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Original article

Challenges in the Diagnosis of Gastroparesis: Divergence Between Gastric Emptying Scintigraphy Results for Liquids and Solids

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Abstract

Introduction: Gastric emptying scintigraphy with solid food is the recommended gold standard for studying gastroparesis in patients after mechanical obstruction has been ruled out, according to the latest clinical guidelines. Although gastric emptying for liquids can also be assessed, the results of these two phases may not always align. **Objective:** To determine the level of concordance between gastric emptying scintigraphy results for solids and liquids in the evaluation of gastroparesis at three nuclear medicine centers in Bogotá, Colombia. **Methodology:** Data from all patients who underwent both phases of the study were reviewed. Patients under 18 years of age, those with accelerated results in either phase, or those with incomplete data were excluded. Cohen's kappa coefficient was calculated to assess agreement between the tests. A bivariate analysis was performed to examine the association between test results, the level of agreement, and sociodemographic and clinical variables. **Results:** A total of 210 patients met the inclusion criteria. Delayed results were observed in the solid phase in 86 patients (41%) and in the liquid phase in 181 patients (86%). The kappa value was $\kappa = 0.082$ (95% confidence interval [CI]: 0.005–0.16), with statistically significant results ($p < 0.05$). The most common pattern of divergence was normal solid-phase emptying with delayed liquid-phase emptying, observed in 102 patients (48.6%). **Conclusion:** The level of concordance between gastric emptying scintigraphy for liquids and solids is low. The solid phase is considered the gold standard, and the results of the liquid phase should be interpreted with caution, taking into account the clinical context of each patient.

Keywords

Gastroparesis, gastric emptying, scintigraphy, food.

INTRODUCTION

Gastroparesis is a syndrome characterized by delayed gastric emptying associated with upper abdominal symptoms in the absence of mechanical gastric obstruction[1]. It falls under the category of functional gastrointestinal disorders, which are highly prevalent and poorly understood, significantly impacting healthcare and socioeconomic systems[2]. Regarding its etiology, the disorder is primarily idiopathic but is also linked to diabetes *mellitus*, postsurgical conditions, and, to a lesser extent, autoimmune diseases, paraneoplastic syndromes, neurological conditions, medications, and eating disorders[3].

The true prevalence of gastroparesis is unknown, though data is available for specific countries. For instance, in the United Kingdom, a prevalence of 13.8 per 100,000 inhabitants and an incidence of 1.9 per 100,000 inhabitants were reported in 2016[4]. Similarly, a study analyzing 43,827,910 medical records in the United States found a prevalence of 0.16% in the general population[5]. In Colombia, no specific data is available; however, worldwide prevalence has been found to range between 20% and 40% in diabetic patients,

with studies consistently reporting a significantly higher prevalence in women compared to men[6].

Gastric emptying scintigraphy (GES) is a nuclear medicine test used to evaluate gastric emptying by consuming a standardized caloric meal containing a total of 255 kcal. It assesses the emptying of solids (solid-phase gastric emptying, SGE) or liquids (liquid-phase gastric emptying, LGE) labeled with radioisotopes (technetium-99m in Colombia) and is currently considered the most appropriate diagnostic method for assessing gastric motility[7,8]. In 2008, the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society reached a consensus that standardized the meal and reference values for SGE (**Table 1**)[9]. However, for LGE, there is no consensus among societies on universally accepted normal values. Nonetheless, multiple studies have established varying normal ranges for the mean gastric emptying time of clear liquids, ranging from 1.5 to 25 minutes[10–13]. In nuclear medicine practice, the upper normal limit proposed by Dr. Harvey Ziessman, set at 26 minutes, is widely accepted[14].

Table 1. Reference Values for Gastric Retention in SGE

Time	Lower Limit of Gastric Retention (%)	Upper Limit of Gastric Retention (%)
1 hour	30%	90%
2 hours	-	60%
3 hours	-	30%
4 hours	-	10%

Adapted from: Abell TL and colleagues. J Nucl Med Technol. 2008;36(1):44–54[9].

Although recent guidelines, such as those published in 2020 by the European Society of Neurogastroenterology and Motility in collaboration with United European Gastroenterology[15] and in 2022 by the American College of Gastroenterology[16], specifically recommend SGE as the diagnostic method for patients with suspected gastroparesis, it is common for both phases to be performed in these patients. However, previous studies have demonstrated that the results of the two phases may not always be consistent. Notably, it has been found that a significant percentage of patients with gastroparesis symptoms and normal SGE results test positive in LGE[8,17,18]. In light of this, the objective of the present study was to determine the concordance between gastric emptying scintigraphy results for solids and liquids in diagnosing gastroparesis at three nuclear medicine centers in Bogotá, Colombia, between July 1, 2020, and July 31, 2023.

