algorithm. Author's own research.

are essential to reduce the risk of this syndrome [3,7,10-12]. A proposed management algorithm is outlined based on the established diagnosis (**Figure 8**).

CONCLUSION

PEG is a widely used method for nutritional support, and BBS is a condition that should be suspected when there is difficulty in feeding and local signs of inflammation. Endoscopic management is feasible in most cases, and the use of laparoscopic forceps through the channel is a more accessible alternative in settings where specific instruments for completely releasing the buried internal bumper are not available.

Conflict of Interests

The authors declare no conflict of interest.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

REFERENCES

1. Hansen E, Qvist N, Rasmussen L, Ellebaek MB. Postoperative complications following percutaneous endoscopic gastrostomy are common in children. Acta Paediatr. 2017;106(7):1165-1169. https://doi.org/10.1111/apa.13865
2. Blumenstein I, Shastri YM, Stein J. Gastroenteric tube feeding: techniques, problems and solutions. World J Gastroenterol. 2014;20(26):8505-24. https://doi.org/10.3748/wjg.v20.i26.8505
3. Furlano RI, Sidler M, Haack H. The push-pull T technique: an easy and safe procedure in children with the buried bumper syndrome. Nutr Clin Pract. 2008;23(6):655-7. https://doi.org/10.1177/0884533608326229
4. Costa D, Despott EJ, Lazaridis N, Woodward J, Kohout P, Rath T, et al. Multicenter cohort study of patients with buried bumper syndrome treated endoscopically with a novel, dedicated device. Gastrointest Endosc. 2021;93(6):1325-1332. https://doi.org/10.1016/j.gie.2020.11.009
5. Anagnostopoulos GK, Kostopoulos P, Arvanitidis DM. Buried bumper syndrome with a fatal outcome, presenting early as gastrointestinal bleeding after percutaneous endoscopic gastrostomy placement. J Postgrad Med. 2003;49(4):325-7.
6. Huynh G, Chan M, Huynh H. Buried bumper syndrome. Videogie. 2019;5(3):104-106.
7. Chimal-Juárez MF, Morales-Chávez CE, Rodríguez-Reséndiz MP. Síndrome del botón enterrado: caso clínico de complicación por gastrostomía endoscópica. Rev Mex Cir Endoscop. 2021;22(3-4):139-144. https://doi.org/10.35366/106478
8. Menni A, Tzikos G, Chatziantoniou G, Gionga P, Papavramidis TS, Shrewsbury A, et al. Buried bumper syndrome: A critical analysis of endoscopic release techniques. World J Gastrointest Endosc. 2023;15(2):44-55. https://doi.org/10.4253/wjge.v15.i2.44
9. Orsi P, Spaggiari C, Pinazzi O, Di Mario F. Is the Buried bumper syndrome a buried problem? Personal experience about a different therapeutic approach and prevention possibilities. Riv. ital. nutr. parenter. enter. 2002;20(3):124-31.
10. Bathobakae L, Leone C, Elagami MM, Shah H, Baddoura W. Acute Buried Bumper Syndrome: A Case Report. Cureus. 2023;15(3):e36289. https://doi.org/10.7759/cureus.36289
11. Rajan A, Wangrattanapranee P, Kessler J, Kidambi TD, Tabibian JH. Gastrostomy tubes: Fundamentals, periprocedural considerations, and best practices. World J Gastrointest Surg. 2022;14(4):286-303. https://doi.org/10.4240/wjgs.v14.i4.286
12. Satiya J, Marcus A. The Buried Bumper Syndrome: A Catastrophic Complication of Percutaneous Endoscopic Gastrostomy. Cureus. 2019;11(3):e4330. https://doi.org/10.7759/cureus.4330

https://doi.org/10.22516/25007440.1088

Case report

Gastric Polyposis in Familial Adenomatous Polyposis: A Case Report. An Approach for the Endoscopist

Maykel Alain Padilla-Ruiz,[1]* Gustavo Ariza-Cotes.[2]

OPEN ACCESS

Citation:
Padilla-Ruiz MA, Ariza-Cotes G. Gastric Polyposis in Familial Adenomatous Polyposis: A Case Report. An Approach for the Endoscopist. Revista. colomb. Gastroenterol. 2024;39(2):205-210.
https://doi.org/10.22516/25007440.1088

[1] Department of Gastroenterology, Hospital Comunitario Dr. Valentín Gómez Farías. Coatzacoalcos, Mexico.
[2] Clínica de Especialidades Digestivas Gastrocentro. Coatzacoalcos, Mexico.

***Correspondence:** Maykel Alain Padilla-Ruiz.
padillagastrohepatologia@gmail.com

Received: 11/06/2023
Accepted: 17/07/2023

Abstract

Familial adenomatous polyposis (FAP) is an autosomal dominant inheritance syndrome. Although the main manifestation of this disease is the presence of numerous colon adenomas, upper gastrointestinal tract involvement also occurs. A report of a young patient with gastric polyposis (more than 100 polyps) was presented. There was a brief updated review of the topic focused on endoscopic findings, including updated suggestions on gastric polyps in FAP management and monitoring.

Keywords

Adenomatous polyposis coli, gastric cancer, endoscopy digestive system.

CASE PRESENTATION

A 28-year-old female patient with a history of familial adenomatous polyposis (FAP) underwent a total proctocolectomy and creation of an ileal pouch six years ago. Biopsy confirmed the presence of adenocarcinoma, necessitating ongoing monitoring with reservoiroscopies. She also has a history of papillary thyroid carcinoma, which was surgically treated four years ago. In April 2023, an upper gastrointestinal endoscopy (UGIE) was performed.

The UGIE revealed no endoscopic alterations in the duodenum, the region corresponding to the papilla, the antropyloric region, and the angular zone. However, in the mid and upper zones of the gastric body and fundus, multiple polyps (more than 100), each smaller than 5 mm were observed. These polyps were scattered, some forming clusters, with mucosa similar to the surrounding area. Multiple biopsies were taken.

The biopsies indicated the presence of a fundic gland polyp, moderate chronic gastritis, follicular, with mild activity; these findings are consistent with *Helicobacter pylori*. There was no evidence of atrophy, metaplasia, or dysplasia. The result was negative for malignant cells (**Figure 1A-C**).

DISCUSSION AND LITERATURE REVIEW

FAP is an autosomal dominant hereditary syndrome caused by a mutation in the APC gene located on chromosome 5q21. While the primary manifestation of this disease is the presence of numerous colon adenomas, the upper gastroin-

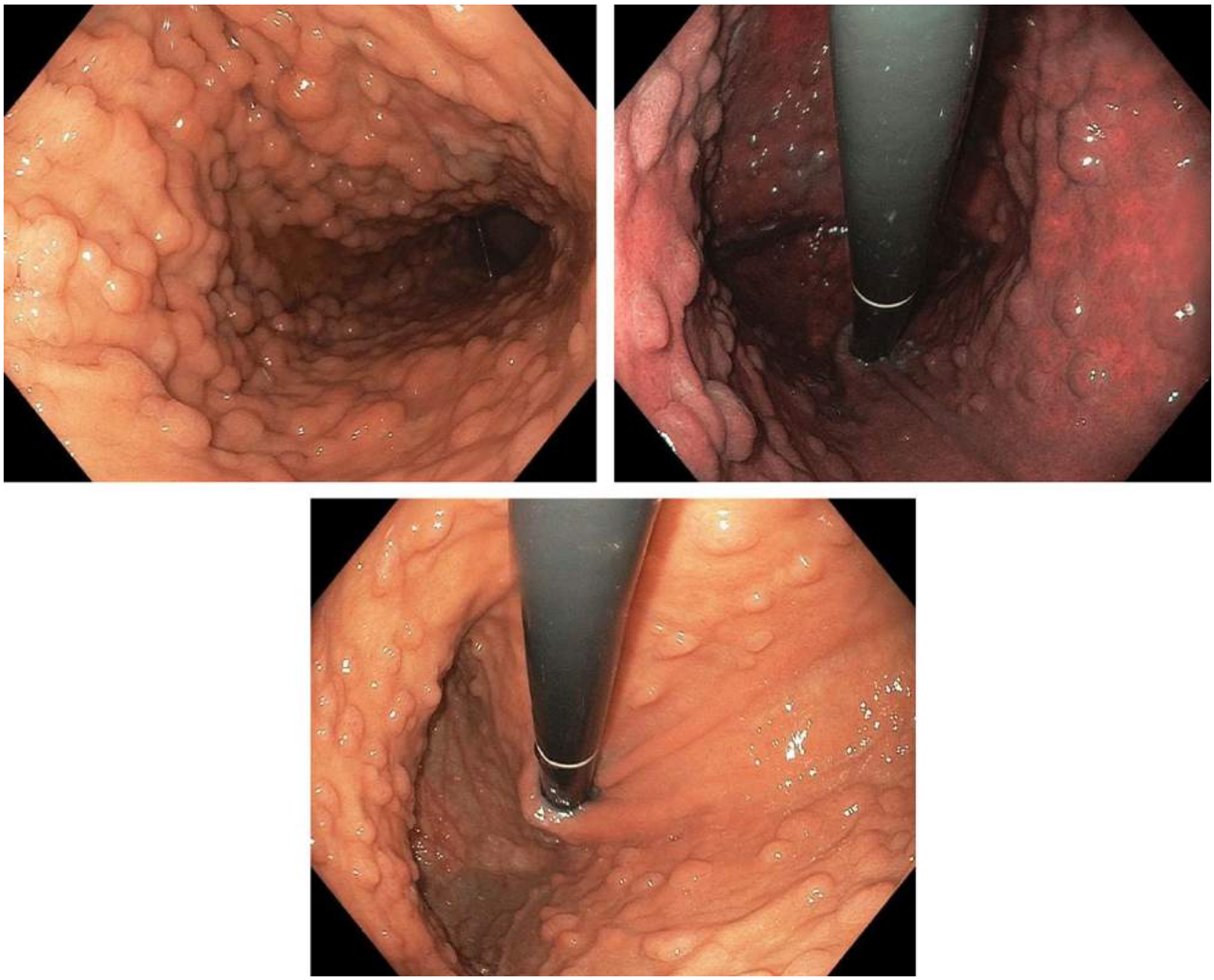


Figure 1. Upper gastrointestinal endoscopy showing extensive diffuse gastric polyposis. Author's file.

testinal tract can also be affected. Patients with FAP have a significant risk of extracolonic malignancies, primarily in the duodenum, but also an increased risk of stomach cancer. Up to 20% to 30% of FAP cases are *de novo*, arising from a new pathogenic variant in APC, and therefore, may lack a family history of FAP[1].

Endoscopic surveillance of the colon and prophylactic colectomy have significantly decreased colorectal cancer mortality and improved the survival of patients with FAP, resulting in a greater need for surveillance of extracolonic malignancies. Endoscopic surveillance in FAP patients is a safe and effective method for diagnosing precancerous lesions, allowing for the treatment of most benign lesions and early-stage cancers. However, surveillance recommendations for the digestive tract are not fully defined.

The initial recommendations for gastric polyp surveillance were based on the Spigelman classification, which in 1989 described a staging system for duodenal polyps to stratify the risk of duodenal cancer in FAP[2].

GASTRIC LESIONS IN FAP

Most patients with FAP develop gastric polyposis and have a higher risk of gastric cancer compared to the general population. According to the National Comprehensive Cancer Network (NCCN) Guidelines Report "Genetic/Familial High-Risk Assessment: Colorectal, Version 1.2022", the estimated lifetime risk of gastric cancer in patients with a hereditary disease with APC mutation is 0.1% to 7.1% compared to 0.8% in the general population,

with the average onset between 52 and 57 years. Cannon and colleagues, in their publication based on data from the U.S. polyposis registry, identify gastric cancer as the leading cause of death in patients with FAP and attenuated FAP (AFAP) after duodenal and ampullary cancers[3,4].

Screening procedures with the removal of suspicious lesions can prevent the vast majority of carcinomas in these patients. Gastric lesions are common in adult patients with FAP; therefore, recognizing the different types of polyps, their early detection, and performing biopsies or removing them are very important in preventing gastric cancer in these patients.

Types of Gastric Polyps in Patients with FAP

These types include fundic gland polyps, gastric foveolar-type adenomas, gastric intestinal-type adenomas, pyloric gland adenomas, hyperplastic polyps, and gastric adenocarcinomas.

Fundic Gland Polyps (FGPs)

FGPs are the most common type of polyps, observed in 40% to 88% of patients with FAP[5,6]. Typically small (< 5 mm), sessile, multiple, and asymptomatic, FGPs are confined to the stomach. FGPs associated with FAP differ from sporadic FGPs, showing a more balanced sex distribution. They often exhibit low-grade dysplasia, although they are not considered precursor lesions for most gastric adenocarcinomas in FAP. There is no established causal link between *H. pylori* and FAP-associated FGPs[5].

Adenomas can appear anywhere in the stomach but are more frequently found in the antrum. They are less common than FGPs in patients with FAP. Antral adenomas are typically flat, sessile, and subtle with a red villiform appearance, whereas those in the gastric body and fundus are more polypoid with a pale yellow surface, making them difficult to differentiate from FGPs.

In patients with FAP, endoscopists should maintain a high degree of suspicion for detecting gastric adenomas and take multiple biopsies. Virtual endoscopy techniques can be useful for detecting these lesions, especially flat ones and subtle mucosal changes. The use of Fujinon Intelligent Chromo Endoscopy (FICE) technology can identify dysplasia and differentiate between adenomatous and non-adenomatous polyps, significantly increasing the detection of adenomas in FAP patients. This can be extrapolated to virtual endoscopy techniques like NBI (Olympus) or iScan (Pentax)[6].

Adenomas located in the antrum of the stomach should be removed via endoscopic submucosal dissection (ESD) or endoscopic mucosal resection (EMR) when there is a high degree of suspicion during esophagogastroduodenoscopy (EGD)[3].

Pyloric Gland Adenomas (PGA)

Pyloric gland adenomas are rare epithelial polyps more frequently found in patients with autoimmune atrophic gastritis and FAP. They are most commonly located in the gastric body and predominantly occur in women. PGAs are clinically significant due to their malignant potential, unlike hyperplasia of metaplastic glands. In some cases, high-grade dysplasia is observed, and invasive carcinoma is associated with 12% to 42% of these lesions[7].

As with other types of adenomas, complete excision of PGAs with biopsy of the surrounding flat mucosa is appropriate in patients with FAP, as PGAs often arise in the context of chronic lesions.

Hyperplastic Gastric Polyps

These polyps are most prevalent in regions with a high incidence of *H. pylori* infection. In contrast, in Western countries, where *H. pylori* prevalence is lower and proton pump inhibitor (PPI) use is common, fundic gland polyps are more frequent. The British Society of Gastroenterology (BSG) guidelines suggest that hyperplastic polyps larger than 1 cm, pedunculated polyps, and those causing symptoms (obstruction, bleeding) should be resected. If *H. pylori* is present, it should be eradicated before re-evaluation. The guidelines also recommend that if adenomas or hyperplastic polyps are present, the fundic mucosa should be endoscopically evaluated for gastric atrophy, intestinal metaplasia, *H. pylori*, and synchronous neoplasia[8].

Inflammatory Fibroid Polyps

These are rare lesions, representing less than 0.1% of all gastric polyps. After resection, inflammatory fibroid polyps generally do not recur, and surveillance is not recommended[9].

Gastric Adenocarcinoma

Gastric adenocarcinoma develops from an adenoma and can occur anywhere in the stomach, potentially being multicentric and metachronous. Studies have shown that gastric cancer tends to appear around two decades after colectomy in FAP patients[10].

Endoscopically, three features are most frequently observed in individuals with gastric cancer and FAP: solitary gastric polyps ≥ 2 cm, a carpet of proximal gastric polyps, and polypoid mounds within a proximal carpet. Another high-risk gastric lesion in FAP is the presence of white gastric plaques, which may reflect underlying adenomatous mucosa and likely indicate a higher risk of gastric cancer[11-13].

