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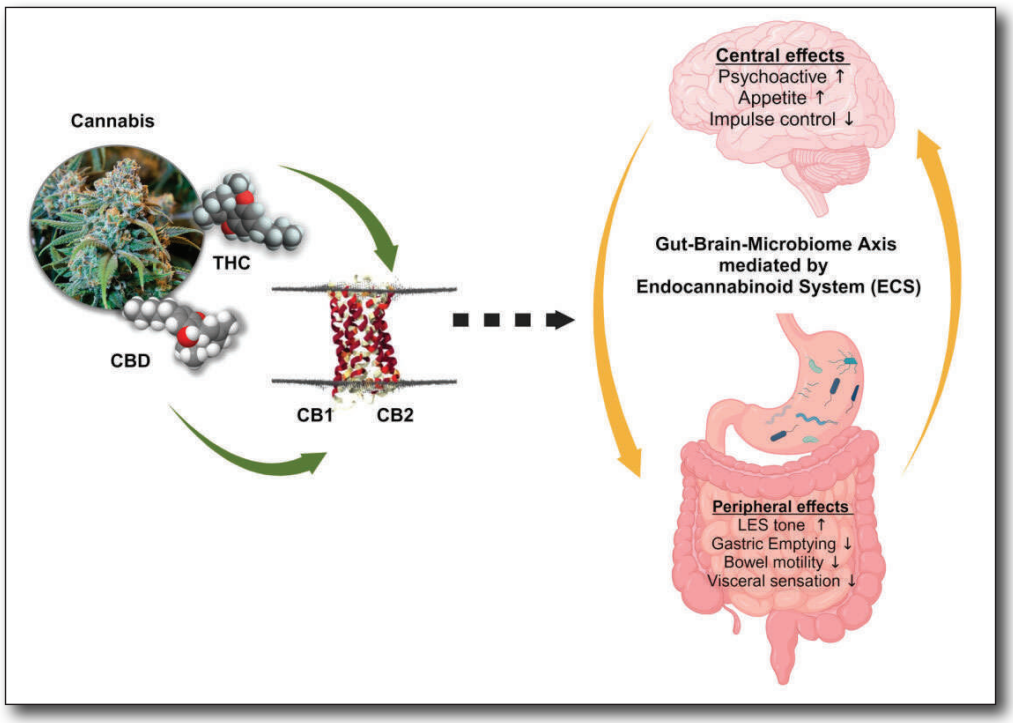
JNMT

Journal of Nuclear Medicine Technology

FEATURED IMAGE

Got the Munchies for an Egg Sandwich? The Effects of Cannabis on Bowel Motility and Beyond. Rutger Gunther et al. See page 8.



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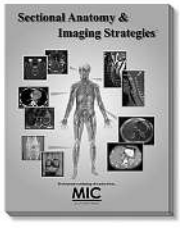

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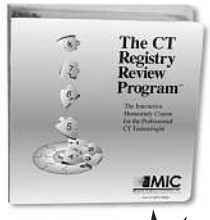

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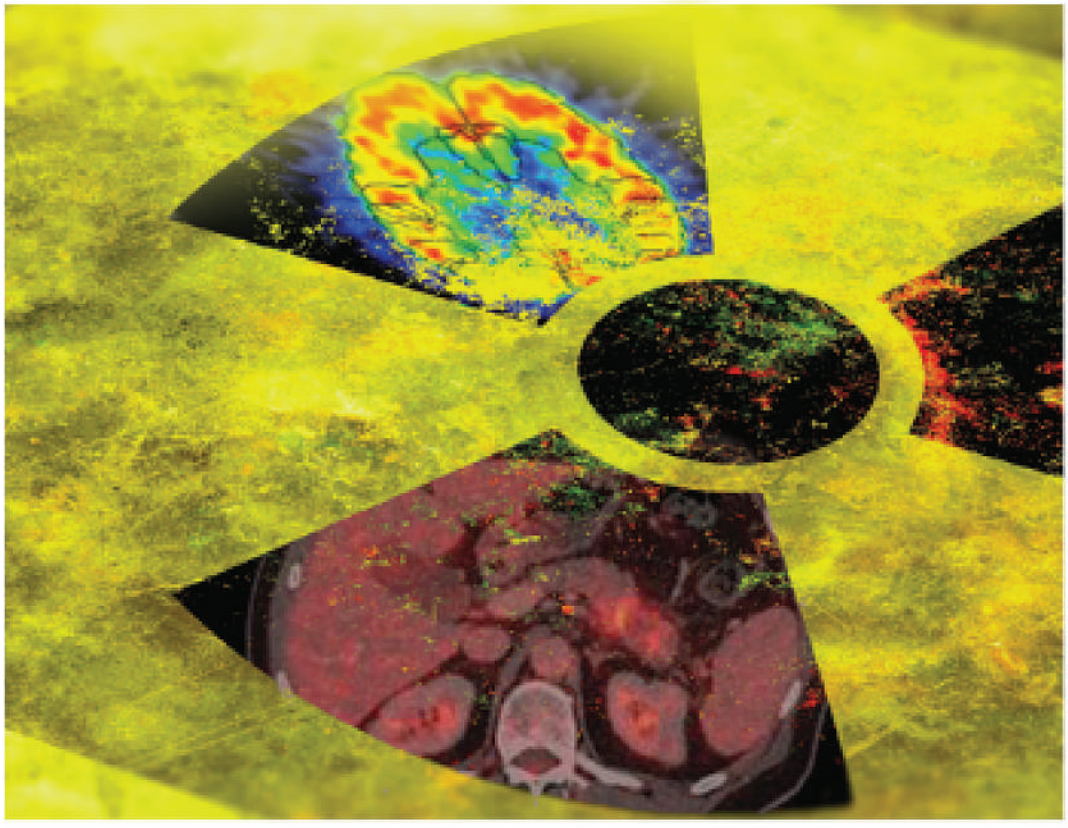

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JNMT

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JNMT Journal of NUCLEAR MEDICINE TECHNOLOGY

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MISSION: SNMMI-TS is dedicated to the advancement of molecular and nuclear medicine technologists by providing education, advocating for the profession, and supporting research to achieve clinical excellence and optimal patient outcomes. **VISION:** To be recognized as the leader in molecular imaging and therapy. To be dedicated to the advancement of the profession through adoption of emerging technologies.

JNMT Journal of NUCLEAR MEDICINE TECHNOLOGY

SNMMI-TS Drives Innovation and Collaboration: Highlights of Recent Initiatives and Educational Programs

Dmitry D. Beyder, MPA, CNMT

Over the past 6 months, SNMMI-TS has been working on innovative new programs and advancing important initiatives. This year we will introduce several new educational offerings as well as new initiatives that expand across imaging modalities. We have strengthened our connections with our international colleagues and continued our efforts to build and renew the workforce pipeline into the field. As we work through Year 1 of the strategic plan, there is still a lot to be done! I am thrilled to share some highlights with you.

In mid-January, the SNMMI-TS announced the new SNMMI-TS Launch Pad program: a $15,000 grant to be awarded to one or more SNMMI-TS members to support an innovative new project or program that will transform technologist education, outreach, advocacy, or pipeline efforts. Recognizing that the field of nuclear medicine and molecular imaging is changing rapidly, the SNMMI-TS identified our vision for the future as being able to drive change within hospitals, institutions, and academia to better educate and advocate for the field of nuclear medicine and molecular imaging; therapy will be practiced in all hospitals around the country, and nuclear medicine technologists—as key members of the care team—will use their enhanced expertise in precision medicine to collaboratively improve patient outcomes. The Launch Pad grant will serve as a "launching" point for this vision—hopefully the first of many new and innovative projects our members will imagine and create. Applications closed March 1; award notifications will be sent by April 1, with project completions by September 30.

The SNMMI-TS Molecular Therapy Task Force (Joby MacLean, chair; Jay Smith, vice-chair; Dmitry Beyder, leadership liaison) has been busy planning the first Technologist Theranostics Tumor Board (T^3B). The goal of this project is to allow technologists to learn and better understand their vital role in theranostics. These "technologist tumor boards" will be reactive case discussions (lessons learned) and will outline the role of technologists in therapy, what concerns they had, what could have been done differently, and what could be done in the future to ensure a higher success rate (scheduling, infusion techniques, collaborations with other entities, etc.). The first T^3B was scheduled for February 27, with leads Dmitry Beyder (Barnes-Jewish Hospital; SNMMI-TS President), Michael Harrod, and Vikas Prasad (both from Washington University School of Medicine). The initial paperwork has been submitted for VOICE/CME approval and will focus on these 3 objectives:

1. Understand key components to consider when treating patients with ^{177}Lu-PSMA.
2. Be able to make patients more prepared and comfortable during workup for and receipt of PSMA therapy.
3. Better respond to challenges that occur in a clinical practice when delivering radiopharmaceutical therapy.

Dmitry D. Beyder, MPA, CNMT

Throughout their discussions, the Molecular Therapy Task Force felt it was KEY to collaborate and partner with the institutions awarded SNMMI Therapy Center of Excellence status and the SNMMI Therapy Centers of Excellence. With the goal of hosting a T^3B event quarterly, the SNMMI-TS Molecular Therapy Task Force has reached out to the president of the Therapy Center of Excellence for help and collaboration in identifying potential institutions and individuals who may be willing to lead the next event (sometime in May or June).

The University of Alabama at Birmingham (UAB) has launched Nuclear Medicine and Molecular Therapy Intensive (NMMTI). SNMMI-TS is excited to be partnering with UAB on this effort and marketing the program to members. The program's mission is to provide qualified individuals with the knowledge and skills needed to succeed in their clinical career and to better prepare them for the future of nuclear medicine. The NMMTI emphasizes a generalist approach so that students can apply these skills to many areas of therapy in the field. The week-long, fast-paced, intensive program includes lectures, hands-on skills, labs, and interactive activities. The NMMTI will hold this workshop from April 29 through May 3, 2024. The complete, tentative schedule can be found at https://www.uab.edu/shp/cds/images/documents/nmmis/UAB-NMMTI-Schedule.pdf.

UAB is also working to reignite the Nuclear Medicine Advanced Associate (NMAA) program. The NMAA program is on the agenda for the Alabama Board of Trustees meeting in Huntsville, Alabama; the SNMMI-TS and SNMMI plan to

submit a letter of support ahead of the meeting. Once approved, the goal is to reopen the program before or during 2026.

The SNMMI-TS Advocacy Committee and the State TAG Team have been working tirelessly over the past 6 months to address state licensure issues and develop a plan for outreach within the chapters. During this spring and fall, the SNMMI-TS will contact chapters to request time at chapter meetings for members to meet with their state TAGs. The SNMMI-TS will be providing $250 per TAG to reimburse expenses and asking chapters to waive meeting registration fees to help reduce TAG expenses. The goal of this outreach effort is to ensure that chapter members know their state TAGs so they can contact them if issues arise in their state. We also hope to provide advocacy-related education to chapter meeting attendees regarding ongoing state issues. We are currently following legislation in Georgia, Indiana, Louisiana, New Hampshire, Ohio, Pennsylvania, and Washington, DC.

The 15th annual SNMMI-TS Leadership Academy was held in conjunction with the SNMMI Mid-Winter Symposium, January 31 through February 3 in Orlando, Florida. The Leadership Academy has been the centerpiece of SNMMI-TS leadership development strategy, actively working on building a team of approximately 15 technologists per year who have demonstrated leadership abilities and engagement at the national/chapter level. This year, the individuals below graduated from the 2024 academy. Congratulations to all!

Leila Alsarag, CNMT (Missouri Valley Chapter)
Fernando Anleu-Escobar, CNMT (Central Chapter)
Jason Cohen, CNMT (Pacific Southwest Chapter)
Danielle Deimer, Med, BS, CNMT, RT(N) (New England Chapter)
Jill Holmquist, CNMT, PET, NMTCB(RS) (Southeastern Chapter)
Summer Khairi, MBA, CNMT (Southwestern Chapter)
Jared LeBlanc, CNMT (New England Chapter)
Carol Long, CNMT (Southeastern Chapter)
Shari Moreau, RT(N)(ARRT) (Mid-Eastern Chapter)
Christopher Morgan (Greater New York Chapter)
Margaret O'Krafka* (Eastern Great Lakes Chapter)
Brianna Reidel* (Greater New York Chapter)
Jeremy Slicker, CNMT, NMTCB(RS) RT(N) (Southeastern Chapter)
Courtney Tronca (New England Chapter)
Isa Weizenegger* (Southwestern Chapter)
Ryan Widener, MBA, CNMT, RT (Southeastern Chapter)
Lindsay Williams, MBA, ARRT(N)(CT), CNMT (Southwestern Chapter)

**denotes student attendee*

We are off to a fast start in 2024, with efforts focused on the 2023 SNMMI-TS Strategic Plan. While much of the current work is around goals 1, 3, and 4 (new technologies, workforce pipeline, and advocacy, respectively), we also continue to look forward and set our eyes for the future beyond this year. We continue to engage our committees, chapters, liaisons, professional partners, and Value Initiative Industry Alliance partners to cover all 6 of our strategic goals and make sure that the profession, our members, and patients are well cared for in the years to come. Please support our work so molecular imaging can continue to be an integral part of the healthcare delivery system.

Thank You, Readers, for Helping to Shape Future *JNMT* Content

Kathy S. Thomas, MHA, CNMT, PET, FSNMMI-TS

Editor, *JNMT*

I would like to begin this editorial with a big "THANK YOU!" to those who took the time to respond to the 2023 *JNMT* Readership Survey. Your responses, candid comments, and suggestions will guide and develop the future content of *JNMT*. Beyond your "thumbs up" for the continuing education articles published in each issue, you provided a very positive response for the newer sections, including the Educators' Forum, Practical Protocol Tips, and Practical Pointers. Readers liked the balance of scientific versus practical information and confirmed that published information was being used in the clinical setting to make changes, as necessary. You mentioned the need for authors to consider the diverse clinical settings around the world when discussing innovative technical and scientific information and how the varied clinical settings can apply that information. There were comments from a few readers noting the desire to receive a printed copy of *JNMT* rather than reading articles online. SNMMI-TS members can opt in to receive print copies of *JNMT* by contacting the membership office at memberinfo@snmmi.org.

The focus of this issue is the brainchild of our continuing education Associate Editor, Mary Beth Farrell. I will let Mary Beth describe her work with a dedicated group of nuclear medicine professionals to present the topic Gastrointestinal System Imaging:

> *"I have a pet peeve (noun = personal grievance or vexation). My main gripe is noncompliance with the Society of Nuclear Medicine and Molecular Imaging guidelines and the consensus recommendations for gastric emptying scintigraphy (GES) (1,2). Nuclear medicine is all about physiology, and the only way to accurately and reliably assess physiology is through standardization.*
>
> *In 2017, I coauthored a study published in the JNMT that looked at accredited laboratories' compliance with the standardized GES protocol (3). Only 35% of laboratories followed the correct meal contents at that time. The variety of ridiculous ingredients, such as honey buns, cornflakes and milk, peanut butter and jelly sandwiches, hard-boiled eggs, or pizza, made my brain explode. In this issue, Tafti et al. reexamines compliance with the standardized protocol (4). The good news is that meal compliance is up to 62%, and ridiculousness is down. The bad news is that one-third of laboratories still do not follow the consensus meal and guidelines.*
>
> *The continued nonadherence with the meal contents and other standardized protocol components was the impetus for several articles. A study by Gunther, Banks, and McWhorter assesses fasting blood glucose screening before GES, a critical variable affecting gastric emptying rate (5). Two continuing education articles discuss new variables to be considered: marijuana and glucagonlike peptide-1 receptor agonists (weight loss medications). Gunther et al. describe marijuana's physiologic effects on GES results (6), while Parkman et al. discuss the new weight loss drugs and gastroparesis (7).*

Kathy S. Thomas, MHA, CNMT, PET, FSNMMI-TS

> *The March issue also contains several GES-related research articles. The first by Maurer et al. evaluates new software and reference values for dynamic antral contraction scintigraphy in patients with gastric dysmotility (8). The second study by Singh and Graham (9) looks at changes in patient management following GES in patients with suspected gastroparesis.*
>
> *The JNMT editors were delighted by the submission of two research studies by students. The first by Green and Johnson evaluates the binding efficiency of ^{99m}Tc sulfur colloid to liquid egg whites when added before and after cooking (10). Regrettably, the previously mentioned study by Tafti et al. found some laboratories still squirt the ^{99m}Tc sulfur colloid on cooked eggs, making Green and Johnson's article opportune. The second study, a survey of working technologists about GES practices by Muskus et al., finds that only 37% of respondents follow the guidelines for meal components (11).*
>
> *An invited perspective by MacLean and el-Chammas looks at a scenario in which the standardized GES protocol often cannot be followed—pediatric patients who may have an*

allergy or do not like eggs (12). The authors explain how GES is performed at their pediatric facility. A practical protocol tip for performing liquid GES is included to assist in imaging pediatric patients (13).

Although not strictly GES but still related to gastrointestinal system imaging, Peacock et al. provides a continuing education article and practical protocol tip for hepatobiliary imaging using a fatty meal cholecystagogue (Ensure-Plus) (14,15). This article is helpful considering recent episodes of cholecystokinin unavailability.

Two articles sum up the overarching intent of this issue: improved standardization, accuracy, and reproducibility of GES. McKee and Farrell discuss the plethora of GES misinformation on social media platforms and the scientific merit of that information (16). Maurer and Donahoe (the authors of the original 2008 Society of Nuclear Medicine and Molecular Imaging GES guideline) describe the state of GES in 2024 and the continuing need for compliance with published guidelines (17). The authors bring the point home: 'Only with adherence to standard protocols will we be able to speak the same language when managing these complex patients'."

I would be remis if I didn't mention in this first issue of 2024 that *JNMT* is continuously looking for new authors and reviewers. Consider adding to your New Year Resolutions the possibility of sharing your expertise as an author or reviewer. Need a mentor? Help is available! Please contact me (ksthomas0412@msn.com) with your ideas, suggestions, or requests for assistance.

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Glucagonlike Peptide-1 Receptor Agonists: The Good, the Bad, and the Ugly—Benefits for Glucose Control and Weight Loss with Side Effects of Delaying Gastric Emptying

Henry P. Parkman, Daniel S. Rim, Jonathan R. Anolik, Simin Dadparvar, and Alan H. Maurer

Gastroenterology Section, Endocrinology and Metabolism Section, and Nuclear Medicine Section, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania

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Glucagonlike peptide-1 (GLP-1) receptor agonists (RAs) are being increasingly used for glycemic control in patients with diabetes and for weight loss and weight management in obese subjects. There has been recent public awareness of the potential of GLP-1 RAs to delay gastric emptying and cause gastroparesis. By delaying gastric emptying, these agents can complicate the clinical evaluation of patients on these drugs by affecting diagnostic testing for gastroparesis. This article discusses GLP-1 RAs and their effects on gastric emptying, gastric food retention, and gastroparesis. This article highlights how physicians should be attuned to the gastric side effects of these popular therapeutic agents for blood glucose control in people with diabetes and for weight loss and weight management in obese patients.

Key Words: GLP-1 receptor agonists; gastric emptying scintigraphy; gastroparesis

J Nucl Med Technol 2024; 52:3–7
DOI: 10.2967/jnmt.123.266800

Glucagonlike peptide-1 (GLP-1) receptor agonists (RAs) are being increasingly used for glycemic control in patients with diabetes and for weight loss and weight management in obese subjects.

By delaying gastric emptying, these agents can complicate the clinical evaluation of patients by affecting diagnostic testing for gastroparesis. Delaying gastric emptying can also increase the risk of aspiration during endoscopic and surgical procedures (*1,2*). This article discusses GLP-1 RAs and their effects on gastric emptying, gastric food retention, and gastroparesis, as well as highlighting how physicians and other medical staff caring for these patients should be attuned to the gastric side effects of these popular therapeutic agents for blood glucose control in people with diabetes and for weight loss and weight management in obese patients.

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For correspondence or reprints, contact Henry P. Parkman (henry.parkman@temple.edu).
Published online Jan. 9, 2024.

GLP-1 Actions

GLP-1 is a naturally occurring incretin peptide hormone, synthesized primarily in intestinal endocrine cells (*2*). On nutrient ingestion, GLP-1 is released, activating GLP-1 receptors in various target tissues, including the pancreas, stimulating insulin release; the hypothalamus, stimulating satiety centers; and gastric neuronal cells, delaying gastric emptying. GLP-1 RAs are peptides developed to control blood glucose by causing insulin release and slowing gastric emptying, which can result in a sensation of fullness that can reduce appetite. Endogenous GLP-1 has a short half-life of 2–3 min, whereas the pharmacologic GLP-1 RAs that have been developed have extended durations of action for the management of type 2 diabetes mellitus (e.g., semaglutide, dulaglutide, and liraglutide) and weight management (e.g., semaglutide and liraglutide). Table 1 lists the GLP-1 agonists that have been developed. GLP-1 RAs can be classified as short-acting or long-acting depending on how long they work in the body and how frequently they are given. Short-acting and long-acting GLP-1 RAs have different characteristics (*3*). Short-acting GLP-1 RAs stay in the body for less than a day and are generally taken once or twice per day; they help control blood sugar levels after meals. For short-acting GLP-1 RAs, such as exenatide and lixisenatide, delayed gastric emptying is the main mechanism of suppression of postprandial hyperglycemia. Long-acting GLP-1 RAs continue to work for a full day or even a week after being taken and help to control blood sugar throughout the day and night. For the long-acting GLP-1 RAs, such as liraglutide, exenatide long-acting release, dulaglutide, and semaglutide, increasing glucose-dependent insulin secretion and suppressing inappropriate glucagon

TABLE 1
Glucagonlike Peptide-1 RAs Used for Glucose Control and Weight Management

Generic name	Brand name	Dosing	Half-life	Indication
GLP-1 RAs				
Short-acting GLP-1 RA				
Exenatide	Byetta (Eli Lilly)	5–10 μg SQ twice daily	2.4 h	Glycemic control in adults with T2DM
Lixisenatide	Adlyxin (Sanofi)	10–20 μg SQ daily	3 h	Diabetes management in conjunction with insulin
Liraglutide	Victoza (Novo Nordisk)	0.6–1.8 mg SQ daily	13 h	Glycemic control in T2DM
Liraglutide	Saxenda (Novo Nordisk)	0.6–3 mg SQ daily	13 h	Weight loss and chronic weight management
Long-acting GLP-1 RA				
Dulaglutide	Trulicity (Eli Lilly)	0.75–4.5 mg SQ weekly	5 d	Improvement of blood sugar in T2DM
Semaglutide	Rybelsus (Novo Nordisk)	3–14 mg orally daily	7 d	Treatment of T2DM, an oral agent
Semaglutide	Ozempic	0.25 to 2 mg SQ weekly	7 d	Diabetes management; off label for weight management
Semaglutide	Wegovy	0.25–2.4 mg SQ weekly	7 d	Approved by Food and Drug Administration for chronic weight management
Exenatide long-acting release	Bydureon Bcise (AstraZeneca)	2 mg SQ weekly	2 wk	Glycemic control in adults with T2DM
Dual glucose-dependent insulinotropic polypeptide/ GLP-1 RAs				
Tirzepatide	Mounjaro	2.5–15 mg SQ weekly	5 d	Treatment for T2DM; off label for weight loss
Tirzepatide	Zepbound (Eli Lilly)	5–15 mg SQ weekly	5 d	Treatment for obesity

SQ = subcutaneously; T2DM = type 2 diabetes mellitus.

secretion are the main mechanisms of suppression of postprandial hyperglycemia.

In recent years, the number of patients with diabetes treated with GLP-1 RAs has increased. Many endocrinologists are using these GLP-1 RAs and sodium–glucose cotransporter 2 inhibitors. Several societies have recommended earlier initiation of these medications, especially in patients with cardiovascular or renal disease (*4,5*). Although gastrointestinal symptoms such as nausea and vomiting and delayed gastric emptying are labeled side effects of the GLP-1 RAs, there are limited reports of actual medication-induced gastroparesis reported.

Drug development has led to strategies to further improve the efficacy of GLP-1 RAs. Dual glucose-dependent insulinotropic polypeptide/GLP-1 RAs have been recently developed, of which tirzepatide is an example (*6*). Because of the complementary actions of the 2 incretins, these compounds may offer improved management options for type 2 diabetes mellitus and obesity. Nausea and delayed gastric emptying are reported side effects of tirzepatide. The gastric emptying delay is largest after the first dose, and this effect diminishes over time. Tirzepatide slows postmeal glucose absorption, reducing postprandial glucose.

GLP-1 and Gastric Emptying and Gastroparesis

Liraglutide is a long-acting GLP-1 RA that activates glucagon receptors on pancreatic β-cells to stimulate glucose-dependent insulin action. Subcutaneous injection of up to 1.8 mg once daily is used for glucose control, whereas higher doses are used for chronic weight management (Table 1). Liraglutide use is associated with slower gastric emptying and increased fasting gastric volume (*7*). In a prospective randomized, placebo-controlled trial of liraglutide in adult patients with obesity and normal gastric emptying at baseline, liraglutide, 3 mg subcutaneously daily, increased weight loss at 5 and 16 wk of treatment and slowed gastric emptying at these times compared with placebo (*7*). Overall, 57% of patients treated with liraglutide developed delayed gastric emptying. In patients developing delayed gastric emptying at 5 wk, 51% of the patients had a persistent delay in gastric emptying to 16 wk. Conversely, of the patients with delayed gastric emptying at 5 wk, 49% of the patients normalized their gastric emptying at 16 wk. Tachyphylaxis due to persistent use of the GLP-1 RA has been suggested as a potential explanation for the initial delay in gastric emptying, with subsequent improvement with continued treatment in some patients.

Case reports have described patients being diagnosed with gastroparesis who had recently started GLP-1 RAs. Rai et al describe a case of liraglutide-induced acute gastroparesis in a 52-year-old man with type 2 diabetes mellitus presenting with symptoms of gastric outlet obstruction (*8*). Treatment involved initial nasogastric suction and discontinuation of liraglutide. Kalas et al. published 2 cases of medication-induced gastroparesis that were initially diagnosed as diabetic gastroparesis but were subsequently found to have been induced by GLP-1 RAs (*9*). Repeat studies after medication discontinuation found improvement in symptoms and resolution of the delayed gastric emptying. In each of these cases, the association of the GLP-1 RAs with the gastroparesis was recognized not initially but only on careful review of medications the patient was taking after presentation. These case reports emphasize the potential to mislabel patients with gastroparesis who have a gastric emptying test performed while taking a GLP-1 RA.

Further research needs to be done to assess the frequency of misdiagnosing diabetic patients with gastroparesis due to medications, specifically GLP-1 RAs. In a review of gastric emptying scintigraphy (GES) tests performed over 2 y (2019–2021), Kalas et al. found that of 384 tests performed, 57% of the patients had diabetes and 24% of the patients with diabetes were on a GLP-1 RA (*10*). Of the patients with diabetes with delayed gastric emptying, 24% were on a GLP-1 RA. This study did not find an association between GLP-1 RA use and delayed gastric emptying. Some studies have reported that the effect of GLP-1 RAs on gastric emptying is more pronounced in the first hour of gastric emptying than at later times postprandially (3 and 4 h).

The association of GLP-1 RAs and delayed gastric emptying is not new. The American College of Gastroenterology guidelines for gastroparesis, published in 2013 (*11*), describe iatrogenic gastroparesis from pharmacologic agents such as narcotic opiate analgesics, anticholinergic agents, and some diabetic medications, including GLP-1 RAs. The most common side effects of GLP-1 RAs are nausea and vomiting, which have been attributed to delayed gastric emptying. Nausea (43.5%) was the most commonly reported adverse event with exenatide treatment, and vomiting was also quite commonly encountered (12.8%) (*12*). These guidelines suggest that for accurate determination of gastric emptying, GLP-1 RAs should be withdrawn before patients undergo a gastric emptying test to evaluate for gastroparesis. Usually, medications that have the potential to delay or even speed up gastric emptying are held for 3–4 half-lives of the drug. For narcotic analgesics, this is often 2–3 d. Three days off treatment would be for the short-acting GLP-1 RAs, which are given on a once- or twice-daily basis, but it would be 3–4 wk for the long-acting GLP-1 RAs, which are often given on a weekly basis, as is more typically done for weight reduction in an obese patient. There is some evidence to suggest that GLP-1 RAs may impair gastric emptying for up to 8 wk (*13*).

Limited studies are available evaluating the use of GLP-1 RAs in patients with preexisting gastroparesis. Beti et al., from Germany (*14*), conducted one of the few studies evaluating the effect of GLP-1 RAs on patients with diabetes with and without preexisting diabetic gastroparesis. In the study, 75% of participants with normal gastric emptying before receiving GLP-1 RAs developed delayed gastric emptying. In addition, 30% of participants with preexisting diabetic gastroparesis had worsening gastric emptying after GLP-1 RA treatment, whereas the remaining 70% had no change or minimal improvement. Linnebjerg et al. reported a dose-dependent delay in gastric emptying in patients with type 2 diabetes mellitus treated with exenatide (*15*). The diabetic patients with slower baseline gastric emptying had less change in gastric emptying after exenatide administration.

The Food and Drug Administration has recently received reports of stomach paralysis, or severe gastroparesis, developing with the antiobesity GLP-1 RA drugs semaglutide and liraglutide (*16*). Surprisingly, some patients have reported that the gastroparesis did not resolve after cessation of the drug, an event that usually does not occur with RAs. Recently, the Food and Drug Administration has added the potential side effect for Ozempic (Novo Nordisk) of ileus or blockage of intestinal contents. This is already present in the label for Wegovy (Novo Nordisk) and Mounjaro (Eli Lilly).