METHODOLOGY

Study Design and Population

A multicenter, cross-sectional study was conducted at the nuclear medicine centers of Clínica Universitaria Colombia, Clínica Reina Sofía, and Medicina Nuclear Palermo in Bogotá, Colombia, from July 1, 2020, to July 31, 2023. All SGE and LGE studies performed during this period were reviewed, and cases involving patients over 18 years of age who had undergone both phases were selected. Patients with a history of gastric surgery, those with accelerated gastric emptying in either phase, or those with incomplete test, clinical, or demographic data were excluded from the analysis.

Data Collection and Result Analysis

All three centers followed the protocol established by the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society for SGE[9]. This protocol standardized the test meal to include 118 mL of egg whites mixed with 1 mCi (37 MBq) of technetium-99m-labeled radiocolloid during preparation in a microwave or non-stick pan. Additionally, the meal included two slices of white bread, 30 grams of jam, and 120 mL of water. The food could be consumed either as a sandwich or separately, ensuring that the patient ate the entire meal or at least 50% within 10 minutes. Afterward, with the patient in the supine position, immediate anterior and posterior projection images were taken at one hour, two hours, and four hours. Gastric retention and emptying percentages were then evaluated with correction for radiopharmaceutical decay.

In the case of LGE, 300 mL of water labeled with 1 mCi (37 MBq) of 99mTc-DTPA was used, and a dynamic study was performed over 40 minutes with the patient in a supine position. The mean gastric emptying time was obtained and evaluated. Both phases were conducted on different days, early in the morning, after a minimum fasting period of six hours and with the discontinuation of all medications that could affect gastric motility (opioids, prokinetics, antispasmodics, and benzodiazepines) 48 hours prior to the study.

The studies provided quantitative results, and for the analysis, the reference values and criteria defined by the Society of Nuclear Medicine and the American Neurogastroenterology and Motility Society were used for the interpretation and diagnosis of SGE[9]. According to the percentages and times obtained, the final result was described as normal SGE if all values were within the normal range, or delayed SGE if at least one measurement was abnormal. For LGE, the reference was the study by Ziessman and colleagues[14], which established an upper

limit of normal at 26 minutes. Times below 26 minutes were classified as normal LGE, and times above 26 minutes were classified as delayed LGE.

The studies were conducted using Infinia™ gamma cameras (GE HealthCare) with detectors positioned in the anterior and posterior planes. Data processing was carried out on Xeleris™ workstations, applying corrections for positioning and time. Study results were visualized through the Carestream VUE PACS platform. Clinical data were obtained from the Carestream VUE RIS, AVICENA, and SOPHIA information systems.

Statistical analysis was performed using R software version 4.3.1[19] and EpiInfo version 7.2.6[20]. Cohen's kappa coefficient was calculated to assess the strength of agreement between tests, based on the study by Landis and Koch (**Table 2**)[21]. Qualitative variables were presented as absolute and relative frequencies, while quantitative variables were described using measures of central tendency and dispersion. A bivariate analysis was conducted between the results of each test and their agreement with sociodemographic and clinical variables using the Wilcoxon rank-sum test and Fisher's exact test for qualitative variables, and Pearson's chi-square test for quantitative variables.

Table 2. Strength of Agreement Based on Kappa Value

Kappa Value	Strength of Agreement
0.00	Poor
0.01-0.20	Slight
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Substantial
0.81-1.00	Almost perfect

Source: Landis JR, and colleagues. Biometrics. 1977;33(1):159–74[21].

Ethical Considerations

This study was approved by the Ethics Committee for Research of Fundación Universitaria Sanitas under Approval Minutes CEIFUS 1221-23. It adhered to the current national and international regulations governing human research, including the Declaration of Helsinki, Resolution 8430 of 1993, Resolution 1995 of 1999, and Resolution 2378 of 2008.