In its 2020 guidelines on the role of endoscopy in FAP, the American Society for Gastrointestinal Endoscopy (ASGE) recommends surveillance every three to six months with random biopsies of polyps and endoscopic resection of polyps > 10 mm, particularly in cases of diffuse gastric

polyposis and large clusters of polyps. The ASGE also recommends the endoscopic removal of all polyps located in the antrum due to the high likelihood of adenomas[5,9].

The 2015 ASGE guidelines on the role of endoscopy in managing premalignant and malignant conditions of the stomach state that sampling gastric polyps with forceps may not reveal dysplastic components. These guidelines recommend complete polypectomy with a snare based on size: fundic polyps > 10 mm, hyperplastic polyps > 5 mm, and all adenomatous polyps. According to the ASGE, surgery should be reserved for patients with FGPs and adenomas harboring advanced histological features that fail endoscopic management. Additionally, they note that mucosal biopsy sampling may not be adequate for assessing malignancy within layers of carpeted polyposis or polypoid mounds and suggest that endoscopic ultrasound (EUS) may help evaluate underlying malignancy[5].

It is crucial to address the extracolonic manifestations of FAP as part of a comprehensive healthcare plan due to the associated risks of duodenal/ampullary, thyroid, and gastric cancer[14].

SURVEILLANCE

The current surveillance guidelines for the upper digestive tract from the American College of Gastroenterology (ACG) and the BSG/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/UK Cancer Genetics Group, published in 2015 and 2020 respectively, strongly recommend initiating upper digestive tract surveillance between the ages of 25 and 30, with intervals every 0.5 to 4 years based on the Spigelman classification of duodenal polyposis. The NCCN guidelines recommend starting upper gastrointestinal endoscopy slightly earlier, between the ages of 20 and 25, due to concerns about the morbidity and mortality associated with duodenal/periampullary cancers in FAP. Gastrectomy may be considered if high-risk lesions cannot be removed endoscopically; ideally, these procedures should be performed in a specialized center experienced in managing FAP and should take patient-specific factors into account.

Additionally, if a patient with FAP needs to undergo a colectomy at an age younger than that recommended for starting upper gastrointestinal tract surveillance, an initial upper gastrointestinal endoscopy should be performed to rule out gastric neoplasia before the colectomy[8,14,15].

Since the introduction of genetic testing and prophylactic colectomy in FAP, the incidence and mortality from colorectal cancer have decreased, and the detection of extracolonic cancer is recommended[2,3].

Current EGD surveillance recommendations do not consider gastric polyposis but are determined by the duodenal stage of polyposis. It is suggested that EGD surveillance intervals should reflect the emerging risk of gastric cancer.

Mankaney and colleagues identified several endoscopic factors in FAP patients who developed gastric adenocarcinoma. As Bianchi suggests, gastric surveillance should include multiple random biopsies of polyps, targeted biopsy of unusually appearing proximal polyps, and snare resection of individual polyps > 10 mm or lesions in the antrum. The severity of gastric polyposis should be based on the size, number, and pathology of gastric polyps. A surveillance interval of three years is recommended for patients with few to numerous small FGPs or FGPs with foveolar low-grade dysplasia (LGD).

In the presence of a proximal gastric polyposis carpet, an EGD should be performed at an interval of one year, and more frequently depending on the size of solitary polyps, the presence of polypoid mounds, and the histology of the polyps. For patients with proximal gastric polyposis mounds, initial EUS with fine-needle aspiration (FNA) of suspicious lesions and endoscopic reduction of the polypoid mounds should be conducted, with follow-up every three to six months based on the pathology. A baseline magnetic resonance imaging or CT scan is recommended to check for metastatic disease when polypoid masses are found, due to the frequent occurrence of metastatic disease. If any pathology sample indicates high-grade dysplasia (HGD), gastrectomy should be recommended (**Table 1**).

Patients with numerous proximal polyposis or carpet without polypoid mounds and with FGP-HGD, PGA-HGD, or TA-HGD should be reviewed every three months or offered prophylactic gastrectomy. Any patient with intramucosal carcinoma or invasive cancer should undergo gastrectomy[9].

The last-mentioned work is an effort to standardize the follow-up of gastric lesions in patients with FAP. However, to date, there are no recommendations from international societies on this matter, so each case must still be individually analyzed, and studies with higher-quality evidence are needed to establish accurate follow-up guidelines.

CONCLUSIONS

More research is needed to identify the causes and determine the optimal approach for the early detection of gastric cancer in FAP. Research on the genetics and environmental associations of gastric cancer in the context of FAP will help advance the prevention of this deadly cancer.

Table 1. Follow-up of Gastric Adenomas in FAP

Number of Polyps, Size, and Presence of Mound Polyps	Histology	Follow-Up Strategy
Multiple, < 10 mm	FGP with or without foveolar LGD	EGD according to Spigelman if duodenal polyp or every 3 years
Multiple or carpet, < 10 mm	PGA or TA	Every year
Multiple or carpet, > 10 mm	FGP with or without foveolar LGD, PGA, or TA	Every 6 to 12 months
Multiple of any size without mound formation	FGP with HGD, PGA with HGD, or TA with HGD	Every 3 to 6 months or offer gastrectomy
Proximal polyp mounds	FGP with or without foveolar LGD, PGA, or TA	Every 3 to 6 months, EUS. Consider CT scan or MRI of the abdomen
Proximal polyp mounds	FGP with HGD, PGA with HGD, or TA with HGD	Prophylactic gastrectomy
Any size or number	Intramucosal or invasive adenocarcinoma	Gastrectomy

PGA: pyloric gland adenomas; TA: tubular adenoma; HGD: high-grade dysplasia; LGD: low-grade dysplasia; EUS: endoscopic ultrasound; MRI: magnetic resonance imaging; CT: computed tomography. Taken from Mankaney GN and colleagues; Endosc Int Open. 2022;10(08):E1080-E7[9].

REFERENCES

1. Paszkowski J, Samborski P, Kucharski M, Cwalinski J, Banasiewicz T, Plawski A. Endoscopic Surveillance and Treatment of Upper GI Tract Lesions in Patients with Familial Adenomatous Polyposis-A New Perspective on an Old Disease. Genes (Basel). 2022;13(12):2329. https://doi.org/10.3390/genes13122329
2. Spigelman AD, Williams CB, Talbot IC, Domizio P, Phillips RK. Upper gastrointestinal cancer in patients with familial adenomatous polyposis. Lancet. 1989;2(8666):783-5. https://doi.org/10.1016/S0140-6736(89)90840-4
3. Campos FG, Martinez CAR, Sulbaran M, Bustamante-Lopez LA, Safatle-Ribeiro AV. Upper gastrointestinal neoplasia in familial adenomatous polyposis: prevalence, endoscopic features and management. J Gastrointest Oncol. 2019;10(4):734-44. https://doi.org/10.21037%2Fjgo.2019.03.06
4. Cannon AR, Keener M, Neklason D, Pickron TB. Surgical Interventions, Malignancies, and Causes of Death in a FAP Patient Registry. J Gastrointest Surg. 2021;25(2):452-6. https://doi.org/10.1007/s11605-019-04412-9
5. Yang J, Gurudu SR, Koptiuch C, Agrawal D, Buxbaum JL, Abbas Fehmi SM, et al. American Society for Gastrointestinal Endoscopy guideline on the role of endoscopy in familial adenomatous polyposis syndromes. Gastrointest Endosc. 2020;91(5):963-82e2. https://doi.org/10.1016/j.gie.2020.01.028
6. Lami G, Galli A, Macri G, Dabizzi E, Biagini MR, Tarocchi M, et al. Gastric and duodenal polyps in familial adenomatous polyposis patients: Conventional endoscopy vs virtual chromoendoscopy (fujinon intelligent color enhancement) in dysplasia evaluation. World J Clin Oncol. 2017;8(2):168-77. https://doi.org/10.5306%2Fwjco.v8.i2.168
7. Wood LD, Salaria SN, Cruise MW, Giardiello FM, Montgomery EA. Upper GI tract lesions in familial adenomatous polyposis (FAP): enrichment of pyloric gland adenomas and other gastric and duodenal neoplasms. Am J Surg Pathol. 2014;38(3):389-93. https://doi.org/10.1097/pas.0000000000000146
8. Banks M, Graham D, Jansen M, Gotoda T, Coda S, Pietro MD, et al. British Society of Gastroenterology guidelines on the diagnosis and management of patients at risk of gastric adenocarcinoma. Gut. 2019;68(9):1545-75. https://doi.org/10.1136/gutjnl-2018-318126
9. Mankaney GN, Cruise M, Sarvepalli S, Bhatt A, Liska D, Burke CA. Identifying factors associated with detection of sessile gastric polyps in patients with familial adenomatous polyposis. Endosc Int Open. 2022;10(08):E1080-E7. https://doi.org/10.1055/a-1839-5185
10. Shibata C, Ogawa H, Miura K, Naitoh T, Yamauchi J-i, Unno M. Clinical Characteristics of Gastric Cancer in Patients with Familial Adenomatous Polyposis. Tohoku J Exp Med. 2013;229(2):143-6. https://doi.org/10.1620/tjem.229.143
11. Leone PJ, Mankaney G, Sarvapelli S, Abushamma S, Lopez R, Cruise M, et al. Endoscopic and histologic features associated with gastric cancer in familial adenomatous polyposis. Gastrointest Endosc. 2019;89(5):961-8. https://doi.org/10.1016/j.gie.2018.12.018

12. Calavas L, Rivory J, Hervieu V, Saurin JC, Pioche M. Macroscopically visible flat dysplasia in the fundus of 3 patients with familial adenomatous polyposis. Gastrointest Endosc. 2017;85(3):679-80. https://doi.org/10.1016/j.gie.2016.03.1499
13. Kunnathu ND, Mankaney GN, Leone PJ, Cruise MW, Church JM, Bhatt A, et al. Worrisome endoscopic feature in the stomach of patients with familial adenomatous polyposis: the proximal white mucosal patch. Gastrointest Endosc. 2018;88(3):569-70. https://doi.org/10.1016/j.gie.2018.04.010
14. Gupta S, Provenzale D, Regenbogen SE, Hampel H, Slavin TP, Hall MJ, et al. NCCN Guidelines Insights: Genetic/Familial High-Risk Assessment: Colorectal, Version 3.2017. J Natl Compr Canc Netw. 2017;15(12):1465-75. https://doi.org/10.6004/jnccn.2017.0176
15. Monahan KJ, Bradshaw N, Dolwani S, Desouza B, Dunlop MG, East JE, et al. Guidelines for the management of hereditary colorectal cancer from the British Society of Gastroenterology (BSG)/Association of Coloproctology of Great Britain and Ireland (ACPGBI)/United Kingdom Cancer Genetics Group (UKCGG). Gut. 2020;69(3):411-44. https://doi.org/10.1136/gutjnl-2019-319915

https://doi.org/10.22516/25007440.1084

Case report

Spontaneous Pneumoperitoneum: A Pathology Not Always Surgical. Presentation of Two Documented Cases in Patients in Association with SARS-CoV-2 Infection

Gustavo Aguirre,[1]* Cristian Torres,[2] Nicolás Arredondo,[2] Andrés Falla.[3]

OPEN ACCESS

Citation:
Aguirre G, Torres C, Arredondo N, Falla A. Spontaneous Pneumoperitoneum: A Pathology Not Always Surgical. Presentation of Two Documented Cases in Patients in Association with SARS-CoV-2 Infection. Revista. colomb. Gastroenterol. 2024;39(2):211-218. https://doi.org/10.22516/25007440.1084

[1] General Surgeon, General Surgery Service, Hospital Militar Central. Specialist in Gastrointestinal Surgery and Digestive Endoscopy, Instituto Nacional de Cancerología. Bogotá, Colombia.
[2] General Surgery Resident, Universidad Militar Nueva Granada, Hospital Militar Central. Bogotá, Colombia.
[3] General Surgeon, General Surgery Service, Hospital Militar Central. Bogotá, Colombia.

***Correspondence:** Gustavo Aguirre.
gustavoaguiber@gmail.com

Received: 23/05/2023
Accepted: 21/07/2023

Abstract

The finding of pneumoperitoneum has traditionally been a surgical emergency–indicative of gastrointestinal tract disruption requiring immediate surgical exploration; however, there are conditions involving non-surgical management. There were two cases of pneumoperitoneum in association with viral pneumonia (severe acute respiratory syndrome type 2 coronavirus [SARSCoV-2]) without a history of intestinal pneumatosis or another risk factor for spontaneous pneumoperitoneum that obtained a favorable outcome without surgical intervention. This is the second report of concurrent pneumoperitoneum and coronavirus disease of 2019 (COVID-19) in the literature. A brief review of this relationship and more recent data between pneumoperitoneum and the pathophysiological mechanism of SARS-CoV-2 was also included. This paper seeks to expand knowledge with these two cases to rethink, in part, the surgical dogma of pneumoperitoneum management and to lead the reader further from the pathophysiology point of view.

Keywords

Pneumoperitoneum, non-surgical, COVID-19, SARS-CoV-2, viral pneumonia, pneumatosis cystoides intestinalis.

INTRODUCTION

The SARS-CoV-2 infection has introduced new challenges for medical personnel, prompting the global community to unify efforts to mitigate the damage caused by this virus and to establish definitive guidelines for managing a relatively new disease (COVID-19), which primarily affects the respiratory system and occasionally exhibits gastrointestinal involvement[(1)].

While most causes of pneumoperitoneum are of surgical origin, there exists a subset known as *spontaneous pneumoperitoneum,* where it has been shown that conservative management can avoid the additional morbidity associated with surgical procedures, anesthetic risks, and increased hospital costs[(2)].

Here, we present two cases of patients who were admitted to the emergency department of Hospital Militar Central in Bogotá: a woman and a man with confirmed SARS-CoV-2 infection.

CASE PRESENTATION

Case 1

An 84-year-old patient with a history of Alzheimer's disease, oxygen-dependent chronic obstructive pulmonary disease (COPD), degenerative osteoarthritis, cholecystectomy four years ago, and right hip osteosynthesis 45 days prior, presented to the emergency department with a 2-day history of drowsiness associated with irritative urinary symptoms, hematuria, and foul-smelling urine. The patient reported occasional cough, denied abdominal pain, and had regular bowel movements. Upon admission, laboratory tests, a chest X-ray, and computed tomography urography (uro-CT) were requested, and the patient was placed in the observation room.

The complete blood count showed no leukocytosis or neutrophilia, mild anemia, normal renal function and arterial blood gases, hyponatremia of 128 mmol/L, and mildly elevated C-reactive protein at 5.4 mg/dL. The urinalysis suggested infection, with subsequent growth of *Enterococcus faecalis* in the urine culture. The chest X-ray (**Figure 1**) revealed diffuse thickening of the central and peripheral interstitium, predominantly on the right side, with patchy areas of ground-glass opacity superimposed on an interstitial pattern, as well as pneumoperitoneum. The uro-CT (**Figure 2**) showed thickening of the bladder walls without other findings in the urinary tract, and evidence of pneumoperitoneum without identifiable lesions, free fluid, or inflammatory processes.