In patients with diabetic gastroparesis, optimal glucose control is suggested to reduce the future risk of complications of diabetes, including gastroparesis. In some patients, glucose control is achieved by use of the GLP-1 RAs. Thus, the GLP-1 RAs are helpful on one hand for glucose control and weight management but may be potentially harmful on the other hand, causing delayed gastric emptying, gastric retention, and gastroparesis symptoms.

GLP-1 Agonists and Gastric Emptying Testing

GES is considered the gold standard for quantifying gastric emptying and diagnosing gastroparesis. Gastric emptying should be assessed when patients have relatively good glucose control because hyperglycemia can itself delay gastric emptying. The current procedure guideline (*17*) and consensus recommendations (*18*) of the Society of Nuclear Medicine and Molecular Imaging and the American Neurogastroenterology and Motility Society for performing GES indicate that imaging centers should check the fasting glucose level on the day of gastric emptying testing to make sure the blood glucose is under control. Although the recommended upper level for serum glucose before performing the test varies slightly between the 2 publications ($<$200 mg/dL (*17*) and $<$275 mg/dL (*18*)), an upper limit of less than 275 mg/dL is generally considered acceptable. Both publications recommend that drugs that can potentially delay gastric emptying should be withheld before a gastric emptying test is performed. However, they give no specifics on how to approach symptomatic patients currently on newly developed GLP-1 RA drugs. With a long half-life of up to 7 d for drugs in common use, this has led to controversy and confusion on how and when to study symptomatic patients who would need to be off their medication for at least 2–3 half-lives.

Most physicians and patients are not willing to withhold these medications for such a long time (3–4 wk).

GLP-1 RAs and Aspiration

In delaying gastric emptying, and with resulting prolonged retention of food in the stomach, these agents might increase the risk of aspiration in patients sedated for endoscopic and surgical procedures. In a retrospective analysis of patients undergoing elective upper endoscopy (*19*), increased residual gastric contents were seen in 8 of 33 (24%) patients receiving semaglutide, compared with only 19 of 371 (5%) patients not receiving semaglutide ($P < 0.001$). Semaglutide use and the presence of preoperative digestive symptoms (nausea/vomiting, dyspepsia, abdominal distension) were associated with increased residual gastric contents. One case of pulmonary aspiration was reported, with that patient being in the semaglutide group. Additional studies have confirmed that GLP-1 RA treatment has been associated with gastric residue in an esophagogastroduodenoscopy in patients with diabetes, with the proportion of gastric residue higher in the GLP-1 RA treatment group than in the non–GLP-1 RA treatment group (5.4% vs. 0.5%) (*3*).

The potential risk of aspiration associated with delayed gastric emptying is of particular concern to anesthesiologists sedating these patients for endoscopy and surgical procedures. Several published case reports have documented instances of aspiration in patients receiving GLP-1 RAs, emphasizing the importance of considering this risk (*1,2*). Several suggestions in the anesthesiology literature have been made for patients taking these medications. One is guidelines on stopping these agents before surgical procedures: to hold the short-acting agents for a day and the long-acting agents for a week (*1*). Another is to consider performing gastric ultrasound to determine residual gastric content before induction of anesthesia in these patients (*1*). Concern was raised since the GLP-1 RAs are often given weekly and often stored in a refrigerator at home; the patient might not report this to the surgeon at the time of the evaluation but may report this to the anesthesiologist on the day of surgery.

Suggestions for Managing Patients Taking GLP-1 RAs

Questions remain on how to deal clinically with patients taking GLP-1 RAs, with their potential to delay gastric emptying, since these agents have ramifications in diagnosing gastroparesis and in performing procedures on patients taking these medications. Here are some suggestions that seem appropriate from the information presented above.

Patients Being Considered for Treatment with a GLP-1 RA. We suggest that patients should be assessed for symptoms of gastroparesis (nausea, vomiting, stomach fullness) before starting treatment with a GLP-1 RA. If symptoms of gastroparesis are present, consider obtaining a gastric emptying test to document delayed gastric emptying before treatment with a GLP-1 RA. Once patients are taking the GLP-1 RA medications (similar to patients starting to take narcotic analgesics), it will be difficult to discern whether they have true gastroparesis or medication-induced gastroparesis. Interestingly, the patients who use them for glucose control in type 2 diabetes mellitus are often at risk for developing gastric emptying abnormalities, primarily gastroparesis, but occasionally rapid gastric emptying can be seen (*20*). Of note, these agents are now being used much earlier in the course of the diabetes and may actually prevent gastroparesis by improving glucose control. If symptoms or delayed gastric emptying is present before treatment, proceed with caution with use of a GLP-1 RA, as symptoms and gastric emptying may worsen on treatment.

Patients being treated with a GLP-1 agonist should be told about potential side effects, that they may develop symptoms such as nausea and fullness, and that these medications can delay gastric emptying. Furthermore, patients should be reminded to tell their physicians that they are on these medications, especially gastroenterologists performing endoscopic procedures, surgeons for surgical procedures, and anesthesiologists sedating the patients for these procedures. These patients should also be instructed to inform other health care providers such as nuclear medicine technologists about such medications, especially before studies such as GES.

Patients Developing Gastrointestinal Symptoms on a GLP-1 RA. If a patient being treated with a GLP-1 RA develops persistent symptoms of gastroparesis—nausea, vomiting, fullness—then the medication should probably be stopped to see whether the symptoms resolve. If they do, providers may need to prescribe a different method of drug control of glucose. If the symptoms do not resolve after the GLP-1 RA is stopped, then evaluation for gastroparesis off the GLP-1 RA is suggested.

Patients on GLP-1 RAs Being Considered for GES. Physicians ordering gastric emptying tests should be aware of whether the patient is taking a GLP-1 RA, just as they should know whether patients are taking narcotic analgesics or are heavy users of cannabis (marijuana), which also delays gastric emptying. The best practice for physicians ordering the test is to have the patient stop these medications before any test to measure gastric emptying. This stoppage should last 3–4 d for patients taking a short-acting, once- or twice-daily GLP-1 RA but 3–4 wk for patients taking a long-acting, often weekly GLP-1 RA. Stopping the GLP-1 RA may be difficult, as it takes time to come off the pharmacologic effects of the GLP-1 RA, and the patient might lose glucose control. Any such decision must be carefully considered between both the patient and the physician.

When patients present to the nuclear medicine department for a gastric emptying test, the current medications of the patients should be reviewed, including ones that can accelerate or delay gastric emptying, such as narcotic pain medications, anticholinergic agents, and GLP-1 RAs. The patient should inform the testing site of use of these medications before testing, and a decision should be made with the referring physician on whether to proceed that day or reschedule the test and, if the latter, for how long the drug should be withheld.

If a GES test is performed on a patient taking a GLP-1 RA, the GES report should state this and indicate that any delay in gastric emptying may be drug-induced. For patients referred for GES with symptoms of gastroparesis and who are taking a GLP-1 RA, the test will not be able to differentiate between delayed gastric emptying caused by diabetic gastroparesis and delayed gastric emptying caused by medication-induced gastroparesis. If GES is performed on patient receiving a GLP-1 RA, a normal result rules out both, allowing one to potentially look for other causes. However, symptoms may still be from the GLP-1 RA despite no delay in gastric emptying, perhaps through effects of GLP-1 RA on the vagus nerve. If gastric emptying is delayed, one therapeutic option would be to stop the medication and see whether the symptoms resolve. If the symptoms do not resolve, patients might need to undergo an additional gastric emptying test after a sufficient time (as much as 4 wk) off the medication to see whether they still have true gastroparesis.

Patients on GLP-1 RAs Who Are Undergoing Endoscopic or Surgical Procedures. Because the GLP-1 RAs delay gastric emptying and increase gastric retention, retained food in the stomach could be aspirated in patients being sedated for procedures. For patients taking GLP-1 RAs, consider holding the drug for at least 3 half-lives before a planned procedure (*21*). For semaglutide, this would be 3 wk. Generally, for these procedures, the patient reports fasting overnight. Often, if patients are known to have gastroparesis, they are instructed to be on a liquid diet for 1–3 d before their procedure to reduce the chance of gastric solid-food retention. This preparation could also be used for patients on GLP-1 RAs. For patients taking GLP-1 RAs for type 2 diabetes mellitus, consider consulting the provider prescribing the agent about the risks and benefits of holding the drug for at least 3 half-lives ahead of the planned procedure.

SUMMARY

GLP-1 RAs are being increasingly used for glycemic control in patients with diabetes and for weight loss and weight management in obese subjects.

By delaying gastric emptying, these agents can complicate the clinical evaluation of patients on these drugs by affecting the diagnostic testing for gastroparesis. Delaying gastric emptying can also increase the risk of aspiration during endoscopic and surgical procedures. Physicians, health care providers, and medical staff caring for these patients should be attuned to the gastric side effects of these popular therapeutic agents.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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Got the Munchies for an Egg Sandwich? The Effects of Cannabis on Bowel Motility and Beyond

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The use of medicinal cannabis has a long history dating back thousands of years. Recent discoveries have shed light on its mechanism of action with the identification of cannabinoid receptors and endocannabinoids, which make up the body's endocannabinoid system. Cannabinoid receptors, particularly the cannabinoid 1 and 2 receptors, play a crucial role in modulating the gut–brain axis and serve as potential therapeutic targets for gastrointestinal motility and inflammatory disorders. With increasing legalization of cannabis and a rising number of users, understanding the effects of cannabis on gut motility is essential for nuclear medicine providers. Although tetrahydrocannabinol, the principal psychoactive constituent of cannabis, may decrease gut motility in experimental settings, it appears to paradoxically improve symptoms in gastroparesis. Treatment effects are difficult to measure given the large number of variables that could significantly alter outcomes, such as cannabinoid type, potency, and route of intake. Another consideration is the highly personalized gut microbiome, which directly interacts with the endocannabinoid system. Further research is required to delineate these multifaceted, complex cannabinoid interactions. The goal of this article is to explore the knowns and unknowns of the impact of cannabis on the alimentary system.

Key Words: gastric emptying; bowel motility; gastroparesis; cannabis; marijuana; gut microbiome

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The use of cannabis can be traced back for millennia. Descriptions of its use for recreational, spiritual, and medicinal purposes have been recorded in ancient texts all over world, such as the Ebers Papyrus from 1550 BCE, which describes its topical application for inflammation (*1*). Despite the long history of cannabis as a medicinal herb, we have only recently begun to understand its mechanism of action. In 1988, the first cannabinoid receptor was identified as a binding site for tetrahydrocannabinol (the principal psychoactive component of cannabis) in the brain (*2*). This discovery led to the identification of endogenous cannabinoids synthesized within our own bodies that regulate the broader endocannabinoid system. The system comprises endocannabinoid substrates (anandamide and 2-archidonoyl glycerol), cannabinoid receptors (primarily the cannabinoid 1 [CB1] receptor and the cannabinoid 2 [CB2] receptor), and other components of the gut–brain axis (Fig. 1).

The CB1 and CB2 receptors are principally responsible for modulating the gut–brain axis. CB1 receptors, located centrally in the dorsal vagal complex of the brain, are responsible for emesis via the vagus nerve. CB1 receptors, located peripherally throughout the intestinal tract, modulate motility. CB2 receptors are found primarily in inflammatory cells lining the gastrointestinal tract and in the peripheral nervous system. Both receptors have been identified as potential therapeutic targets in functional gastrointestinal disorders and inflammatory bowel disease (*3*).

With expanding legalization of cannabis, use has become increasingly more common in the United States. As of 2023, 38 states allow the medical use of cannabis, 23 states allow the recreational use of cannabis, and 9 states allow cannabis with a low-tetrahydrocannabinol–to–high-cannabidiol ratio. Only 3 states, that is, Idaho, Nebraska, and Kansas, lack a public access cannabis program (*4*). According to the 2021 National Survey on Drug Use and Health, 18.7% of people 12 y or older (52.5 million people) used marijuana, with the rates being highest among young adults 18–25 y old (35%) (*5*). With increased accessibility and surging user population, understanding the effects of cannabinoids on gastrointestinal motility is essential for physicians who treat and manage patients with gastrointestinal disorders.

Although the gastroenterology literature has described the effects of cannabinoids on the gut, there is a paucity of research in the field of nuclear medicine. This continuing education article attempts to examine and summarize our current knowledge on this complex topic and provide

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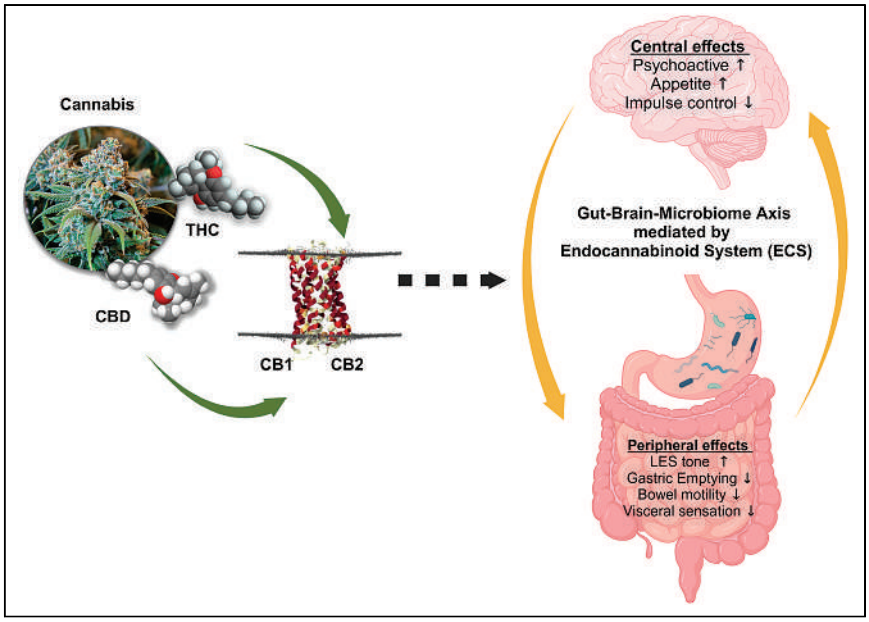

FIGURE 1. Primary effects of cannabis on human body. Principal phytocannabinoids (tetrahydrocannabinol and cannabidiol) interact primarily with CB1 and CB2 receptors found in brain and gastrointestinal tract. These receptors, combined with endocannabinoids, define endocannabinoid system, which mediates complex bidirectional interactions among gut, brain, and microbiome (*43–46*). CBD = cannabidiol; LES = lower esophageal sphincter; THC = tetrahydrocannabinol. (Created with BioRender.com; cannabis image courtesy of Cannabis Training University [https://creativecommons.org/licenses/by-sa/4.0/].)

recommendations for gastric emptying and bowel transit scans performed in an era with near-ubiquitous cannabis access.

Gastric emptying scintigraphy (GES) remains the primary imaging modality for evaluating functional disorders of the stomach. The procedural standard of the Society of Nuclear Medicine and Molecular Imaging has become a useful benchmark to define abnormal delayed gastric emptying. First, it is important to distinguish delayed gastric emptying from gastroparesis—terms that are not synonymous. Gastroparesis is a clinical condition for which delayed gastric emptying is used as one of several required diagnostic criteria. Gastroparesis requires characteristic symptomatology (nausea, vomiting, regurgitation, dyspeptic symptoms) and the absence of gastric outlet obstruction. Although gastroparesis is commonly attributed to idiopathic or diabetic causes, numerous conditions that mimic gastroparesis can also demonstrate delayed gastric emptying. The differential diagnosis for delayed gastric emptying includes functional gastrointestinal disorders, gastroesophageal reflux disease, medications, postsurgical states, eating disorders, connective tissue disease (scleroderma), neuromuscular conditions (myasthenia gravis), neurodegenerative conditions (Parkinson), and neuropsychiatric conditions (stress, anxiety). Such functional disorders defined by the Rome IV criteria include functional dyspepsia, rumination syndrome, cyclic vomiting syndrome, and cannabinoid hyperemesis syndrome (*6*,*7*). Since patients may use cannabis recreationally or self-medicate for these specific conditions, understanding the physiologic effects of cannabis is essential for accurate interpretation of GES.

LET'S GET INTO THE WEEDS: DEFINING CANNABIS, CANNABINOIDS, AND NOMENCLATURE

Because of the variety of cannabis plants and cannabinoid compounds, we will first review some definitions and nomenclature. *Cannabis sativa, Cannabis indica,* and *Cannabis ruderalis* are the primary plant species from which commercial cannabis is derived. These plants are known by many other street names, such as marijuana, Mary Jane, weed, pot, grass, ganja, hash, and purple haze, to name a few. Inhalation of smoked cannabis is the most common form of intake.

The principal psychoactive component of cannabis is δ-9-tetrahydrocannabinol, which activates CB1 receptors and decreases bowel motility. The other primary cannabinoid of interest is cannabidiol, which may have desirable antiinflammatory effects and play a role in motility. There are approximately 80 other naturally occurring, plant-based phytocannabinoids within cannabis whose actions continue to be studied.

Pharmaceutical (synthetic) tetrahydrocannabinol includes drugs such as dronabinol (Marinol; Unimed Pharmaceuticals), which shares the same chemical structure as organic tetrahydrocannabinol found in cannabis. It has been approved by the U.S. Food and Drug Administration for appetite stimulation in HIV/AIDS anorexic patients and treatment of chemotherapy-induced nausea and vomiting. It is also used off-label for innumerable other illnesses. A pharmaceutical synthetic form of cannabidiol also exists (Epidiolex; Jazz Pharmaceuticals), which has been approved for rare intractable seizure disorders. Hemp is legally defined in the United States as all other parts of the cannabis plant, such as the fibrous stem, which contain less than 0.3% tetrahydrocannabinol and are used in various industrial products.

Synthetic (neo)cannabinoids have an altered chemical structure but mimic the effect of tetrahydrocannabinol on cannabinoid receptors. These drugs were marketed as "legal highs" or "fake weed" and became popular in the early 2000s because of their commercial availability and undetectability on drug tests. Common product names include K2 and Spice. Early synthetics are now illegal because of their unregulated status and dangerous potency, but newer

agents continue to enter the market. Drug companies are attempting to synthesize new, safer formulations (*8*).

Endocannabinoids are lipid substrates made endogenously by the human body. Anandamide was first discovered in 1992 and was characterized as a neurotransmitter. The more recently discovered endocannabinoid is 2-archidonoyl glycerol. It is now known that the action of these endocannabinoid bioactive lipids extends far beyond the central nervous system. Beyond their function at the CB1 and CB2 receptors, anandamide and 2-archidonoyl glycerol also interact with a multitude of other receptors such as transient receptor potential vanilloid type 1, peroxisome proliferator-activated receptor-α and -γ, and G-protein–coupled receptor. A complex interplay with other pathways exists, which can lead to the synthesis and degradation of prostaglandins and other bioactive lipids such as palmitoyl ethanolamide and anorexigenic oleoyl ethanolamide. Each has actions linked to motility and the inflammatory cascade. A recent article by Srivastava et al. provides a thorough review on this topic (*9*).

EFFECT OF CANNABINOIDS ON GUT MOTILITY

Although decreased gastrointestinal motility due to cannabinoids has been established in both human and experimental animal models, it has not been definitively established in cannabis users with gastroparesis. To clarify these potentially discordant findings, we will examine the literature.

In Vitro and In Vivo Studies

In vitro studies have demonstrated a physiologic braking effect of tetrahydrocannabinol on gastrointestinal and colonic motility (*10*). Decreased smooth muscle contractility and peristaltic action are the result of CB1 receptor activation by tetrahydrocannabinol, resulting in the inhibition of acetylcholine neurotransmitter release. In vivo animal studies validated these findings by measuring intragastric pressures and the gastrointestinal transit times of radiopaque or radiolabeled meals (*11*). In a mouse model of terminal ileitis, CB1 receptors are overexpressed, thereby decreasing motility. It is hypothesized that this upregulation of CB1 receptors is a protective mechanism regulated by the endocannabinoid system to counteract the pathophysiologic hypermotile state, which defines inflammatory bowel disease and possibly other functional disorders of the gut such as irritable bowel syndrome (*12*). Relaxation of the lower esophageal sphincter is also inhibited by tetrahydrocannabinol, preventing gastroesophageal reflux (*13*).

Human Experimental Studies

Only 2 double-blind, experimental studies conducted in 1990 and 2006 validated delayed gastric emptying in healthy volunteers after oral tetrahydrocannabinol intake by scintigraphy (*14*,*15*). Of note, both studies predate the current procedural standards for gastric emptying. As such, they used different imaging times (2-h vs. 6-h endpoints) and different standard solid meals (cooked chicken liver, beef stew, crackers, and water vs. eggs, buttered toast, and 1% milk). Both studies were also limited by a small sample size (n = 13 and 30), with results applicable to the measurable effects of only orally ingested dronabinol–tetrahydrocannabinol at dosages prescribed for antiemetic use. The study with 13 healthy volunteers (*15*) demonstrated statistically significant delays in gastric emptying at 30 min and 2 h. The greatest difference was detected at 2 h, with a 40% increase in average percentage retention (45.6% ± 7.2% vs. 73.9% ± 7.1%). The study with 30 volunteers (*14*) demonstrated a weaker but statistically significant delay in gastric emptying evidenced by an increased half-time over a 6-h time frame (150 ± 6 vs. 175 ± 11). Post hoc analysis showed that the delays were significant only among women, for which there is no clear explanation.

Human experimental research has failed to definitively establish a significant measurable effect of cannabinoids on small- or large-bowel transit (*14*). Future research that focuses on cannabis users is necessary. Small- and large-bowel transit scintigraphy is infrequently encountered in daily practice but could be used to measure the effect of novel selective cannabinoid therapies designed for disorders of hyper- or hypomotility such as irritable bowel syndrome (*13*). At present, conditions that are characterized by abnormal small- or large-bowel motility, such as celiac disease, small-intestinal bacterial overgrowth, and inflammatory bowel disease, are more commonly evaluated with fluoroscopy or CT/MR enterography. However, these studies lack the dynamic, quantitative, functional assessment ascertained by scintigraphy (*16*).

Gastric Emptying in Cannabinoid Users

Recent cross-sectional studies have examined the prevalence of cannabinoid use in patients with gastroparesis, and no significant difference in gastric emptying times was found between users and nonusers. Two studies benefited from a large sample size (n = 197 and 506) and use of the current Society of Nuclear Medicine and Molecular Imaging procedural standards for GES (*17–19*). Their analysis also considered the effects of cannabinoid type, routes of intake, and chronicity or frequency of use. However, a major limitation of these studies was the lack of a baseline GES before cannabis exposure. This would control confounding variables that may contribute to significant interindividual differences in gastric emptying times. A population-based study comparing rates of gastric emptying among states or countries with a higher incidence of cannabis exposure could be informative and establish an association but not causality (*20*). Additionally, the reference ranges for GES may be unique for certain populations because of population genetics or unique gut microbiota cultivated by region-specific foods and dietary habits (*21*).

Perceived Benefits of Cannabis for Gastroparesis

Perhaps the most interesting result comes from a recent large National Institutes of Health–sponsored trial in which 81% of cannabis users perceived benefits in their gastroparesis

symptoms. The investigators reported that cannabis users represented a minority of all gastroparesis patients (12% of 506 patients) and had higher baseline scores for nausea, vomiting, and upper abdominal pain. There are 2 possible explanations for these findings—that is, either cannabis causes more severe gastrointestinal symptoms or gastroparetic patients with worse symptoms were prone to use cannabis. A baseline symptom inventory before cannabis exposure may have clarified the temporal relationship (*19*).

Further evidence that supports the clinical benefit of cannabis comes from a small prospective cohort study ($n = 24$) by Barbash et al. (*22*). Patients with delayed gastric emptying by GES were selected and prescribed dronabinol–tetrahydrocannabinol, medical cannabis, or both via vaporized inhalation or sublingual drops. The tetrahydrocannabinol-to-cannabidiol ratio of the medical cannabis was determined by the dispensary for each patient and not considered in the analysis. A significant improvement was found in abdominal pain and all symptoms measured by the Gastroparesis Cardinal Symptom Index. Key limitations were small sample size and the lack of a placebo-controlled masked study design. Additionally, because the study could not control the highly variable ratios of tetrahydrocannabinol to cannabidiol prescribed to patients by dispensaries, the treatment effect is difficult to measure and cannot be attributed to a particular cannabinoid (tetrahydrocannabinol vs. cannabidiol). The lack of standardization inherent in the heterogeneous cannabis marketplace limits the analysis. Additionally, a follow-up GES at the time of symptom improvement was unfortunately not performed (*22*).

The seemingly contradictory cannabinoid effects that improve gastroparetic symptoms but likely delay gastric emptying have yet to be elucidated. Experts hypothesize that these perceived benefits are unrelated to effects on gastric emptying via CB1 receptors but are instead the result of tetrahydrocannabinol or cannabidiol action on other cannabinoid receptors that blunt visceral sensation possibly via CB2 receptor activation. To clarify these questions, a recent study evaluated the efficacy of cannabidiol in patients with gastroparesis and demonstrated a significant improvement in symptoms despite slower GES times. However, the same researchers using a near-identical study design to evaluate patients with functional dyspepsia and normal baseline GES failed to demonstrate a significant change in GES times. No such randomized controlled trial exists for a tetrahydrocannabinol treatment group. Regardless, any measurable treatment effects discovered by a randomized controlled trial would be limited to a specific patient population treated with pharmaceutical cannabinoid formulations. It would be inappropriate to extrapolate the results to commercial cannabis use comprising a diverse cannabinoid marketplace with heterogeneous tetrahydrocannabinol and cannabidiol potencies, variable pharmacokinetic profiles dependent on route of intake, and individualized gut microbiota (*23–25*).

Cannabinoid Hyperemesis Syndrome

Chronic heavy cannabinoid intake can result in a clinical syndrome characterized by bouts of cyclic hyperemesis and relieved by prolonged hot baths or showers. An increase in incidence has been attributed to the expanding access to cannabis nationwide. Originally characterized as a subtype of cyclic vomiting syndrome because of overlapping features, it is now separately defined by the Rome IV criteria. Cannabinoid hyperemesis syndrome may be distinguished by delayed gastric emptying compared with the rapid gastric emptying of cyclic vomiting syndrome (*26*,*27*).

Despite the strong correlation between frequent cannabis use and cannabinoid hyperemesis syndrome, a case series by Simonetto et al. demonstrated that only 30% of 98 patients had delayed gastric emptying, whereas 45% had normal emptying and 25% had rapid emptying (*28*). Such paradoxical findings underscore the perplexing relationship between cannabis and potentially delayed gastric emptying among chronic users.

From a technical perspective, the timing of scintigraphy relative to cannabis intake may also contribute to inconsistent results. It is plausible that the timing of GES acquisition may be stalled for patients who have hyperemesis because they cannot tolerate the radiolabeled meal or in whom radioactive contamination from uncontrolled hyperemesis needs to be avoided. With the 4-h half-life of tetrahydrocannabinol, it is possible that the GES may not capture the delayed gastric emptying that had been present at initial presentation. The initial human experimental studies that reported delayed gastric emptying in healthy subjects started GES within 1 h of dronabinol–tetrahydrocannabinol administration. Follow-up GES in patients with delayed gastric emptying after cannabis cessation would help clarify these findings. In the initial case series, in which Allen et al. described cannabinoid hyperemesis syndrome, the single patient who demonstrated severely delayed gastric emptying was the only patient evaluated during an acute episode (*29*). The other patients demonstrated normal gastric emptying when evaluated between bouts of illness. Regardless, the diagnosis of cannabinoid hyperemesis syndrome should be based on drug history, symptomatology, and resolution of symptoms after cessation rather than GES.

THERAPEUTIC POTENTIAL OF ENDOCANNABINOID SYSTEM

The endocannabinoid system plays a crucial role in maintaining gastrointestinal balance and has therapeutic potential. Cannabinoids have demonstrated antiinflammatory and pain-relieving properties and may benefit patients with gastrointestinal conditions, as suggested by small studies on patients with inflammatory bowel disease. However, findings from epidemiologic studies contradict some animal and human research, particularly regarding potential benefits in obesity, fatty liver, gastroparesis, and irritable bowel syndrome. These inconsistencies highlight the complex

interactions between the endocannabinoid system and other systems such as the gut microbiome. Current studies focusing mainly on CB1 and CB2 receptors and exploring substrates responsible for the synthesis and degradation of endocannabinoids could open new therapeutic possibilities (*17*,*23*).

DRUGS AND BUGS: CANNABINOIDS AND GUT MICROBIOME

Further complicating our understanding of the endocannabinoid system is its relationship to the gut microbiome (Fig. 1). The gut microbiome has emerged as a key component of human health in recent years, with far-reaching effects on nutrition, cancer susceptibility, and gastrointestinal disorders, among others. Consumers are inundated by marketing which claims that pre- or probiotic products will enhance our health through recolonization of healthy gut flora. Although the efficacy of these products is debated, there is a plethora of evidence demonstrating that the microbiome in our gut does impact our health. The homeostatic imbalance between the microbiome and the human host is termed dysbiosis as opposed to the ideal state of symbiosis (*9*). A recent large systematic review found that nearly half of patients with gastroparesis are also affected by small-intestinal bacterial overgrowth, further strengthening the connection between motility and the gut microbiome (*30*).