RESULTS

During the study period, a total of 1,217 gastric emptying scintigraphies were performed across the three centers. After excluding patients under 18 years of age or those who had undergone only one phase of the test, 242 eligible patients were identified. Of these, 32 met at least one exclusion criterion, resulting in a total of 210 patients included in the analysis. The sociodemographic and clinical characteristics of the included patients are summarized in **Table 3**. The median age was 56 years (interquartile range [IQR]: 40–65), and 85% of the study population was female. Normal nutritional status, as defined by body mass index, accounted for 47% of the population. Diabetes was present in 19% of patients, and 24% had a history of autoimmune disease. Regarding the gastric emptying results, 41% of patients showed delayed solid-phase gastric emptying, while 86% showed delayed liquid-phase gastric emptying. Concordance between the two phases was observed in 101 patients (48.1%), while 109 patients (51.9%) showed discordant results.

Table 3. Demographic, Clinical, and Gastric Emptying Scintigraphy Results of Studied Patients

Variable	n = 210
Demographic Characteristics	
Age in years, median (IQR)	56 (40-65)
Sex, n (%)	
- Female	178 (85)
- Male	32 (15)
Clinical Characteristics	
Nutritional status, n (%)	
- Underweight	9 (4.3)
- Normal	99 (47)
- Obesity	25 (12)
- Overweight	77 (37)
Diabetes, n (%)	39 (19)
Autoimmune disease, n (%)	50 (24)
Scintigraphy result	
Delayed solid-phase emptying, n (%)	86 (41%)
Delayed liquid-phase emptying, n (%)	181 (86%)
Time (days) between tests	5 (2-9)

IQR: Interquartile Range. Author's own research.

Table 4 shows that being female was associated with delayed gastric emptying scintigraphy results for liquids ($p = 0.004$). No other variables showed significant differences.

Table 4. Demographic and Clinical Variables by Gastric Emptying Scintigraphy Results

Variable	Liquid-Phase Scintigraphy Results			Solid-Phase Scintigraphy Results		
	Delayed n = 181	Normal n = 29	*p*-Value	Delayed n = 86	Normal n = 124	*p*-Value
Age in years, median (IQR)	56.00 (39.00-65.00)	55.00 (43.00-65.00)	>0.9[a]	57.50 (40.00-67.75)	55.00 (39.75-64.00)	0.5[a]
Sex, n (%)			0.004			0.2[c]
- Female	159 (88%)	19 (66%)		76 (88%)	102 (82%)	
- Male	22 (12%)	10 (34%)		10 (12%)	22 (18%)	
Nutritional status, n (%)			0.3[b]			0.4[b]
- Underweight	7 (3.9%)	2 (6.9%)		6 (7.0%)	3 (2.4%)	
- Normal	89 (49%)	10 (34%)		42 (49%)	57 (46%)	
- Obesity	20 (11%)	5 (17%)		10 (12%)	15 (12%)	
- Overweight	65 (36%)	12 (41%)		28 (33%)	49 (40%)	
Diabetes, n (%)	35 (19%)	4 (14%)	0.5	16 (19%)	23 (19%)	>0.9[c]
Autoimmune disease, n (%)	45 (25%)	5 (17%)	0.4	20 (23%)	30 (24%)	0.9[c]

[a]Wilcoxon rank-sum test. [b]Fisher's exact test. [c]Pearson's chi-square test. Author's own research.

Table 5 provides a comparison of the results from both phases for all patients, stratified by the variables studied. It was found that 48.6% of patients exhibited delayed gastric emptying in the liquid phase (LGE) while presenting normal results in the solid phase (SGE), representing the most common pattern of divergence between the two tests. No statistically significant differences were identified when analyzing the results by sex, diabetes, autoimmune disease, or obesity. Cohen's kappa coefficient was calculated to assess the agreement between the results of gastric emptying scintigraphy for solids and liquids. The κ value was 0.082 (95% confidence interval [CI]: 0.005–0.16), which was statistically significant ($p < 0.05$).

DISCUSSION

Gastroparesis is a condition predominantly of idiopathic origin, and due to the non-specific nature of its symptoms, it presents a diagnostic challenge in some cases and represents a significant cause of morbidity[22]. This study evaluated the level of agreement between the two phases of the diagnostic test currently considered the gold standard for diagnosing this condition: gastric emptying scintigraphy[8].

In this study, most of the patients with gastroparesis were female, consistent with reports in the literature[6]. Female sex was the only factor associated with delayed gastric emptying in the liquid phase (LGE). However, previous studies have not demonstrated sex differences in liquid gastric emptying, unlike solid gastric emptying. For instance, a study by Lorena and colleagues showed that the solid gastric emptying time was longer in women than in men[23]. Similarly, when evaluating the divergence between the results of both tests by sex, no statistically significant differences were found.