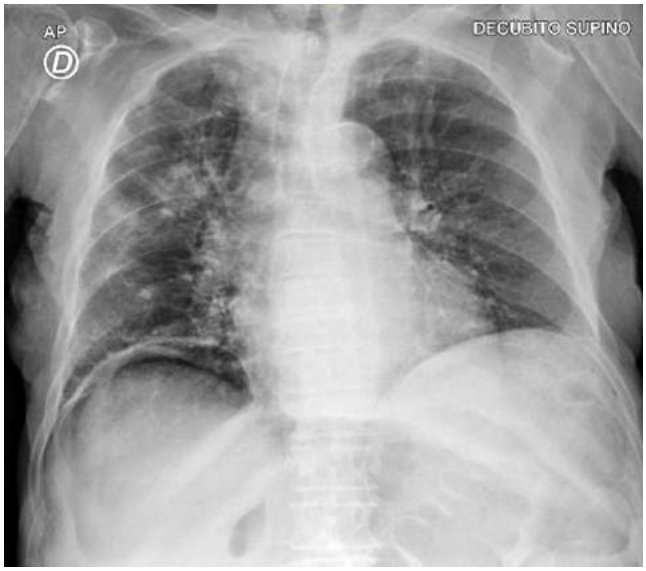


Figure 1. Case 1. Pneumoperitoneum on chest X-ray. Author's file.

Due to the imaging findings, the patient was transferred to the COVID isolation area where a polymerase chain reaction (PCR) test was performed, resulting positive for SARS-CoV-2 infection. Consequently, a consultation with the general surgery service was requested due to the presence of pneumoperitoneum.

The patient, bedridden, was assessed using the Barthel index, which scored 40/100. She experienced coughing fits, was asymptomatic gastrointestinally, had a distended and soft abdomen without pain, and showed no signs of peritoneal irritation. However, due to the pneumoperitoneum found in the uro-CT, an abdominal CT with double contrast was requested (**Figure 3**). This scan revealed bladder wall thickening related to her urinary tract infection, significant pneumoperitoneum, no inflammatory processes or free fluid, and air bubbles in the intestinal walls compatible with pneumatosis cystoides intestinalis. These findings were not present in a contrast-enhanced abdominal CT performed seven months earlier during an acute diarrheal disease study.

The patient was managed expectantly, tolerated oral intake, had regular bowel movements, and never reported abdominal pain. She was administered ampicillin-sulbactam antibiotic therapy for seven days to treat her urinary tract infection, which resulted in an adequate clinical response and improvement in delirium. Follow-up tests showed no leukocytosis or neutrophilia, but correction of her hyponatremia, decreasing C-reactive protein levels, and renal function and electrolytes within normal limits. After 13 days, the patient was discharged with instructions for outpatient follow-up, warning signs, and home oxygen therapy.

Case 2

A 25-year-old patient with a history of inguinal herniorrhaphy, appendectomy, and left lower limb amputation due to a fragmentation weapon injury, presented to the emergency department with a six-day history of dry cough, clear rhinorrhea, fever, and liquid stools. This was followed by left flank pain radiating to the ipsilateral lumbar region. The patient was admitted to the COVID observation area, and laboratory tests and a uro-CT were ordered due to suspicion of urolithiasis.

The complete blood count showed leukopenia of 3340 cells/mm^3 without neutrophilia, positive C-reactive protein, arterial blood gases with acid-base balance, and slightly elevated lactate at 1.9. The PCR test was positive for SARS-CoV-2 infection. The chest CT scan (**Figure 4**) showed typical findings of COVID-19 pneumonia, and the uro-CT scan (**Figure 5**) revealed punctate nephrolithiasis



Figure 2. Case 1. Falciform ligament sign. Author's file.

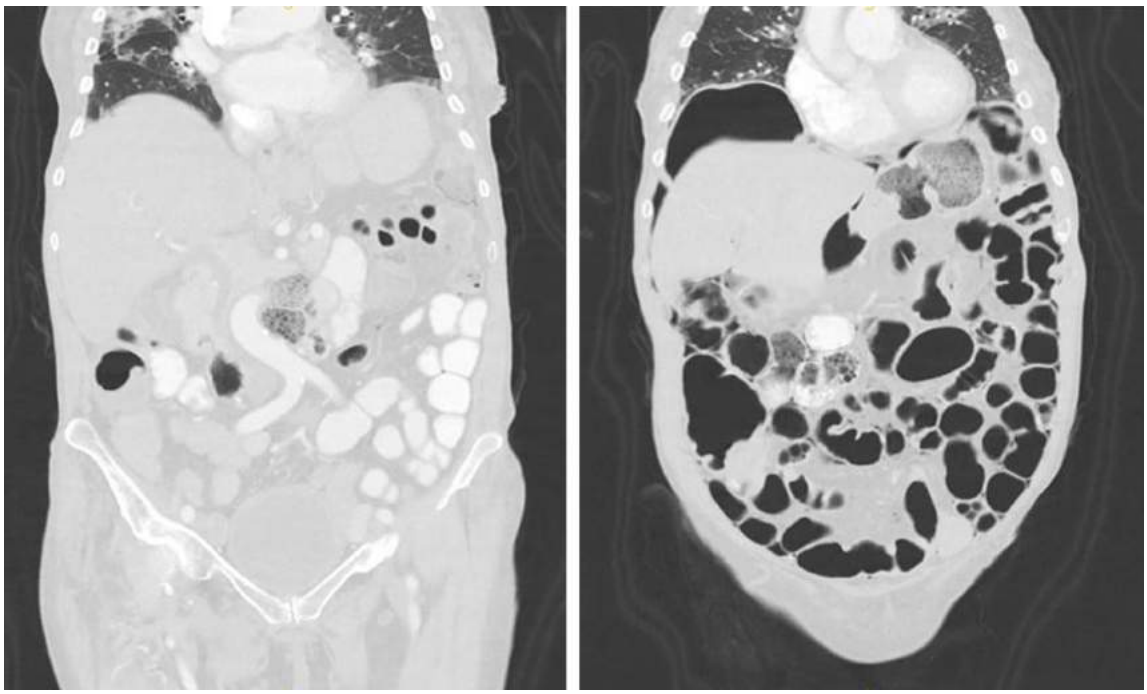


Figure 3. Case 1. Gas bubbles in the intestinal wall. Author's file.



Figure 4. Case 2. Free air bubbles in the left hypochondrium. Author's file.

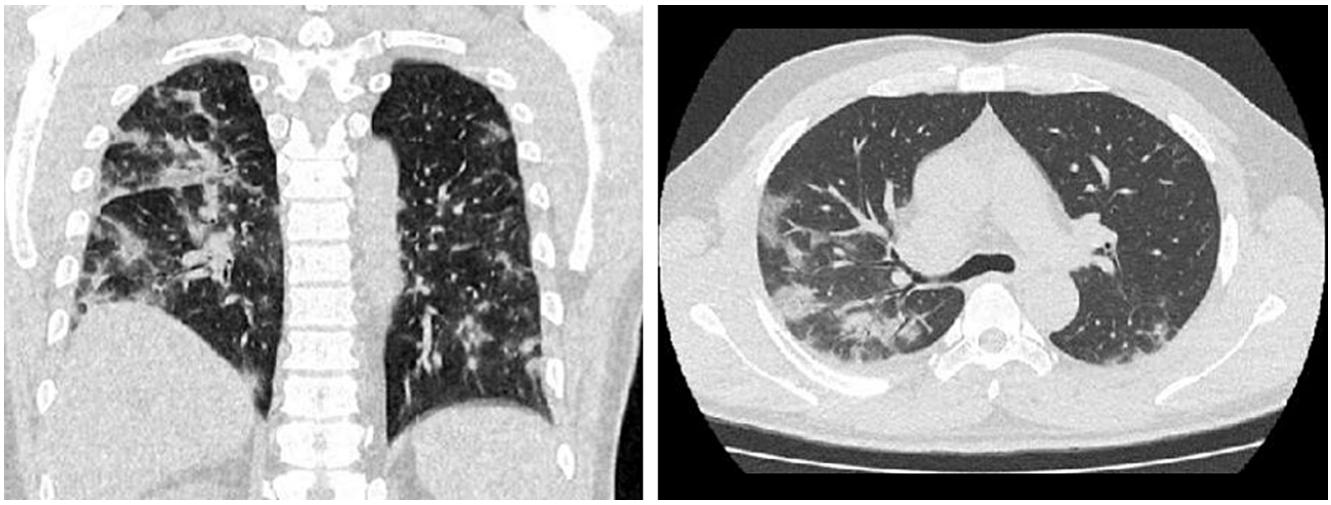


Figure 5. Case 2. Changes in lung parenchyma due to COVID-19. Author's file.

on the right side without obstructive effect and pneumoperitoneum adjacent to the splenic flexure of the colon, prompting a consultation with the general surgery service.

In the clinical evaluation, the patient was clinically stable, with occasional cough, using supplemental oxygen, without tachycardia, and had a soft abdomen with no peritoneal irritation. The double-contrast abdominal CT scan (**Figure 6**) showed pneumoperitoneum bubbles in the left hypochondrium without inflammatory changes, leading to expectant management. The patient tolerated oral

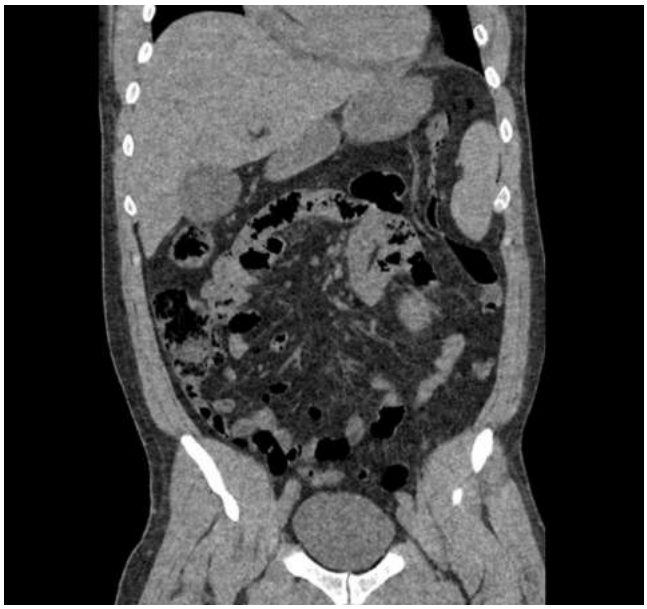


Figure 6. Case 2. Air bubbles in the colonic wall. Author's file.

intake well and showed improvement in pain and resolution of liquid stools. Seventy-two hours after admission, the patient experienced resolution of respiratory and gastrointestinal symptoms and was discharged with warning signs and outpatient follow-up.

DISCUSSION

SARS-CoV-2 infection was first identified in December 2019 in Wuhan, Hubei province, China. Initially referred to as the novel coronavirus, the International Committee on Taxonomy of Viruses officially named it SARS-CoV-2, while the World Health Organization (WHO) designated the disease caused by the virus as COVID-19[1].

It is believed that the virus originated in bats and subsequently transmitted to humans through other animal hosts, exhibiting a high rate of transmissibility. The outbreak was declared a pandemic in March 2020[1].

SARS-CoV-2 primarily spreads through the respiratory tract via droplets, respiratory secretions, and direct contact. However, the virus has also been isolated from fecal and blood samples, suggesting multiple routes of transmission[1]. The primary symptoms are respiratory, ranging from mild flu-like symptoms to acute respiratory distress syndrome (ARDS), respiratory failure, multiorgan failure, and even death[1].

Common clinical manifestations of COVID-19 include fever (88.7%), cough (67.8%), fatigue (38.1%), sputum production (33.4%), dyspnea (18.6%), sore throat (13.9%), and headache (13.6%). Gastrointestinal symptoms are less common, such as diarrhea (3.8%) and vomiting (5.0%)[1]. The occurrence of pneumoperitoneum is even rarer, with only one case reported in the literature by Gemio Del Rey and colleagues[2], associated with SARS-CoV-2 infection. This rarity highlights the importance of presenting these two new cases of spontaneous pneumoperitoneum associated with COVID-19.

Pneumoperitoneum is defined as the accumulation of free air in the peritoneal cavity[3]. It was first described by Popper in 1915[4], and it typically indicates visceral perforation in 85% to 95% of all cases, necessitating surgical intervention[3-5]. However, in 5% to 15% of cases, pneumoperitoneum does not indicate perforation and arises from other sources that do not require emergency surgery[3-5]. This subset warrants further exploration.

According to Mularski and colleagues, non-surgical pneumoperitoneum can be classified into five categories based on its origin: thoracic (43.4%), abdominal (30.6%), gynecological (7.6%), and idiopathic (18.4%) (**Table 1**)[5].

Thoracic-origin pneumoperitoneum has two proposed mechanisms for the passage of air from the thoracic cavity to the abdominal cavity: direct passage through pleural and diaphragmatic defects, and the classic route through the mediastinum along perivascular connective tissue or larger diaphragmatic portals to the retroperitoneum and finally to the peritoneum; this passage is known as the *Macklin effect*[4]. Idiopathic pneumoperitoneum is defined as pneumoperitoneum without a clearly established etiology[4,5]. Finally, non-surgical abdominal-origin pneumoperitoneum arises from residual air from surgical procedures (60%), peritoneal dialysis (11%-34%), gastrointestinal endoscopic procedures (25%), and is associated with findings of pneumatosis cystoides intestinalis (PCI)[4,5]. The absorption rate varies for each patient, and pneumoperitoneum can be found in 50% of patients in control tomography on the sixth day[5].

As demonstrated in the two presented cases, most patients with spontaneous pneumoperitoneum are asymptomatic or present with vague symptoms, a characteristic that is very clear in patients who do not require surgical management. It is also important to consider the presence of systemic inflammatory response signs in the context of each patient, as the finding of pneumoperitoneum, as noted, is incidental in patients with symptoms secondary to extraintestinal pathologies[5].

One of these patients presents findings related to pneumatosis cystoides intestinalis, which recently developed alongside the noted symptoms, as it was not documented in previous CT studies during earlier hospitalizations. Pneumatosis cystoides intestinalis is a rare condition first described by Du Vernoy in autopsies in 1730 and later

Table 1. Causes of Non-Surgical Pneumoperitoneum

Thoracic	Abdominal	Gynecological	Idiopathic
Mechanical ventilation: – airway pressure >40-60 cmH_2O – high volumes – pre-existing lung disease	- Previous abdominal surgery	- Sexual intercourse/oral sex	- Cocaine consumption
- Cardiopulmonary resuscitation	- Peritoneal dialysis	- Vaginal douching	- Scleroderma without pneumatosis cystoides intestinalis
- Pneumothorax/pneumomediastinum	- Gastrointestinal endoscopic procedures	- Anatomical anomalies	- Decompression diving
- Airway/chest procedures	- Pneumatosis cystoides intestinalis	- Pelvic inflammatory disease	- Tooth extraction
		- Hysterosalpingography	- Other unclear
		- Childbirth	
		- Gynecological medical examination	

Adapted from: Williams NM, et al. Postgrad Med J. 1997;73(863):531-7[4]; Mularski RA, et al. Crit Care Med. 2000;28(7):2638-44[5].

named by Mayers in 1825[8]. It is defined as the presence of air dissecting the intestinal wall[9] and can be divided into two types: primary (15%) and secondary (85%)[10]. Its severity can range from a benign condition to one that is life-threatening[9].

The exact incidence is unknown since most patients are asymptomatic; however, autopsy series reports have found an incidence of 0.03% in the general population[9].

There are three main hypotheses regarding the pathophysiology of the condition:

1. The mechanical theory involves an increase in intraluminal pressure caused by conditions such as intestinal obstructions, inflammatory bowel diseases, mesenteric ischemia, gastrointestinal tract tumors, anorectal surgeries, or endoscopic procedures. This pressure causes mechanical damage to the mucosa, allowing the migration of intraluminal gas into the intestinal wall. However, this theory does not explain the persistence of these cysts once formed.
2. The pulmonary theory suggests that chronic lung diseases such as COPD, asthma, or pneumonia cause alveolar rupture, leading to mediastinal emphysema and the release of gas along the aorta and mesenteric vessels to the intestinal wall. This theory does not account for the fact that 50% of the gas found in the cysts is hydrogen, a gas not produced by mammals.
3. The bacterial theory proposes that bacterial translocation to the intestinal wall and subsequent gas production by fermentation can generate this condition; however, the presence of gas-producing bacteria in these cysts has not been confirmed[8,10,11].