The endocannabinoid system, which links the gut to the brain, is affected by the gut microbiome. It is postulated that their interaction occurs via 3 pathways: the hypothalamic–pituitary–adrenal axis, the vagus nerve, and systemic neurotransmitter–hormonal regulation. Researchers have validated these relationships by measuring changes in endocannabinoid tone after introducing specific bacteria to germ-free mice. Manipulation of gut microbiota through antibiotics, probiotics, a high-fat diet, and gene-knockout expression results in alterations of endocannabinoid levels (anandamide and 2-archidonoyl glycerol) and cannabinoid receptor expression. Conversely, the opposite is true when endocannabinoid tone is manipulated, thereby altering microbiota composition. Even more astounding, researchers have discovered receptor sites on bacteria (e.g., *Helicobacter pylori, Escherichia coli,* and *Pseudomonas aeruginosa*) that respond to human neurotransmitters (epinephrine, norepinephrine serotonin), hormones (gastrin, somatostatin, insulin, steroids), and immune factors resulting in measurable changes in microbiota composition and virulence, reinforcing the bidirectional aspect of the gut–brain–microbiome axis (*31*,*32*). Mouse models can mimic a variety of pathophysiologic disease states, thereby enabling researchers to study the effect of microbiota in inflammatory conditions, metabolic disorders, and stress (*9*). Although this research is limited to endocannabinoid signaling, phytocannabinoids likely have a similar effect given their shared receptors. Animal models and human cross-sectional studies have successfully demonstrated alterations in gut microbiota caused by phytocannabinoid exposure. More importantly, inflammatory markers and clinical symptoms were improved after correction of the pathologic dysbiosis in animal models (*33*–*35*).

The highly personalized microbiota among individuals, cultures, and geographic regions could significantly impact the effect of cannabinoids. In the age of precision medicine, emerging technologies that rely on big data attempt to uniquely characterize an individual's microbiome (*36*). Researchers have identified unique subpopulations of microbiota along different segments of the gastrointestinal tract within single individuals and have expanded their work to characterize the gut virome (*37*,*38*). Continued advances within molecular imaging such as attempts to radiolabel microorganisms may allow us in the future to visually assess the collective function of our gut flora (*39*). One could postulate that careful selection of one's diet could cultivate gut microbiota optimized for desirable therapeutic effects.

THE MUNCHIES

This article would not be complete without a discussion of the well-known phenomenon of a surge in appetite and food consumption after cannabis use, colloquially known as the munchies. Tetrahydrocannabinol activates CB1 receptors in the brain, thereby increasing appetite and the desirability of food. This homeostatic balance is regulated by the endocannabinoid system's action on the hypothalamus, which modulates the hunger hormones ghrelin and leptin. Ghrelin stimulates appetite and increases motility, whereas leptin curbs hunger and decreases motility. Because endocannabinoids exert their action on the upstream hypothalamic homeostatic regulator, it is possible that the interaction between exogenous cannabis exposure and the native endocannabinoid system could produce both promotile and antimotile effects depending on the incompletely understood physiologic feedback loop (*40*,*41*). Cannabinoids also act on pleasure pathways in the brain that increase dopamine and result in the characteristic insatiable hunger. An animal study looked at the relationship between different macronutrient stimuli and endocannabinoid signaling in mice. They found that endocannabinoid levels highly regulate dietary fat intake, whereas no measurable response was identified in carbohydrate- or protein-based meals. These effects have led to medications that either stimulate or block cannabinoid signaling. At present, they can be prescribed as an appetite stimulant in anorexic patients. CB1 receptor antagonists have been tried for weight loss in obesity but were stopped because of severe neuropsychiatric side effects (*15*,*42*).

HIGH-YIELD CLINICAL CONSIDERATIONS IN NUCLEAR MEDICINE

There is limited evidence that cannabinoids result in significant delays in gastric emptying. Any significant delays would likely be limited to instances of very recent intake ($<$12 h). The social history should be reviewed for all forms of cannabinoids (medical or recreational marijuana,

dronabinol–tetrahydrocannabinol, synthetic cannabinoids such as K2 or Spice). To avoid false-positive results, it is recommended to avoid cannabinoid intake for at least 72 h before GES, although no cannabis after midnight would likely suffice (*43*). This measure is conservative and extends several half-lives beyond the 4-h serum half-life of tetrahydrocannabinol. Cannabinoids should be added to the list of medications that may affect gastric emptying per the Society of Nuclear Medicine and Molecular Imaging procedure standards for GES.

If GES is requested for a chronic cannabis user, it is important to recognize that a negative result is more helpful. In patients with gastroparetic symptoms and a normal GES result, other functional gastrointestinal disorders should be considered such as functional dyspepsia. If the result is positive, cannabis may or may not contribute to the result and should be correlated with the timing of intake. The collective research does not suggest a significant difference in gastric emptying times in chronic users. A trial of prolonged cessation to assess improvement in symptoms and repeat GES could be considered. If gastroparetic symptoms improve with cannabis, abnormal GES times should yield to symptom index scoring systems as the primary measure of treatment effect.

GES has limited utility in differentiating cannabinoid hyperemesis syndrome from cyclic vomiting syndrome. Rapid gastric emptying is more characteristic of cyclic vomiting syndrome but should serve only as a supporting criterion given the significant overlap of GES times between the two conditions. A history of cannabis use and resolution of symptoms after cessation are the primary differentiating diagnostic features of cannabinoid hyperemesis syndrome.

Cannabinoids should be suspended before small- or large-bowel transit studies to avoid false-positive (slow transit) results, unless measuring the cannabinoid effect is the purpose of the examination. Although this issue is incompletely studied, our current understanding is that cannabinoids could decrease bowel motility and thereby increase transit times. The effect on transit times in chronic users is currently unknown.

CONCLUSION

Given the increased availability of medical and recreational cannabis nationwide, its effects on bowel motility and inflammatory bowel disease have garnered significant attention. Historically, cannabis has been associated with decreased gastrointestinal motility, although recent research strongly suggests a paradoxical clinical improvement in gastroparesis. At present, there is no convincing evidence that cannabis results in significant delays in gastric emptying. More robust double-blinded trials that use the GES procedure standard, test various cannabinoid intake types at different time intervals, and enroll both naïve and chronic users could help clarify the relationship under specific experimental conditions. However, the generalizability of the results would be significantly limited when considering the heterogeneous cannabinoid marketplace accessible to our patients. Instead, studies that assess its clinical utility in symptom management would be of greater utility. We are just beginning to understand the complex interplay among other phytocannabinoids (cannabidiol), endocannabinoids (anandamide and 2-archidonoyl glycerol), and CB1 and CB2 receptors within the broader endocannabinoid system. The multifaceted effect on the gut–brain–microbiome axis requires further research within each of these domains to decipher its many potential benefits on the gut.

DISCLOSURE

Mary Beth Farrell is an employee of the IAC. The views expressed are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of Defense, or the U.S. government. No other potential conflict of interest relevant to this article was reported.

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Use of a Fatty Meal Cholecystagogue Protocol in Hepatobiliary Scintigraphy for Chronic Functional Gallbladder Disease

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Chronic functional gallbladder disorder, characterized by biliary pain in the absence of structural pathology, poses a diagnostic challenge necessitating reliable cholecystagogues for accurate evaluation. However, recurrent shortages of synthetic cholecystokinin analogs have prompted the exploration of alternative agents. This paper describes the efficacy of Ensure Plus as a viable fatty meal substitute for hepatobiliary scintigraphy in assessing chronic functional gallbladder disorder. Through comparative studies, Ensure Plus demonstrates comparable diagnostic accuracy to cholecystokinin in similar patient populations. Furthermore, Ensure Plus demonstrates significant symptom improvement after cholecystectomy in patients with anomalous gallbladder ejection fractions. This paper offers a detailed protocol for the seamless integration of Ensure Plus into hepatobiliary scintigraphy, providing clinicians with a valuable tool to navigate cholecystokinin shortages while maintaining diagnostic precision in cases of chronic functional gallbladder disorder. The use of Ensure Plus not only addresses practical supply challenges but also underscores its potential as a cost-effective and clinically sound alternative in biliary diagnostics.

Key Words: hepatobiliary scintigraphy; chronic functional gallbladder disorder; gallbladder ejection fraction; fatty meal; Ensure Plus

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The gallbladder is a saccular organ attached to and extending along the underside of the liver (Fig. 1A). The primary function of the gallbladder is to serve as a reservoir for bile salts, lipids, and other macromolecules involved in the digestion of fats (*1*). Bile enters and exits the gallbladder via the cystic duct, which connects directly with the common hepatic duct to form the downstream common bile duct, which empties into the duodenum after passing through the pancreas and sphincter of Oddi (Fig. 1A). The sphincter of Oddi contracts between episodes of feeding to create back pressure within the biliary system, which results in retrograde passage of bile through the cystic duct into the gallbladder for storage. On feeding and neurohormonal stimulation, the smooth muscle within the muscularis layers of the gallbladder walls contracts and the sphincter of Oddi relaxes to allow for differential pressure dynamics that push bile out of the gallbladder, through the common bile duct, and out of the sphincter of Oddi to the duodenum. Cholecystokinin is the most potent hormonal stimulator of gallbladder smooth muscle contraction and sphincter of Oddi relaxation, but acetylcholine released from the vagal or enteric nerves can also produce a similar effect (*2–10*). Gallbladder functioning and the biliary system require patent ducts and effective management of pressure dynamics to ensure that bile is appropriately delivered from the gallbladder to the food bolus. Disruption of the duct patency or biliary pressure dynamics will result in gallbladder pathology, including acute and chronic disease (Fig. 1B).

Obstruction of the biliary duct system or disruption of the smooth muscle dynamics involved in the passage of bile through the duct system results in common biliary pathologies (Table 1) (*1*,*11*). Acute blockage of biliary transit out of the gallbladder, usually from a gallstone, results in increased pressure within the gallbladder lumen and resultant inflammation throughout the gallbladder walls (acute calculous cholecystitis). This results in pain of the right upper quadrant along with other gastrointestinal symptoms. Rarely, a more serious form of acute cholecystitis can result without gallstone blockage (acalculous cholecystitis); this form is commonly secondary to gallbladder injury or systemic disease. Acute cholecystitis is commonly evaluated with ultrasound, but it can be confirmed or further assessed with hepatobiliary scintigraphy, CT, or MRI. On hepatobiliary scintigraphy, acute cholecystitis is

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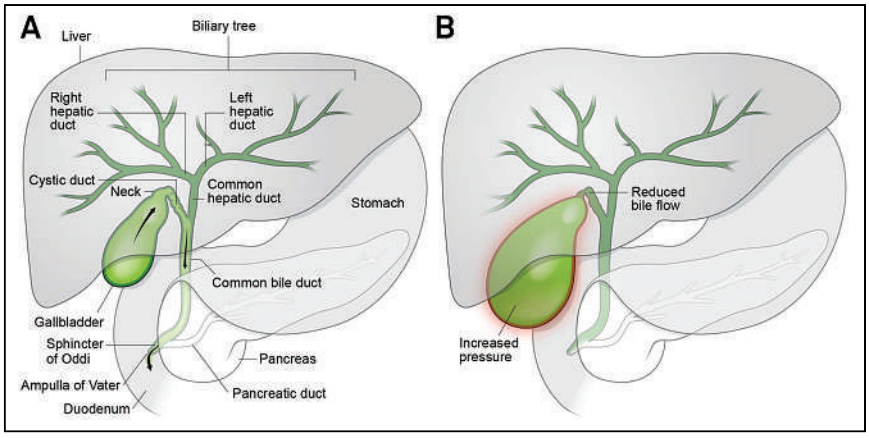

FIGURE 1. Normal and abnormal biliary transit. (A) Normal anatomy and physiology of hepatobiliary system, with hepatic production of bile, excretion via hepatic ducts, localization to gallbladder, and excretion, on stimulation, through common bile duct and ampulla of Vater to small bowel. Sphincter of Oddi acts as pressure valve for bile passing into small bowel near junction of biliary system and duodenum. (B) Reduced bile flow (which in case of chronic functional gallbladder disorder is due to gallbladder dysmotility), which results in increased pressure and inflammation within gallbladder (cholecystitis).

confirmed by blockage of radiopharmaceutical passing through the cystic duct to the gallbladder (*1*,*12*).

In contrast to acute cholecystitis cases, chronic cases of cholecystitis can develop in patients either through obstruction or through disruption of pressure dynamics in the biliary system. Like acute cholecystitis, chronic cholecystitis can also develop in the setting of gallstones (chronic calculous cholecystitis). Some cases of chronic gallbladder disease are also found in patients without gallstones (acalculous). Physicians and researchers have historically questioned whether chronic acalculous gallbladder disease, termed chronic functional gallbladder disorder, was a true entity (*13*,*14*). Chronic functional gallbladder disorder is defined as biliary pain without gallstones or other structural pathology (Fig. 1B) (*14–17*). Biliary pain is described as epigastric or right upper quadrant pain that builds up, occurs at different intervals, and is not significantly associated with bowel movement, position changes, or acid suppressants (*11*,*18*,*19*). It can result in nausea and vomiting and radiate to the back. Supportive evidence for chronic functional gallbladder disorder includes a low gallbladder ejection fraction on hepatobiliary scintigraphy, normal liver or pancreatic enzymes, and normal bilirubin (*11*,*12*,*14*,*20*). Mimicking physiologic biliary physiology, stimulated hepatobiliary scintigraphy can help to assess the gallbladder ejection fraction in cases of possible chronic functional gallbladder disorder. In this article, we will describe the history and use of a standardized fatty meal, Ensure Plus (Abbott), to determine gallbladder ejection fractions in possible cases of chronic functional gallbladder disorder.

BACKGROUND

Before hepatobiliary scintigraphy came into use, cholegraphy was performed with intravenous and oral contrast agents and radiographic or fluoroscopic imaging (*3*,*21*). During this time, researchers made discoveries regarding biliary physiology and pathogenesis that are important for hepatobiliary scintigraphy. Initial work on gallbladder contraction and biliary excretion resulted from cholegraphic studies in which patients were administered an oral cholecystagogue (*22–25*). Examples of the reported oral cholecystagogues include milk, corn oil emulsion, Cholex (egg yolk, soya lecithin, glycerin, and peanut oil), D-sorbitol solution, safflower oil emulsion, vegetable oil, fatty meal (Lipomul), and Ensure Plus (*5*,*8*,*12*,*22*,*23*,*25–33*). In 1957, cholecystokinin was developed as an intravenous cholecystagogue demonstrating prompt and strong contraction of the gallbladder and opening of the sphincter of Oddi (*2*,*3*). Beginning with the development of radiolabeled iminodiacetic acid analogs in 1976, followed

TABLE 1
Gallbladder/Biliary Pathologies, Common Symptoms, and Hepatobiliary Scintigraphy Findings

Pathology	Symptom	Finding
Acute calculous cholecystitis	Acute biliary colic with or without fever, nausea, vomiting	Nonvisualization of gallbladder
Acute acalculous cholecystitis	Critical illness, sepsis, jaundice, pain in right upper quadrant	Nonvisualization of gallbladder (variable false positive due to illness)
Chronic calculous cholecystitis	Variable: biliary colic, nausea, reflux, bloating	Delayed gallbladder ejection fraction; stones on hepatobiliary scintigraphy or ancillary imaging
Chronic functional gallbladder disorder	Variable: biliary colic, nausea, reflux, bloating	Delayed gallbladder ejection fraction (other reported signs not diagnostic)
Sphincter-of-Oddi syndrome	Biliary colic, nausea, vomiting	Radiopharmaceutical concentration in biliary tree; delayed bowel excretion
Enterogastric reflux	Epigastric pain, vomiting, nausea, heartburn	Reflux of radiopharmaceutical in bowel proximal to ampulla of Vater
Hepatic dysfunction	Pain in right upper quadrant; severe illness pending cause	Delayed extraction by liver and delayed excretion from liver

by ^{99m}Tc-mebrofenin, which demonstrated better hepatic extraction and decreased renal excretion, hepatobiliary scintigraphy gradually replaced oral cholegraphy for imaging functional gallbladder pathologies (*1*,*12*,*34–36*).

As a predominantly functional gallbladder pathology, chronic functional gallbladder disorder began to be characterized using cholecystagogues to determine gallbladder ejection fractions. Using different cholecystokinin administration protocols with hepatobiliary scintigraphy, researchers found the least variation in results with a 60-min continuous cholecystokinin infusion (*12*,*36*,*37*). Using this protocol, researchers found that the lower limit of normal gallbladder ejection fractions was 38%, with gallbladder ejection fractions less than 38% considered abnormal. Unfortunately, sincalide (the commercial analog of cholecystokinin) has been prone to shortages over the years; oral cholecystagogues have therefore been used to continue assessments for chronic functional gallbladder disorder (*38*). Among the oral cholecystagogues, milk, corn oil emulsions, Lipomul, and Ensure Plus have been investigated to assess for normal gallbladder ejection fractions (*8*,*26*,*29*,*39*). In adults, researchers found normal gallbladder ejection fractions to be at least 40% for milk after 60 min, at least 20% for corn oil emulsions after 60 min, and at least 33% for a fatty meal (i.e., Ensure Plus) after 60 min. In pediatric patients given Lipomul, researchers found normal gallbladder ejection fractions to be at least 35% after 30 min. Among these options, Ensure Plus is well tolerated, with a variety of flavors, consistent preparation (11.4 g of fat), and low lactose content (*8*). In contrast to sincalide administration, which occurs over 60 min, Ensure Plus is administered orally within 5 min and is better tolerated. Ensure Plus is much more affordable than compounded or commercial preparations of sincalide. Ensure Plus is also more accessible to any nuclear medicine practice.

In a comparison of cholecystokinin to Ensure Plus in hepatobiliary scintigraphy for suspicion of chronic functional gallbladder disorder, we found that patients receiving cholecystokinin or Ensure Plus did not significantly differ in the percentage of abnormal gallbladder ejection fractions identified in similar patient populations (*28*). The descriptive statistics from that same study found that the sensitivity, specificity, positive predictive value, and negative predictive value for chronic cholecystitis on histopathology or for a subjective reduction in postoperative biliary-type pain in patients undergoing cholecystectomy. Li et al. assessed the symptoms for patients undergoing hepatobiliary scintigraphy with Ensure Plus for suspected chronic functional gallbladder disorder, comparing the symptom outcomes after cholecystectomy or conservative management in patients with normal or abnormal gallbladder ejection fractions (*27*). In patients with abnormal gallbladder ejection fractions on Ensure Plus hepatobiliary scintigraphy, 97% experienced symptom improvement after cholecystectomy, compared with 65% who were treated conservatively. Although these are retrospective studies, these findings suggest that Ensure Plus can be used instead of cholecystokinin for gallbladder ejection fraction evaluation in suspected cases of chronic functional gallbladder disorder. This is particularly helpful during sincalide shortages and as a cost-saving measure. In this article, we will describe our institutional approach to using Ensure Plus as the cholecystagogue in hepatobiliary scintigraphy for evaluation of chronic functional gallbladder disorder.

Preparation

In preparation for Ensure Plus hepatobiliary scintigraphy for gallbladder ejection fraction, patients should fast for at least 2 h and preferably 4–6 h (*1*,*12*). Ingested food stimulates endogenous release of cholecystokinin, which can interfere with the hepatobiliary scintigraphy study. If the patient has been fasting for more than 24 h, bile and sludge can accumulate in the gallbladder and interfere with the passage of radiopharmaceutical into the gallbladder. For these patients, one can pretreat with sincalide. The Society of Nuclear Medicine practice guideline recommends pretreating patients with 0.02 μg/kg sincalide IV over 3–60 min, approximately 15–30 min before injecting the radiopharmaceutical (*12*). For pretreatment at our institution, we have found that sincalide administration over 3–5 min, 30 min before radiopharmaceutical administration, is sufficient. If sincalide is not available, a fatty meal can be given at least 2 h before the hepatobiliary scan for gallbladder ejection fraction. If patients have been fasting for more than 24 h, there may be other factors that may impact the accuracy of the gallbladder ejection fraction results, including systemic illness. In such patients, it may be advisable to postpone gallbladder ejection fraction imaging until the patient is more stable (*1*).

Additionally, it is important to withhold opiate medications for at least 6 h or 3–4 half-lives before Ensure Plus hepatobiliary scintigraphy for gallbladder ejection fraction (*12*). Opiates can result in inaccurate results due to their effects on the sphincter of Oddi. In some cases, the reversal agent, naloxone hydrochloride, can be administered.

Patients should be instructed to remain still and breathe normally during the imaging phases of the hepatobiliary scintigraphy study. They should avoid coughing, clearing their throat, taking deep breaths, or falling asleep.

Radiopharmaceutical

Historically, ^{99m}Tc-labeled iminodiacetic acid molecules, such as hepatobiliary iminodiacetic acid, were used for hepatobiliary scintigraphy, but because of poor uptake in cases of hyperbilirubinemia, they are no longer widely used (*1*). Currently, ^{99m}Tc-disofenin (2,6-diisopropylacetanilido iminodiacetic acid) and ^{99m}Tc-mebrofenin (bromo-2,4,6-trimethylacetanilido iminodiacetic acid) are approved for use in hepatobiliary scintigraphy. These radiopharmaceuticals have improved hepatic extraction, including in cases of elevated bilirubin levels up to 20–30 mg/dL (*1*). These bilirubin analogs are extracted by the liver and excreted through the biliary system on the basis of pressure dynamics with the biliary system (Fig. 1A). ^{99m}Tc-disofenin and ^{99m}Tc-mebrofenin are administered intravenously at activities of

111–185 MBq (3–5 mCi). In cases of hyperbilirubinemia, the activities can be raised to 185–370 MBq (5–10 mCi). For children, activities are weight-based, at 1.8 MBq/kg (0.05 mCi/kg) (*12*).

Cholecystagogue Precautions

Precautions for sincalide administration include standard allergic reactions and those related to the mechanism of action (*10*). Severe hypersensitivity reactions have been reported, including anaphylaxis. Sincalide has also been reported to induce preterm labor or abortion in pregnant patients because of effects on smooth muscles. Some patients report severe biliary colic symptoms, particularly patients with gallstones. If the pain is severe, it is recommended to stop sincalide infusion, report the symptoms, and continue imaging. For some surgeons, reproduction of the initial patient-reported symptoms during the scan is used as a positive factor for recommending cholecystectomy. Additional symptoms include nausea, vomiting, dizziness, and flushing.

Precautions for Ensure Plus predominantly involve allergic reactions. Patients with lactose intolerance generally do not have problems with Ensure Plus because of the low amounts of lactose in the formula (*40*). Patients with galactosemia, particularly severe galactosemia, should avoid Ensure Plus. As an oral agent, Ensure Plus may not be suitable for patients who cannot tolerate oral intake. Patients with gastric feeding tubes may undergo Ensure Plus hepatobiliary scintigraphy, but if the enteric tube is in a significantly postpyloric position, Ensure Plus may not have the intended effect on gallbladder contraction; this has not been studied.

Acquisition

After the patient is positioned supine with a pillow beneath the knees and arms on the sides and supported, the radiopharmaceutical (^{99m}Tc-disofenin or ^{99m}Tc-mebrofenin) is injected intravenously. Dynamic imaging with a large-field-of-view γ-camera and a low-energy all-purpose or low-energy high-resolution collimator ensures that the liver, gallbladder, biliary tree, and bowel can be simultaneously visualized (*12*). The optimal image matrix with such a collimator is 128 × 128. Dynamic imaging at a rate of 1 frame/min for 60 min is then performed. Within this time frame, the gallbladder should fill, and some radiopharmaceutical may pass into the bowel. If the gallbladder does not fill in 60 min, it is recommended to evaluate the patient for signs of acute cholecystitis. Repeat imaging could be obtained after sincalide pretreatment.

After pre–Ensure Plus imaging is completed, 237 mL (8 oz) of Ensure Plus is then administered by mouth to the patient. Ideally, the patient should try to drink the Ensure Plus within 5 min. The patient is then again positioned supine. At our institution, we then position the γ-camera detector in the left anterior oblique position and perform dynamic imaging at 30 s/frame for 120 frames. This approach allows for finer time resolution, but 1 min/frame for 60 frames would also suffice.

Processing

Pre– and post–Ensure Plus dynamic images are then processed to determine the gallbladder ejection fraction. A region of interest (ROI) is drawn around the gallbladder (Fig. 2). The individual who is processing the images should ensure that there is no significant gallbladder motion during the pre– or post–Ensure Plus dynamic imaging. If the gallbladder moves significantly outside the ROI during the scan, then the technologist cannot batch process the images and should instead process the images individually to ensure that the gallbladder lies within the ROI at each time point. The individual who is processing the images should also ensure that there is no significant biliary tree radiopharmaceutical overlap with the ROI over the course of dynamic pre– or post–Ensure Plus imaging. The counts from the ROI are then processed by the imaging software to generate a time–activity curve (Fig. 2). The gallbladder ejection fraction percentage is calculated from the maximum and minimum gallbladder ROI counts as [(maximum count − minimum count)/maximum count] × 100 (*12*).

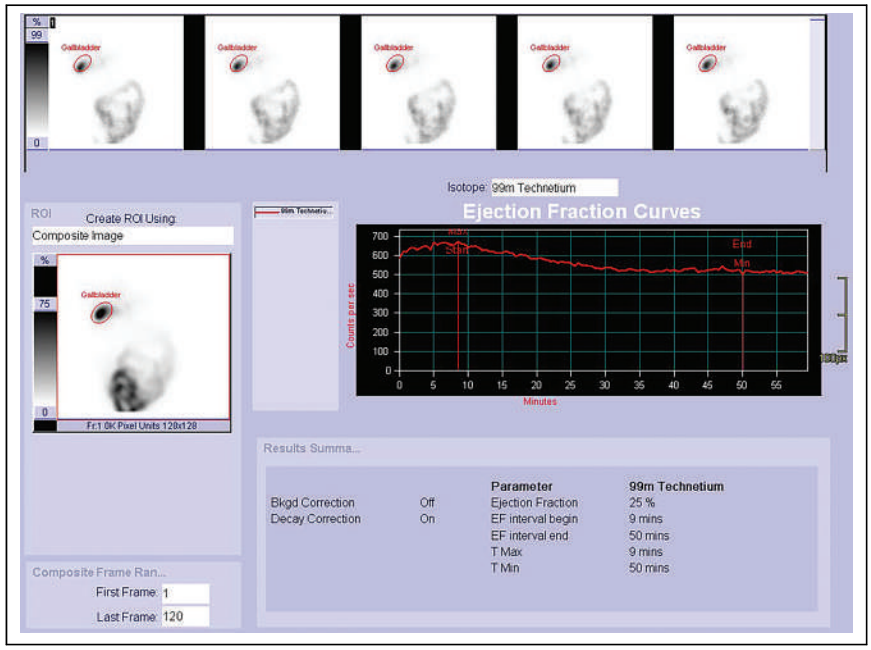

FIGURE 2. Ensure Plus hepatobiliary scintigraphy results for patient with chronic functional gallbladder disorder (gallbladder ejection fraction, 25%). Appropriate gallbladder ROI placement is shown. Ejection fraction was calculated from demonstrated time–activity curve. Low ejection fraction (<33%) is consistent with chronic functional gallbladder disorder. EF = ejection fraction; Fr:1 = frame 1; T max = time of maximum counts/s; T min = time of minimal counts/s.

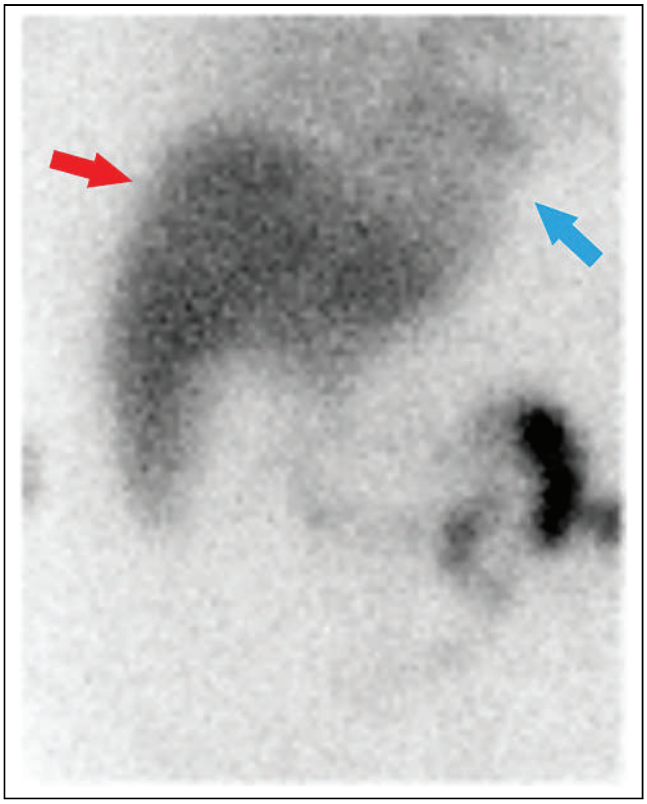

FIGURE 3. In this patient with severe hepatic dysfunction, image at 60 min after ^{99m}Tc-mebrofenin injection demonstrates significant persistent uptake in cardiac blood pool (blue arrow) and liver (red arrow), with little passage into bowel and nonvisualization of gallbladder.

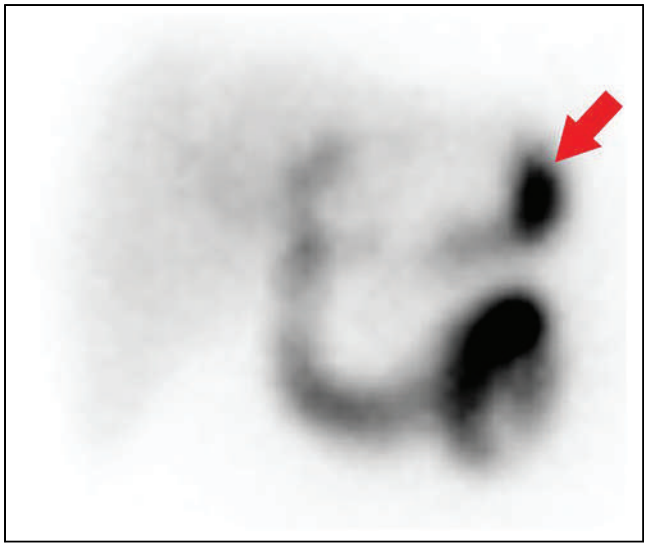

FIGURE 4. In this selected hepatobiliary scintigraphy image 40 min after injection of ^{99m}Tc-mebrofenin, there is moderate reflux (arrow) of radiopharmaceutical in retrograde fashion to stomach. Enterogastric reflux can be cause of abdominal symptoms in patients and should be reported if seen.