Of note, a higher proportion of patients had a history of autoimmune diseases than diabetes, and the percentage of diabetic patients was lower than that reported in the literature, which is approximately 30%[6]. It is essential to remember that in clinical practice, diagnosing gastroparesis in diabetic individuals involves multiple criteria. Diagnosis is not based solely on symptoms, history, and the exclusion of mechanical causes; a noninvasive test confirming delayed gastric emptying is also required[24].

In some previous studies, such as the one conducted by Sachdeva and colleagues[17], both phases were assessed simultaneously using a dual-isotope radioisotopic study, where solid food was labeled with 99mTc and liquid with 111In. In Colombia, 111In is not available for dual studies, so the two phases were conducted on different days. Nevertheless, similar and adequate preparation was ensu-

Table 5. Comparison of Results from Both Phases by Studied Variables

Variables	LGE	GVS			Kappa	*p*-Value
			Delayed	Normal		
All patients		Delayed	79	102	0.08	0.03
		Normal	7	22		
Female		Delayed	71	88	0.06	0.11
		Normal	5	14		
Male		Delayed	8	14	0.12	0.32
		Normal	2	8		
Diabetes		Delayed	15	20	0.06	0.4
		Normal	1	3		
Autoimmune disease		Delayed	17	28	-0.06	0.37
		Normal	3	2		
Obesity		Delayed	9	11	0.14	0.28
		Normal	1	4		

LGE: Liquid-Phase Gastric Emptying; SGE: Solid-Phase Gastric Emptying. Author's own research.

red for both studies. Additionally, institutional protocols did not require that one specific phase be performed first, making the order of the tests irrelevant.

Although previous studies had shown that 26% to 32% of patients exhibit discordant results between LGE and SGE[14,17,18], this is the first study to evaluate the strength of agreement between the two tests. The study found a low level of agreement, likely due to the substantial proportion of patients with delayed results in LGE but normal results in SGE (**Table 5**).

A significant factor to take into account is that, during the SGE study, patients stand up from the gamma camera and remain seated between imaging sessions, whereas, for the LGE study, patients remain in a supine position for 40 minutes immediately after ingesting the radiolabeled water. It has been shown that body position and gravity can significantly influence liquid gastric emptying. Although the documented mean time for liquid emptying in the supine position is approximately 28 minutes[12], the reference time used in this study was 26 minutes.

The process of gastric emptying involves complex neuromuscular interactions that are not yet fully understood. However, it has been determined that liquid gastric emptying occurs exponentially due to the pressure gradient generated by the tone of the gastric fundus and the relaxation of the pylorus. In contrast, solids are initially retained in the proximal stomach (lag phase) before moving to the antrum, where they are triturated through phasic contractions[25].

Failures in antral contractions and inadequate pyloric relaxation are likely the primary pathophysiological disruptions in gastroparesis[25]. Ziessman and colleagues suggested that LGE might identify patients with a primary abnormality in the gastric fundus[14]. While this hypothesis remains unproven, it has been observed that delayed emptying of caloric meals involves more complex mechanisms, including alterations in gastric accommodation and antral motility index[26].

The strengths of this study include the comparison of patients against themselves, ensuring robust correlation of results. Additionally, the outcomes of both SGE and LGE are purely quantitative, which guarantees adequate reproducibility. However, the main limitation of the study is its retrospective nature, with data extracted from multiple information systems. Nonetheless, as the participating institutions operate within a common academic and clinical framework, the procedures are highly similar. Furthermore, a stratified analysis was conducted based on the study variables to control for potential confounders. Prospective studies are necessary to confirm the findings of this research.

A comprehensive understanding of the pathophysiology of gastroparesis and the mechanisms by which LGE may yield a higher rate of positive results in suspected cases of this condition still requires further scientific development. Although our findings demonstrate that this phenomenon is not limited to previously studied international populations, only the protocols and values for SGE are internationally standardized and endorsed by scientific societies. Moreover, SGE is recommended in the latest guidelines from European and American gastroenterology societies as the diagnostic test of choice[15,16].

In this study, the degree of agreement between gastric emptying scintigraphy for liquids and solids was found to be low in our population. The most common pattern of divergence was normal solid-phase results with delayed liquid-phase results. While gastric emptying scintigraphy for solids remains the gold standard, LGE results should be interpreted cautiously and within the individual clinical context of each patient. Prospective studies are warranted to investigate this discordance and the associated factors in a controlled manner.

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Conflict of Interest

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

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