Additional theories have been described, such as the chemical or nutritional deficit theory, which explains how malnutrition can prevent the digestion of carbohydrates, leading to increased fermentation, large volumes of gas, intestinal distension, ischemia, and subsequently gas dissecting the submucosa. Finally, there have been reports of intestinal pneumatosis secondary to chemotherapy, hormone therapy, and connective tissue diseases, although the pathophysiology remains unknown[8].

In a systematic analysis conducted by Wu and colleagues, the average age of patients was found to be 45.3 ± 15.6 years, with variable symptoms. The most common symptoms, in order of frequency, were abdominal pain, diarrhea, distension, nausea and vomiting, bloody diarrhea, mucus in stools, and constipation[8]. Lesions were primarily located in the colon (46%), followed by the small intestine (27%), a combination of the colon and small intestine (7%), and the stomach (5%)[10].

Pneumoperitoneum is a manifestation of an underlying disorder, and its management focuses on treating the

underlying cause. Wu and colleagues found that most patients (93%) with primary spontaneous pneumoperitoneum were cured with conservative management, and the effectiveness of antibiotic treatment was only 26.3%[8], indicating that the cause is not always infectious.

During the COVID-19 pandemic, cases associating SARS-CoV-2 with imaging findings of intestinal pneumatosis have been reported, similar to other viruses such as the human immunodeficiency virus (HIV), norovirus, and cytomegalovirus[12]. It has been described that the virus uses the angiotensin-converting enzyme 2 (ACE2) receptor to enter the cell and the transmembrane serine protease 2 (TMPRSS2) to initiate its protein production. These two molecules play a crucial role as they are expressed in both type 2 alveolar cells and enterocytes, suggesting how the virus can invade the gastrointestinal tract mucosa[12]. Additionally, the virus has been reported to cause degenerative changes in intestinal lymphoid tissue, resulting in a marked decrease in lymphocytes[13].

In the two presented cases, it is considered that these patients may have pneumoperitoneum associated with COVID-19. However, it is crucial to differentiate whether the pneumoperitoneum is amenable to medical management. In a case series, Bhayana and colleagues described abdominal imaging findings in COVID-19 and found that 20% (4/20) of their ICU patients had intestinal pneumatosis. Of these, three showed clear signs of ischemia or intestinal necrosis during laparotomy, and only one had pneumatosis cystoides intestinalis[14].

While the finding of pneumoperitoneum can be alarming for the medical team, the interpretation and individualization of each case, along with proper evaluation by the surgical team, can help identify patients who are suitable for medical management. This challenges the traditional surgical dogma that "all pneumoperitoneum is surgical".

CONCLUSIONS

SARS-CoV-2 infection, or COVID-19, is a recent disease with high transmissibility that has affected a significant portion of the global population. Healthcare personnel are still learning about it. While respiratory symptoms are well-known, gastrointestinal symptoms such as distension, abdominal pain, diarrhea, and vomiting[1] have also been documented. Some patients may present with imaging findings of pneumatosis cystoides intestinalis[12,15] and spontaneous pneumoperitoneum[2], often asymptomatic. Therefore, it is crucial to discern which patients benefit from surgical management and which from conservative management[3-5].

Not all patients with pneumoperitoneum require surgical intervention. Supported by the literature, this article highlights that 5% to 15% of patients benefit from conservative management. It is essential to individualize patient care, conduct a thorough medical history to identify potential causes, and follow up to avoid increasing patient morbidity with unnecessary surgical procedures and costs[3-5].

To date, these two reported cases of spontaneous pneumoperitoneum associated with COVID-19 are the first to be published in the Americas. In Europe, only one similar case has been reported by Gemio Del Rey and colleagues[2], involving a patient with SARS-CoV-2 infection who required mechanical ventilation, potentially explaining the pneumoperitoneum. However, the two presented cases have a more challenging pathophysiological explanation, hypothesizing the invasion of the virus into gastrointestinal cells via ACE2 and TMPRSS2 receptors found on the surface of enterocytes[12], leading to the presentation of pneumatosis cystoides intestinalis and, consequently, pneumoperitoneum. While an intrathoracic cause might be considered due to the pronounced pulmonary presentation in COVID-19 patients, this theory loses weight as the Macklin effect cannot be demonstrated with imaging[6].

It is interesting to observe the complex and diverse clinical manifestations of the new SARS-CoV-2 infection, which continues to challenge healthcare personnel. Since there are no definitive management guidelines for the new infection yet, more cases of spontaneous pneumoperitoneum are expected to arise. It is crucial to consider that not all patients presenting with this finding require surgical management. Cases should be individualized, and with appropriate clinical evaluation, the risk of morbidity and mortality from unnecessary surgical interventions can be reduced.

REFERENCES

1. Ludwig S, Zarbock A. Coronaviruses and SARS-CoV-2: A Brief Overview. Anesth Analg. 2020;131(1):93-96. https://doi.org/10.1213/ANE.0000000000004845
2. Gemio Del Rey IA, de la Plaza Llamas R, Ramia JM, Medina Velasco AA, Díaz Candelas DA. Neumoperitoneo espontáneo no quirúrgico en paciente COVID-19 positivo con neumonía bilateral severa [Non-surgical spontaneous pneumoperitoneum in a COVID-19 positive patient with severe bilateral pneumonia]. Cir Esp. 2021;99(6):469-471. https://doi.org/10.1016/j.ciresp.2020.05.030

3. Hanna M, Ng C, Slater K. Small Bowel Diverticulosis As a Cause of Chronic Pneumoperitoneum. Cureus. 2020;12(3):e7303. https://doi.org/10.7759/cureus.7303
4. Williams NM, Watkin DF. Spontaneous pneumoperitoneum and other nonsurgical causes of intraperitoneal free gas. Postgrad Med J. 1997;73(863):531-7. https://doi.org/10.1136/pgmj.73.863.531
5. Mularski RA, Sippel JM, Osborne ML. Pneumoperitoneum: a review of nonsurgical causes. Crit Care Med. 2000;28(7):2638-44. https://doi.org/10.1097/00003246-200007000-00078
6. Ahmed K, Amine EG, Abdelbaki A, Jihene A, Khaoula M, Yamina H, et al. Airway management: induced tension pneumoperitoneum. Pan Afr Med J. 2016;25:125. https://doi.org/10.11604/pamj.2016.25.125.9038
7. Cadena M, Solano J, Caycedo N, Gomez D, Vinck EE, Quiroga P, et al. Tension pneumoperitoneum: Case report of a rare form of acute abdominal compartment syndrome. Int J Surg Case Rep. 2019;55:112-116. https://doi.org/10.1016/j.ijscr.2019.01.014
8. Wu LL, Yang YS, Dou Y, Liu QS. A systematic analysis of pneumatosis cystoids intestinalis. World J Gastroenterol. 2013;19(30):4973-8. https://doi.org/10.3748/wjg.v19.i30.4973
9. Feuerstein JD, White N, Berzin TM. Pneumatosis intestinalis with a focus on hyperbaric oxygen therapy. Mayo Clin Proc. 2014;89(5):697-703. https://doi.org/10.1016/j.mayocp.2014.01.026
10. Ling F, Guo D, Zhu L. Pneumatosis cystoides intestinalis: a case report and literature review. BMC Gastroenterol. 2019;19(1):176. https://doi.org/10.1186/s12876-019-1087-9
11. Wang YJ, Wang YM, Zheng YM, Jiang HQ, Zhang J. Pneumatosis cystoides intestinalis: six case reports and a review of the literature. BMC Gastroenterol. 2018;18(1):100. https://doi.org/10.1186/s12876-018-0794-y
12. Meini S, Zini C, Passaleva MT, Frullini A, Fusco F, Carpi R, et al. Pneumatosis intestinalis in COVID-19. BMJ Open Gastroenterol. 2020;7(1):e000434. https://doi.org/10.1136/bmjgast-2020-000434
13. Kielty J, Duggan WP, O'Dwyer M. Extensive pneumatosis intestinalis and portal venous gas mimicking mesenteric ischaemia in a patient with SARS-CoV-2. Ann R Coll Surg Engl. 2020;102(6):e145-e147. https://doi.org/10.1308/rcsann.2020.0145
14. Bhayana R, Som A, Li MD, Carey DE, Anderson MA, Blake MA, et al. Abdominal Imaging Findings in COVID-19: Preliminary Observations. Radiology. 2020;297(1):E207-E215. https://doi.org/10.1148/radiol.2020201908
15. Lakshmanan S, Toubia N. Pneumatosis Intestinalis in COVID 19. Clin Gastroenterol H. 2020;S1542-3565(20):30755-2. https://doi.org/10.1016/j.cgh.2020.05.048

https://doi.org/10.22516/25007440.1082

Case report

Primary Congenital Intestinal Lymphangiectasia: A Case Report

Tatiana Díaz-Gómez,[1*] Pablo Sempértegui-Cárdenas,[2] Ana Tinoco-Ochoa.[2]

OPEN ACCESS

Citation:
Díaz-Gómez T, Sempértegui-Cárdenas P, Tinoco-Ochoa A. Primary Congenital Intestinal Lymphangiectasia: A Case Report. Revista. colomb. Gastroenterol. 2024;39(2):219-223. https://doi.org/10.22516/25007440.1082

[1] Third-Year Resident of the Pediatrics Postgraduate Program. Universidad de Cuenca, Hospital Vicente Corral Moscoso. Cuenca, Ecuador.
[2] Vicente Corral Moscoso Hospital, Department of Pediatrics. Cuenca, Ecuador.

***Correspondence:** Tatiana Diaz-Gómez.
tatidi2404@hotmail.com

Received: 12/05/2023
Accepted: 27/07/2023

Abstract

Primary intestinal lymphangiectasia (PIL) is a rare disease that was discovered in 1961 by Waldmann et al., who first described the concept of intestinal lymphangiectasia. PIL is manifested by large and dilated intestinal lymphatic vessels that lead to the loss of lymphatic fluid to the intestinal lumen, including severe hypoalbuminemia and, consequently, generalized edema. The etiology of PIL is unknown; however, several genes are involved in the development of the lymphatic system. The case of a two-month-old patient with a prenatal diagnosis of ascites on third-trimester ultrasound was presented. The patient was born with rapidly progressive ascites and showed an endoscopic study with evidence of snowflake images and histology compatible with intestinal lymphangiectasia. The patient remained on octreotide infusion at baseline and subsequently with refractory ascites the dose was increased. Several evacuatory paracentesis were performed and he remained on enteral nutrition based on an extensively hydrolyzed formula with a 54% contribution of medium chain triglycerides (MCTs) and parenteral nutrition (PN). Subsequently, the patient was switched to a subcutaneous infusion of octreotide, which allowed hospital discharge and adequate outpatient follow-up with a favorable evolution.

Keywords

Ascites, intestinal lymphangiectasia, octreotide, children.

INTRODUCTION

Primary intestinal lymphangiectasia (PIL) is a rare disease characterized by the presence of large, extensive intestinal lymphatic vessels, leading to the loss of lymphatic fluid into the intestinal lumen. This condition results in severe hypoalbuminemia and consequently generalized edema[(1)]. PIL was first described in 1961 by Waldmann, who observed varying degrees of lymphatic vessel dilation in 18 patients[(2)]. The etiology of PIL remains unknown; however, several genes, including VEGFR3, PROX1, FOXC2, and SOX18, are implicated in the development of the lymphatic system[(3)].

PIL can be suspected at birth or during pregnancy based on ultrasound imaging, which can detect fetal ascites or lower limb lymphedema[(2)]. In a child with symptoms suggestive of PIL, routine tests typically indicate hypoalbuminemia, lymphopenia, and hypogammaglobulinemia. The diagnosis is confirmed through endoscopy, which reveals the characteristic snowflake appearance of the affected duodenal mucosa, and histological examination of biopsies showing lymphatic vessel dilation[(4)].

The primary treatment strategy for PIL involves dietary modification, specifically a low-fat diet supplemented with medium-chain triglycerides (MCT)[2]. When dietary measures are insufficient, dietary supplements or enteral nutrition based on fat-free formulas or formulas with MCTs[5] as the main lipid content are utilized[5]. In cases where dietary interventions fail, additional options can be considered, either alone or in combination with a low-fat diet and MCT supplementation[2]. Second-line therapies include surgical interventions (ranging from laparoscopic resection to major surgery such as *duodenopancreatectomy*), radiological interventions, and medications. The choice of treatment depends on the extent of the disease[6]. The prognosis of PIL can be severe and potentially fatal, particularly when malignant complications (such as lymphoma) or pleural or pericardial effusions occur[2].

CASE PRESENTATION

The patient is a two-month-old girl with a prenatal diagnosis of ascites identified on a third-trimester ultrasound, which led to a planned cesarean section. She was born weighing 3500 grams and was discharged with furosemide and instructions for exclusive breastfeeding. At one and a half months of age, she presented with an increased abdominal circumference and had five episodes of food vomiting, leading to her hospitalization.

On physical examination, the following data were recorded: weight: 6.8 kg, height: 60 cm, weight/height index (+2SD) unreliable due to ascites, mid-upper arm circumference (-3SD) indicating severe malnutrition, and abdominal circumference: 53 cm. The abdomen displayed a collateral venous network and was globular, tense, with a positive fluid wave and crescent-shaped dullness. The remainder of the examination was apparently normal.

Paraclinical test results were as follows: white blood cells: 4900/µL, neutrophils: 41.8%, lymphocytes: 39.9%, hemoglobin: 11 g/dL, platelets: 531,000, fibrinogen: 351 mg/dL, total proteins: 4.9 g/dL, albumin: 3.4 g/dL, globulin: 1.5 g/dL, urea: 9.1 mg/dL, creatinine: 0.21 mg/dL, cholesterol: 138.9 mg/dL, triglycerides: 5512.6 mg/dL, C-reactive protein (CRP): 0.28 mg/dL, immunoglobulin A (IgA): 0.2 g/L, immunoglobulin G (IgG): 2.2 g/L, immunoglobulin M (IgM): 0.4 g/L, immunoglobulin E (IgE): 3.4 IU/mL, alpha-fetoprotein: 434 IU/mL, carcinoembryonic antigen: 1.5 ng/mL, CA 125: 568.1 IU/mL, CA 15-3: 6 U/mL, CA 19-9: 10 U/mL, fecal fats: positive. The ascitic fluid study showed a milky white appearance, albumin: 0.8 g/dL, amylase: 16 U/L, glucose: 133.5 mg/dL, proteins: 2.7 g/dL, lactate dehydrogenase (LDH): 442 U/L, white blood cell count: 0.209 cells/mL, lymphocytes 79%, neutrophils: 21%, ascitic fluid culture: negative, acid-fast bacilli (AFB) and GeneXpert in ascitic fluid: negative.

Imaging studies included a chest-abdominal X-ray, which revealed abundant free fluid. Both the abdominal ultrasound and the triphasic abdominal computed tomography (CT) scan (**Figure 1**) indicated marked ascites. Upper gastrointestinal endoscopy showed snowflake-like images in the first, second, and third portions of the duodenum (**Figures 2A** and **B**). Duodenal biopsy revealed villi with a preserved crypt-villus ratio (greater than 2.5/1), and no increase in intraepithelial lymphocytes (less than 30%) was observed with routine techniques. Slightly dilated mucosal and submucosal lymphatic vessels surrounded by scant lymphoplasmacytic infiltrate were noted in the lamina propria of some villi, without macrophages suggesting xanthomatous lesions. Immunohistochemical staining with podoplanin (D-240) highlighted lymphatic vascular structures in isolated villi, findings consistent with focal duodenal lymphangiectasia (**Figures 3A** and **B**).