Interpretation

Interpretation of the Ensure Plus hepatobiliary scintigraphy for gallbladder ejection fraction involves evaluating the pre–Ensure Plus dynamic imaging for physiologic extraction of the radiopharmaceutical from the blood pool into the liver parenchyma, excretion through the hepatic biliary system, localization to the gallbladder, and then post–Ensure Plus excretion from the gallbladder through the extrahepatic biliary system to the bowel. If there is a significant delay (>5–10 min) in extraction from the blood pool to the liver, it may be a sign of hepatic dysfunction, such as liver failure or acute hepatitis (Fig. 3) (*1*). Extraction to the liver but a lack of excretion to the biliary system may also suggest poor hepatic function or a high-grade biliary obstruction. As previously noted, if the gallbladder fails to fill, it may indicate a sign of acute cholecystitis versus cold bile or sludge obstructing entrance of the radiopharmaceutical. After assessment of the patient, one can consider rescheduling the hepatobiliary scintigraphy with sincalide pretreatment to ensure radiopharmaceutical localization to the gallbladder.

In pre– or post–Ensure Plus imaging, a delay in passage to the small bowel may suggest dysfunction of the sphincter of Oddi, characterized by a functional or anatomic obstruction (*41*,*42*). On hepatobiliary scintigraphy, the sphincter of Oddi manifests as decreased clearance of the radiopharmaceutical from the liver, dilation of the intra- and extrahepatic biliary ducts, and increased radiopharmaceutical concentration in the biliary system.

During excretion of the radiopharmaceutical from the biliary system into the small bowel, it is important to also assess for retrograde localization of the radiopharmaceutical to the stomach or esophagus (Fig. 4). This enterogastric reflux should be documented in the report, as it can result in an alkaline gastritis and may be a source of pain for the patient.

The most important step in evaluation and interpretation of Ensure Plus hepatobiliary scintigraphy for gallbladder ejection fraction is to report the gallbladder ejection fraction, which is normal if it is at least 33% (*8*). Rapid emptying of the gallbladder has also been reported and suggested as a possible cause of symptoms. Rapid emptying is reported as greater than 65%–80% (*43*). Case reports have reported that cholecystectomy in these cases of biliary colic can lead to symptomatic relief. Although a gallbladder ejection fraction is not the only determining factor for most surgeons, it can be a helpful quantitative measure in defining chronic functional gallbladder disorder in patients with biliary-type symptoms.

CONCLUSION

Determining the gallbladder ejection fraction is an important quantitative tool that assists surgeons in deciding whether a patient's biliary-type pain is due to chronic functional gallbladder disorder. Unfortunately, the primary cholecystagogue used to stimulate gallbladder contraction and sphincter of Oddi relaxation, sincalide, is often underproduced and faces chronic shortages. Consequently, nuclear medicine practitioners need to be aware of other effective oral cholecystagogues that can be used to determine

gallbladder ejection fractions. The best studied of these cholecystagogues is Ensure Plus, an affordable, palatable oral fatty meal that similarly induces gallbladder contraction and sphincter of Oddi relaxation for accurate gallbladder ejection fraction determination.

DISCLOSURE

The opinions and assertions expressed here are those of the authors and do not necessarily reflect the official policy or position of the Uniformed Services University or the Department of Defense. No potential conflict of interest relevant to this article was reported.

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Fatty Meal Hepatobiliary Scintigraphy for Gallbladder Ejection Fraction Determination

Justin G. Peacock and Amanda M. Adams

RATIONALE/INTRODUCTION

The gallbladder stores and concentrates bile. Bile is a mixture of salts and lipids that break down fat and are released into the duodenum during digestion (*1*). Cholecystokinin, which is released by the proximal intestine in response to fat stimulation, causes gallbladder contraction and relaxation of the sphincter of Oddi.

Determination of gallbladder ejection fraction can be used to characterize gallbladder disorders, such as chronic functional gallbladder disease (*2*,*3*). The gallbladder ejection fraction can be calculated during hepatobiliary scintigraphy by inducing contraction of the gallbladder and relaxation of the sphincter of Oddi.

Historically, cholecystokinin analogs such as sincalide have been used; however, because these analogs are often subject to supply shortages, alternative cholecystagogues have been evaluated (*4*,*5*). A well-studied oral cholecystagogue is Ensure Plus (Abbott Laboratories), a liquid fatty meal (*6*–*8*). Ensure Plus is readily available, inexpensive, and effective in assessing gallbladder ejection fraction. A gallbladder ejection fraction of at least 33% is considered normal (*6*).

INDICATIONS

- Evaluation of chronic functional gallbladder disorder.
- Determination of gallbladder ejection fraction.

CONTRAINDICATIONS

- Severe galactosemia, a rare hereditary disorder affecting how the body processes galactose. (This is a possible contraindication. Although patients with lactose intolerance can generally tolerate Ensure Plus, in cases of severe galactosemia, sincalide hepatobiliary scintigraphy should be considered.)
- A patient not properly prepared for the procedure.
- Pregnancy or breastfeeding. (Pregnancy must be excluded according to local institutional policy. If the patient is breastfeeding, appropriate radiation safety instructions should be provided.)
- A recent nuclear medicine study (radiopharmaceutical-dependent).

PATIENT PREPARATION

- The patient should fast for at least 2 h but preferably 4–6 h.
- Ideally, the patient should have eaten within 24 h before the meal. If the test is scheduled in advance, consider having the patient ingest a fatty meal within 24 h to ensure emptying of the gallbladder before the scan.
- The patient should not take opioids for at least 6 h before the examination.
- A focused patient history containing the following elements should be obtained:

TABLE 1
Radiopharmaceutical Identity, Dose, and Route of Administration

Identity	Dose	Route of administration
^{99m}Tc-disofenin	111 MBq (3 mCi); range, 111–185 MBq (3–5 mCi)	Intravenous
^{99m}Tc-mebrofenin	111 MBq (3 mCi); range, 111–185 MBq (3–5 mCi)	Intravenous
^{99m}Tc-mebrofenin or ^{99m}Tc-disofenin	Pediatric dose: 1.85 MBq/kg (0.05 mCi/kg); minimum, 18.5 MBq (0.5 mCi)	Intravenous
Sincalide	For pretreatment, if needed: 0.02 μg/kg over 30–60 min, with infusion completed 15–30 min before radiopharmaceutical administration	Intravenous

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TABLE 2
Dynamic and Static Acquisition Parameters

Parameter	Description	Standard, preferred, or optional
Camera type	Large field of view	Standard
Energy peak	140 keV	Standard
Energy window	20%	Standard
Collimator	Low-energy all-purpose or low-energy high-resolution	Standard
Patient position	Supine	Standard
Camera position	Anterior with liver in left upper quadrant of field of view	Standard
Injection-to-imaging time	Acquisition started within 5 min of injection	Standard
Acquisition type	Dynamic	Standard
Views	Anterior	Standard
Additional views	Left anterior oblique and right lateral	Optional
Matrix	128 × 128	Standard
Number of views	60	Standard
Frame rate per time	1 frame/min	Preferred
	Post–Ensure Plus images: 1 frame/30 s	Standard
Additional view time per projection	2 min	Optional

- Pain location and timing relative to eating and bowel movements.
- Previous history of gallbladder or liver disease.
- Current medications.
- Imaging findings, including ultrasound, CT, or MRI.
- Lab results, including hepatic function tests and bilirubin.
- Time and content of the last meal.

DYNAMIC AND STATIC IMAGE ACQUISITION

The radiopharmaceutical identity, dose, and route of administration are described in Table 1, and the acquisition parameters are described in Table 2.

Pre–Ensure Plus Imaging

- Establish intravenous access.
- Position the patient supine on the imaging table, with the γ-camera anterior to the region of the liver.
- Administer the radiopharmaceutical intravenously as a bolus, begin imaging within 5 min of injection, and image for 60 min.
- If the gallbladder does not fill during this period, assess the patient for pain and consider repeat imaging with the sincalide pretreatment described under "Common Options."
- After dynamic pre–Ensure Plus imaging, obtain static left anterior oblique and right lateral views to confirm gallbladder radiopharmaceutical localization.

Post–Ensure Plus Imaging

- Administer 237 mL (8 oz) of Ensure Plus by mouth. Ideally, the patient should drink the total amount within 5 min.
- Reposition the patient as in the Pre–Ensure Plus imaging.
- Reduce liver background by positioning the γ-camera in the left anterior oblique position.
- Perform dynamic imaging for 60 min.

COMMON OPTIONS

- A higher administered activity (5–10 mCi) may be needed in patients with hyperbilirubinemia.

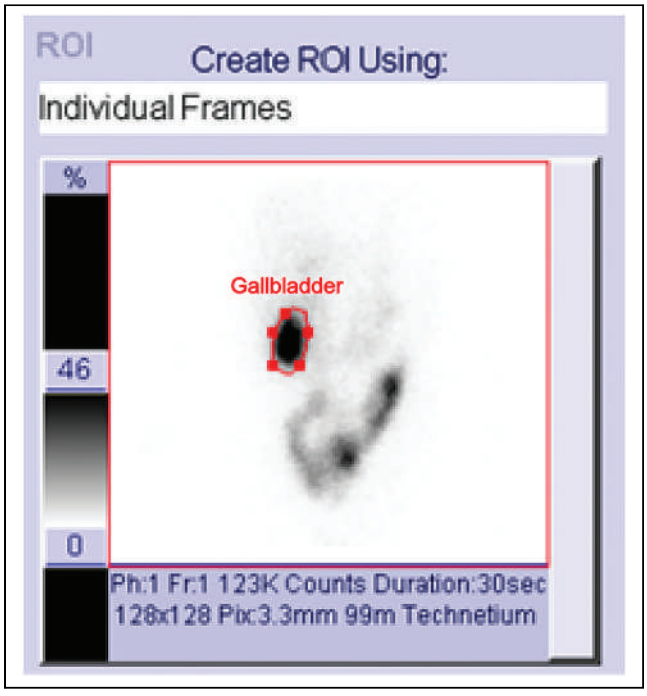

FIGURE 1. Creation of region of interest (ROI) encircling radiopharmaceutical-outlined gallbladder. Ensure that gallbladder remains within ROI throughout post–Ensure Plus dynamic imaging.

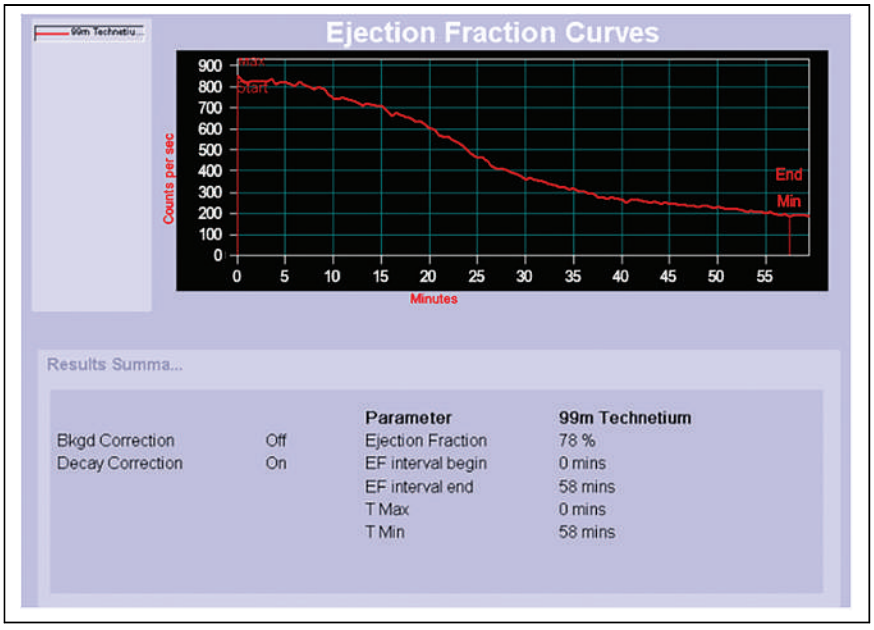

FIGURE 2. Time–activity curve for gallbladder ejection fraction, determined from counts within gallbladder ROI throughout course of post–Ensure Plus dynamic imaging. Bkgd = background; EF = ejection fraction; T Max = time of maximum counts/s; T Min = time of minimum counts/s.

- If the gallbladder is not visualized during the pre–Ensure Plus imaging, sincalide (cholecystokinin) may be administered at 0.02 μg/kg over 30–60 min.
- A booster dose of radiopharmaceutical may be needed to fill the gallbladder (usually half the standard dose).
- Recommend waiting 15–30 min after completion of sincalide infusion before having the patient drink the Ensure Plus and acquiring the post–Ensure Plus dynamic images.

PROCESSING INSTRUCTIONS

- On the post–Ensure Plus dynamic images, place a region of interest over the region of the gallbladder (Fig. 1).
- Ensure that the gallbladder remains within the ROI throughout the post–Ensure Plus dynamic imaging, manually shifting the region of interest if needed, as the position can change with patient motion or respiration.
- Generate a time–activity curve (Fig. 2).
- Determine the percentage gallbladder ejection fraction as [(gallbladder maximum − gallbladder minimum)/gallbladder maximum] ×100.

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Gastric Emptying Scintigraphy 2024: Still A Need for Compliance with Published Guidelines

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Since first introduced by Griffith et al. in 1966 (*1*), gastric emptying scintigraphy (GES) of a radiolabeled meal has been considered the gold standard for measuring gastric emptying. With a properly radiolabeled ordinary meal, the volume of gastric emptying of solids or liquids is accurately measured without the need for geometric assumptions used by other imaging modalities.

The stomach is a complex organ. It is much more than a receptacle to store food before it enters the small bowel. This complexity includes multiple receptors in the wall of the stomach that are sensitive to physical and chemical stimuli as well as electromechanical and hormonal controls, all helping to sense and then respond to the gastric contents so that the ingested meal can be appropriately processed. As with any complex physiologic system, there are many ways the system response can be altered through changes in input and output stimuli. Therefore, the key to the reproducibility of GES, particularly the ability to compare results from one imaging center to another, is adherence to the technical requirements of the test, which include patient preparation (including but not limited to overnight fasting before testing, elimination of drugs that may affect gastric emptying, and patient glucose control), meal preparation, standardized image acquisition times and image processing, and final interpretation based on comparison to healthy control subjects.

In a 1995 review of gastrointestinal nuclear medicine, the following question was asked: "Can we prevent tarnishing a gold standard?" (*2*). Despite the recognition that GES was the most physiologic test for measuring gastric motor function, there was a need for more consistency in how GES was being performed and interpreted. This lack of consistency was underlined by the first Society of Nuclear Medicine and Molecular Imaging (SNMMI) procedure guideline for gastric emptying—published in 1999 (*3*)—which listed several meal options with the caveat that the results should be compared with normal values established for the meal in use. However, normal values for specific meals were hard to come by, and when they were provided, the normal values were often poorly documented with healthy control subjects. It was not until the publication of Tougas et al. in 2000 that critical, multiinstitutionally and internationally based normal values for the emptying of the liquid egg-white meal became available (*4*).

Although the publication of the Tougas meal with its associated normal values was immediately recognized as a major step forward for standardizing GES, there was limited progress in getting nuclear medicine imaging centers to change their practice patterns. Many continued to use their local favorite meal based on no or poorly established normal control values. Protocols for the frequency and timing of imaging and processing of the data were also inconsistent, and the reported results were often based on only 1–2 h of imaging.

Complaints from referring gastrointestinal physicians who could not compare results between imaging centers, and patient complaints that GES studies often were being repeated by different physicians with different meals and imaging protocols, generated a joint project of the SNMMI and the American Neurogastroenterology and Motility Society to develop an updated GES guideline in 2005. The joint committee of these 2 societies approved a final report, which resulted in 2 publications: "Consensus Recommendations for Gastric Emptying Scintigraphy: A Joint Report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine" (*5*) and the "Procedure Guideline for Adult Solid-Meal Gastric-Emptying Study 3.0" (*6*). In an editorial in *The Journal of Nuclear Medicine* in 2008, an urgent message was published that stressed the importance of these guidelines and appealed to the nuclear medicine community to "quickly adopt these new standards so we can achieve consistency and reliable results for our patients and referring physicians" (*7*).

In 2017, Farrell et al. (*8*) reviewed 127 labs for their compliance with the SNMMI GES procedure guideline 3.0. They used reports to the Intersocietal Accreditation Commission database to evaluate the GES protocols from all labs applying for accreditation from 2013 to 2015. They studied 14 key compliance variables, including medication withholding, medication withholding time, blood glucose measurement, blood glucose recording, fasting before testing, full versus partial meal ingestion, radiopharmaceutical dose, imaging protocol, calculation of geometric mean, proper decay correction, and reporting of percentage meal retention for all time points. They found that 69.3% of

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sites were not compliant with the content or preparation of the consensus meal and that only 3.1% of labs were fully compliant with all 14 variables. Over 50% of the labs were compliant with only 5 variables or fewer. Two of the most critical compliance variables—proper withholding of medications and checking of blood glucose—had the lowest levels of compliance. These authors pointed out that such low compliance was found 8 y after publication of the SNMMI GES 3.0 guideline while citing a report that it usually takes an average of 9.3 y for such practice guidelines to become customary (*9*).

Unfortunately, yet another recent report confirmed significant noncompliance with GES guidelines. In "Gastric Emptying Scans: Poor Adherence to National Guidelines" in 2021, Wise et al. used a questionnaire looking at key GES protocol requirements (*10*). In total, 121 of 872 medical institutions responded. Only 4 of 88 (4.5%) adhered to 3 critical measures: 4-h study duration, controlled blood glucose levels, and proper restriction of medications. Only 59% used the recommended meal, and 19% did not include in the report whether the patient had eaten the entire meal.

The group from the Intersocietal Accreditation Commission has done a recent follow-up (*11*) on whether there has been any improvement in compliance with the SNMMI guidelines since the Intersocietal Accreditation Commission's earlier study. For sites that had applied for accreditation from 2018 to 2021, the Intersocietal Accreditation Commission again used its database to look at the same 14 variables used in its 2017 publication. From 118 labs applying, the study found that "compliance is improving in some key areas but remains suboptimal in others." Overall, labs were compliant on average with 8 of 14 variables, but only 4 sites were compliant with all variables. An improvement was noted in the use of the consensus meal, now 62% versus 30% previously, and greater compliance found with measurement of retention percentages instead of half-emptying times (65% vs. 35% 5 y prior). The variable with lowest compliance was the recording of blood glucose (3%). As there is a well-known association between elevated blood glucose and slow gastric emptying, this is a critical value to check before performing a GES test (*12–14*). Many labs had earlier said that glucose testing was not a point-of-care test available in their departments; however, today blood glucose is routinely measured for all ^{18}F-FDG PET studies and should therefore be routinely available for patients undergoing GES.

The recent publications cited above (*8,10,11*) show that there remains an inadequate response on the part of nuclear medicine departments to comply with the most basic guidelines and technical requirements for performing GES. It is clear that our understanding of the complexity and multifactorial components that contribute to overall gastric motility and ultimate gastric emptying of a meal has increased significantly since the publication of the current SNMMI 3.0 guideline. Recent advances have demonstrated that other measurements available from GES, such as fundal accommodation and analysis of antral contractions using dynamic antral contraction scintigraphy, have clinical value and may eventually be added to the current acquisition and processing of GES (*15,16*). The SNMMI committee on procedure standards has recently initiated an update to the GES practice guideline (Kevin Donohoe, oral communication, 2023). So, although this is an exciting time marked by our ability to provide more advanced scintigraphic information for detecting abnormal gastric motor function, the addition of more advanced imaging and processing will only increase the complexity of the test and therefore the need for adherence to standard study protocols. Only with adherence to standard protocols will we be able to speak the same language when managing these complex patients.

In the report from Wise et al. noted above, the authors state: "The significant impact of a gastroparesis diagnosis, or misdiagnosis, on both patients and the health care system mandates that GES be performed according to a validated protocol" (*10*). It is essential that there be greater compliance with current and future guidelines if we are to maintain GES as the go-to gold standard test for the diagnosis and management of patients with suspected gastroparesis.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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Reexamining Compliance with Gastric Emptying Scintigraphy Guidelines: An Updated Analysis of the Intersocietal Accreditation Commission Database

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Many variables can influence the results of gastric emptying scintigraphy (GES). A lack of standardization causes variability, limits comparisons, and decreases the credibility of the study. To increase standardization, in 2009 the Society of Nuclear Medicine and Molecular Imaging (SNMMI) published a guideline for a standardized, validated GES protocol for adults based on a 2008 consensus document. Laboratories must closely follow the consensus guideline to provide valid and standardized results as an incentive to achieve consistency in patient care. As part of the accreditation process, the Intersocietal Accreditation Commission (IAC) evaluates compliance with such guidelines. The rate of compliance with the SNMMI guideline was assessed in 2016 and showed a substantial degree of noncompliance. The aim of this study was to reassess compliance with the standardized protocol across the same cohort of laboratories, looking for changes and trends. **Methods:** The IAC nuclear/PET database was used to extract GES protocols from all laboratories applying for accreditation from 2018 to 2021, 5 y after the initial assessment. The number of labs was 118 (vs. 127 in the initial assessment). Each protocol was again evaluated for compliance with the methods described in the SNMMI guideline. The same 14 variables were assessed in a binary fashion: patient preparation (4 variables—types of medications withheld, withholding of these medication for 48 h, blood glucose $\leq$ 200 mg/dL, blood glucose recorded), meal (5 variables—use of consensus meal, nothing by mouth for 4 h or more, meal consumed within 10 min, documentation of percentage of meal consumed, meal labeled with 18.5–37 MBq [0.5–1.0 mCi]), acquisition (2 variables—anterior and posterior projections obtained, imaging each hour out to 4 h), and processing (3 variables—use of the geometric mean, decay correction of data, and measurement of percentage retention). **Results:** Protocols from the 118 labs demonstrated that compliance is improving in some key areas but remains suboptimal in others. Overall, labs were compliant with an average of 8 of the 14 variables, with a low of 1-variable compliance at 1 site, and only 4 sites compliant with all 14 variables. Nineteen sites met an 80% threshold for compliance (11+ variables). The variable with the highest compliance was the patient's taking nothing by mouth for 4 h or more before the exam (97%). The variable with the lowest compliance was the recording of blood glucose values (3%). Notable areas of improvement include the use of the consensus meal, now 62% versus previously only 30% of labs. Greater compliance was also noted with measurement of retention percentages (instead of emptying percentages or half-times), with compliance by 65% of sites versus only 35% 5 y prior. **Conclusion:** Almost 13 y after the publication of the SNMMI GES guidelines, there is improving but still suboptimal protocol adherence among laboratories applying for IAC accreditation. Persistent variation in the performance of GES protocols may significantly affect patient management, as results may be unreliable. Using the standardized GES protocol permits interpretation of results in a consistent manner that allows interlaboratory comparisons and fosters acceptance of the test validity by referring clinicians.

Key Words: gastric emptying scintigraphy; guidelines; accreditation; protocols; standardization

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Since its inception in 1966, nuclear medicine gastric emptying scintigraphy (GES) has evolved to demonstrate significant interinstitutional protocol variation (*1,2*). Lack of protocol consistency across institutions limits the ability to compare studies across hospitals and laboratories and can affect clinical management. GES studies are perhaps particularly prone to a lack of standardization because of the numerous parameters intrinsic to the exam, which can potentially affect study credibility among both imagers and referring clinicians. Principally, these parameters include variation in image acquisition, meal components/composition, and factors involving patient preparation. The American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine and Molecular Imaging (SNMMI) published a consensus statement in 2008 addressing the need for standardization (*3*). SNMMI, in 2009, summarized key points of these recommendations in its publication *Procedure Guideline for Adult Solid-Meal Gastric-Emptying Study 3.0* (*4*). Providing a standardized GES protocol allowed for a reproducible and reliable exam that better supports the needs of clinicians and their patients. Parameters addressed in the guideline include meal labeling and composition, patient preparation, and image acquisition and interpretation criteria.

As part of its mission, the Intersocietal Accreditation Commission (IAC) evaluates the quality of care being provided by

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nuclear medicine laboratories. The IAC does this through assessment of evaluation protocols, staff qualifications, and quality of imaging, among other factors. Specifically, protocol compliance and reporting are evaluated on the basis of accepted practices, to include published professional society guidelines such as those provided in the 2009 SNMMI GES publication. In 2016, an evaluation of protocol adherence noted a substantial degree of noncompliance across institutions seeking accreditation. This low adherence pointed to the need for greater education on consensus efforts for the standardization of GES studies. Subsequently, a separate group of researchers performed an in-depth survey of 121 sites performing GES, using 51 metrics derived from the consensus recommendations (*5*). These sites included both academic and nonacademic facilities, and similar results were revealed, with sites self-reporting compliance with less than two thirds of the measured metrics and no sites 100% compliant. Now, 13 y since the original guideline publication, this study aimed to reassess protocol adherence across the same cohort of laboratories undergoing IAC accreditation.

MATERIALS AND METHODS

Laboratories applying for general nuclear medicine accreditation from April 2018 to October 2022 were reviewed, and their respective GES protocols were examined, with corresponding deidentified facility information extracted from the IAC database. No patient data were collected or used. An Institutional Review Board waiver was obtained. From the IAC database, 7 demographic variables were recorded, which included lab or facility type (hospital vs. nonhospital), accreditation cycle (first time vs. reaccreditation), annual gastrointestinal-study volume, annual general nuclear medicine–study volume (excluding nuclear cardiology and PET), number of physicians, number of technologists, and number of γ-cameras (Table 1). On the basis of the SNMMI GES procedure guideline, 14 variables were selected for assessment (*4*). Compliance with these variables was considered the minimum needed for optimally accurate and reproducible performance of GES by laboratories. The 14 variables were divided into 4 categories: patient preparation, meal content, image acquisition, and image processing (Table 2). Meals administered were further categorized into 5 subgroups based on content (Table 3). Scores were computed on the basis of compliance with and adherence with the 14 variables. For example, a score of 14 constituted full compliance with all 14 variables. Associations were investigated to see if the 14 adherence variations were related in any way to the demographic variables. The total number of correct variables was also correlated with the demographic variables.

The data were cleaned and examined for outliers, normality of distribution, and correlations. Frequency and percentage compliance were reported for the 14 compliance variables, meal subgroup, and categoric demographic variables. Mean, median, and range were reported for the continuous demographic variables.

RESULTS

In total, 128 laboratories applied for general nuclear medicine accreditation from 2018 to 2022. Of these laboratories, 118 applied for gastrointestinal imaging accreditation, submitting GES protocols that were evaluated. The remaining laboratories did not provide GES protocols because they either did not perform GES or submitted other types of gastrointestinal imaging protocols for evaluation.

Demographics

Demographic frequency distributions are listed in Table 1. Most laboratories were hospital-based (69%). Laboratories performed a mean of 1,623 general nuclear medicine studies annually, with a median of 1,180. Laboratories performed a mean of 426 gastrointestinal nuclear medicine studies annually, with a median of 306. Most laboratories had been through the accreditation process more than once, with only 3% of labs undergoing their initial accreditation.

Guideline Adherence

Of the 4 variable categories (patient preparation, meal, acquisition, and processing/reporting), laboratories were most compliant with the variables related to patient preparation and meal delivery (Fig. 1). Specifically, the areas of greatest compliance were having instructions for patients to fast a minimum of 4 h (97%), using an appropriate radiotracer dose of 18.5–37 MBq (0.5–1.0 mCi) (77%), and having the patient consume the test meal in 10 min or less (73%). The areas of lowest compliance were having instructions for blood glucose testing before meal ingestion (97%) and, relatedly, having instructions for documenting the patient blood glucose level (92%).

TABLE 1
Laboratory Demographic Data (n = 118)

Variable	Category	Frequency (n)	%
Laboratory type	Hospital-based	82	69.5
	Nonhospital	36	30.5
First time vs. reaccreditation application	First time	3	2.5
	Reaccredited	115	97.5
	Mean	**Median**	**Range**
Gastrointestinal study annual volume	426	306	6–1,736
General nuclear medicine annual volume	1,623	1,180	45–9,077
Number of medical staff	12	9.5	1–77
Number of technical staff	6.8	7	1–31
Number of γ-cameras	3.6	2	0–20

TABLE 2
Standard Protocol Variables

Category	Variable	Definition
Patient preparation	Medication withholding	Prokinetic agents: metoclopramide, tegaserod (Zelnorm; Alfasigma USA, Inc.), domperidone, erythromycin, and cisapride; opiates; anticholinergic and antispasmodic agents; atropine, nifedipine, progesterone, octreotide, theophylline, benzodiazepine, and phentolamine
	Withholding time	Two days
	Blood glucose	Testing of blood glucose level before study to ensure level is <200 mg/dL
	Blood glucose recording	Recording of blood glucose level and including it in final report
Meal	Consensus meal	Proper preparation of meal with all 4 listed ingredients and no other ingredients (e.g., no butter or juice): 118 mL (4 oz) of liquid egg whites, 120 mL of water, 2 slices of toast, 30 g of jam or jelly
	Nothing by mouth	No food or water by mouth for minimum of 4 h
	Meal ingestion time	Consumption of meal as quickly as possible and in less than 10 min
	Partial meal	Instructions in cases of vomiting or if patient ingests only a portion of meal
	Radiopharmaceutical dose	18.5–37 MBq (0.5–1.0 mCi) of ^{99m}Tc sulfur colloid
Acquisition	Image projections	Acquisition of both anterior and posterior images
	Image frequency	Acquisition of images immediately on meal completion and hourly until 4 h
Processing	Geometric mean	Calculation of geometric mean using anterior and posterior projections (geometric mean = $\sqrt{}$ (anterior counts × posterior counts)
	Decay-corrected	Decay correction of counts in region of interest
	Percentage retention	Reporting of final measurements as percentage gastric retention at each time point

Compliance with the Consensus Meal

Thirty-eight percent of laboratories were not compliant with the consensus meal, with 62% of laboratories using the exact meal content of 2 egg whites, 2 slices of white toast, jelly, and 120 mL of water as recommended in the guidelines (Table 4). Incorrect ingredients were used in place of the 2 egg whites in 23% of laboratories. These included a variety of similar, but invalid, ingredients ranging from a single whole egg to powdered eggs and water. Additional ingredients not recommended in the guidelines were used by 6% of the laboratories. For example, added ingredients included butter, peaches, or additional water. Also, oatmeal was still inappropriately being used as an alternative meal by 8 laboratories. Approximately 3% of laboratories used highly unusual GES meals. These included tuna sandwiches, peanut butter and jelly sandwiches, beef stew, and the patient's favorite meal.