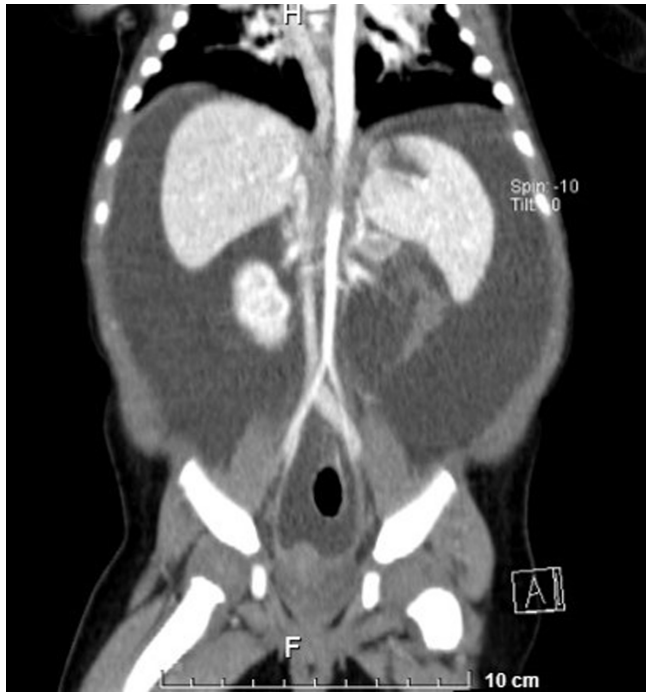


Figure 1. Triphasic abdominal CT scan showing homogeneous parenchyma of the liver and spleen, pancreas with a normal tissue attenuation pattern, normal kidneys, spontaneous ascites, bilateral posterobasal subsegmental pulmonary atelectasis, and no identifiable tumors. Source: Patient's medical records.

Upon admission, the patient received an intravenous dose of albumin at 1 g/kg and was started on prophylactic cefazolin before the diagnostic and therapeutic paracentesis. A milky fluid of 370 mL was obtained (**Figure 4**), prompting

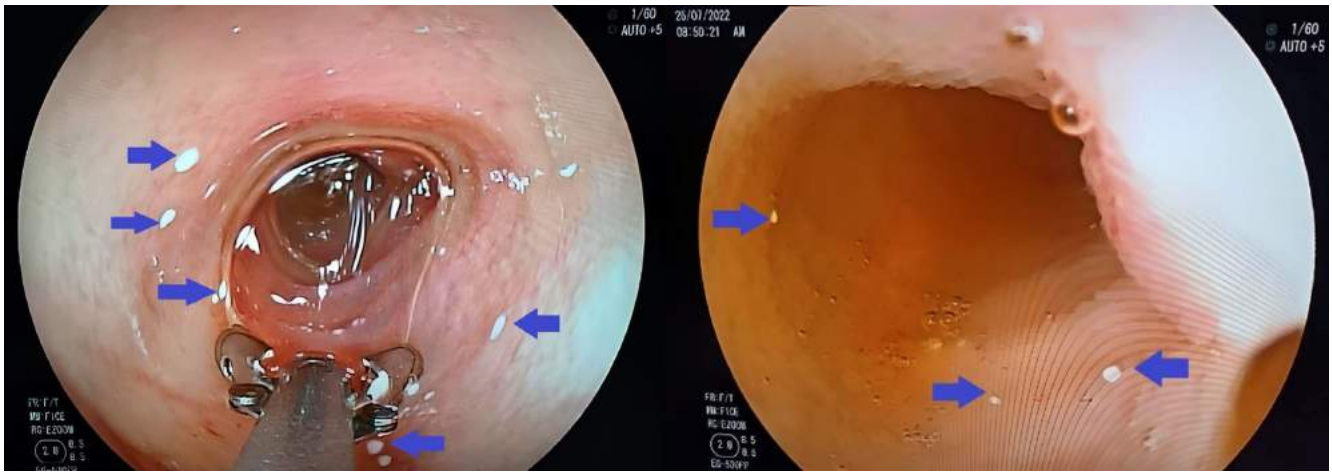


Figure 2. Endoscopic images of the first, second, and third portions of the duodenum displaying white speckling with a snowflake appearance that does not disappear with pressure washing. Pathological findings are indicated by blue arrows. Source: Patient's medical records.

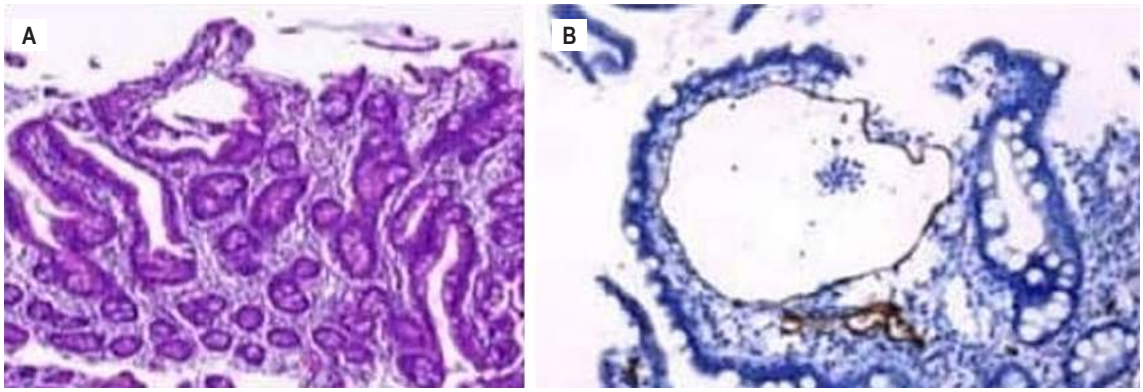


Figure 3. A. Duodenal mucosa. **B.** Histological sections of duodenal biopsy with podoplanin (D2-40) immunohistochemical staining highlighting lymphatic vascular structures in isolated villi. Source: Patient's medical records.

the initiation of octreotide infusion at 1 µg/kg/h along with total parenteral nutrition (TPN). This regimen was maintained initially and later increased to 3 µg/kg/h due to refractory ascites. Several evacuative paracenteses were performed, draining volumes up to 900 mL, with concurrent albumin administration for replacement. Due to the unavailability of formulas with exclusive medium-chain triglycerides (MCT) in the country, an extensively hydrolyzed formula containing MCT was used. Subsequently, the octreotide infusion was switched to subcutaneous administration at 100 µg every eight hours, which allowed the discontinuation of parenteral nutrition after 25 days of hospitalization. On day 26, the patient was discharged with an abdominal circumference of 38 cm and treatment that included an extensively hydrolyzed formula, MCT, subcutaneous octreotide, spironolactone, fat-soluble vitamins, and folic acid. During follow-up in the outpatient service, she required hospitalization once more for a therapeutic paracentesis, but she continued to show favorable progress.

DISCUSSION

PIL is a rare disease, and the prevalence of its clinically manifest form is unknown due to the presence of asymptomatic cases. Few cases have been reported in Latin America, and none in Ecuador. In children, it is generally diagnosed before the age of three but can present later in childhood or even in adulthood(2).

The main clinical manifestation is peripheral edema of varying degrees, which is usually symmetrical. However, moderate serous effusions such as pleural effusion, pericarditis, or chylous ascites are common and can be life-threatening in severe forms[2]. In this case, the patient presented with ascites detected on ultrasound during pregnancy,



Figure 4. Paracentesis showing the extraction of milky ascitic fluid. Source: Patient's medical records.

which was already a warning sign for appropriate management at birth. Unfortunately, adequate management was not initiated until she was one month old, by which time the ascites had become severe.

Although several methods have been proposed to investigate PIL, none can replace the histological examination of biopsies for confirming the diagnosis[2]. Routine imaging tests at the onset, such as abdominal ultrasound and computed tomography (CT), can typically identify diffuse thickening of the small intestine wall and edema, which are consequences of dilated lymphatic vessels within the villi[2].

Diet modification is the cornerstone of PIL treatment, involving a high-protein diet (2 g/kg/day) and low-fat content (< 25 g/day). The fat component should consist of more than 90% MCTs and short-chain triglycerides SCTs because these components are transported directly to the portal circulation instead of the lymphatic system, thereby decreasing intestinal lymphatic flow and preventing the rupture of lymphatic vessels with the resultant loss of proteins and T cells[2,6]. TPN allows for digestive rest and a reduction in splanchnic and subsequently chylous flow. TPN is not recommended as an initial nutritional support measure but is an option for patients who cannot tolerate or have contraindications to oral feeding, do not respond to dietary treatment, have an underlying disease requiring more aggressive nutritional therapy, or are malnourished[5].

Other treatment options depend on the extent of the disease. Focal segmental PIL refractory to dietary therapy can be treated by intestinal resection or radiological embolization. Diffuse intestinal lymphangiectasia and extensive lymphangiectasia require treatment with drugs such as octreotide, propranolol, and tranexamic acid[6].

Octreotide is a somatostatin analogue that decreases splanchnic blood flow, intestinal motility, and triglyceride absorption. Therefore, it can be optimally used in patients with intestinal lymphatic vessel involvement only[6]. Complete resolution of chylous effusion has been observed after initiating octreotide therapy in newborns[7]. An induction therapy with a subcutaneous injection of 1 to 10 μg/kg/dose twice daily for two weeks is recommended, followed by the same dose injected subcutaneously at four-week intervals as maintenance therapy[6]. However, in our patient, we initially opted for an octreotide infusion, which has shown good response in cases of congenital chylothorax, before transitioning to subcutaneous administration at doses up to 40 μg/kg/day[8]. Albumin infusion is a symptomatic treatment proposed for patients with significant ascites[9] or severe lower limb edema, but its effectiveness is transient due to persistent lymph leakage into the intestinal lumen[2].

Other therapeutic options include propranolol, which appears to have a therapeutic effect on the endothelium of lymphatic vessels[6]. Tranexamic acid has demonstrated utility, as intestinal protein loss can occur during increased fibrinolytic activity[10].

CONCLUSIONS

- PIL is a rare disease characterized by large, extensive intestinal lymphatic vessels leading to lymphatic fluid loss into the intestinal lumen.
- The diagnosis of PIL is confirmed by histological examination of intestinal biopsy samples.
- Diet modification is the cornerstone of PIL treatment.

RECOMMENDATIONS

Healthcare professionals should be made aware of the suggestive symptoms of this rare disease to facilitate early and appropriate intervention, thereby improving the quality of life for these patients. No other cases of PIL have been reported in Ecuador, making it important to note that the treatment was successful despite local challenges.

Conflict of Interest

The authors declare no conflict of interest.

Funding Sources

This research did not receive any specific grants from public, commercial, or non-profit funding agencies.

REFERENCES

1. Altın Z, Atabay Y, Özer S, Karakoyun M, Ekmekçi S, Yürekli EY, et al. Primary intestinal lymphangiectasia and a review of the current literature. Turk J Gastroenterol. 2018;29(6):714-716. https://doi.org/10.5152/tjg.2018.18596
2. Vignes S, Bellanger J. Primary intestinal lymphangiectasia (Waldmann›s disease). Rev Med Interne. 2018;39(7):580-585. https://doi.org/10.1016/j.revmed.2017.07.009
3. Hokari R, Kitagawa N, Watanabe C, Komoto S, Kurihara C, Okada Y, et al. Changes in regulatory molecules for lymphangiogenesis in intestinal lymphangiectasia with enteric protein loss. J Gastroenterol Hepatol. 2008;23(7 Pt 2):e88-95. https://doi.org/10.1111/j.1440-1746.2007.05225.x
4. Asakura H, Miura SM, Morishita T, Aiso S, Tanaka T, Kitahora T, et al. Endoscopic and histopathological study on primary and secondary intestinal lymphangiectasia. Dig Dis Sci. 1981;26(4):312-20. https://doi.org/10.1007/BF01308371
5. Sánchez P, Rodríguez B, Díaz O, Vázquez N, Murcia C, Rodeiro S. Manejo de la ascitis quilosa y revisión de la literatura. Nutr Clín Diet Hosp. 2022;42(1):126-133.
6. Kwon Y, Kim MJ. The Update of Treatment for Primary Intestinal Lymphangiectasia. Pediatr Gastroenterol Hepatol Nutr. 2021;24(5):413-422. https://doi.org/10.5223/pghn.2021.24.5.413
7. Zaki SA, Krishnamurthy MB, Malhotra A. Octreotide Use in Neonates: A Case Series. Drugs R D. 2018;18(3):191-198. https://doi.org/10.1007/s40268-018-0237-9
8. Mas E, Borrelli O, Broekaert I, de-Carpi JM, Dolinsek J, Miele E, et al. Drugs in Focus: Octreotide Use in Children With Gastrointestinal Disorders. J Pediatr Gastroenterol Nutr. 2022;74(1):1-6. https://doi.org/10.1097/MPG.0000000000003294
9. Lopez RN, Day AS. Primary intestinal lymphangiectasia in children: A review. J Paediatr Child Health. 2020;56(11):1719-1723. https://doi.org/10.1111/jpc.14837
10. MacLean JE, Cohen E, Weinstein M. Primary Intestinal and Thoracic Lymphangiectasia: A Response to Antiplasmin Therapy. Pediatrics. 2002;109(6):1177-1180. https://doi.org/10.1542/peds.109.6.1177

https://doi.org/10.22516/25007440.1090

Case report

Celiac Disease, A Silent Enemy: A Case Report

Diana Carolina Urbano-Albán,[1]* Bairon Díaz-Idrobo,[2] Rosales Sebastián Hooker-Herrera,[3] Julio César Hooker-Mosquera.[4]

OPEN ACCESS

Citation:
Urbano-Albán DC, Díaz-Idrobo B, Hooker-Herrera RS, Hooker-Mosquera JC. Celiac Disease, A Silent Enemy: A Case Report. Revista. colomb. Gastroenterol. 2024;39(2):224-229. https://doi.org/10.22516/25007440.1090

[1] General Practitioner, Hospital Physician, Hospital Universitario San José. Popayán, Colombia.
[2] General Practitioner, Hospital Physician, Hospital Universitario San José. Popayán, Colombia.
[3] Internist, Hospital Universitario San José. Popayán, Colombia.
[4] Gastroenterologist Internist, Digest Center S.A.S. Cali, Colombia.

***Correspondence:** Diana Carolina Urbano-Albán.
dianaurbano@unicauca.edu.co

Received: 21/06/2023
Accepted: 04/10/2023

Abstract

Celiac disease (CD) is an immune-mediated enteropathy with systemic compromise in genetically susceptible individuals, caused by an immune response to ingested gluten. The only therapy for CD is a gluten-free diet (GFD).

A case of a 55-year-old woman who reported to the emergency room for early satiety, intolerance to legumes, abdominal distension, and chronic diarrhea, including paresthesias in the upper and lower limbs, was presented. In addition, she described a functional decline due to dyspnea and involuntary weight loss of approximately 20 kilograms in the last 2 years. An esophagogastroduodenoscopy with CD protocol was performed, along with serology for CD, which confirmed the initial diagnostic suspicion. Treatment with a gluten-free diet and nutritional supplementation was indicated, which yielded a significant improvement in the clinical picture.

Keywords

Celiac disease, gluten-free diet, malabsorption syndrome, case reports.

INTRODUCTION

Celiac disease (CD) is a systemic immune-mediated disorder, characterized by a specific serological and histological profile associated with gluten intake, and a broad range of gastrointestinal and extra-gastrointestinal clinical manifestations[(1)]. It affects approximately 1% of the global population, although most cases remain undiagnosed due to nonspecific symptoms and a general lack of awareness about the disease. The incidence and prevalence of CD are on the rise, likely due to industrialization, increased consumption of gluten-containing foods, heightened clinician awareness for diagnosing the disease, and advancements in diagnostic methods[(2)]. CD affects individuals of various ages, races, and ethnic groups. The epidemiological behavior of this disorder in Colombia is largely unknown, with very few reported cases and even fewer published studies on the topic[(3-5)].

CASE PRESENTATION

A 55-year-old female patient with no relevant medical history presented with a three-week clinical course of early satiety, weight loss, intolerance to legumes, abdominal distension, and chronic watery diarrhea, along with paresthesias initially in the upper limbs and subsequently affecting the lower limbs. During the systems review, the patient reported experiencing similar symptoms for the past two

© 2024 Asociación Colombiana de Gastroenterología

years, accompanied by a decrease in functional class due to dyspnea with moderate to minor exertion and an unintentional weight loss of approximately 20 kg over the same period. Due to the exacerbation of symptoms, she sought emergency care. On physical examination, her vital signs were normal, her weight was 34 kg, and notable findings included pale oral mucosa, a smooth and geographic tongue, and epigastric pain upon deep palpation, without signs of peritoneal irritation.

Laboratory tests revealed macrocytic hyperchromic anemia, leukopenia, thrombocytopenia, normal renal function, hypokalemia, hypocalcemia, hypomagnesemia, prolonged international normalized ratio (INR), and deficiencies in vitamins B^{12} and D (**Table 1**). Intravenous electrolyte replacement was administered, and additional studies were conducted. Endoscopic studies of the upper and lower digestive tracts, tumor markers, and thoracic and abdominal CT scans were unremarkable.

Based on the clinical and laboratory findings, celiac disease (CD) was suspected. Additional studies were conducted, including a duodenal biopsy following the protocol for CD, which reported findings consistent with Marsh 1 (**Figure 1**) and Marsh 2 (**Figure 2**) classifications, and an endoscopic ultrasound showing findings consistent with chronic pancreatitis (**Figure 3**). After discharge, the patient had positive anti-tissue transglutaminase IgA antibody results and normal IgA levels.

The patient was treated with a gluten-free diet (GFD), pancreatic enzyme supplementation, vitamin D, calcium, and monthly intramuscular vitamin B_{12}. Following adherence to medical recommendations and a healthy lifestyle, the patient showed significant clinical improvement, gained 16 kg, normalized her bowel habits, and recent laboratory tests showed normal vitamin B_{12} levels and improved 25-hydroxyvitamin D levels (**Table 2**).

A periodic follow-up plan at 3, 6, and 12 months was indicated, and recommendations were given for family members to undergo screening for the disease.

DISCUSSION

Celiac disease (CD) is a systemic, immune-mediated disorder that occurs in genetically predisposed individuals in response to the ingestion of gluten, a protein found in wheat, rye, and barley[6]. More than 95% of patients with CD express HLA-DQ2, while the remaining patients express HLA-DQ8, along with other non-HLA genes[7,8].

CD affects about 1% of the global population, with prevalence estimates ranging from 1.4% to 1.8%. There are significant regional differences and intra-regional variations, with cumulative incidences reaching up to 3%. These differences are not fully understood and cannot be

Table 1. Admission Laboratory Results

Laboratory Test	Result	Reference Values
Hemogram		
- Leukocytes	2.1 x 10^3/µL	4.5-10 x 10^3/µL
- Red blood cell count	3.8 x 10^6/µL	4.2-5.4 x 10^6/µL
- Hemoglobin	6.6 g/dL	12.5-16 g/dL
- Hematocrit	18.90%	37%-47%
- Mean corpuscular volume	129.5 fL	79-101 fL
- Mean corpuscular hemoglobin	35.2 pg	29-35 pg
- RDW-CV	12.00%	11%-16%
- Platelets	58 x 10^3/µL	150-450 x 10^3/µL
Electrolytes		
- Potassium	2.7 mmol/L	3.5-5.1 mmol/L
- Sodium	141 mmol/L	136-146 mmol/L
- Chloride	106 mmol/dL	101-109 mmol/L
- Magnesium	1.15 mg/dL	1.9-2.5 mg/dL
- Serum calcium	5.4 mg/dL	8.9-10.3 mg/dL
Renal function		
- Creatinine	0.56 mg/dL	0.55-1.02 mg/dL
- Blood urea nitrogen	8 mg/dL	7-25 mg/dL
Liver function		
- AST	38 U/L	0-35 U/L
- ALT	31 U/L	0-35 U/L
- INR	1.46	0.8 a 1.2
- Albumin	3 g/dL	3.4 a 5.4 g/dL
- Total bilirubin	0.81 mg/dL	0.1 a 1.2 mg/dL
- LDH	642 U/L	85-227 U/L
Deficiencies		
- Folic acid	4.3 ng/mL	2.7 a 17 ng/mL
- Vitamin B_{12}	< 83 pg/mL	200 a 800 pg/mL
- 25-hydroxyvitamin D	6.9 ng/mL	30-40 ng/mL
- Ferritin	194 ng/mL	23.9-336.2 ng/mL
Thyroid function		
- Free T4	1 ng/dL	0.9 a 2.3 ng/dL
- TSH	0.39 mUI/L	0.37 a 4.7 mUI/L
Others		
- Anti-tissue transglutaminase IgA antibodies	**1.41**	Negative: less than 0.9 Undetermined: 0.9-1.1 **Positive: greater than 1.1**

RDW: red cell distribution width; AST: aspartate aminotransferase; ALT: alanine aminotransferase; IgA: immunoglobulin A; INR: international normalized ratio; LDH: lactate dehydrogenase; TSH: thyroid-stimulating hormone. Source: Author's File.

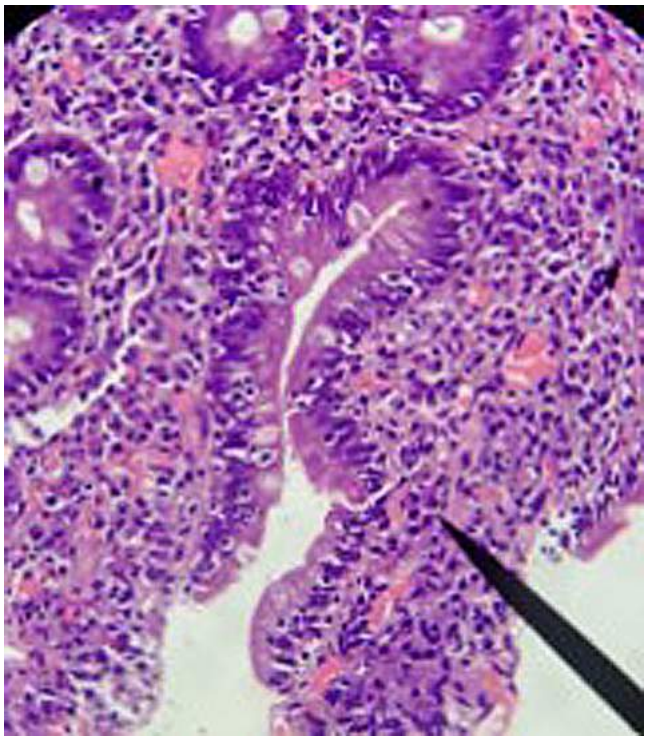


Figure 1. Marsh 1 Classification (Infiltrative). Duodenal bulb mucosa showing preservation of the glandular population with occasional intraepithelial lymphocytes (10 lymphocytes per 100 epithelial cells). Courtesy of the Pathology Department of Hospital Universitario San José, Popayán, with reading amplification (Dr. Nohelia Muñoz).

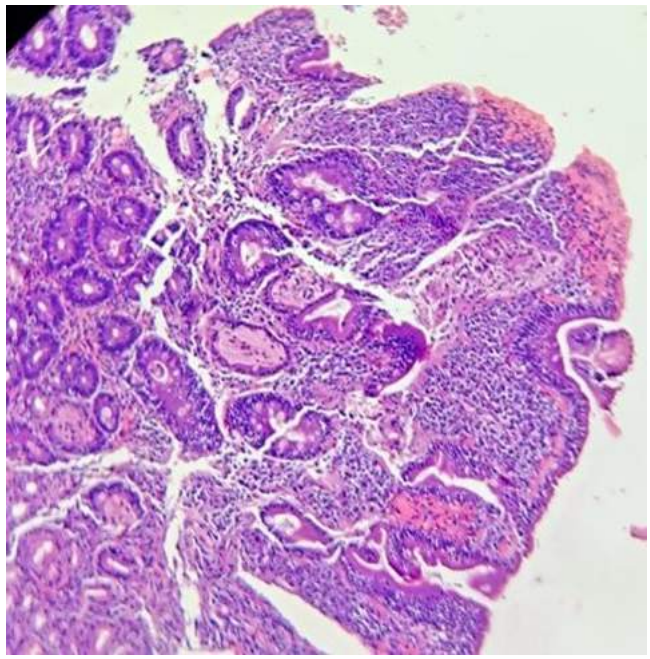


Figure 2. Marsh 2 Classification (Hyperplastic). Mucosa of the second portion of the duodenum showing slight glandular hyperplasia with 30 intraepithelial lymphocytes per 10 epithelial cells. There is no presence of villous atrophy. Courtesy of the Pathology Department of Hospital Universitario San José, Popayán, with reading amplification (Dr. Nohelia Muñoz).

Table 2. Outpatient Laboratory Results

Laboratory Test	Result	Reference Values
Vitamin B_{12}	733.4 pg/mL	200 a 1100 pg/mL
25-hydroxyvitamin D	17.7 ng/mL	30-100 ng/mL

Source: Author's File.

explained by the known genetic and environmental risk factors[1]. The majority of cases present during childhood, with a higher prevalence in females. Risk factors include having a first-degree relative with CD, type 1 diabetes, Hashimoto's thyroiditis, other autoimmune diseases (such as autoimmune liver diseases, Sjögren's syndrome, and IgA nephropathy), Down syndrome, Turner syndrome, and IgA deficiency[9].

In Colombia, there are no established protocols for the diagnosis or treatment of CD, leading to low suspicion and underreporting of the disease. This may also be attributed to lower gluten consumption compared to industrialized countries, variations in gut microbiota, or early childhood exposure to infections that might prevent the development of autoimmunity[10].

The classic clinical presentation of CD includes chronic diarrhea, abdominal distension, and weight loss, as seen in the patient under discussion. Other common symptoms include recurrent abdominal pain, constipation, chronic fatigue, headache, aphthous stomatitis, dermatitis herpetiformis, osteoporosis, iron deficiency, anemia, elevated transaminases, and neurological symptoms such as anxiety, depression, and paresthesias, the latter being present in the described patient. Up to 21% of patients are asymptomatic. This patient presented with severe anemia, deficiencies in vitamins B_{12} and D, and possibly vitamin K deficiency (suggested by the prolonged INR). These findings, along with the clinical symptoms, indicated a malabsorption syndrome, leading to the suspicion of CD[1,9].

Patients with CD are at an increased risk of developing acute or chronic pancreatitis, which can worsen their overall prognosis. The prevalence of CD in patients with

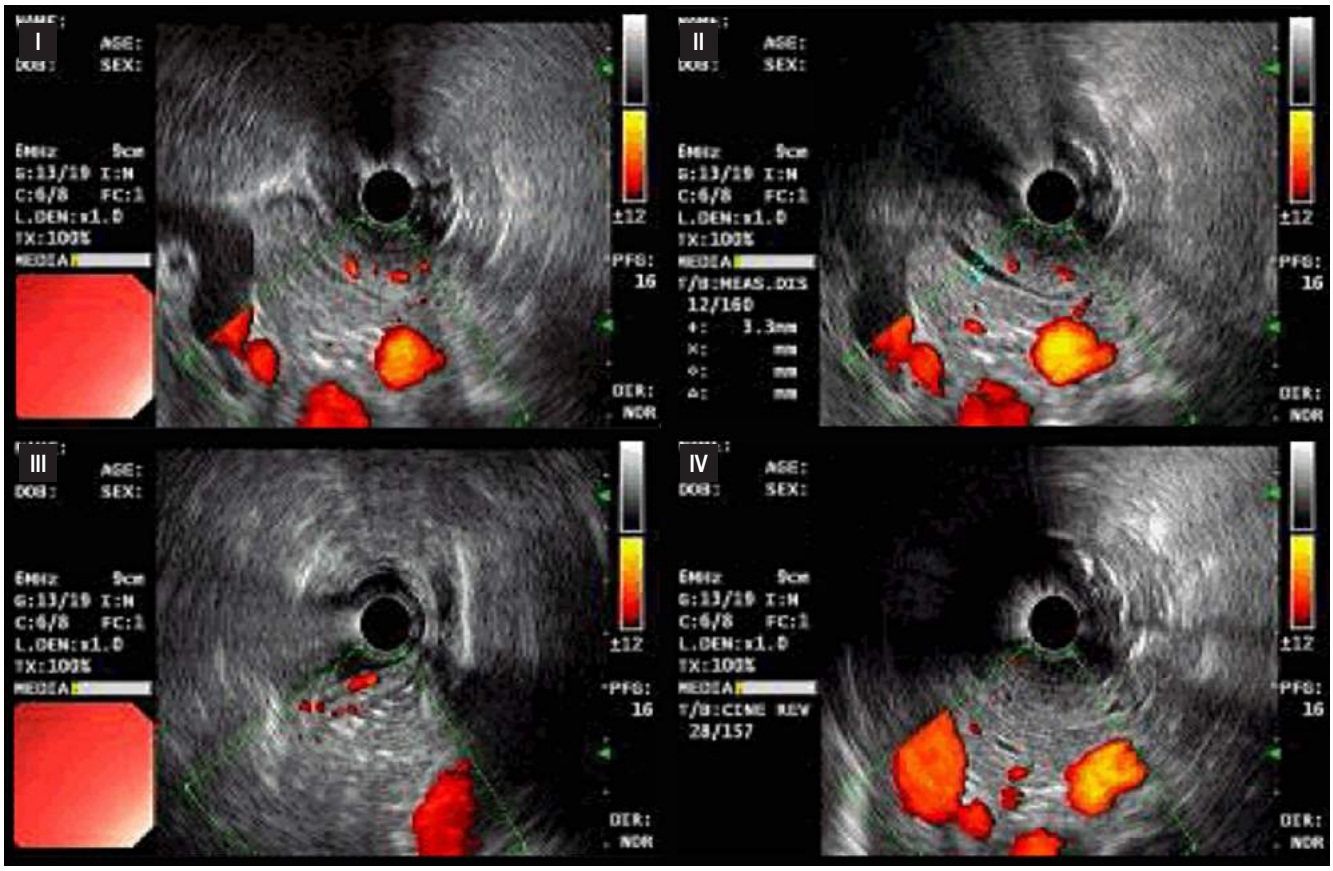


Figure 3. Endoscopic Ultrasound. Pancreatic parenchyma showing changes in its echostructure (**I**), with the presence of hyperechoic bands between 3 and 5 mm (**II**) and diffuse nodularity throughout the gland (**III**). The duct of Wirsung is dilated, measuring approximately 3.5 mm towards the head, with wall reinforcement and irregularity (IV). Source: Author's File.

chronic pancreatitis can be as high as 7.4%, as seen in the case of the patient described. Several theories have been proposed to explain this increased risk: malnutrition associated with CD affecting pancreatic secretion and causing atrophy; chronic inflammation of the duodenum and the papilla area leading to stenosis and subsequent pancreatic disease; and an autoimmune phenomenon involving specific autoantibodies against pancreatic islets, which is considered one of the most significant contributors to the relationship between pancreatitis and CD. Both endocrine and exocrine pancreatic functions can be affected, with exocrine insufficiency being more common in CD patients due to reduced secretin production resulting from duodenal involvement. This exacerbates the patients' nutritional status and prognosis[11].

The gold standard for diagnosing CD is a combination of positive serological tests—anti-tissue transglutaminase antibodies (tTGA-IgA), anti-endomysial antibodies, and antibodies against deamidated gliadin peptides—along with a duodenal biopsy following the CD protocol[8,12]. It is noteworthy that up to 80% of individuals with CD remain undiagnosed, as the prevalence of biopsy-diagnosed CD is approximately 0.7%[1]. In the patient described, positive serological tests and duodenal biopsy findings classified as Marsh 1 and 2 confirmed the diagnosis of CD[13].