Variable Compliance and Changes Since 2016

Overall, labs were compliant with an average of 7.9 of the 14 variables, with a low of single-variable compliance at 1 site and a high of 14-variable compliance at 1 site (Fig. 2). Previously, the average was compliance with 4.8 variables, with a low of zero variables at 2 sites, but 4 sites were compliant with all 14 variables. The variable with the highest compliance included instructing the patient to take nothing by mouth for 4 h (97%), similar to the 95% compliance found in 2016. The variable with the lowest compliance was the assessment of blood glucose levels at 3%, previously 13%. This value increases to 24% if looking only at sites that check blood glucose levels in patients with known diabetes. Since 2016, notable areas of improvement include use of the consensus meal, now in 62% of labs versus previously in only 31%, as well as measurement of retention percentages instead of emptying percentages or half-times by 65% of sites versus only 35% 5 y prior.

TABLE 3
Meal Content Subgroups

Meal type	Ingredients
Full consensus	Egg white, white toast, jelly, and water
Partial	Partial components of consensus meal
Consensus plus	Consensus meal with addition of nonstandard ingredients such as egg yolk (whole eggs)
Oatmeal	Oatmeal alone or with other ingredients
Other	Unusual meals such as burrito or peanut butter sandwich

DISCUSSION

Practice guidelines have been shown to improve the quality of patient care through evidence-based protocol standardization and serve to reduce variability in patient care (*6–8*). SNMMI published *Procedure Guideline for Adult Solid-Meal Gastric-Emptying Study 3.0* in 2009, which provided standardized guidance on performing GES (*4*). GES studies have previously been shown especially prone to protocol variability, with a wide range of meals administered to patients across institutions (*2,5*). The 2009 GES consensus guideline, therefore, was developed to reduce the GES-related variations between nuclear medicine laboratories and represented a consensus across different professional societies. The data presented in this study, obtained from laboratories applying for IAC accreditation, have shown areas of improved compliance since the previous analysis

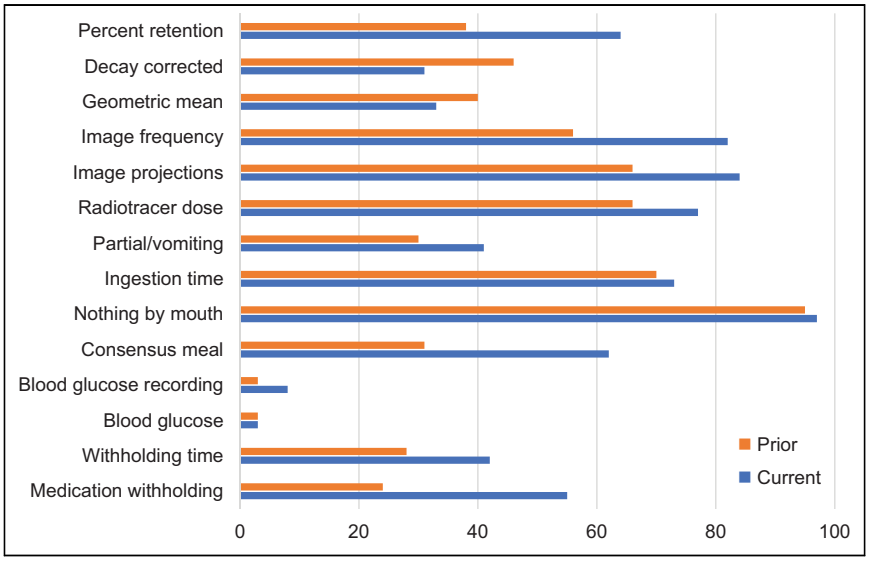

FIGURE 1. Comparison of prior survey vs. current survey results: compliance with 14 individual protocol variables from prior study (*2*) and current evaluation. Highest-compliance variables in current study included instructions on taking nothing by mouth for 4 h before procedure at 97%, and variable with lowest compliance was provision of blood glucose instructions at 3%. Overall average of compliance across all variables increased from 43% in 2017 to 54% currently.

of data in 2016. However, whereas there has been increased compliance with regard to guideline adherence since 2016 with specific variables, there is still, overall, a relatively low rate of compliance with the guideline GES protocol in the current study group of 118 laboratories.

GES Variability

Patient Preparation. Patient preparation is especially important in gastrointestinal nuclear medicine studies because of the physiologic sources of error that can be introduced. Approximately 55% of laboratories were compliant with providing medication-withholding instructions, an improvement from a prior compliance rate of 26% in 2016 and the 31%–35% reported in 2021 by Wise et al. (*2,5*). A variety of drugs, including those known for their prokinetic properties, should be withheld for approximately 48 h before a procedure (Table 2). Different nuclear medicine studies can have their own list of medications that need to be withheld before a procedure (such as an ^{123}I-MIBG study or a hepatobiliary scan). As such, providing lists of medications in respective study protocols is an optimal way of educating nuclear medicine technologists on appropriate patient preparation. Considering the well-described effects of drugs such as opiates and anticholinergics on gastric emptying, even in small doses, compliance with specific medication discontinuation before a GES study is paramount to assess gastric motility under ideal physiologic conditions (*9,10*).

Compared with 2016, a suboptimal level of compliance was again noted vis-à-vis instructions for measuring the patient's blood glucose level before the exam, with only 24% of laboratories checking it in known diabetics and 8% of labs assessing it in all patients. This is in line with Wise's results of only 16% of facilities measuring blood glucose in diabetic patients (*5*). Considering that hyperglycemia is an understood cause of delayed gastric emptying, results should be interpreted in the setting of this known physiologic derangement (*11*). As such, annotating glucose levels (and ensuring that levels were <200 mg/dL) was considered an important variable in our study. Some of the lack of compliance may arise from a small but significant variation between the original 2008 consensus document and subsequent SNMMI guidelines on solid gastric emptying (*3,4*). The consensus document used 275 mg/dL as the upper limit for an acceptable blood glucose level before GES, but that number was revised down to 200 in the SNMMI guidelines and in the American College of Radiology practice parameter (*12*).

Meal Content and Preparation. Previously, the composition and preparation of meals were noted to be a source of major variability (*2*). A variable meal composition can affect the reliability of a GES study, considering that carbohydrates empty more quickly than fatty and protein-rich foods and that liquids empty more quickly than semisolids, which empty more quickly than solids (*13*). Food volume and resulting gastric wall stress are also known factors that affect emptying (*14*). A nonstandardized meal with a varying nutrient composition and volume can therefore lead to spurious study interpretation if there are no published normal values for the specific meal administered. The consensus meal consists of 2 slices of white toast, 30 g of strawberry jelly, 120 mL of water, and 120 g of liquid egg white (Egg Beaters [Post Holdings] or generic) scrambled with 18.5–37 MBq (0.5–1.0 mCi) of ^{99m}Tc-sulfur colloid (*4*). Consensus meal adherence has reassuringly improved since 2016, with compliance now being at 62% versus the previous 31% (*2*).

A few labs have continued to include nonstandard meals such as tuna sandwiches and beef stew, which would be doubtful to have a comparable emptying rate to the known rate for a standard consensus meal. Cooking the liquid egg

TABLE 4
Meal Component Variation (n = 118)

Meal type	Frequency (n)	%
Full consensus	74	62.7%
Partial	27	22.8%
Consensus plus	6	5.1%
Oatmeal	10	8.5%
Other	3	2.5%

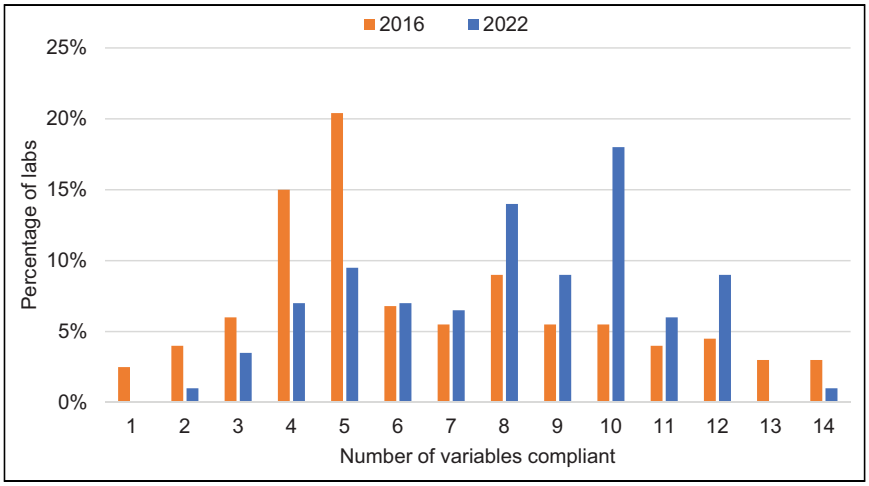

FIGURE 2. Number of variables compliant with guidelines per laboratory in current and previous 2016 studies. Smaller percentage of laboratories was compliant with all 14 variables. However, greater percentage of laboratories was compliant with more guideline variables.

whites with the sulfur colloid allows for bond formation and appropriate labeling of the egg whites with the radiotracer. Otherwise, the radiotracer can separate from the egg protein component, resulting in a potentially early transit of a radiotracer-predominant emulsion. Some labs were noted to diverge from the concomitant cooking of the egg whites and the sulfur colloid. For example, at least 1 lab injected sulfur colloid into a single hard-boiled egg, a meal often administered in the past, but now antiquated and likely resulting in inaccurate exam results. Many labs continued to use whole eggs, a problematic divergence considering that ^{99m}Tc-sulfur colloid binds to the albumin in the egg white and not to the egg yolk. Egg yolk also contains a higher fat content, which can artifactually delay transit compared with the liquid egg whites in the consensus meal.

Acquisition and Processing. Since 2016, there was an improvement in protocol compliance with respect to image acquisition. Approximately 85% of laboratories were compliant with imaging in both the anterior and the posterior views, whereas the previously compliance was 65% in 2016 (*2*). Images were acquired at the appropriate frequency by 83% of laboratories, an improvement from 55% compliance in 2016. Guidelines recommend that both anterior and posterior images be acquired, not only to assist with proper quantification of meal retention but also to serve as an added interpretation tool in the setting of potential artifacts and abnormal anatomy. The consensus protocol also recommends imaging immediately on meal completion and at 1, 2, 3, and 4 h afterward, as this timing provides information on transit dynamics. Greater than 10% administered meal retention at 4 h constitutes an abnormal exam result, and hence protocol omission of this data point can result in a false-negative interpretation in up to 30% of cases (*15*). Greater compliance with reporting percentage retention was also noted in the current study, constituting 65% of laboratories, an increase from the 35% in the 2016 study (*2*). Fewer labs are reporting the half-time of emptying for assessment, an encouraging trend considering the limitations in reporting half-time in patients due to the data's being collected at hourly intervals and the potential need for data extrapolation (*3*). Similar poor adherence was noted with regard to calculating retention using the geometrics of anterior and posterior projections and decay correcting the counts in the region of interest, constituting 33% and 31% compliance, respectively.

Guideline Implementation

Overall, there has been a trend toward greater guideline adherence since 2016. Although some aspects of the consensus guidelines remain to be widely adopted, compliance with the standardized meal and with providing instructions to withhold interfering medications have improved, as have some variables concerning the imaging-and-processing portion of the exam and the reporting of meal percentage retention at each time point. The fact that other variables have continued to demonstrate low rates of implementation in laboratory protocols suggests a need for continued education on the consensus guidelines with attention to these particular variables. Specifically, these include testing blood glucose before the exam to ensure a level below 200 mg/dL, recording this level in the final report, calculating the geometric mean (using the anterior and posterior projections), and using decay correction for the counts in the region of interest.

Limitations

This study was a retrospective evaluation of application materials submitted to the IAC for accreditation. The IAC database was designed for management of accreditation and not for observational research purposes. It is possible that laboratories are following the guidelines but that actual practice is not documented in the protocol. Such a possibility is unlikely, however, given the similar findings of Wise et al. in a study of GES guideline compliance using a survey technique (*5*). A final limitation is that adherence with guidelines was chosen as a surrogate for quality because measuring direct patient outcomes in diagnostic medicine is complicated.

CONCLUSION

Since the publication of the SNMMI GES guidelines, there has been a gradual increase in protocol adherence among laboratories applying for IAC nuclear/PET accreditation. Certain specific recommendations in the guidelines have gained greater acceptance, whereas lack of adherence with other practice variables persists. Greater efforts on

disseminating the specific gaps in guideline adherence would likely be helpful.

DISCLOSURE

Mary Beth Farrell is an employee of the IAC. The views expressed are those of the authors and do not reflect the official policy or position of Brooke Army Medical Center, the U.S. Army Medical Department, the U.S. Army Office of the Surgeon General, the Department of the Army, the Department of Defense, or the U.S. government. No other potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: What is the degree of laboratory protocol adherence with the GES guideline published in 2009, and has adherence improved since it was assessed in 2016?

PERTINENT FINDINGS: Protocol adherence with the guidelines was examined for 118 laboratories, and adherence has improved in some areas since 2016 but remains suboptimal in others. Overall, labs complied with an average of 8 of the 14 variables, and only 19 laboratories met an 80% threshold for compliance (11+ variables).

IMPLICATIONS FOR PATIENT CARE: Persistent variation in the performance of GES protocols may significantly affect patient management, as results may be unreliable.

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Fourier Phase Analysis of Dynamic Antral Contraction Scintigraphy: New Software, Reference Values, and Comparisons to Conventional Gastric Emptying

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Dynamic antral contraction scintigraphy (DACS) has been used to evaluate for gastric dysmotility by measuring antral contraction frequency and ejection fraction (EF). Fourier phase image analysis has the potential to assess gastric antral contractions for dyssynchrony as has been used for analyzing nuclear cardiology ventriculography (multigated acquisition studies) for cardiac dyssynchrony. The aims of this study were to determine whether Fourier phase analysis helps to characterize antral motility physiology, whether Fourier phase analysis correlates with conventional gastric emptying scintigraphy (GES), and which DACS parameters may aid in diagnosing gastric dysmotility, particularly delayed gastric emptying (GE). **Methods:** DACS and GES of healthy volunteers ($n = 22$) were compared with patients ($n = 99$) with symptoms of gastroparesis. New DACS Fourier phase analysis software was developed. **Results:** GE was delayed ($n = 53$) or normal ($n = 46$) in patients. There was a linear correlation between the time for the stomach to empty 50% of the meal and the percentage total proximal and distal in-phase antral pixels at 30 min ($r = 0.37$, $P = 0.0001$) and 60 min ($r = 0.26$, $P = 0.007$). In healthy volunteers, the mean proximal-to-distal ratio of in-phase antral pixels increased from 1.67 (30 min) to 2.65 (120 min) ($P = 0.035$), and EF increased from 23% (30 min) to 32% (120 min) ($P = 0.022$). Multivariable regressions of percentage total proximal and distal in-phase antral pixels (30 min) and EF (60 min) were the best predictors of abnormal GE (adjusted odds ratio, 3.30 [95% CI, 1.21–9.00] and 2.97 [95% CI, 1.08–8.21], respectively). **Conclusion:** This study used Fourier phase analysis to analyze DACS in healthy volunteers and patients with symptoms of gastroparesis. In addition to establishing reference values, new physiologic information on antral motility was obtained. In healthy volunteers, there was an increasing proximal-to-distal ratio of in-phase antral pixels and antral EF over time after meal ingestion. The percentage total proximal and distal in-phase antral pixels at both 30 and 60 min correlated well with GE values for the time for the stomach to empty 50% of the meal. For symptomatic patients, the percentage total proximal and distal in-phase antral pixels at 30 min and the EF at 60 min after meal ingestion correlated with delayed GE on conventional GES. Thus, Fourier phase analysis of DACS appears to have potential to further aid in diagnosing gastric dysmotility in GES.

Key Words: gastric emptying scintigraphy; antral contractility; antral dyssynchrony; Fourier analysis

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Although in widespread clinical use, conventional gastric emptying scintigraphy (GES), which measures only the percentage of total gastric emptying (GE) of a standardized meal, does not always correlate well with symptoms of gastroparesis. In some studies, GES is able to detect abnormal GE in only up to 40% of patients when there is a high clinical suspicion of gastroparesis (*1*). Because conventional GES fails to detect gastric dysmotility as a cause of symptoms in some patients when there is a high clinical suspicion of impaired GE, efforts have been made to augment GES using more advanced analysis of GES, particularly dynamic antral contraction scintigraphy (DACS), which permits assessment of antral contractility (*2–4*).

Antral hypomotility has been shown to be directly related to impaired GE using invasive manometric studies (*5*). In patients with dyspepsia and symptoms of gastroparesis, antroduodenal manometry has been associated with infrequent, low-amplitude pressure waves in the antrum (*6*). However, other investigations, even in patients with severe dyspepsia, have failed to identify a strong positive correlation between symptoms, GE, and postprandial manometric recordings of antral contractility (*7*).

Although DACS was introduced over 20 y ago, the methodology and technical aspects of performing DACS have not been standardized. Furthermore, prior DACS used research software available only at the small number of institutions performing those studies, limiting the more widespread use of DACS. Two variables from Fourier analysis of DACS, antral contraction frequency and amplitude, have typically been used to characterize antral contractility. The dominant antral contraction frequency has been calculated as the frequency with the highest Fourier amplitude. Antral contraction amplitude has been measured using either the amplitude of the Fourier

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analysis (*4*) or ejection fraction (EF) (*2*) derived from the percentage of radioactive content displaced by an average contraction from a region in the mid antrum.

These prior studies have shown the potential of DACS to characterize both the normal and the abnormal physiology of antral contractions. Urbain et al. demonstrated in longstanding diabetes that the lag phase of GE was prolonged and was associated with a reduction in the amplitude of antral contractions (*4*). Knight et al. showed that slower GE in women than in men directly related to a mid-antral decrease in the EF, which correlated with antral manometry (*2*). More recently, we demonstrated that DACS can be used to assist in partitioning the stomach into proximal and distal sections allowing measurement of fundic accommodation and to measure antropyloroduodenal contractions in healthy volunteers (*3,8*).

Fourier analysis of nuclear cardiac ventriculography (multigated acquisition studies) has been well established for cardiac dyssynchrony. Left ventricular dyssynchrony is present when there are temporal differences in the activation and contraction of various left ventricular myocardial segments. Impairment of left ventricular systolic function and reduced cardiac output can be the result of such left ventricular dyssynchrony (*9*). Nuclear medicine DACS of the stomach is performed in a similar manner to nuclear cardiac multigated acquisition studies. The software needed to analyze either cardiac or antral contractions assigns a phase angle to each pixel of the Fourier phase image, which is derived from the first Fourier harmonic. The phase angle reflects the similarity or difference in timing to the onset of contraction in each adjacent image pixel. Similar to its application in nuclear cardiology, this type of Fourier phase image analysis has the potential to assess gastric antral contractions for dyssynchrony.

The aims of this study were to investigate the potential of antral Fourier phase analysis to add physiologic information on antral motility, to investigate how Fourier phase analysis of DACS correlates with conventional GES, and to study which DACS parameters may contribute to diagnosing delayed GE. To accomplish these aims, we developed and validated a new DACS processing software package allowing performance of Fourier phase analysis and established reference DACS results in healthy volunteers.

MATERIALS AND METHODS

All healthy volunteers included in this study were the same as those included in our prior study using DACS to measure antropyloroduodenal contractions (*3*). Our institutional review board approved this study, and all healthy volunteers gave written informed consent. The retrospective symptomatic patient studies included 100 sequential patients referred for GES with DACS between September 26, 2018, and March 24, 2021, who had symptoms suggesting gastroparesis. An institutional review board waver was issued for review of the retrospective studies.

All healthy volunteers were questioned to ensure they had no prior history of gastrointestinal disease or prior gastrointestinal surgery and that they were not taking medications that might affect gastrointestinal function. All healthy volunteers and symptomatic patients came to the Nuclear Medicine Department on the morning after an overnight fast. GES was performed using the 4-h liquid egg white protocol described initially by Tougas et al. (*10*) and recommended in the current Society of Nuclear Medicine and Molecular Imaging guideline (*11*) and the consensus report of the Society of Nuclear Medicine and Molecular Imaging and the American Neurogastroenterology and Motility Society (*12*). The meal consists of 120 g (4 oz) of liquid egg white radiolabeled with ^{99m}Tc-sulfur colloid and served with 2 pieces of white bread and jelly. In addition, patients were given 120 mL of water immediately after ingestion of the solid portion of the meal. The dose of ^{99m}Tc-sulfur colloid given to the healthy volunteers for GES with DACS ranged from 74 to 370 MBq (2–10 mCi) as previously described (*3*). All patient studies were performed with a minimal dose of 74 MBq (2 mCi).

After meal ingestion, conventional static GES using a 128 × 128 matrix was performed at 0, 0.5, 1, 2, 3, and 4 h, with the subject upright in the anterior and then the posterior position for 30 s in each position. DACS was performed using continuous anterior list-mode 1-s images obtained for 10 min (total of 600 images) immediately after the static imaging and at 0.5, 1, and 2 h as previously described (*2,8*).

Total-stomach conventional GES results were analyzed from the static images as the percentage of radioactivity retained in the whole stomach using the geometric mean of the decay-corrected anterior and posterior counts for each time point. Because Fourier analysis of the DACS images does not require depth correction of counts using the geometric mean, the DACS images were acquired and processed using anterior images only. Delayed GE was defined as more than 60% gastric retention of the ^{99m}Tc-labeled solid meal at 2 h, more than 10% at 4 h, or a $T^1/_2$ (time for the

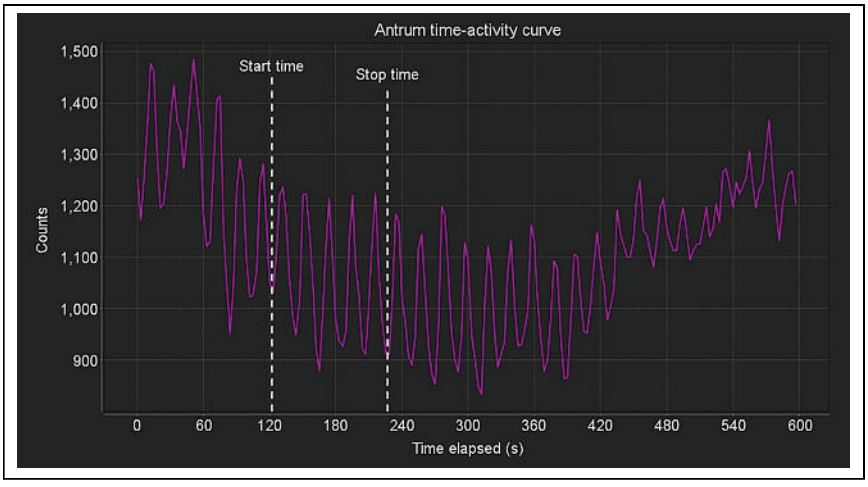

FIGURE 1. User selection of set of antral contractions for DACS analysis. This example of time–activity curve from patient study shows that even after use of image motion correction software, patient motion can result in significant motion artifacts in time–activity curve. Software workflow allows user to select optimum subset of image peaks and valleys (as shown between start time and end time), where antral contractions are stable and will be used for DACS processing.

stomach to empty 50% of the meal) of more than 132 min, computed by a power exponential curve fit (*10,12*).

All DACS images were analyzed using a β-version MIM Software workflow developed for this study. Before processing of the DACS images, the serial continuous dynamic images consisting of a total of 600 images of 1 s each were first reviewed and motion-corrected using standard motion correction software to help eliminate patient movement artifacts. A 2-cm region of interest was then placed over the mid antrum to record a time–activity curve for antral contractions from the serial DACS image set. To further minimize patient movement artifacts and to ensure analysis of consistent peristaltic contractions, the time–activity curve from the continuous dynamic set was visually reviewed and a minimum set of 4 consecutive antral peristaltic waves that demonstrated consistent frequency and amplitude of contractions was selected for analysis (Fig. 1).

During visual review of the serial images used to create the final DACS composite image sequence, we observed, as others have reported (*13*), short intermittent periods of irregular antral contractions. Any such periods of antral dysrhythmia were excluded from the final DACS analysis. To establish how often these occurred in the healthy volunteers, both readers measured the percentage of time these were observed during the 10-min DACS recordings. The average percentage of the time these episodes of antral dysthymias were observed in healthy volunteers was calculated for the 2 readers.

The software workflow calculates the mean frequency of antral contractions by measuring the peak-to-peak time intervals from the time–activity curve. The mean EF is then calculated from the time–activity curve, with the EF for the time interval (i) for each individual contraction being given by…

$$EF_i\ (\%) = 100 \times (\text{maximum}_i - \text{minimum}_i) / \text{maximum}_i,$$

where maximum and minimum refer to the number of counts derived from the antral time–activity curve for each time interval.

The software reformats a grouped image series using the set of selected antral contractions for Fourier analysis. This final composite cinematic image series provides a movie display of the temporal movement of the antral peristaltic wave, which typically starts in the area of the incisura and propagates distally toward the pylorus. The results of the Fourier analysis for all antral pixels are color-coded in a final display of the Fourier-derived phase angles and amplitude (Fig. 2).

After visual display and review of the phase and amplitude maps, the software permits the operator to manually define regions of interest for the proximal, distal, and total area of the antrum. The software then applies an automated threshold (40% threshold of the antrum-derived phase angles) to calculate the number of pixels in the proximal and distal antral areas, which, as a group, are in phase and have similar timing in their onset of contraction, where…

$$\text{Percentage total} = \left(\begin{array}{l}\text{no. of proximal antral in-phase pixels} \\ + \text{no. of distal antral in-phase pixels}\end{array}\right) / \text{total no. of antral pixels.}$$

The ratio of in-phase proximal pixels to distal pixels is also calculated to characterize the relative contribution of proximal versus distal antral pixels with in-phase contractions.

The DACS results of the patients with suspected gastroparesis were compared with the results of the normal volunteers and correlated with the results of conventional GES, including the percentage of total GE at 2 and 4 h and measurement of a power exponential fit to calculate the $T^1/_2$ of GE. For classification of the results of conventional GES, a patient was considered to have delayed GE if any one of the following criteria was met: abnormal

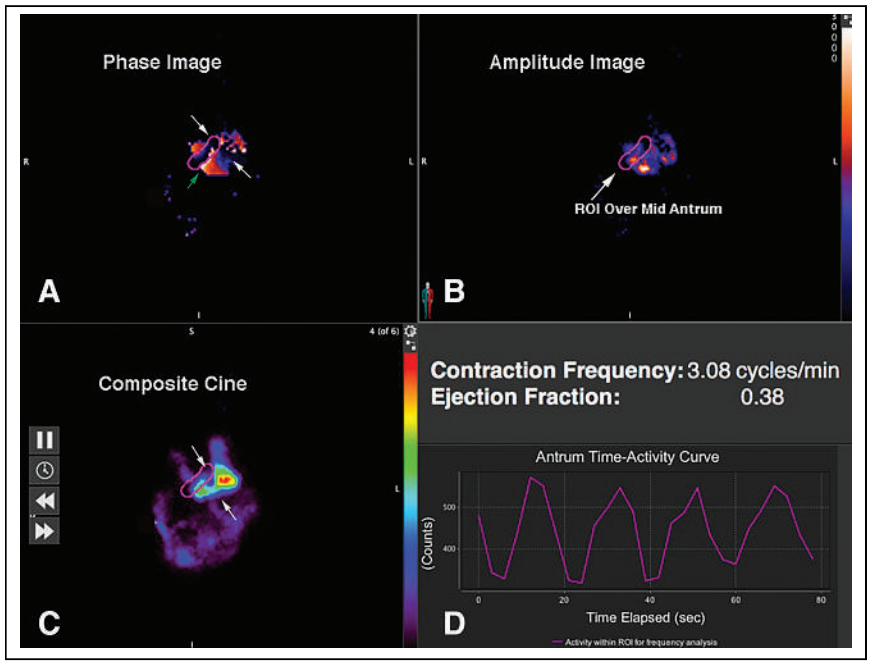

FIGURE 2. Healthy volunteer. (A) Fourier phase image showing color-coded pixels of Fourier phase analysis. Two-centimeter-wide region of interest drawn over mid antrum is same as obtained from those pixels in mid antrum with highest amplitude as shown in B. Antral peristaltic wave originates at incisura (white arrows). Resulting phase image shows those pixels that have similar color-coded phase angles clustered in proximal and distal antrum to left and right of mid antral region of interest. Leading edge of in-phase pixels appears as band of pixels (shown here with white color scale or 0° phase angle [green arrow]) in proximal antrum. To left of mid antral region of interest, group of pixels appears (~180° from leading edge, red/orange color scale) corresponding to retrograde contractions arising in distal antrum. (B) Amplitude image showing color-coded pixels of Fourier amplitude. Image demonstrates cluster of high-amplitude pixels in mid antral region of interest (arrow) and in adjacent proximal antrum. (C) Single frame of composite cine image, with colored pixels representing total counts of radiolabeled solid-food activity in stomach. When viewed as movie display, antral peristaltic wave can be seen to originate at incisura (white arrows) and propagate distally through antrum across mid antral region of interest, followed by retrograde bolus movement back into proximal antrum. (D) Time–activity curve from mid antral region-of-interest–derived gastric counts, which are used to calculate antral contraction frequency and EF. ROI = region of interest.