The severity of histological changes in the small intestine does not necessarily correlate with the severity of clinical manifestations. In 2007, Brar and colleagues studied 499 CD patients and demonstrated a trend towards a higher proportion of patients presenting with atypical or silent (non-diarrheal) CD. This was accompanied by a trend towards less severe duodenal pathology; however, most patients still had the more severe form of villous atrophy, indicating a lack of correlation between clinical presentation and the degree of villous atrophy[14]. This was further evidenced in a 2013 Italian study, which included histological data from over

1400 adult CD patients and found that patients with mild enteropathy could not be distinguished from those with villous atrophy based on laboratory characteristics, with the possible exception of the t-TG antibody index[15].

The management of CD relies on strict adherence to a GFD[4]. Symptom improvement and resolution typically occur within days or weeks and often precede the normalization of serological markers and the atrophy of duodenal villi[1]. All patients with CD should be tested for micronutrient deficiencies, including iron, folic acid, vitamin B_{12}, and vitamin D, to enable timely supplementation if deficiencies are identified. Additionally, treatment with digestive enzymes is essential while managing CD with the GFD[11].

Periodic follow-up and monitoring of CD patients are recommended to assess the response to treatment, detect associated diseases, and monitor the progression to refractory forms of CD or neoplastic complications arising from the condition.

CONCLUSION

Celiac disease is a systemic, immune-mediated, and multifactorial pathology with a rising prevalence due to increased gluten consumption in the diet and greater clinical awareness for its diagnosis. It can affect individuals of any age and manifests predominantly in children and women. CD presents a diagnostic challenge, requiring high clinical suspicion and physician awareness to perform timely serological and histological studies for early management, thus significantly impacting patients' quality of life.

It is crucial to suspect CD in patients with compatible gastrointestinal symptoms, particularly those that are recurrent or refractory to conventional therapy, as well as in patients with chronic, resistant, or recurrent idiopathic pancreatitis.

Acknowledgments

We extend our gratitude to the patient and Dr. Nohelia Muñoz, pathologist at Hospital Universitario San José

Conflict of Interest

The authors report no conflicts of interest in relation to this article.

REFERENCES

1. Lebwohl B, Sanders DS, Green PHR. Coeliac disease. Lancet. 2018;391(10115):70-81. https://doi.org/10.1016/S0140-6736(17)31796-8
2. Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, et al. Global Prevalence of Celiac Disease: Systematic Review and Meta-analysis. Clin Gastroenterol Hepatol. 2018;16(6):823-836.e2. https://doi.org/10.1016/j.cgh.2017.06.037
3. Suarez-Correa J, López-Barreto JC, Mejía-Cardona AF, Paredes-Fernández AJ. Enfermedad celíaca: un reto diagnóstico en Colombia. Repert. Med. Cir. 2022; 31(2):123-32. https://doi.org/10.31260/RepertMedCir.01217372.1159
4. Cabrera-Chávez F, Granda-Restrepo DM, Arámburo-Gálvez JG, Franco-Aguilar A, Magaña-Ordorica D, Vergara-Jiménez MJ, et al. Self-Reported Prevalence of Gluten-Related Disorders and Adherence to Gluten-Free Diet in Colombian Adult Population. Gastroenterol Res Pract. 2016;2016:4704309. https://doi.org/10.1155/2016/4704309
5. Paredes-Echeverri S, Rodríguez AN, Cárdenas WA, Mendoza de Molano B, González JM. Seroprevalence of Antitransglutaminase and Antiendomysium Antibodies in Adult Colombian Blood Bank Donors. Can J Gastroenterol Hepatol. 2020;2020:7541941. https://doi.org/10.1155/2020/7541941
6. Lebwohl B, Rubio-Tapia A. Epidemiology, Presentation, and Diagnosis of Celiac Disease. Gastroenterology. 2021;160(1):63-75. https://doi.org/10.1053/j.gastro.2020.06.098
7. Denham JM, Hill ID. Celiac disease and autoimmunity: review and controversies. Curr Allergy Asthma Rep. 2013;13(4):347-53. https://doi.org/10.1007/s11882-013-0352-1
8. Caio G, Volta U, Sapone A, Leffler DA, De Giorgio R, Catassi C, et al. Celiac disease: a comprehensive current review. BMC Med. 2019;17(1):142. https://doi.org/10.1186/s12916-019-1380-z
9. Fasano A, Catassi C. Clinical practice. Celiac disease. N Engl J Med. 2012;367(25):2419-26. https://doi.org/10.1056/NEJMcp1113994
10. Parra-Medina R, Molano-Gonzalez N, Rojas-Villarraga A, Agmon-Levin N, Arango MT, Shoenfeld Y, et al. Prevalence of celiac disease in latin america: a systematic review and meta-regression. PLoS One. 2015;10(5):e0124040. https://doi.org/10.1371/journal.pone.0124040
11. Balaban DV, Enache I, Ciochina M, Popp A, Jinga M. Pancreatic involvement in celiac disease. World J Gastroenterol. 2022;28(24):2680-2688. https://doi.org/10.3748/wjg.v28.i24.2680
12. Husby S, Murray JA, Katzka DA. AGA Clinical Practice Update on Diagnosis and Monitoring of Celiac Disease-

Changing Utility of Serology and Histologic Measures: Expert Review. Gastroenterology. 2019;156(4):885-889. https://doi.org/10.1053/j.gastro.2018.12.010
13. Moscoso F, Quera R. Enfermedad celíaca. Revisión. Rev. méd. Chile. 2016;144(22):211-221. https://doi.org/10.4067/S0034-98872016000200010
14. Brar P, Kwon GY, Egbuna II, Holleran S, Ramakrishnan R, Bhagat G, et al. Lack of correlation of degree of villous atrophy with severity of clinical presentation of coeliac disease. Dig Liver Dis. 2007;39(1):26-9. https://doi.org/10.1016/j.dld.2006.07.014
15. Zanini B, Caselani F, Magni A, Turini D, Ferraresi A, Lanzarotto F, et al. Celiac disease with mild enteropathy is not mild disease. Clin Gastroenterol Hepatol. 2013;11(3):253-8. https://doi.org/10.1016/j.cgh.2012.09.027

https://doi.org/10.22516/25007440.1087

Case report

Metastasis of Lung Cancer in the Pancreas, Diagnosis Using Endoscopic Ultrasound: A Case Report

Estefanía García,[1*] Edgar Julián Ferreira,[2] Germán Tovar-Fierro,[3] Diana Gaona.[4]

OPEN ACCESS

Citation:
García E, Ferreira EJ, Tovar-Fierro G, Gaona D. Metastasis of Lung Cancer in the Pancreas, Diagnosis Using Endoscopic Ultrasound: A Case Report. Revista. colomb. Gastroenterol. 2024;39(2):230-235. https://doi.org/10.22516/25007440.1087

[1] Physician and Surgeon; Sedation Physician, GASTROCAL. Floridablanca, Santander, Colombia.
[2] Gastroenterologist and Advanced Endoscopist; Physician and Surgeon, Universidad Industrial de Santander (UIS); General Surgeon, UIS; Gastroenterologist, Universidad de Caldas, GASTROCAL, Los Comuneros – Hospital Universitario de Bucaramanga and Hospital Manuela Beltrán del Socorro. Floridablanca, Santander, Colombia.
[3] General Practitioner, Universidad Industrial de Santander; Specialist in Internal Medicine and Gastroenterology, Universidad Militar Nueva Granada and Hospital Militar Central; Undergraduate and Postgraduate Internal Medicine Professor, Universidad Autónoma de Bucaramanga (UNAB). Floridablanca, Santander, Colombia.
[4] Physician and Surgeon, Universidad Industrial de Santander (UIS); Specialist in Pathology, Universidad de Antioquia; Advanced Specialization in Oncological Pathological Anatomy, Universidad Autónoma de México; Oncological Pathologist, Laboratorio Isabel Bolívar and Hospital Universitario de Santander. Floridablanca, Santander, Colombia.

***Correspondence**: Estefanía García.
faniagarcia.95@gmail.com

Received: 09/06/2023
Accepted: 25/08/2023

Abstract

Only 2% of malignant tumor lesions in the pancreas represented metastatic lesions. Endoscopic biliopancreatic ultrasonography, with the possibility of guided biopsy, is one of the main diagnostic methods currently available for lesions in the pancreas. A case of a male patient with a history of small cell carcinoma of the lung with findings of a tumor lesion in the pancreas corresponding to metastasis was described.

Keywords

Endoscopic ultrasound, fine needle aspiration guided by endoscopic ultrasound, metastasis, pancreas.

INTRODUCTION

Adenocarcinoma is the most common solid tumor lesion in the pancreas, accounting for approximately 85% of cases, followed by neuroendocrine tumors, which make up 5%, and only 2% of cases are metastatic lesions. The remaining cases include other types of lesions such as pancreatic lymphoma, solid pseudopapillary tumor, pancreatoblastoma, and neurogenic tumors[1-5]. The primary tumors most likely to metastasize to the pancreas include renal cell carcinoma, lung cancer, melanoma, breast cancer, colon cancer, bladder cancer, and others[1,2,5-7]. Biliopancreatic endoscopic ultrasound is considered the most effective study for detecting pancreatic masses compared to other imaging studies, with sensitivity and specificity rates of 84.9% and 95.9%, respectively, for detecting pancreatic metastases[8,9].

Moreover, fine-needle aspiration guided by endoscopic ultrasound is the first-line diagnostic tool for the histopathological identification of these lesions, with reported accuracy rates of 93.4% for lesions larger than 20 mm,

© 2024 Asociación Colombiana de Gastroenterología

83.5% for lesions between 10 mm and 20 mm, and 82.5% for lesions smaller than 10 mm[10]. Complications from the procedure are infrequent, with an approximate rate of 2.5%, the most common being abdominal pain, and rare cases including pancreatitis, bleeding, perforation, and biliary peritonitis[11-13]. Additionally, this method has been shown to have advantages over other sample acquisition techniques such as percutaneous puncture and endoscopic retrograde cholangiopancreatography, whether used as a first diagnostic option or as an alternative after the failure of these procedures. Studies have found false negatives that were later confirmed as positive by fine-needle aspiration[12,14]. This article describes the case of a patient with small cell lung carcinoma metastasis in the uncinate process and body of the pancreas.

CLINICAL CASE

A 58-year-old male patient initially presented in August 2021 with an episode of hemoptysis, constitutional symptoms, progressive dyspnea, and decreased functional status. A contrast-enhanced computed tomography (CT) scan of the chest and abdomen revealed a large mediastinal mass infiltrating and compressing the esophagus, vascular, and bronchial structures, with no evident abdominal infiltration (**Figures 1** and **2**). A biopsy confirmed a small cell lung neuroendocrine carcinoma through immunohistochemistry. Staging studies at that time were negative for metastatic lesions, making the patient a candidate for chemotherapy and radiotherapy. He completed three cycles of chemotherapy with cisplatin and etoposide, along with 23 sessions of consolidative radiotherapy to the mediastinum, between December 2021 and March 2022, achieving an adequate response at that time.

The patient subsequently returned to the emergency department in May 2023 due to progressive dyspnea. A chest CT scan revealed mediastinal involvement from a mass infiltrating and compressing the vascular structures, esophagus, and bronchi. An abdominal CT scan showed a tumor lesion in the uncinate process extending to the body of the pancreas (**Figures 3** and **4**). Consequently, a linear biliopancreatic endoscopic ultrasound was performed, identifying a tumor lesion measuring 62 x 54 mm in diameter, originating from the uncinate process and extending to the body of the pancreas (**Figure 5**). The ultrasound also revealed periportal lesions compatible with multiple adenopathies and distal bile duct invasion without secondary dilation (**Figure 6**).

A biopsy was performed using endoscopic ultrasound guidance, employing a transgastric approach with a modified wet suction technique and a 19G needle. The sample obtained was analyzed for cytopathology and histopathology, leading to a final diagnosis of a high-grade malignant tumor with small round cell morphology (**Figures 7** and **8**). The patient received an additional dose of chemotherapy in the emergency department, which resulted in an unfavorable clinical outcome and a decline to NYHA functional class III/IV. As a result, it was ultimately determined that the patient was a candidate for a home palliative care package.

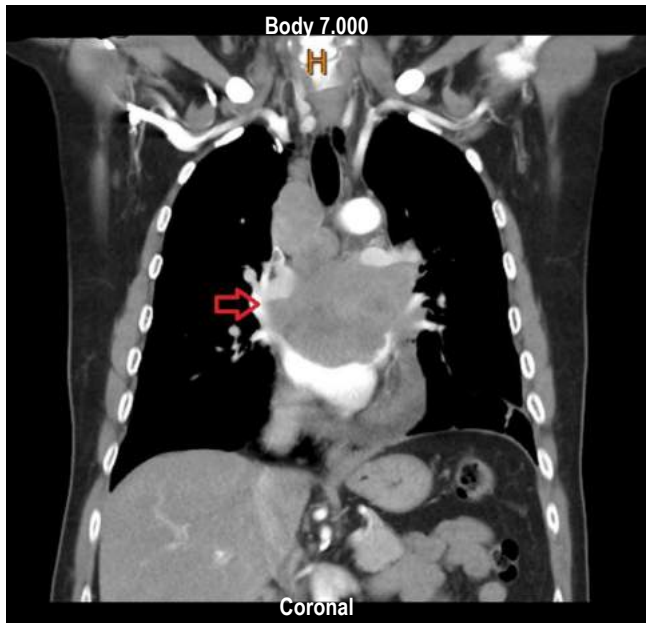


Figure 1. Contrast-enhanced chest CT, coronal view. Mediastinal mass compressing and infiltrating the esophagus and vascular structures. Author's File.

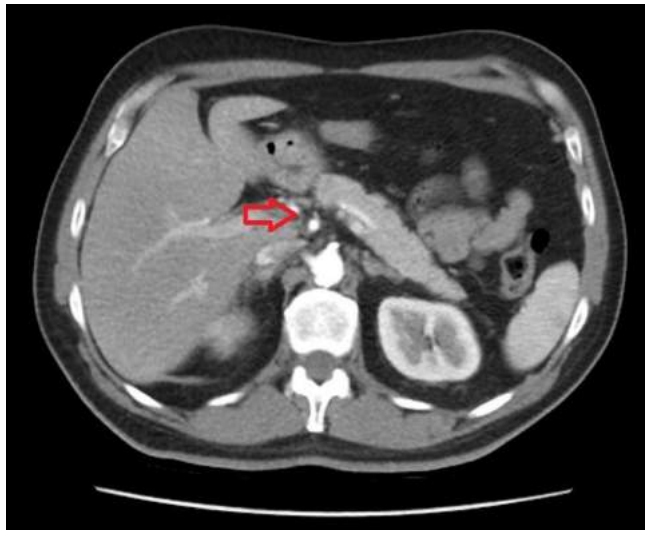


Figure 2. Contrast-enhanced abdominal CT, transverse view. Pancreas without evidence of tumor lesions or infiltration. Author's File.