2-h retention (>60% retained), abnormal 4-h retention (>10% retained), or a $T^1/_2$ of more than 132 min (*10*).

The DACS data on healthy volunteers for percentage total, proximal-to-distal ratio, EF, and contraction frequency were tested for normality using the Kolmogorov–Smirnov test and found to depart from being normally distributed at almost all time points (30, 60, and 120 min). The reference results by DACS were therefore expressed using medians and 90% intervals for all time points for these 4 parameters based on the healthy volunteers' data. Linear (mixed-effects) regression analysis was used to correlate the DACS data with the data of conventional GES on $T^1/_2$ and percentages of gastric retention at 2, 3, and 4 h, as well as to perform time trend analyses for the 4 DACS parameters among patients or healthy volunteers. The 90% DACS intervals based on the healthy volunteers were used to define abnormality by DACS and associated with or used to predict conventional GES results. Group comparisons of DACS abnormality between patients or healthy volunteers with normal results and patients with abnormal results by conventional GES were performed using the Fisher exact test. Univariable and multivariable logistic regression analyses were performed to determine which DACS parameters could be used to help predict abnormal GES results, and raw and adjusted odds ratios (95% CIs) were reported from such logistic regression models, with the multiple regression model selected using the stepwise variable selection method. *P* values of less than 0.05 were considered statistically significant. SAS, version 9.4 (SAS Institute Inc.), was used for all data analyses. There was no adjustment for multiple comparisons because this study was exploratory and observational and not meant to confirm any a priori hypothesis or to make a statement regarding 2 or more parameters combined at the same time.

RESULTS

Study Subjects

Conventional GES results were normal for all 22 healthy volunteers (13/22 [59.1%] male; median age, 34.5 y [range, 23.0–69.0 y]). Of the 100 patients studied, 99 had studies suitable for analysis. One patient's DACS study could not be analyzed because of marked motion artifacts at all time points and was therefore excluded. Of the 99 patients, 53 had delayed GE (12/53 [22.6%] male; median age, 42.0 y [range, 19.0–82.0 y]) and 46 had normal GE (6/46 [13.0%] male; median age, 40.0 y [range, 19.0, 78.0 y]).

DACS in Healthy Volunteers

An example of a healthy volunteer's DACS software analysis output is shown in Figure 2. The healthy volunteers' DACS results consistently demonstrated 2 well-defined areas of in-phase, color-coded pixels that localized in the proximal and distal antrum. The pixels with similar phase angles were separated by a band of pixels with no in-phase pixels, which correlated with a mid-antral area showing the highest Fourier-derived amplitude. This mid-antral region corresponded on the cine images visually to the peaks of bolus food antegrade and retrograde movements through the mid antrum (Fig. 2B).

A summary of the healthy volunteers' (n = 22) DACS results for percentage total in-phase antral pixels, proximal-to-distal ratio, EF, and contraction frequency for all time points is shown in Table 1. The proximal-to-distal ratio significantly increased over time from a median of 1.67 at 30 min to 2.65 at 120 min (P = 0.035). Figure 3 shows an example of how the Fourier phase images demonstrate this normal increase in the proximal-to-distal ratio for in-phase pixels from 30 to 120 min. Similarly, the EF significantly increased with time from a median of 23% at 30 min to 32% at 120 min (P = 0.022). In healthy volunteers, the percentage total in-phase antral pixels did not change significantly over time from a median of 45% at 30 min to 51% at 120 min (P = 0.11). The frequency of antral contractions also did not significantly change over time, ranging from a median of 3.08 cycle/min at 30 min to 2.91 cycle/min at 120 min (P = 0.11).

The mean percentage irregular contractions recorded by the 2 readers were 9.9% (range, 0%–34.7%) at 30 min, 11.7% (range, 0%–35.4%) at 60 min, and 11.3%% (range, 0%–23.1%) at 120 min.

DACS in Healthy Volunteers and Patients

Linear regression of the percentage total versus the $T^1/_2$ of GE using the healthy volunteers and all patients (n = 121)

TABLE 1
Descriptive Summary and 90% Percentile Intervals Based on Healthy Volunteers for Conventional GES Parameters

Variable	*n*	Median	Range	*P**	5%, 95% CI
Percentage total, 30 min	19	45%	31%–63%	0.11	31%, 63%
Percentage total, 60 min	22	40%	17%–63%		19%, 62%
Percentage total, 120 min	13	51%	32%–61%		32%, 61%
Proximal-to-distal ratio, 30 min	19	1.67	0.36–6.62	0.035	0.36, 6.62
Proximal-to-distal ratio, 60 min	22	1.89	0.71–4.71		0.88, 3.15
Proximal-to-distal ratio, 120 min	13	2.65	1.25–6.38		1.25, 6.38
EF, 30 min	21	23%	8%–44%	0.022	14%, 36%
EF, 60 min	22	27%	19%–42%		19%, 40%
EF, 120 min	14	32%	11%–41%		11%, 41%
Frequency (cycle/min), 30 min	21	3.08	2.58–3.45	0.11	2.67, 3.33
Frequency (cycle/min), 60 min	22	2.86	2.40–3.57		2.76, 3.48
Frequency (cycle/min), 120 min	14	2.91	2.42–3.20		2.42, 3.20

**P* value for testing time effect of each variable.

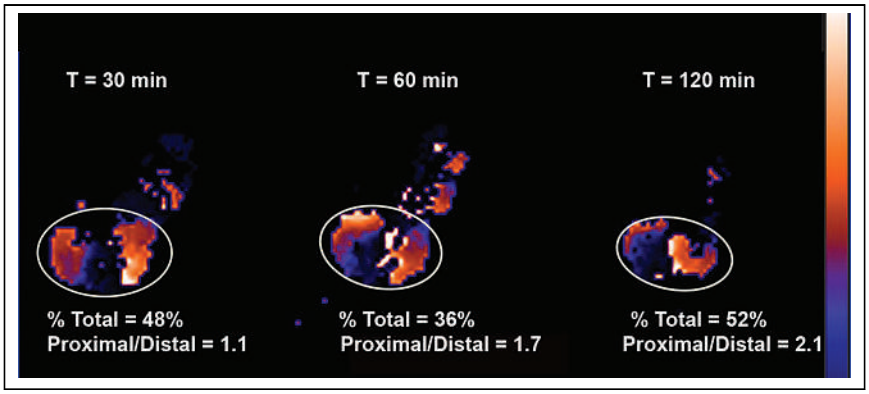

FIGURE 3. Patient with normal GE and normal phase analysis. Shown are Fourier phase results at 30, 60, and 120 min. Elliptic region of interest (white) shows total antral area used for analysis. Similarly colored clusters of pixels in proximal and distal antrum are those that have similar phase angles by Fourier analysis. Typically, ratio of proximal-to-distal ratio for in-phase pixels increases from 30 to 120 min.

revealed a significant linear correlation at the 30- and 60-min time points (Fig. 4). At 30 min, the percentage total was $0.4630–0.0008 \times T^1/_2$ ($r = 0.37$, $P = 0.0001$). At 60 min, the percentage total was $0.4415 + -0.0005 \times T^1/_2$ ($R = 0.2559$, $P = 0.0065$). A similar linear trend seemed to exist for percentage total at 120 min but did not achieve statistical significance ($0.4024 + -0.0003 \times T^1/_2$ ($R = 0.1456$, $P = 0.1680$).

The proximal-to-distal ratios at 30 and 120 min did not significantly correlate linearly with $T^1/_2$. There was, however, a fair linear correlation for proximal-to-distal ratio at 60 min ($1.3361 + 0.0072 \times T^1/_2$, $r = 0.19$, $P = 0.049$). Antral contraction frequency at 30 min had a good linear correlation with $T^1/_2$ ($2.8237 + 0.0017 \times T^1/_2$, $r = 0.30$, $P = 0.003$). EF showed no significant linear relationship with $T^1/_2$.

DACS in Patients with Delayed GE

Table 2 summarizes performance using the DACS parameters one at a time for detection of abnormal results on conventional GES. Measurement of the percentage total at all times (30, 60, and 120 min) appeared to correlate with abnormal results on conventional GES, with the strength of this correlation decreasing over time and achieving statistical significance only at 30 min. Among all the DACS parameters, the percentage total at 30 min ($P = 0.001$), proximal-to-distal ratio at 60 min ($P = 0.017$), and EF at 60 min ($P = 0.011$) were the only three that had a statistically significant predictive capability for abnormal results compared with conventional GES (sensitivity ≥ 35%, specificity ≥ 75%). The raw odds ratios of having abnormal results on conventional GES were 4.49 (95% CI, 1.81–11.15), 2.72 (95% CI, 1.23–5.99), and 3.47 (95% CI, 1.33–9.06), when comparing the group that had abnormal DACS results with the group that had normal DACS results for the 3 DACS parameters, respectively. Figure 5 shows an example of how the Fourier phase images demonstrate the lack of a consistent increase in the proximal-to-distal ratio for in-phase pixels from 30 to 120 min.

On the basis of the multivariable logistic regression results, 2 abnormal values (the percentage total antral pixels at 30 min and the EF at 60 min) as defined using the healthy volunteers' DACS data were the best subset of all DACS values for predicting abnormal results on conventional GES (Table 3; adjusted odds ratio, 3.30 (95% CI, 1.21–9.00) and 2.97 (95% CI, 1.08–8.21), respectively).

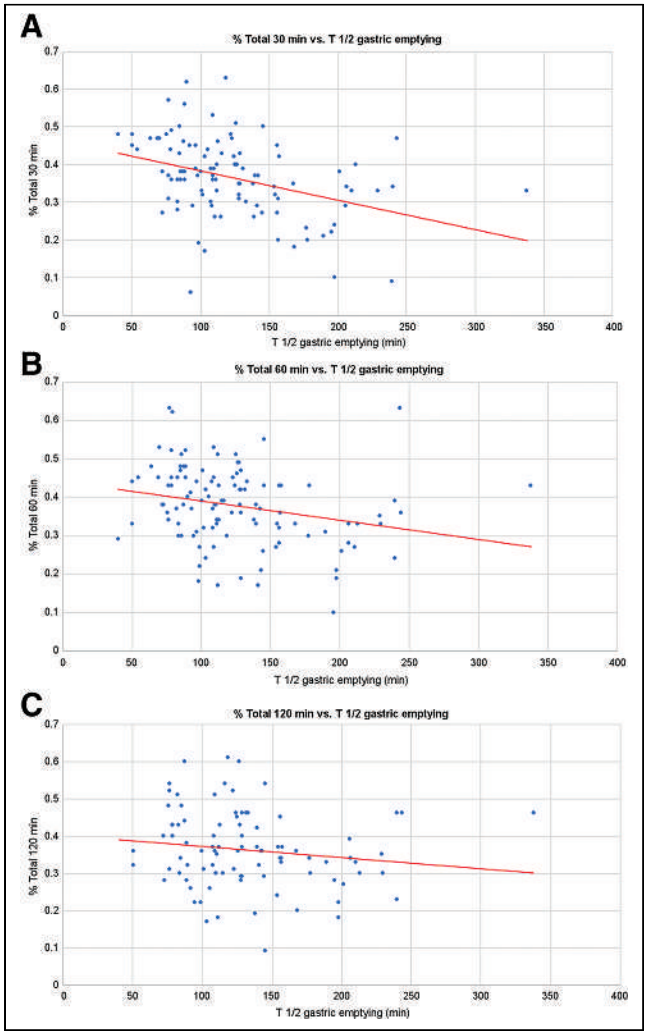

FIGURE 4. Linear regressions of percentage total compared with $T^1/_2$ of GE. (A) 30 min (percentage total = $0.4630 + -0.0008 \times T^1/_2$, $R = 0.3746$, $P = 0.0001$). (B) 60 min (percentage total = $0.4415 + -0.0005 \times T^1/_2$, $R = 0.2559$, $P = 0.0065$). (C) 120 min (percentage total = $0.4024 + -0.0003 \times T^1/_2$, $R = 0.1456$, $P = 0.1680$).

DISCUSSION

There is increasing interest in the use of advanced imaging to more completely characterize the complex coordination of gastric motility within different functional areas of the stomach and how each contributes to overall GE and

TABLE 2
Predictive Capability of DACS Parameters for Abnormal Results Compared with Conventional GES

DACS grouping by…	Overall (n = 121)	Conventional GES results: Abnormal (n = 53)	Conventional GES results: Normal (patients + healthy volunteers) (n = 68)	P*	Raw odds ratio†	95% CI
Percentage total, 30 min				0.001		
Abnormal, <31% or >63%	30 (27.5%)	21 (43.8%)	9 (14.8%)		4.49	1.81–11.15
Normal, 31%–63%	79 (72.5%)	27 (56.3%)	52 (85.2%)		Reference	
Percentage total, 60 min				0.17		
Abnormal, <19% or >62%	9 (7.6%)	6 (11.8%)	3 (4.5%)		2.84	0.68–11.97
Normal, 19%–62%	109 (92.4%)	45 (88.2%)	64 (95.5%)		Reference	
Percentage total, 120 min				0.21		
Abnormal, <32% or >61%	34 (35.1%)	21 (41.2%)	13 (28.3%)		1.78	0.76–4.16
Normal, 32%–61%	63 (64.9%)	30 (58.8%)	33 (71.7%)		Reference	
Proximal-to-distal ratio, 30 min				1.00		
Abnormal, <0.36 or >6.62	7 (6.4%)	3 (6.3%)	4 (6.6%)		0.95	0.20–4.46
Normal, 0.36–6.62	102 (93.6%)	45 (93.8%)	57 (93.4%)		Reference	
Proximal-to-distal ratio, 60 min				0.017		
Abnormal, <0.88 or >3.15	39 (33.3%)	23 (46.0%)	16 (23.9%)		2.72	1.23–5.99
Normal, 0.88–3.15	78 (66.7%)	27 (54.0%)	51 (76.1%)		Reference	
Proximal-to-distal ratio, 120 min				0.83		
Abnormal, <1.25 or >6.38	37 (38.9%)	20 (40.8%)	17 (37.0%)		1.18	0.51–2.69
Normal, 1.25–6.38	58 (61.1%)	29 (59.2%)	29 (63.0%)		Reference	
EF, 30 min				0.48		
Abnormal, <14% or >36%	25 (24.8%)	12 (29.3%)	13 (21.7%)		1.50	0.60–3.72
Normal, 14%–36%	76 (75.2%)	29 (70.7%)	47 (78.3%)		Reference	
EF, 60 min				0.011		
Abnormal, <19% or >40%	24 (22.6%)	16 (34.8%)	8 (13.3%)		3.47	1.33–9.06
Normal, 19%–40%	82 (77.4%)	30 (65.2%)	52 (86.7%)		Reference	
EF, 120 min				0.26		
Abnormal, <11% or >41%	15 (18.3%)	10 (23.3%)	5 (12.8%)		2.06	0.64–6.68
Normal, 11%–41%	67 (81.7%)	33 (76.7%)	34 (87.2%)		Reference	
Frequency, 30 min				0.047		
Abnormal, <2.67 or >3.33	11 (10.9%)	8 (19.5%)	3 (5.0%)		4.61	1.14–18.57
Normal, 2.67–3.33	90 (89.1%)	33 (80.5%)	57 (95.0%)		Reference	
Frequency, 60 min				0.32		
Abnormal, <2.76 or >3.48	10 (9.4%)	6 (13.0%)	4 (6.7%)		2.10	0.56–7.93
Normal, 2.76–3.48	96 (90.6%)	40 (87.0%)	56 (93.3%)		Reference	
Frequency, 120 min				1.00		
Abnormal, <2.42 or >3.20	11 (13.4%)	6 (14.0%)	5 (12.8%)		1.10	0.31–3.95
Normal, 2.42–3.20	71 (86.6%)	37 (86.0%)	34 (87.2%)		Reference	

*P value for testing association of DACS abnormality with standard clinical diagnosis based on conventional GES using Fisher exact test.

†Raw odds ratio of being diagnosed as abnormal by conventional GES comparing DACS abnormal to normal.

potential treatment of gastroparesis (*14,15*). Up to now, DACS has focused primarily on measuring the frequency and amplitude of antral contractions. We have previously shown that DACS can significantly enhance the information provided by GES not only by measuring antral contraction amplitude and frequency (*8*) but also by assessing antropyloric contractions that produce coordinated, antropyloroduodenal bolus propagation (*3*). Analogous to cardiac multigated acquisition studies assessing for ventricular dyssynchrony, DACS may provide information on the in-phase relationship of the timing to the onset of antral contractions. In this study, we have investigated the use of Fourier phase analysis to augment DACS analysis of the contractility of the proximal and distal antrum. We have also correlated how DACS measurements of antral contraction frequency, EF, and proximal and distal antral phase analysis correlate with conventional measurement of overall $T^1/_2$. This study showed that DACS percentage total in-phase antral pixels at 30 min and EF at 60 min are potential new measures of antral contractility that may have added value for predicting abnormal GE. Importantly, this study has led to development of a software package and associated reference values that can eventually be made available to others and offer the potential for more widespread clinical use.

Other imaging techniques have been used to assess for antral contractility, particularly most recently MRI, which

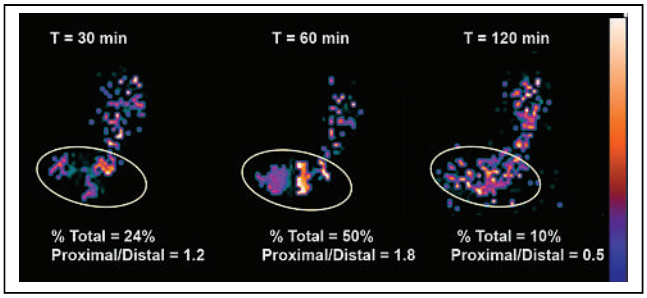

FIGURE 5. Patient with abnormal GE and abnormal phase analysis. Shown are Fourier phase angle images for patient with delayed GE ($T^1/_2$ = 188 min). Elliptic ROI as in Figure 4 again shows total antral area used for analysis. There is lack of synchronous in-phase proximal and distal antral pixels at 30 and 120 min compared with normal pattern (Fig. 4). At 60 min, there is cluster of proximal antral phasic activity but no coordinated distal phasic contractions.

can be used to measure gastric volumes and the phasic and amplitude components of gastric contractions (*16*). Although MRI has greater spatial and temporal resolution than scintigraphy, MRI for gastric motility currently has limitations, including use of nonphysiologic meals, limited scanner time for prolonged imaging, high costs, and current availability limited to only research centers.

This study showed that DACS in healthy volunteers demonstrates a consistent pattern of 2 in-phase areas of the antrum that show coordinated contractions. The first area is the proximal antrum, where antral contractions originate. This is separated from the distal antrum by a mid-antral segment, where the peristaltic wave propagates bolus movements of food through the antrum. The second area is in the distal antrum, where rhythmic contractions repel the incoming bolus in a retrograde fashion. The study also showed that the percentage of total proximal and distal antral pixels that are in phase by DACS analysis correlated well with the overall $T^1/_2$, suggesting that this quantitative measurement may serve as a new physiologic measurement of antral contractility. In addition, the study found that in healthy volunteers, the in-phase proximal-to-distal ratio for antral pixels significantly increased over time from 30 to 120 min after meal ingestion, a finding that agrees with early observations of Rees et al., who showed that the motility index of the distal antrum decreased in the postprandial period (*17*). This supports an important role of increasing proximal antrum contractions over time after meal ingestion as the fundus progressively moves solids into the antrum (Fig. 5). In a similar fashion, the antral EF in healthy volunteers increased with time. Finally, univariant and multivariant regressions showed that the percentage total in-phase antral pixels at 30 min and the antral EF at 60 min appeared to be predictors of delayed GE. We acknowledge that additional multiinstitutional clinical studies with more patients will be needed to see whether these findings can be confirmed and expanded to help explain symptoms in patients with suspected gastroparesis when conventional GES results are normal.

The final composite of dynamic images for the Fourier analysis used only a subset of the antral contractions (4 cycles) that occur during the 10 min of continuous list-mode DACS. We acknowledge that the quality of the Fourier analysis could improve using more gastric contraction cycles. We found, however, that the current β-software, which uses existing MIM cardiac phase-amplitude software, required typically a 10- to 15-min run time for 4 cycles. When we used more than 4 cycles, the processing time became greater than 20 min, which was not practical for the large number of patient studies and imaging time points needing analysis. The lengthy processing time of the current DACS MIM workflow is likely related to the need to reformat all the individual list-mode gastric images without the benefit of electrocardiography gating. Such gating, which is performed during cardiac multigated acquisition, helps create a single summed cardiac cycle for analysis.

The β-software used for DACS analysis in this study is still under development by MIM and not currently commercially available. We anticipate that as demand for processing DACS data grows, the current β-software processing time will be improved. It is our hope that based on the results of this study, a final commercial DACS software package with the potential for more widespread availability will make acquisition and processing of DACS available for routine clinical use.

Although processing of only 4 gastric contraction cycles could be considered a potential limitation of the analysis, this choice permitted us to select a set of the best reformatted, summed antral contraction cycles for measurement of phase, amplitude, frequency, and EF across multiple time points. Others have observed with DACS that although most antral contractions appear regular in frequency and amplitude within the time of observation, some antral contractions

TABLE 3
Multivariable Logistic Regression Identifying Best Subset of DACS Abnormality Parameters Associated with Standard Clinical Diagnosis Using Data from All Subjects (n = 121)*

DACS abnormality variable	Adjusted odds ratio	95% CI	*P*
By percentage total, 30 min, to <31% or >63% vs. 31%–63%	3.30	1.21–9.00	0.02
By EF, 60 min, to <19% or >40% vs. 19%–40%	2.97	1.08–8.21	0.036

*24 subjects had missing data on at least 1 variable and hence dropped out of model.

are irregular (*13*). We observed a low occurrence (average of 11%) of irregular antral contractions during DACS in healthy volunteers. Such short periods of spontaneous gastric arrythmias (which may be ≤35%) could affect the DACS analysis. Thus, we believe that visual review of the DACS imaging data and selection of an optimum set of gastric cycles before final analysis, as performed in this study, is desired and important to exclude not only irregular gastric contractions but also potential patient motion artifacts. Such selection of the regular antral contractions should be performed routinely as a part of DACS analysis. Further characterization of whether short periods of antral dysrhythmias affect overall GE in symptomatic patients will require additional study.

CONCLUSION

In this study, Fourier phase analysis of proximal and distal antral phasic contractions was added to DACS in addition to measurements of antral contraction frequency and EF. The study established new reference values and demonstrated new physiologic information on antral motility with a normal increasing proximal-to-distal ratio of in-phase pixels and EF with time after meal ingestion. The percentage total proximal and distal in-phase pixels correlated well with early $T^1/_2$ values. Further, for symptomatic patients, the percentage of in-phase proximal and distal antral pixels (at 30 min) and EF (at 60 min) after meal ingestion are potential new parameters to assess for abnormal antral contractility and delayed GE. Use of Fourier analysis of DACS has the potential to provide added understanding of the underlying pathophysiology of antral contractility.

KEY POINTS

QUESTION: Does Fourier phase analysis of DACS add physiologic information on antral motility that can augment conventional GES for diagnosing gastric dysmotility?

PERTINENT FINDINGS: In healthy volunteers, the proximal-to-distal ratio for in-phase antral pixels and antral EF increases with time after meal ingestion. The percentage total proximal and distal in-phase antral pixels at both 30 and 60 min correlated well with $T^1/_2$. For symptomatic patients, the percentage total proximal and distal in-phase antral pixels at 30 min and the antral EF at 60 min after meal ingestion have potential to further aid in diagnosing delayed GE.

IMPLICATIONS FOR PATIENT CARE: New software and associated reference values for antral contraction frequency, in-phase contractions, and EF have been developed and offer the potential for more widespread application of DACS to aid in the diagnosis of abnormal GE.

DISCLOSURE

A β-version of the MIM software was provided for these studies. Natalie Cole is a software engineer employed by MIM Software. As a salaried employee, she has no potential conflicts of interest in terms of any monetary gain for any potential sales of the software or patent ownership. No other potential conflict of interest relevant to this article was reported.

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Gastric Emptying Studies in Pediatrics: A Cincinnati Children's Hospital Experience

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Gastric emptying studies are routinely performed in many nuclear medicine departments; however, there are many different techniques used to perform the procedure across the country. Creating consistency in clinical practice will aid gastroenterologists in diagnosing and treating illnesses associated with abnormalities related to gastric emptying. In 2017, Cincinnati Children's Hospital adopted adult standards for pediatric gastric emptying studies that included a standard meal along with imaging over the course of 4 h. Gastric emptying studies are the second-highest-volume examination performed in the nuclear medicine section at Cincinnati Children's Hospital. Accommodating this volume required changes in the scheduling template, scheduling questionnaire, and epic order sets, as well as identification of specific days and locations for gastric emptying studies. Both protocol standardization and workflow optimization are critically important in creating consistency in patient care. Gastric emptying can be evaluated with solid food, liquid food, or solid and liquid food simultaneously. The methodology of the study is initially determined by the ordering provider but may require special accommodations based on what the patient will tolerate. In coordination with the ordering and interpreting physicians, the nuclear medicine technologists at Cincinnati Children's Hospital have the decision-making ability to deviate from the provider's request as necessary, which helps expedite workflow and eliminates wasted time. Any deviation from the standardized protocol is documented by the nuclear medicine technologist and incorporated into the final report by the interpreting physician, as dietary information is meaningful to the ordering provider. Reference values associated with the standardized or modified protocol are also included in the final report.

Key Words: dual-phase gastric emptying; gastric emptying; pediatrics

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Gastric emptying studies have become increasingly common, not because they are exceptionally awesome to look at or overly fun to perform but because they provide gastroenterologists with information on how well a patient's stomach is functioning. The primary indication for performing gastric emptying studies is to rule out gastroparesis, a condition in which the stomach empties too slowly. A secondary indication is to rule out dumping syndrome, in which the stomach empties too quickly. Assessment of gastric emptying in nuclear medicine is based on the meal consumed. Challenges in performing gastric emptying studies in a pediatric population include food allergies (*1*) and the fact that many children are picky eaters. To accommodate young patients, there needs to be flexibility in the performance of the gastric emptying study so that it will continue to provide meaningful results to the ordering providers.

Performing a gastric empty protocol is relatively simple; however, several considerations need to be factored into clinical practice, especially when the volume of studies continues to rise. Most of the considerations fall into 2 categories: technical aspects of the study, and logistics and patient workflow. The structure of the nuclear medicine department is critical when performing a large volume of gastric emptying studies, including the number of available cameras in the department, the available collimators for each camera, and the available patient prep rooms. Assessing these key elements ahead of time will be helpful when developing a workflow pattern to support a high volume of gastric emptying studies. This article summarizes Cincinnati Children's Hospital's camera acquisition protocols, scheduling templates, and patient and meal preparation, as well as briefly discussing what the results of the gastric emptying study can provide for patient care.

Variety of Gastric Emptying Studies

At Cincinnati Children's Hospital, there are 3 different types of gastric emptying studies routinely performed: dual-phase (solid and liquid), single-phase (solid only), and liquid phase (liquid only). Gastric emptying studies begin with evaluating a patient for a dual-phase study and, from there, cascade to either a solid phase or liquid phase. The study performed is determined by what radiolabeled food the patient can consume. Dual-phase gastric emptying uses ^{99m}Tc-sulfur colloid–radiolabeled egg whites as the solid phase and ^{67}Ga-citrate mixed with apple juice or water as the liquid phase (*2,3*). In our department, the solid-phase gastric emptying study is performed with radiolabeled egg whites, Ensure Plus (Abbott Laboratories) (*4*), or plain oatmeal (*5*). Liquid gastric emptying studies use the patient's

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formula, milk, or clear liquid. Flexibility is essential in this patient population and is dependent on what the child will or will not eat. At Cincinnati Children's Hospital, the nuclear medicine technologist is permitted to modify the dual-phase study as needed (Fig. 1).

Schedule Considerations

Patient preparation includes having the patient eat and drink nothing for 4 h before the study. We have found that scheduling the studies in the morning helps with patient satisfaction and staff satisfaction, with the standard meal more closely resembling breakfast or brunch. Adopting a standard meal for the study creates consistency, and the study results are comparable with reference values in the literature (*2,6*). The standard-meal study with solid food (egg whites), or a solid-food substitute (Ensure Plus) requires periodic imaging over the course of 4 h. At our institution, we needed to build a schedule template that would accommodate a high volume of gastric emptying studies while allowing the department to offer other nuclear medicine studies as well. This was accomplished by dedicating one of our γ-cameras to gastric emptying studies on Mondays, Tuesdays, Thursdays, and Fridays. Even though the study is 4 h in length, we schedule patient appointments in 1-h blocks to allow 3 or even 4 patients to be scheduled on a single day.

Our patient preparation on the day of the study is often the slowest phase of the study. The patient is brought to the prep room, where the technologist will obtain a patient history, explain the study, review allergies, answer any questions the patient (or parents) may have, and then give the patient the meal.

Patients have 10 min to consume the standard meal. Patients do not need to be in the γ-camera room while eating the meal; thus, use of the patient prep rooms aids in facilitating patient workflow. Patients simply leap-frog each other for imaging (Fig. 2).

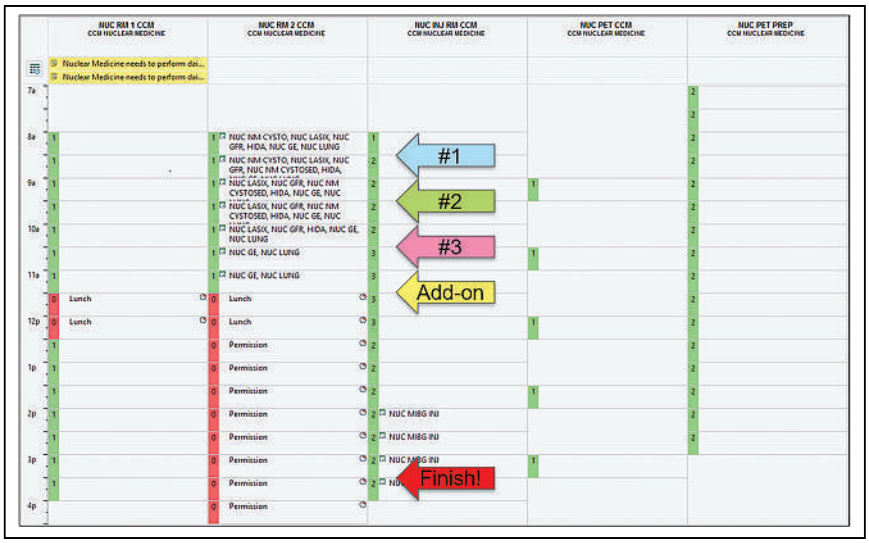

FIGURE 1. Epic schedule template for gastric emptying studies. Central scheduling can schedule 3 gastric emptying studies in 1 d. Scheduling template is blocked as "permission" in afternoon to allow for gastric emptying studies to be performed over 4 h.

Dual-Phase Gastric Emptying

The dual-phase gastric emptying components include a solid phase and a liquid phase. The solid phase consists of 118 mL (4 oz) of ^{99m}Tc-sulfur colloid–labeled egg whites. We use commercially available Egg Beaters (Bob Evans Farms, LLC) at our institution.^{99m}Tc-macroaggregated albumin can be substituted for ^{99m}Tc-sulfur colloid in the event of a sulfur colloid shortage. The liquid phase consists of 118 mL (4 oz) of ^{67}Ga-citrate apple juice or water, whichever the patient prefers. We radiolabel the egg whites in the hot lab and cook them in a microwave oven that is designated for radioactive material use only. We use a disposable measuring cup and pour 118 mL (4 oz) of Egg Beaters into a 473-mL (16-oz) microwave-safe bowl. Liquid egg whites expand when cooking.

For the liquid phase, ^{111}In-diethylenetriaminepentaacetic acid (DTPA) may be substituted for ^{67}Ga-citrate if ^{67}Ga-citrate is not available or if ^{111}In-DTPA is preferred. There are significant cost differences between ^{67}Ga-citrate and ^{111}In-DTPA that should be considered. Unit doses of ^{67}Ga-citrate are purchasable, whereas ^{111}In-DTPA is typically sold in a 55.5-MBq (1.5-mCi) vial at a price that is approximately 35 times higher than a unit dose of ^{67}Ga-citrate. One counter advantage to using ^{111}In-DTPA over ^{67}Ga-citrate, despite the cost, is that ^{111}In-DTPA production is more reliable than ^{67}Ga-citrate production.

When performing gastric emptying studies, we have found it advisable to provide patients with an emesis bag to contain any radioactivity in case they vomit. Cleaning up radioactive contaminants from a waiting room is not fun and will often alarm other patients and families when they see spill kits and radiation detection equipment in use. If a patient vomits during the gastric emptying study, the study must be terminated; accurate gastric emptying can no longer be calculated because of the change in stomach volume.

Dual-Phase Imaging Protocol

γ-cameras will need to be configured to accept 2 energy windows for the dual-phase study. When building the acquisition protocol for the dual-phase study, one should refer to the manufacturer guidelines for the specific camera to set the required energy peaks. At our institution, the photo peak for ^{99m}Tc is set at 140.5 keV with a window of ±10% and the ^{67}Ga photo peak is set at 184 keV with a window of ±10%. The computer program (Xeleris; GE Healthcare) used for processing our gastric emptying studies requires ^{99m}Tc to be the first nuclide

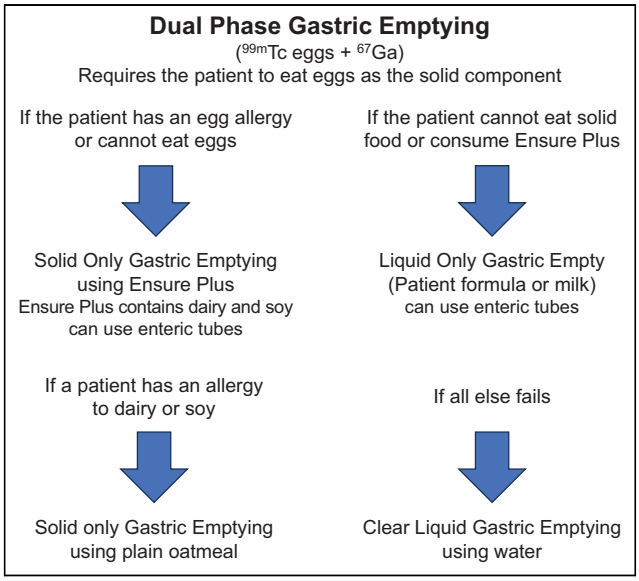

FIGURE 2. Flow diagram of gastric emptying studies starting with dual-phase gastric emptying. Changes based on what patient can be fed are permitted.

set or the program will not work correctly. We set our acquisition protocol with a 128 × 128 matrix and 2-min acquisitions at the standard time points: 0 min, 1 h, 2 h, 3 h, and 4 h.

A medium-energy general-purpose collimator must be used for the 184-keV photons generated by ^{67}Ga. If we use ^{111}In-DTPA for the liquid phase, the second energy setting is built for the 2 primary energy peaks of 171 and 245 keV for ^{111}In. The higher-energy γ-emissions from ^{111}In also require the use of a medium-energy general-purpose collimator.

Before the patient consumes the solid meal and the liquid, we prepare and acquire the ^{67}Ga standard. The ^{67}Ga standard is used to capture the total ^{67}Ga activity to be administered to the patient and will be needed for postprocessing. The ^{67}Ga standard allows the γ-camera to separate the 2 radiopharmaceuticals to calculate the solid ^{99m}Tc phase and the liquid ^{67}Ga phase emptying. In preparing the ^{67}Ga standard, we pour a small amount of apple juice or water (whichever the patient has chosen to drink) into a disposable cup—covering the bottom surface of the cup—and then squirt the ^{67}Ga-citrate dose into the cup and rinse the syringe multiple times by pushing and pulling the plunger to ensure complete delivery of the ^{67}Ga into the liquid. We center the ^{67}Ga standard in the field of view, approximately 30 cm away from the camera head. We acquire a posterior view of the ^{67}Ga standard for 2 min. Approximately 20% of the ^{67}Ga 184-keV backscatter photons will bleed into the ^{99m}Tc window and will need to be subtracted when the data are processed.

The full standard meal for the solid-phase study consists of 118 mL (4 oz) of radiolabeled scrambled egg whites (e.g., Egg Beaters), 2 slices of white bread or toast, 2 packs of jelly (30 g), and 118 mL (4 oz) of water. Gluten-free bread is not allowed because it was not studied when the adult standard protocol was developed. If a patient has a gluten sensitivity, bread should not be included with the standard meal. Patients will likely forego the 2 packs of jelly if bread is not available to spread the jelly on. If the meal is modified in any way, what the patient consumed should be recorded. Once the standard meal is prepared, we encourage the patient to start eating the standard meal before we offer the ^{67}Ga liquid dose (Table 1) in the disposable cup. We record what the patient ate and how long it took the patient to consume the meal. We do not let the patient eat for longer than 10 min, as the stomach can begin to empty before the 0-min image is acquired. We follow the image acquisition camera protocol and acquire a 2-min conjugate view (anterior and posterior) geometric mean image approximately every hour for up to 4 h. We conclude the study at 4 h or when 90% emptying of the solid meal is achieved.

When several dual-phase gastric emptying studies are performed on a single γ-camera in a single day, some images are of greater importance than others. The 0-min image is the baseline image with which the stomach counts are

TABLE 1
Gastric Emptying Dose Chart

Examination	Radiopharmaceutical	Target dose	Other
Dual-phase gastric emptying	Solid (^{99m}Tc-sulfur colloid)	7.4 MBq (0.200 mCi)	Liquid eggs
	Liquid (^{67}Ga-citrate)	3.0 MBq (0.080 mCi)	Water or apple juice
Solid gastric emptying	^{99m}Tc-sulfur colloid	7.4 MBq (0.200 mCi)	Liquid eggs or Ensure Plus
Liquid gastric emptying	^{99m}Tc-sulfur colloid	7.4 MBq (0.200 mCi)	Patient formula or water
Liquid gastric emptying gastroesophageal reflux	^{99m}Tc-sulfur colloid	9.3 MBq (0.250 mCi)	<2 y
		11.1 MBq (0.300 mCi)	2–4 y
		14.8 MBq (0.400 mCi)	≥5 y

Radiopharmaceutical dose chart taken from Cincinnati Children's Hospital Medical Center's Department of Nuclear Medicine radiopharmaceutical target dose schedule. ^{99m}Tc-macroaggregated albumin can be substituted for ^{99m}Tc-sulfur colloid if ^{99m}Tc-sulfur colloid is not available. ^{99m}Tc-DTPA can be used for clear-liquid gastric emptying studies using water.

TABLE 2
Reference Values for Various Types of Gastric Emptying Studies

Study type	Reference value
Dual phase with egg (4-h study) (delayed solid emptying at 2 or 4 h is considered abnormal; delayed clear emptying at 1 or 2 h is considered abnormal)	Liquid: >40% at 1 h; >78% at 2 h
	Solid: >10% but <70% at 1 h; >40% at 2 h; >90% at 4 h
Solid-only with egg (4-h study) (delayed solid emptying at 2 or 4 h is considered abnormal)	>10% but <70% at 1 h; >40% at 2 h; >90% at 4 h
Solid-only with Ensure Plus (4-h study)	>10% but <70% at 1 h; >40% at 2 h; >90% at 4 h
Solid-only with oatmeal (1-h study)	>50% at 1 h
Liquid-only with formula or milk (2-h study)	>51% at 2 h
Clear liquid–only with water (30-min study)	Half-time < 25 min

compared over time to calculate emptying. Stomach emptying can begin before the 0-min acquisition if a patient takes too long to eat or if there is hypermotility. If the small bowel is visualized on the 0-min image, we include total abdominal counts (stomach and small bowel) as the region of interest for the baseline image so that total gastric emptying can be calculated. We acquire the 1-h image to rule out dumping syndrome, a stomach that empties too quickly. We acquire the 2-h image to compare with reference values for both solids and liquids at the 2-h time point. The 3-h image may be omitted if there are patient workflow issues or if the camera room is needed for other patients. We have found that one advantage of acquiring the 3-h image is that patients may achieve 90% emptying of solids at this time and the study can be completed. The 4-h image is needed if 90% emptying of the solid food phase has not been achieved at 3 h and final percent emptying calculations are needed to compare with reference values (Table 2).

Single-Phase Gastric Emptying: Egg Whites or Ensure Plus

If a dual-phase study cannot be performed for any reason, such as if the radiopharmaceutical used for the liquid phase is not available or if the patient has an egg allergy or simply does not like eggs and refuses to eat them, we perform a single-phase gastric emptying study. In our department, labeled-food options for performing a single-phase gastric emptying study include liquid egg whites, Ensure Plus, or plain oatmeal. Our protocol for liquid egg whites or Ensure Plus (*4*) is the same as for the dual-phase study. The only difference is that ^{67}Ga or ^{111}In is not used to radiolabel liquid. Patients able to eat scrambled egg whites are offered apple juice or water to drink with the study. Patients consuming Ensure Plus or oatmeal for the study are not offered apple juice or water with the meal. Our camera acquisition protocol for the single-phase study uses only the ^{99m}Tc energy of 140.5 keV with a window of ±10%. We acquire conjugate-view geometric mean images for accurate emptying measurements (*7*). We have found that acquiring anterior and posterior conjugate-view static images improves the accuracy of the study by accounting for individual patient body habitus, patient attenuation, and scatter correction. In our experience, true stomach activity is higher when conjugate-view images are acquired than when single-projection (anterior or posterior) acquisition methods are used. The images of importance are the same as for a dual-phase study. Imaging at 3 h can also expedite completion if 90% gastric emptying has been achieved.

Single-phase studies using labeled egg whites, Ensure Plus, or plain oatmeal can be performed using either low-energy collimators or medium-energy collimators. Our technologists do not change collimators when they are performing multiple gastric emptying studies that vary between dual-phase and single-phase. The study is only collecting count data; image resolution is not relevant. Not changing collimators between patients is a significant time saver. We use medium-energy collimators if a dual-phase study is on the schedule even if single-phase gastric studies are also scheduled.

Single-Phase Gastric Emptying with Oatmeal

The last option for performing a single-phase gastric emptying study is to use plain oatmeal if a patient cannot consume liquid egg whites or Ensure Plus. ^{99m}Tc-sulfur colloid is the radiopharmaceutical of choice to radiolabel oatmeal (*5*). Unlike dual-phase or single-phase studies using Ensure Plus, the duration of a single-phase gastric emptying study with oatmeal is 1 h. Like dual-phase or other single-phase studies, low-energy or medium-energy collimators can be used. We still acquire an initial image (0 min) after the patient consumes the oatmeal but will also acquire an image at 30 min to rule out dumping syndrome. The image at 60 min will be the last image acquired. Reference values are greater than 50% emptying at 60 min.

Liquid-Only Gastric Emptying

In our department, a liquid gastric emptying study consists of any radiolabeled food that is not scrambled egg whites, Ensure Plus, or oatmeal. Liquid gastric emptying studies are performed when children are too young to consume solid food offered as part of a standard meal for solid studies. Allergens to ingredients such as eggs, dairy, or soy can steer patients to a liquid gastric emptying study. Additionally, a liquid-only study may be required for children with specific formula or dietary restrictions.

Unlike dual-phase or single-phase studies, in which conjugate view images are acquired, posterior images are acquired for liquid gastric emptying studies. A patient being fed via an enteric tube should be positioned with the left side down to prevent premature emptying of the stomach before the initial image can be acquired. After feeding is complete, the patient is positioned supine for imaging. Nasogastric tubes can be removed for imaging if the ordering provider so advises, as they may keep the cardiac sphincter open and potentially mimic gastroesophageal reflux. The image acquisition times of importance are the initial image after feeding (0 min) and the 1-h and 2-h images. If the ordering provider requests gastroesophageal reflux imaging, a 60-min dynamic protocol is applied to acquire images after the 0-min image and before the 1-h image. Dynamic acquisitions for reflux imaging use a 128×128 matrix and a 30-s frame time for 120 frames. Liquid gastric emptying studies can be completed if greater than 51% of gastric emptying is reached after 1 h of imaging. A 2-h posterior static image is acquired if 51% gastric emptying has not been achieved at 1 h.

Clear-Liquid Gastric Empty

Gastric emptying studies using clear liquid (i.e., water) may also be performed if patients cannot consume solid food, milk, or formula. There are some advantages to performing a gastric emptying study using only radiolabeled water. First, most pediatric patients do not have a problem drinking water. Second, the entire study is only 30 min (*8*). Third, adding an inpatient clear-liquid gastric emptying study to the daily workflow is much more feasible given that the length of the study is only 30 min. Clear-liquid gastric emptying studies are useful for evaluating gross gastroparesis. The main disadvantage is that clear-liquid studies do not provide specific details captured in a 4-h dual-phase or single-phase gastric emptying study.

The imaging protocol for a clear-liquid study begins with the patient drinking 237 mL (8 oz) of radiolabeled water. Anterior dynamic images are acquired using a 128×128 matrix at a rate of 1 min per frame for 30 frames. Conjugate views may be acquired; however, the processing program requires only the anterior view for the dynamic phase. At Children's Cincinnati Hospital, a Xeleris workstation (GE Healthcare) is used to process dynamic images. The reference value for clear-liquid gastric emptying is a half-time of less than 25 min.

Patient Care Management

The results of the gastric emptying study can help guide therapy for patients with upper gastrointestinal symptoms, especially if they have delayed emptying (gastroparesis) or rapid emptying (dumping syndrome). Symptoms include nausea, vomiting, early satiety, postprandial fullness, and abdominal pain, which may be caused by gastric sensory or motor dysfunction or both (overlap).

With delayed gastric emptying or gastroparesis, the severity of the symptoms guides the level of supportive care that may be needed (*9*). Patients with grade 1 or mild gastroparesis have intermittent, easy-to-control symptoms and can maintain their weight and nutrition with dietary modifications such as low-fat small, frequent meals. Patients with grade 2 or compensated gastroparesis have partially controlled symptoms and benefit from pain control medications, antiemetics (ondansetron, promethazine, prochlorperazine, lorazepam), and prokinetics (erythromycin, prucalopride, metoclopramide, domperidone, cisapride) to improve their symptoms and avoid hospitalization. Although not a prokinetic agent, Cyproheptadine is widely used in clinical practice for dyspeptic symptoms and may have a role in alleviating symptoms of delayed gastric emptying because of its plausible effects on gastric accommodation.

Patients with grade 3 gastroparesis (gastric failure) respond less to dietary modification or medications, cannot maintain oral nutrition or hydration, and need frequent emergency room visits and hospital admissions; these patients may benefit from enteral tube feeds (gastrostomy tube or gastrostomy–jejunostomy tube), parenteral nutrition, endoscopic procedures (pyloric onabotulinumtoxinA [Botox; Allergan, Inc.] injection and dilation), surgical intervention (pyloroplasty and peroral pyloromyotomy), or neuromodulation (gastric electric stimulation) (*10–12*). Although the consensus recommendations for gastric emptying scintigraphy by the American Neurogastroenterology and Motility Society combined with the Society of Nuclear Medicine and Molecular Imaging are based on a standardized solid meal, dual-phase gastric emptying studies may help target therapy in dyspeptic children. A recent study showed that over half of children with dyspepsia had delayed liquid gastric emptying, and one quarter had delayed liquid emptying with normal solid emptying, highlighting the utility of dual-phase scans (*11*).

Rapid gastric emptying can be seen with iatrogenic dumping syndrome (after esophageal, gastric, or bariatric surgery, as well as in diabetes mellitus, autonomic neuropathy, postural orthostatic tachycardia syndrome, and disorders of gut–brain interaction [dyspepsia, cyclic vomiting syndrome]). Symptoms of rapid emptying or dumping include abdominal pain, bloating, borborygmi, nausea, and diarrhea, as well as vasomotor symptoms such as flushing, palpitations, perspiration, tachycardia, hypotension, fatigue, or syncope, and are attributed to osmotic effects, peptide hormone release, and autonomic neural responses. Treatment of dumping syndrome includes dietary modifications, pharmacologic interventions, surgical intervention, or continuous tube feeding. Dietary modification is usually beneficial for most patients and reduces the amount of food consumed at each meal. Acarbose (an α-glycosidase hydrolase inhibitor that decreases carbohydrate digestion in the small intestine and limits postprandial hyperglycemia and subsequent hypoglycemia), somatostatin analogs, diazoxide (a potassium channel activator that inhibits calcium-induced insulin release), and glucagonlike peptide 1 receptor antagonist exendin 9-39 (corrects hypoglycemia after gastric bypass) are some of the medications used in patients with rapid emptying. Maintaining the patient's nutrition with gastrostomy or even jejunostomy feeds may be necessary (*12*).

CONCLUSION

At Cincinnati Children's Hospital, performing gastric emptying studies for pediatric patients starts with a dual-phase gastric emptying study and branches off from there depending on what radiolabeled food the patient can consume for the study. Creating an environment of flexibility while simultaneously adhering to standardization is critical so that meaningful results can be reported to ordering providers. Treatment for patients with upper gastrointestinal symptoms can vary depending on the results provided by gastric emptying studies.

KEY POINTS

QUESTION: How are gastric emptying scans performed in pediatrics?

PERTINENT FINDINGS: This article discusses the possible variations from standardized protocols when gastric emptying scanning is performed in pediatrics. The scans may be performed as solid only, liquid only, or a dual phase that includes both solid and liquid emptying data.

IMPLICATIONS FOR PATIENT CARE: For patients with upper gastrointestinal symptoms, the results of gastric emptying scans can help guide therapy, which includes dietary modifications, pharmacologic interventions, surgical intervention, or continuous tube feeding.

DISCLOSURE

Joby MacLean is a consultant for GE Healthcare. No other potential conflict of interest relevant to this article was reported.

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Gastric Emptying Study: Liquids

Mary Beth Farrell

RATIONALE

Gastric emptying is a simpler process for liquids than solids because liquids do not need to be mixed with gastric juices and ground into small particles to pass through the pyloric sphincter. As liquids enter the stomach, it relaxes to accommodate the volume. Then, the stomach's smooth muscle contracts, creating a pressure gradient between the stomach and pylorus that pushes liquid through the pyloric sphincter into the duodenum.

The volume of liquid is the main determinant of the rate of liquid gastric emptying. The larger the volume of liquid, the quicker the rate of emptying. Liquid begins leaving the stomach almost as soon as it reaches the stomach and usually empties in approximately 30 min.

CLINICAL INDICATIONS

- Determination of gastric emptying rate.
- Evaluation of mechanical and anatomic obstruction.
- Evaluation of nausea, vomiting, upper abdominal discomfort, bloating, gastroesophageal reflux/chronic aspiration, and early satiety.
- Evaluation of weight loss.
- Evaluation of rapid gastric emptying.

CONTRAINDICATIONS

- Hypoglycemia with blood glucose level less than 40 mg/dL.
- Hyperglycemia with blood glucose level greater than 275 mg/dL.
- Improper preparation of the patient for the procedure.
- Pregnancy or breastfeeding. Pregnancy must be excluded according to local institutional policy. If the patient is breastfeeding, radiation safety instructions should be provided.
- Recent nuclear medicine study (radiopharmaceutical-dependent).

PATIENT PREPARATION/EDUCATION

- The patient should have nothing to eat or drink overnight or 4–6 h before the test.
- The patient may not smoke the morning of the test or until after test completion.
- If the patient has insulin-dependent diabetes:
  - The patient should bring a blood glucose monitor and insulin to the test.
  - The blood glucose level should be determined and recorded before meal ingestion and should ideally be less than 200 mg/dL.
  - If more than 275 mg/dL, a small dose of short-acting insulin should be administered before meal ingestion, and the patient should be monitored. The meal should be withheld until the blood glucose level falls below 275 mg/dL.
- Studies on menstruating patients should be performed during the first 10 d of their menstrual cycle.
- Treatment with prokinetic agents (metoclopramide [Reglan; ANI Pharmaceuticals Inc.], tegaserod [Zelnorm; Alfasigma USA, Inc.], domperidone [Motilium; Janssen], and erythromycin) should be stopped 2 d before the test unless the test is being performed to assess the efficacy of these drugs.

TABLE 1
Radiopharmaceutical Identity, Dose, and Route of Administration

Identity	Dose	Route
^{99m}Tc-sulfur colloid	18.5 MBq (0.5 mCi); range, 18.5–37 MBq (0.5–1.0 mCi)	Oral bolus
^{99m}Tc–diethylenetriaminepentaacetic acid	18.5 MBq (0.5 mCi); range, 18.5–37 MBq (0.5–1.0 mCi)	Oral bolus
Pediatric dose: ^{99m}Tc-sulfur colloid	No weight-based dose; minimum administered activity, 9.25 MBq (0.25 mCi); maximum administered activity, 37 MBq (1.0 mCi)	Oral bolus

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- Medications that delay gastric emptying should be stopped 2 d before the test. These include opiates (meperidine, codeine, morphine, oxycodone hydrochloride, and oxycodone acetaminophen), antispasmodic agents (dicyclomine, phenobarbital, hyoscyamine sulfate, glycopyrrolate), atropine, nifedipine, progesterone, octreotide, theophylline, benzodiazepines, and phentolamine.
- A focused history containing the following elements should be obtained:
  - Symptoms such as nausea, vomiting, abdominal pain, or early satiety.
  - Related diseases, such as hiatal hernia, gastroesophageal reflux, esophageal motility disorders, diabetes, infections, neuromuscular disorders, autoimmune disorders, and connective tissue disorders (previous interventions, including prior stomach or abdominal surgery, because previous surgery may alter the shape or route of emptying; medications as listed above).

PROTOCOL/ACQUISITION INSTRUCTIONS

- Radiopharmaceutical identity, dose, and route of administration are provided in Table 1.
- Planar acquisition parameters are provided in Table 2.
- Acquisition instructions:
  - Mix 18.5–37 MBq (0.5–1.0 mCi) of ^{99m}Tc-sulfur colloid or ^{99m}Tc-diethylenetriaminepentaacetic acid in 300 mL of water (substitution of juice, milk, or formula based on patient and clinical indication is permitted).
  - Instruct the patient to drink the liquid rapidly through a straw.
  - Position the patient semiupright (30°–45° angle) with the camera in the left anterior oblique position and the stomach and upper abdomen in the field of view.
  - Obtain dynamic images at 60 s/frame for 30 min.

IMAGE PROCESSING

- Draw regions of interest around the activity in the entire stomach on the left anterior oblique view.
- Generate a time–activity curve.

TABLE 2
Planar Acquisition Parameters

Parameter	Standard
Field of view	Large and small
Energy peak	140 keV
Energy window	20%
Collimator	Low-energy high-resolution
Patient position	Semiupright (30°–45°)
Camera position	Left anterior oblique
Time of imaging after ingestion	Immediate
Acquisition type	Dynamic
View	Left anterior oblique
Additional views	Not applicable
Matrix	128 × 128
Number of views	Not applicable
Time per view	60 s/frame for 30 min
Additional view time per projection	Not applicable

- Calculate half-emptying time (time required for emptying half the liquid) and best-fit mathematic exponential emptying rate. The normal half-emptying time for clear liquids is less than 25 min. Adding salt, sugar, or other caloric content to the clear liquid meal slows the emptying rate.
- Do not account for radioactive decay or correct for attenuation; these are unnecessary for liquid gastric emptying studies.

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Change in Management After Radionuclide Gastric Emptying Studies Showing Slow Emptying

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The radionuclide gastric emptying study is the gold standard for the diagnosis of gastroparesis. **Methods:** We performed a retrospective analysis of 510 patients to evaluate how often a diagnosis of slow gastric emptying determined by gastric emptying scintigraphy (GES) changes clinical management at our institution. **Results:** We found evidence of gastroparesis in 100 patients. A change in management was recommended for 62% within 1 mo of the GES. **Conclusion:** Our results illustrate the importance of performing GES on patients with clinically suspected gastroparesis.

Key Words: gastric emptying scintigraphy; slow gastric emptying; nutrition education counseling; prokinetics; cholinergics

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Historically, gastric emptying has been assessed using many different methods, beginning in the late 19th century with Walter B. Cannon, who pioneered the first imaging-based method, which used fluoroscopy to assess gastric function after a meal labeled with a radiopaque contrast agent (*1*). More recently, Griffith et al. (*2*) showed in 1966 that it was feasible to quantitatively assess gastric emptying with scintigraphy. The meal, "a breakfast of porridge, scrambled eggs, milk, bread and butter," was labeled with ^{51}Cr, and imaging was done with a rectilinear scanner immediately after the meal had been consumed and at half-hour intervals. Since then, the methodology has evolved, with at least 1,814 papers having been published on gastric emptying scintigraphy (GES) at the time this article was being prepared.

A major area of variability in the reported studies has been the composition of the standard meal. Several different types of standard meals have been proposed. Concern has been raised that unless all subjects eat the same meal, results could vary significantly, which would make interpretation of the results more difficult or impossible. The reality is that the emptying times for most of the proposed standard meals are very similar and minor differences are indistinguishable because of the large physiologic variation between individuals. This was illustrated in a study by Tougas et al., in which a low-fat egg-based meal was compared against a high-fat liver-based meal (*3*). Their conclusion was, "There are no data to indicate that using a meal incorporating an egg or an egg substitute is superior to using a meal incorporating liver as a screening test for delayed gastric emptying."

Although it may not matter whether eggs or chopped liver is used in the meal, the caloric content definitely makes a difference. Lobo et al. looked at gastric emptying of a meal consisting of a single pancake and 100 mL of water compared with a meal of 2 pancakes and a strawberry milkshake (*4*). The half-time for emptying was more than twice as long for the larger meal.

This difference certainly suggests that it is inappropriate to allow complete freedom in meal selection and that some degree of standardization is necessary, at least ensuring that the caloric content of all meals is similar. Standardization allows comparison of results between centers and the use of normal standards for half-time and percentage emptying.

In 2008, a true standard was proposed in "Consensus Recommendations for Gastric Emptying Scintigraphy: A Joint Report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine" (*5*). The meal proposed in these recommendations is that used for many of the published studies, including the one by Tougas et al. (*3*), which is the largest published study in terms of subject numbers.