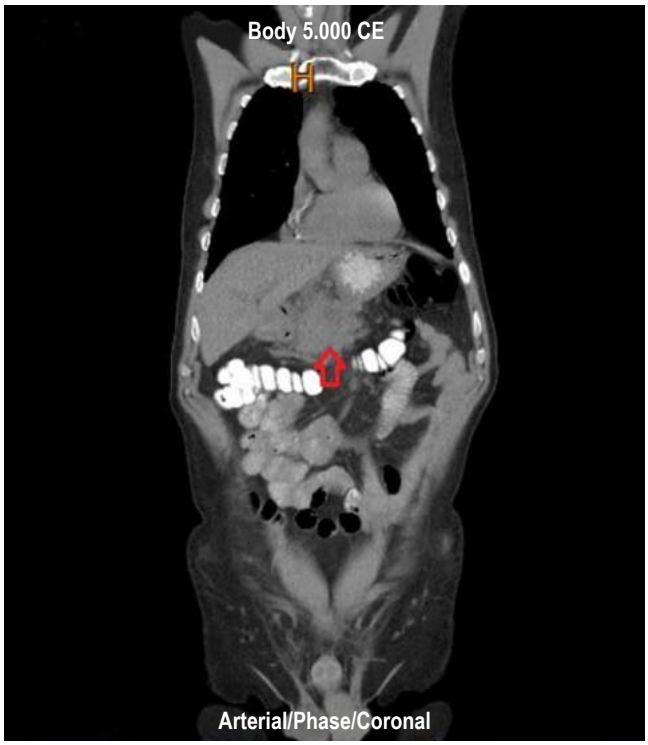


Figure 3. Contrast-enhanced abdominal CT, coronal view. Mass occupying the uncinate process and extending to the body of the pancreas. Author's File.



Figure 4. Contrast-enhanced abdominal CT, transverse view. A window from the stomach for eventual ultrasound-guided biopsy is observed. Author's File.

DISCUSSION

Biliopancreatic endoscopic ultrasound is regarded as the most effective imaging technique for detecting biliopancreatic lesions[15]. Its sensitivity for detecting pancreatic masses is significantly higher compared to contrast-enhanced CT, with rates of approximately 98% versus 74%, respectively, particularly for lesions smaller than 2 cm[10,11]. The sensitivity and specificity for detecting pancreatic metastases using endoscopic ultrasound are 84.9% and 95.9%, respectively[16]. Moreover, fine-needle aspiration biopsy guided by endoscopic ultrasound is considered the first-line histopathological diagnostic method for pancreatic lesions, boasting high sensitivity and specificity for



Figure 5. Linear biliopancreatic endoscopic ultrasound. Mass originating from the uncinate process and extending to the body of the pancreas. Author's File.



Figure 6. Linear biliopancreatic endoscopic ultrasound. Partial invasion of the bile duct. Author's File.

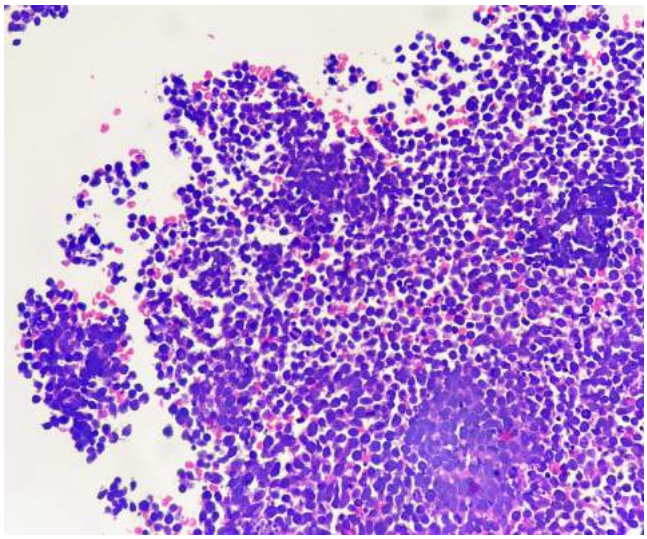


Figure 7. Hematoxylin and eosin stain, 40x. Small cells with hyperchromatic round nuclei arranged in sheets, with frequent mitotic figures and cellular debris. Author's File.

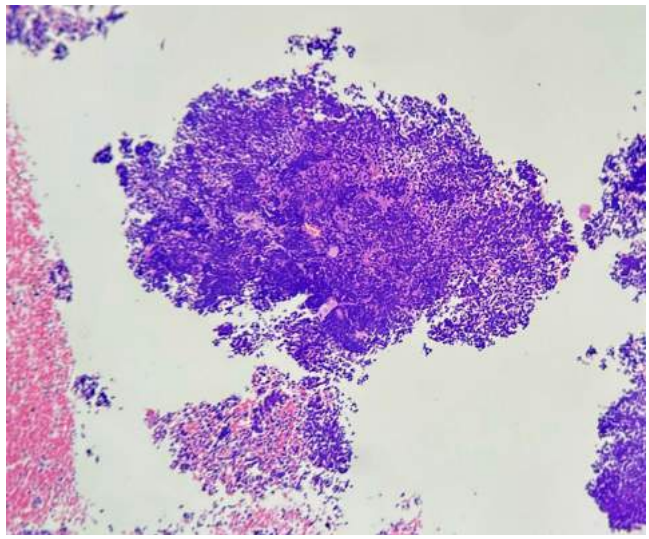


Figure 8. Hematoxylin and eosin stain, 10x. Sheets of small cells with round nuclei and frequent areas of necrosis. Author's File.

detecting metastases, ranging from 84% to 92% and 96% to 98%, respectively, with an overall diagnostic accuracy of 89.3% to 93.3%[1,4,7-9,16-19]. Reported accuracy is 93.4% for lesions larger than 20 mm, 83.5% for lesions between 10 mm and 20 mm, and 82.5% for lesions smaller than 10 mm[10]. While CT and MRI are recommended for diagnosis and staging, they perform poorly in detecting small masses compared to endoscopic ultrasound[10,18,20-24]. Sensitivity is influenced not only by lesion size but also by factors such as solid consistency and location in the neck and body of the pancreas, which enhance diagnostic potential[9,25]. Some literature suggests endoscopic ultrasound as a screening tool for high-risk patients, such as those with a first-degree family history of pancreatic cancer or genetic mutations and syndromes associated with lesion development, like Peutz-Jeghers syndrome[26,27].

Pancreatic metastases are rare, with limited reports in the literature, and their prevalence is approximately 2%[1-5]. The primary tumors most frequently metastasizing to the pancreas include cancers of the kidney, lung, gastrointestinal tract, and breast[1,2,5-7]. Most metastatic lesions appear as solid, hypoechoic, and hypovascularized[1,5]. A recent retrospective study involving 2560 patients found that 28 had pancreatic metastases (1%), with only 20 undergoing endoscopic ultrasound. Among these, five had lung cancer (2 with small cell carcinoma and 3 with squamous cell carcinoma). The small cell carcinoma lesions showed hypervascularization, contrasting with the predominantly hypoechoic, hypovascularized lesions[1]. In this case, conventional linear biliopancreatic endoscopic ultrasound was performed along with fine-needle aspiration, revealing solid, hypoechoic lesions without Doppler signal, aligning with most studies and differing from the last mentioned study.

It can be asserted that the presented case corresponds to metastasis of small cell lung neuroendocrine carcinoma to the pancreas. At the time of diagnosis, imaging showed only a mediastinal mass with local involvement of the esophagus and vascular structures, without any intra-abdominal lesions suggestive of neoplasia or other findings in other systems that could indicate a primary tumor different from the lung. Moreover, biopsy results along with immunohistochemistry confirmed the pulmonary origin. Additionally, the sample taken from the pancreatic lesion via endoscopic ultrasound showed histopathological results consistent with a small round cell malignant tumor, correlating with the pathology findings of the lung mass. This rules out the possibility of a new primary pancreatic tumor. This latter biopsy is crucial for determining the prognosis and guiding treatment or interventions that would benefit the patient.

CONCLUSIONS

Biliopancreatic endoscopic ultrasound is an essential tool for diagnosing pancreatic tumor lesions. It has demonstrated high diagnostic performance and safety when obtaining biopsy samples. It should be considered a first-line diagnostic tool for such lesions. Pancreatic metastases are very rare, and obtaining a histopathological sample is crucial for the defi-

nitive diagnosis of these lesions. Biliopancreatic endoscopic ultrasound enables this by allowing guided puncture, providing greater accuracy and fewer complications compared to other diagnostic methods. The imaging characteristics of the metastatic small cell carcinoma lesion in the pancreas in this clinical case, obtained via ultrasound, align with the majority of studies with similar histopathological results.

REFERENCES

1. Teodorescu C, Bolboaca SD, Rusu I, Pojoga C, Seicean R, Mosteanu O, et al. Contrast enhanced endoscopic ultrasound in the diagnosis of pancreatic metastases. Med Ultrason. 2022;24(3):277–283. https://doi.org/10.11152/mu-3495
2. Adsay NV, Andea A, Basturk O, Kilinc N, Nassar H, Cheng JD. Secondary tumors of the pancreas: an analysis of a surgical and autopsy database and review of the literature. Virchows Arch. 2004;444(6):527–535. https://doi.org/10.1007/s00428-004-0987-3
3. Palazzo M. Role of contrast harmonic endoscopic ultrasonography in other pancreatic solid lesions: Neuroendocrine tumors, autoimmune pancreatitis and metastases. Endoscopic Ultrasound. 2016;5(6):373–376. https://doi.org/10.4103/2303-9027.195870
4. Atiq M, Bhutani MS, Ross WA, Raju GS, Gong Y, Tamm EP, et al. Role of endoscopic ultrasonography in evaluation of metastatic lesions to the pancreas: a tertiary cancer center experience: A tertiary cancer center experience. Pancreas. 2013;42(3):516–523. https://doi.org/10.1097/MPA.0b013e31826c276d
5. Ardengh JC, Lopes CV, Kemp R, Venco F, de Lima-Filho ER, dos Santos JS. Accuracy of endoscopic ultrasound-guided fine-needle aspiration in the suspicion of pancreatic metastases. BMC Gastroenterology 2013;13(1):63. https://doi.org/10.1186/1471-230X-13-63
6. Fusaroli P, D'Ercole MC, De Giorgio R, Serrani M, Caletti G. Contrast harmonic endoscopic ultrasonography in the characterization of pancreatic metastases (with video). Pancreas. 2014;43(4):584–587. https://doi.org/10.1097/MPA.0000000000000081
7. El Hajj II, LeBlanc JK, Sherman S, Al-Haddad MA, Cote GA, McHenry L, et al. Endoscopic ultrasound-guided biopsy of pancreatic metastases: a large single-center experience. Pancreas. 2013;42(3):524–530. https://doi.org/10.1097/MPA.0b013e31826b3acf
8. Otsuka Y, Kamata K, Kudo M. Contrast-enhanced harmonic endoscopic ultrasound-guided puncture for the patients with pancreatic masses. Diagnostics (Basel). 2023;13(6):1039. https://doi.org/10.3390/diagnostics13061039
9. Wang M, Huang S, Pei R, Lin J, Yang X. Endoscopic ultrasonography guided transgastric trans-portal system fine needle aspiration for diagnosing pancreatic head and uncinate process malignancy. Ann Transl Med. 2019;7(23):719. https://doi.org/10.21037/atm.2019.11.137
10. Kitano M, Yoshida T, Itonaga M, Tamura T, Hatamaru K, Yamashita Y. Impact of endoscopic ultrasonography on diagnosis of pancreatic cancer. J Gastroenterol. 2019;54(1):19–32. https://doi.org/10.1007/s00535-018-1519-2
11. Mosquera GA, Carvajal JJ, Gómez AA, Niño S, Cañadas R. Ultrasonido endoscópico, aplicaciones actuales en tumores sólidos gastrointestinales. Rev. colomb. Gastroenterol. 2020;35(4):506–518. https://doi.org/10.22516/25007440.521
12. Iglesias J, Domínguez JE. Endoscopic ultrasound-guided biopsy for the evaluation of pancreatic tumors. Gastroenterol Hepatol. 2007;30(10):597–601. https://doi.org/10.1157/13112588
13. Eloubeidi MA, Tamhane A, Varadarajulu S, Wilcox CM. Frequency of major complications after EUS-guided FNA of solid pancreatic masses: a prospective evaluation. Gastrointest Endosc. 2006;63(4):622–629. https://doi.org/10.1016/j.gie.2005.05.024
14. Gress F, Gottlieb K, Sherman S, Lehman G. Endoscopic ultrasonography-guided fine-needle aspiration biopsy of suspected pancreatic cancer. Ann Inter Med. 2001;134(6):459–464. https://doi.org/10.7326/0003-4819-134-6-200103200-00010
15. Razpotnik M, Bota S, Essler G, Weber-Eibel J, Peck-Radosavljevic M. Endoscopic ultrasound (EUS) in pancreatic masses with inconclusive radiologic workup - a case series and short review of the literature. Med Ultrason. 2021;23(1):107–110. https://doi.org/10.11152/mu-2408
16. Tanaka H, Matsusaki S. The utility of endoscopic-ultrasonography-guided tissue acquisition for solid pancreatic lesions. Diagnostics (Basel). 2022;12(3):753. https://doi.org/10.3390/diagnostics12030753
17. Masuda S, Koizumi K, Shionoya K, Jinushi R, Makazu M, Nishino T, et al. Comprehensive review on endoscopic ultrasound-guided tissue acquisition techniques for solid pancreatic tumor. World J Gastroenterol. 2023;29(12):1863–1874. https://doi.org/10.3748/wjg.v29.i12.1863
18. Levine I, Trindade AJ. Endoscopic ultrasound fine needle aspiration vs fine needle biopsy for pancreatic masses, subepithelial lesions, and lymph nodes. World J Gastroenterol. 2021;27(26):4194–4207. https://doi.org/10.3748/wjg.v27.i26.4194

19. Melita G, Pallio S, Tortora A, Crinò SF, Macrì A, Dionigi G. Diagnostic and interventional role of endoscopic ultrasonography for the management of pancreatic neuroendocrine neoplasms. J Clin Med. 2021;10(12):2638. https://doi.org/10.3390/jcm10122638
20. Terada S, Kikuyama M, Kawaguchi S, Kanemoto H, Yokoi Y, Kamisawa T, et al. Proposal for endoscopic ultrasonography classification for small pancreatic cancer. Diagnostics (Basel). 2019;9(1):15. https://doi.org/10.3390/diagnostics9010015
21. Wang W, Shpaner A, Krishna SG, Ross WA, Bhutani MS, Tamm EP, et al. Use of EUS-FNA in diagnosing pancreatic neoplasm without a definitive mass on CT. Gastrointest Endosc. 2013;78(1):73–80. https://doi.org/10.1016/j.gie.2013.01.040
22. Dietrich CF, Jenssen C. Modern ultrasound imaging of pancreatic tumors. Ultrasonography. 2020;39(2):105–113. https://doi.org/10.14366/usg.19039
23. D'Onofrio M, Crosara S, Signorini M, De Robertis R, Canestrini S, Principe F, et al. Comparison between CT and CEUS in the diagnosis of pancreatic adenocarcinoma. Ultraschall Med. 2013;34(4):377–381. https://doi.org/10.1055/s-0032-1325324
24. Khashab MA, Yong E, Lennon AM, Shin EJ, Amateau S, Hruban RH, et al. EUS is still superior to multidetector computerized tomography for detection of pancreatic neuroendocrine tumors. Gastrointest Endosc. 2011;73(4):691–696. https://doi.org/10.1016/j.gie.2010.08.030
25. Choi SY, Kim JH, Eun HW, Ryu H. Factors affecting the ability of abdominal ultrasonography to detect focal pancreatic lesions identified using endoscopic ultrasonography. Ultrasonography. 2020;39(3):247–256. https://doi.org/10.14366/usg.19078
26. Yousaf MN, Chaudhary FS, Ehsan A, Suarez AL, Muniraj T, Jamidar P, et al. Endoscopic ultrasound (EUS) and the management of pancreatic cancer. BMJ Open Gastroenterol. 2020;7(1):e000408. https://doi.org/10.1136/bmjgast-2020-000408
27. Chari ST, Kelly K, Hollingsworth MA, Thayer SP, Ahlquist DA, Andersen DK, et al. Early detection of sporadic pancreatic cancer: summative review: Summative review. Pancreas. 2015;44(5):693–712. https://doi.org/10.1097/MPA.0000000000000368