The proposed standard meal consists of egg white from 2 large eggs, 2 slices of white bread, 30 g of strawberry jam, and 120 mL of water. The egg white is mixed with 18.5–37 MBq (0.5–1.0 mCi) of ^{99m}Tc-sulfur colloid and then scrambled. The scrambled eggs, along with the jam, is placed between the bread slices to form a sandwich.

Various other aspects occur in practice that introduce significant variability into the test. The most common problem is that the subject does not eat the entire meal. If that happens, it is likely that gastric emptying will be more rapid than if the entire meal had been eaten. Other common circumstances that can influence gastric emptying are medications, smoking, posture during the test, and general well-being (a mild viral illness will slow gastric emptying). Accordingly, it is important to note how much of the meal was consumed, although there is no standard method to correct for partial meal consumption. Subjects should be advised not to smoke on the day of the study, and imaging should be done in a

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standardized manner, that is, with the subject standing or lying supine during imaging and sitting in a chair or walking around between images.

Although there has been agreement on a standardized approach for gastric emptying, in actual practice there continues to be moderate variability in many of the technical details because of continuation of past practices and following of preferences at many sites. In general, as long as there is local standardization and interpretation of results, it is likely that the results will be clinically useful. For instance, at the University of Iowa, we omit the jam from the standard meal and image patients supine. Patients are allowed to walk or sit between images. Both anterior and posterior images are acquired, and counts over the stomach are combined using geometric averaging. The locally generated normal emptying curves almost exactly match the published curves.

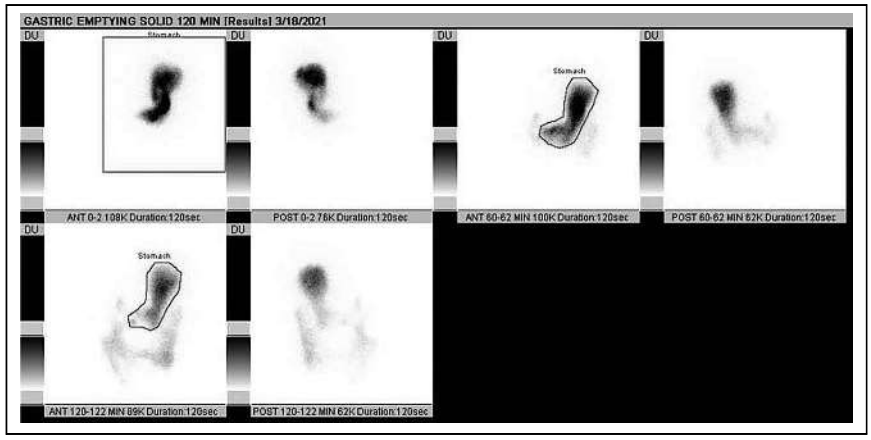

FIGURE 1. γ-camera images and regions of interest of gastric emptying study. At top left are anterior and posterior images of stomach just after intake of radiolabeled meal. Large region of interest is always used on first image to contain all activity ingested. Subsequent regions of interest are drawn to conform to stomach. Images at top right were obtained 1 h after meal intake. Images at bottom show retention of meal after 2 h. Regions of interest are mirrored and applied to posterior images. Anterior and posterior counts are averaged using geometric mean, and count is decay-corrected to beginning of emptying.

Although we have been conducting 2–3 gastric emptying studies per day for decades at the University of Iowa, we have been unaware of the impact of these studies on patient management. The study reported here was a determination of changes in management that have occurred in response to our reports of abnormally slow gastric emptying.

MATERIALS AND METHODS

This retrospective study was performed at a single institution, the University of Iowa Hospitals and Clinics, and was approved by the Institutional Review Board, which waived the need for informed consent. Electronic medical records were accessed for 510 patients (age range, 17–84 y; median age, 52 y). The exclusion criteria were normal or rapid gastric emptying results on GES. The only inclusion criterion was the diagnosis of slow gastric emptying (half-time > 2 h, <40% emptying at 2 h, or <90% emptying after 4 h). Parameters that were recorded and included in the data analysis included sex, age, symptoms, body mass index, presence of diabetes, and the date and type of any change in management.

All patients received the same meal: 2 scrambled eggs mixed with 37 MBq (1 mCi) of ^{99m}Tc-sulfur colloid before cooking, along with a slice of toast and 120 mL of water. Anterior and posterior γ-camera imaging was done immediately after the meal had been eaten and at 1 and 2 h later (Fig. 1). The patients lay supine during the imaging and sat in a chair between images. Geometric means of the anterior and posterior counts were calculated and corrected for radionuclide decay. The results were assessed by comparison to standard curves for solid gastric emptying, similar to plots shown by Hansrod et al. (*6*)

RESULTS

Of the 510 patients analyzed, 100 (19.6%) had slow gastric emptying (Fig. 2). Their mean age was 56 y (range, 17–84 y).

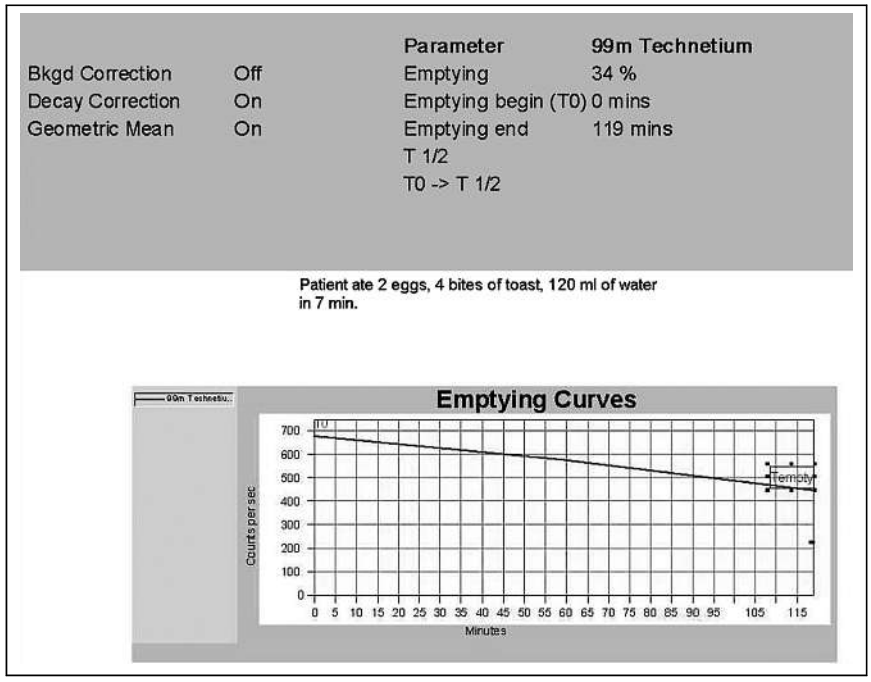

FIGURE 2. Typical slow gastric emptying curve (time points at 0, 60, and 120 min). Analysis was done using esoft software (Siemens). T 1/2 = half-time.

TABLE 1
Change in Management in Patients with Slow Gastric Emptying

Recommendation given for…	Patients (*n*)
Any change in management	62 (62%)
Nutrition education only	41 (41%)
Medication only	10 (10%)
Medication and nutrition education	6 (6%)
Intervention	4 (4%)
Imaging	1 (1%)

There were 22 male patients and 78 female patients; 88% had 2 or more symptoms of gastroparesis (nausea/vomiting, fullness/early satiety, bloating/distension, and upper abdominal discomfort/pain) for over 2 mo. A change in clinical management was recommended for 62% of the patients within 1 mo of diagnosis (Table 1). Nutritional counseling (41%) and medication changes (10%) were the 2 most common recommendations, with prokinetics (e.g., metoclopramide) and cholinergics (e.g., bethanechol) being the medications added most often. Weight loss, gastric pacemakers, endoscopic or surgical procedures, and psychologic interventions were some of the other recommendations for these patients. Change in clinical management did not significantly differ between diabetic (64%) and nondiabetic (60%) patients or between obese (65%) and nonobese (59%) patients (Table 2).

DISCUSSION

Disorders of gastrointestinal transit and motility are common, causing either slow or rapid transit through the stomach, small intestine, or colon and affecting one or more regions of the gastrointestinal system. Although current knowledge of the mechanisms responsible for slow gastric emptying is limited, it is clear that gastroparesis arises from a spectrum of motor dysfunctions. Clinical symptoms are insufficient to make a diagnosis; therefore, objective measurement is required for the diagnosis of gastroparesis. Scintigraphic measurement of gastric emptying is at present the gold standard for establishing the diagnosis, although other techniques, such as radioisotopic breath tests and ultrasound, show considerable promise (*7*). Assessment of regional or whole-gut transit times can also provide direct measurements and diagnostic information to explain the etiology of symptoms and plan therapy (*8*).

TABLE 2
Patient Distribution by Body Mass Index

Body mass index	Patients (*n*)	Change recommended (*n*)
<18.5 (underweight)	4	1 (25%)
18.5–24.9 (normal weight)	29	17 (37%)
25–30 (overweight)	20	13 (39%)
>30 (obese)	47	31 (40%)

Gastroparesis can be idiopathic or diabetic in origin, with little difference seen in their presentations. Patients with suspected gastroparesis often report symptoms referable to other sources of motility impairment in the stomach and extragastric regions. Gastroparesis is a heterogeneous disorder; its etiology affects symptoms and severity. Long-term studies are needed to determine whether the differences in symptoms and gastric emptying affect progression and treatment response. Symptoms attributed to the gastroduodenal region represent one of the main subgroups among functional gastrointestinal disorders.

A slightly modified classification into 4 categories has been proposed (*9*). The first, functional dyspepsia, is characterized by one or more of the following symptoms if unexplainable after a routine clinical evaluation: postprandial fullness, early satiation, epigastric pain, and epigastric burning. This category includes 2 subgroups: postprandial distress syndrome, which is characterized by meal-induced dyspeptic symptoms, and epigastric pain syndrome, which does not occur exclusively postprandially; these subgroups can overlap. The second category, belching disorders, defined as audible escapes of air from the esophagus or stomach, is classified into 2 subgroups—gastric belch and supragastric (or esophageal) belch—depending on the origin of the refluxed air as detected by intraluminal impedance measurement. The third category, nausea and vomiting disorders, includes 3 subgroups: chronic nausea and vomiting syndrome, cyclic vomiting syndrome, and cannabinoid hyperemesis syndrome (caused by long-term cannabis use). The fourth category, rumination syndrome, is characterized by effortless regurgitation of most meals after consumption.

Symptoms due to rapid gastric emptying are often indistinguishable from those of gastroparesis; hence, it is important to differentiate the two to correctly identify the etiology and treat the patient appropriately. A range of treatments has been used for gastroparesis, including dietary modifications, nutritional supplements, medications to stimulate gastric motility, antiemetic drugs, endoscopic or surgical procedures, and psychologic interventions. Most treatments have not been subjected to controlled testing in patients with gastroparesis. Active ongoing research is providing important insights into the pathogenesis, diagnosis, treatment, and outcomes of this disease (*10*).

Patients with gastroparesis often have other comorbidities, including obesity and diabetes. Most patients with slow gastric emptying were recommended to receive nutrition education, which primarily included the recommendation to eat 4–6 small meals, decrease fiber and fat in the diet, and increase protein intake. These patients were encouraged to increase consumption of vitamins and other nutrients in a smoothie-consistency meal. Patients with a high body mass index were encouraged to lose weight. Some patients who were already on a gastroparesis diet were started on metoclopramide (which speeds gastric emptying), taken 15–20 min before meals at least 3 times a day. Patients for whom gastroparesis treatment was not

recommended were often those found to have serious comorbidities, including cardiac failure, a severe eating disorder, and diabetic neuropathy. All of these needed urgent treatment.

In this retrospective study, we used the electronic medical records to analyze and track management of each patient who was reported to have slow gastric emptying on GES testing. Information obtained from medical records can be variable, but generally the case notes showed the clinician's reason for referring a patient and gave reliable clues to any changes in management. We are aware, however, that the results derived from this study alone may not form a basis to draw firm conclusions about any specific management recommendations for patients with gastroparesis on GES testing. A more structured characterization of management recommendations is provided by previous studies that prospectively compared how GES and wireless motility capsule testing inform recommendations for treatments and additional diagnostic evaluations (*11*).

CONCLUSION

Gastroparesis is a disorder that is heterogeneous not only in symptoms but also in severity. Clinical symptoms such as nausea, vomiting, fullness, early satiety, bloating, distension, or upper abdominal pain are not reliable for the diagnosis of gastroparesis, as some of these symptoms can also be due to rapid gastric emptying. GES is the gold standard for diagnosis of gastroparesis. A diagnosis of gastroparesis by GES resulted in a change in clinical management in 62% of such patients in our study, thus illustrating the importance of performing GES on patients with clinically suspected gastroparesis.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Does a slow gastric emptying on GES study change clinical managment?

PERTINENT FINDINGS: Symptoms of rapid gastric emptying and gastroparesis are similar; therefore, differentiating the two is important for proper treatment determination.

IMPLICATIONS FOR PATIENT CARE: Depending on the clinical diagnosis, patients with gastroparesis can be managed by surgery, medication, or conservatively with alterations in diet.

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Universal Fasting Glucose Screening Before Gastric Emptying Scintigraphy and the High Prevalence of Undiagnosed Diabetes and Prediabetes

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The aim of this study was to assess the rates of undiagnosed diabetes mellitus (DM) and pre-DM in patients undergoing gastric emptying scintigraphy (GES). Diabetes is an epidemic in the United States, and the disease is associated with altered gut motility. As a result, we suspected that a significant number of patients referred for GES may have undiagnosed DM or pre-DM. Given that established procedure standards for GES require all patients to prepare with an 8-h fast, an opportunity is provided to measure the fasting blood glucose (FBG) in all individuals before they undergo the examination. **Methods:** The charts of patients undergoing GES were reviewed for a history of DM and correlated with FBG and GES results. FBG values, obtained by point-of-care testing, were categorized as normal, pre-DM, or DM. **Results:** Patients with known DM made up 23% of those referred for GES, and most (55%) had a normal FBG. In those without a history of DM, there were a significant number with undiagnosed pre-DM (12%) and DM (33%). **Conclusion:** Our study provides the first measure of the likely prevalence of undiagnosed DM and pre-DM and characterizes the different gastric emptying patterns among patients with normal FBG, likely undiagnosed pre-DM, likely undiagnosed DM, and known DM.

Key Words: quality assurance; diabetes; fasting plasma glucose; gastric emptying scintigraphy; gastroparesis; prediabetes

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The diabetes mellitus (DM) epidemic in America is a public health crisis with projections that indicate a continual rise in the coming years (*1*). Further amplifying the issue is the staggering one third of the total DM population who are undiagnosed and hence untreated (*2*). The burden of DM is particularly high in certain ethnic groups, such as South Asians living in America, who have a higher prevalence of DM than others (*3*). Complications associated with DM, including retinopathy, nephropathy, cardiomyopathy, neuropathy, and atherosclerosis, contribute to significant morbidity, mortality, and cost to health care.

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Efforts to manage and prevent DM through early identification of pre-DM are routine. The fasting blood glucose (FBG) measured before the start of a gastric emptying scintigraphy (GES) examination is an opportunity to lessen the burden on patients and society.

MATERIALS AND METHODS

Under approval by the institutional review board, we conducted a retrospective chart review of all patients undergoing GES from January 2019 to June 2021 ($n = 260$). The demographics of the studied population were unique to the diverse group of U.S. military beneficiaries comprising active-duty soldiers, family-member dependents, and veterans. From this initial query, 251 met the inclusion criteria for the study. Each patient's chart was reviewed for a history of DM and correlated with FBG and GES results. FBG values, obtained by point-of-care testing (StatStrip; Nova Biomedical), were categorized as normal, concerning for pre-DM, or concerning for DM on the basis of the diagnostic criteria defined by the American Diabetes Association (*4*). GES was performed in accordance with established procedure standards of the Society of Nuclear Medicine and Molecular Imaging and with international accreditation committee guidelines (*5*,*6*). Patients with DM were not categorized by type.

RESULTS

Patients with known DM made up 23% of those referred for GES, and most (55%) had a normal FBG. In those without a history of DM, there were a significant number with likely undiagnosed pre-DM (12%) and DM (33%) (Tables 1 and 2; Fig. 1).

Approximately half the patients who underwent GES had abnormal results (53%). A higher proportion of those with likely undiagnosed DM than with likely undiagnosed pre-DM had abnormal GES results (75% vs. 50%). Among those with undiagnosed pre-DM and DM, rapid emptying studies were more common than delayed emptying studies. Likely undiagnosed DM patients had an average FBG of 166 mg/dL with a maximum FBG of 263 mg/dL. There were 5 undiagnosed patients with an FBG of more than 200 mg/dL, which exceeds the recommend cutoff for GES as defined by the Society of Nuclear Medicine and Molecular Imaging guidelines.

DISCUSSION

The clinical impact of FBG before GES is twofold. In patients with normal gastric emptying results, FBG can be

TABLE 1
GES Results Based on DM Status

GES result	Diagnosed DM	Undiagnosed DM	Undiagnosed pre-DM	No DM	All
Normal	23 (40%)	6 (25%)	32 (50%)	58 (55%)	119 (47%)
Abnormal	34 (60%)	18 (75%)	32 (50%)	48 (45%)	132 (53%)
Total	57 (23%)	24 (10%)	64 (25%)	106 (42%)	251

used to screen DM or pre-DM. And for those with abnormal gastric emptying results, FBG can be used to characterize the patient's delayed GES as likely DM or pre-DM gastroparesis rather than idiopathic. The impact of these findings is significant given the high volume of GES examinations performed each year.

Public Health Impact

A significant number of patients referred for GES likely have undiagnosed pre-DM or DM (45%). This statistic is not surprising given that an estimated third of all patients with DM in the United States are undiagnosed and that DM is the number one cause of gastroparesis. The potential clinical impact of detecting these cases of undiagnosed DM or pre-DM is significant given the large volume of GES procedures performed across the country. A 2021 nationwide survey reported that the average nuclear medicine clinic performed about 200 GES procedures per year, with large academic centers performing up to 2,000 annually. These numbers were limited to just 121 of 872 potential medical institutions who responded to the survey (*7*).

Improved Accuracy of Fasting Plasma Glucose (FPG) Compared with Hemoglobin A1C (HbA1c) When Screening for DM or Pre-DM

The use of FPG as a screening test will improve detection of pre-DM or DM in patients who have already been screened. Many patients referred for GES will have already been screened for DM with the less sensitive test HbA1c instead of the more sensitive FPG or 2-h oral glucose tolerance test. HbA1c is more commonly ordered because of its greater convenience (no fasting required) and performance as a marker of chronic hyperglycemia; however, its sensitivity is poor and differs between ethnicities. HbA1c will diagnose only 30% of cases, many of which would have been detected by FPG. The glucose tolerance test is an alternative screening and diagnostic test. This test is uncommonly ordered because of its logistic barriers but is the most sensitive for both pre-DM and DM, outperforming FPG and HbA1c (*2*,*8*). Collectively, each of these tests can categorize patients into normal, pre-DM, or DM status but evaluates different pathophysiologic processes within the broader diagnosis of dysglycemia. Abnormal FPG denotes impaired fasting glucose with a primary deficiency in insulin secretion. In contrast, an abnormal 2-h oral glucose tolerance test reflects impaired glucose tolerance from abnormal insulin resistance (*9*).

A review of the current literature on our studied population within the military health system reveals similar findings. Although our study included family members and retirees, poor screening practices among those on active duty within the U.S. military across all branches presents an opportunity for an even greater clinical impact. Clutter et al. reported that roughly 50% of all service members met criteria for screening (>45 y old or 18–25 y old with a body mass index $> 25\ kg/m^2$) but only 6% were screened (*10*).

More Accurate Identification of DM or Pre-DM Gastroparesis

The high rates of undiagnosed pre-DM or DM result in significant clinical implications due to potential mischaracterization of the type of gastroparesis. If patients referred for GES have already been screened with HbA1c and the results were negative, then an abnormal GES may not be properly attributed to diabetic gastroparesis. Instead, the patient's delayed gastric emptying may be labeled as idiopathic gastroparesis, which has an extensive list of potential causes, including medications, infectious disorders, autoimmune disorders, neurodegenerative disorders, and other functional gastrointestinal disorders (*11*).

Rapid Gastric Emptying as an Early Indicator of Pre-DM

Multiple studies have shown a potential relationship between rapid gastric emptying and early type 2 DM. It is possible that rapid gastric emptying may be one of the earliest indicators of abnormal postprandial hyperglycemia before abnormal screening by FPG, glucose tolerance testing, or HbA1c. Our results demonstrate a significant number of patients with rapid gastric emptying and normal FBG, and it is

TABLE 2
Distribution of Abnormal GES Results Based on Diagnosis of DM Vs. FBG in Non-DM Patients

		No history of DM			
Abnormal GES result	Known DM	FBG > 125 mg/dL	FBG of 100–125 mg/dL	FBG < 100 mg/dL	All
Delayed	15 (24%)	7 (11%)	13 (21%)	27 (44%)	62 (47%)
Rapid	15 (24%)	10 (18%)	16 (27%)	18 (31%)	59 (45%)
Both	4 (12%)	1 (6%)	3 (3%)	3 (6%)	11 (8%)

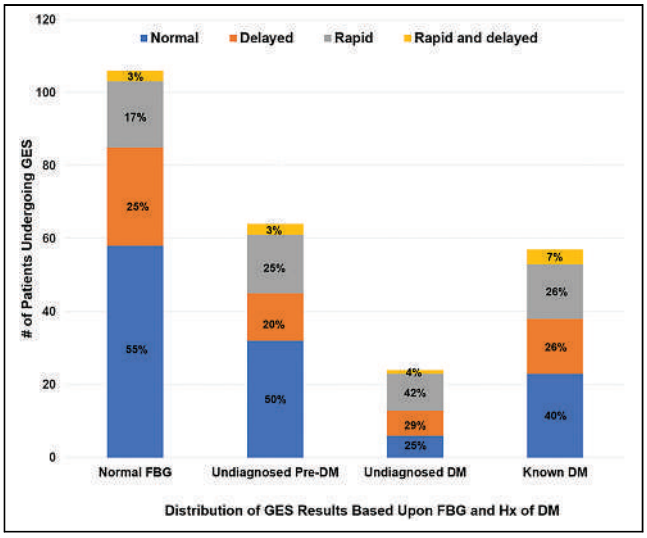

FIGURE 1. Distribution of GES results based on FBG and whether patient had history of DM.

possible that this subgroup of patients may progress to pre-DM and should be monitored (*12*).

Implementation of Routine FBG Before GES

Preimaging FBG is built into the standard workflow of GES at our institution and presents an opportunity to screen for DM or pre-DM in patients referred for suspected gastroparesis. Our results suggest that nuclear medicine imaging centers should routinely perform FBG before GES and, more importantly, document the results in the impression. This should be considered in addition to the reporting recommendations in the GES guidelines. Language such as "FBG of X is concerning for DM or pre-DM and warrants further testing with FPG or a 2-h oral glucose tolerance test to confirm" should be used. Unfortunately, long-standing poor adherence to current GES procedure standards suggests a significant barrier to implementation (*13*).

CONCLUSION

This study highlights the diagnostic implications of undiagnosed DM or pre-DM in patients referred for GES detected through FBG screening. The high prevalence of likely undiagnosed DM or pre-DM in this population emphasizes the need for early detection and intervention. The identification of impaired fasting glucose during GES not only allows for the identification of likely DM or pre-DM but also provides insights into the underlying causes of delayed gastric emptying, allowing for differentiation of DM or pre-DM gastroparesis from idiopathic gastroparesis. The public health impact of screening for undiagnosed DM or pre-DM in patients referred for GES is significant, given the large volume of GES procedures performed annually. Additionally, the use of FBG as a screening test improves the accuracy of DM or pre-DM detection compared with HbA1c, and the necessary preparation is already built into the standardized workflow for GES as recommended by societal guidelines. Furthermore, the high prevalence of rapid gastric emptying in patients with normal FBG may serve as an early indicator of pre-DM in certain high-prevalence populations. Implementing routine FBG assessment before GES can aid in the early identification and management of DM or pre-DM and diabetic gastroparesis.

DISCLOSURE

No potential conflict of interest relevant to this article was reported. The Department of Defense and Defense Health Agency do not necessarily endorse, support, sanction, encourage, verify, or agree with the comments, opinions, or statements contained herein.

KEY POINTS

QUESTION: What are the rates of undiagnosed pre-DM and DM in patients undergoing GES?

PERTINENT FINDINGS: 45% of patients undergoing GES had FBG concerning for undiagnosed DM or pre-DM.

IMPLICATIONS FOR PATIENT CARE: The implementation of universal FBG for all patients undergoing GES provides an excellent opportunity to screen for a prevalent and debilitating disease that remains markedly underdiagnosed and undertreated.

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Gastric Emptying Solid-Meal Content and Misinformation on Social Media Platforms

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Several nuclear medicine technologist–specific groups exist on social media sites such as Facebook and LinkedIn. Although these sites provide a valuable resource and forum for technologists to interact and pose questions, any recommendations, especially those regarding patient care, should be carefully scrutinized and evaluated on the basis of scientific merit and not opinion. Recently, an assortment of unvalidated ingredients for solid-meal gastric emptying scintigraphy has been suggested on these social media sites. Often, these ingredients do not comply with the peer-reviewed guidelines and can potentially produce unreliable results and misdiagnosis. Thus, before implementing advice from an unvetted source, technologists must distinguish between low- and high-quality information. Currency, reliability, authority, and purpose—a test of the trustworthiness of an information source—can help technologists evaluate recommendations and avoid the use of unsupported solid-meal gastric emptying scintigraphy ingredients.

Key Words: gastric emptying scintigraphy; guidelines; compliance; social media

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Marie Curie once famously said, "If it's on the Internet, it must be true." Okay, you caught us; we are lying. Madame Curie did not say that. If the Internet had been in existence in Curie's time, she might have said something such as, "Don't believe everything you read on social media" (Fig. 1). Just because something is on the Internet or social media does not mean it is necessarily true. However, some nuclear medicine technologists seem to think that information and opinions posted on social media can be trusted. We are here to debunk that notion.

Several nuclear medicine technologist–specific groups exist on sites such as Facebook (Meta Platforms, Inc.), LinkedIn (Microsoft Corp.), and X (formerly Twitter; X Corp.). These groups are a valuable resource and forum for technologists to interact and pose questions to their peers (*1*). However, those asking the questions should remember that any response or recommendation related to imaging techniques, especially those affecting patient care, should be scrutinized and evaluated on the basis of scientific merit instead of opinion.

Over the past few years, several technologists have posted questions about gastric emptying scintigraphy (GES) solid-meal ingredients. As expected, many obliging technologists shared the gastric emptying meal currently used at their laboratory.

Unfortunately, many of the recommended meal ingredients are eyebrow-raising and observably not compliant with the standardized meal prescribed in the Society of Nuclear Medicine and Molecular Imaging (SNMMI) procedure guideline (*2*). A casual review of one social media group over the past year revealed a wide range of recommended solid GES meals: oatmeal, grits, Egg McMuffin or breakfast biscuit (McDonald's Corp.), egg salad sandwich, whole eggs, chicken salad sandwich, hard-boiled eggs, turkey sandwich, precooked scrambled eggs (from cafeteria), peanut butter and jelly sandwich, plant-based eggs, tofu, pancakes/French toast, rice *idli* (optional 10 mL of maple syrup), applesauce, cottage cheese, meatballs, mashed potatoes with or without butter, pizza, Dinty Moore beef stew (Hormel Foods Corp.), Kraft Mac and Cheese (Kraft Heinz Co.), and "Whatever the patient wants to bring."

WHAT IS THE BIG DEAL?

What is the big deal, you ask? GES meal composition and preparation method are two of the most critical variables affecting GES accuracy and reproducibility (*3*). First, meal composition, specifically volume, caloric content, and fat content, significantly affects the rate at which material empties from the stomach. For example, liquids, proteins, and carbohydrates empty more quickly than solids, fiber, and fats (*4–7*).

The established reference values for solid GES are based on the standardized meal described in Figure 2 (*2*). Note that the reference emptying values are based on the precise volume, caloric content, and fat content of this meal. Thus, the results of a solid-meal gastric emptying study deviating from this standardized meal may not be valid. Depending on their specific meal, laboratories using differing meal contents must establish their own reference values in healthy patients.

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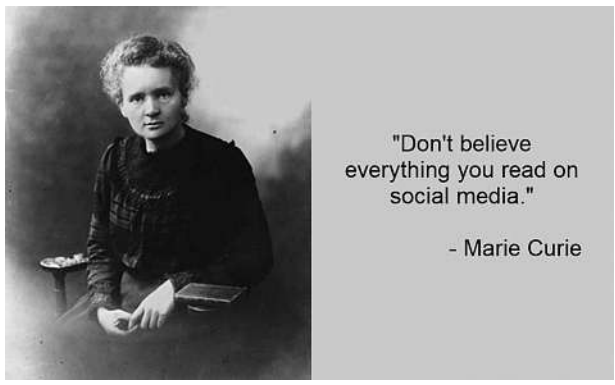

FIGURE 1. Marie Curie, the first woman to receive a Nobel prize (for her research on radioactivity), was a brilliant scientist and would have investigated the veracity of recommendations posted on social media.

Second, the egg preparation method also affects the results of GES. The standardized meal dictates the use of liquid egg whites (e.g., Egg Beaters; Bob Evans Farms, LLC) for a good reason. Liquid egg whites cooked with ^{99m}Tc-sulfur colloid (SC) form a bond with the protein component (i.e., egg white albumin) from denaturing caused by heat (*8*). The binding of ^{99m}Tc-SC to the egg white produces a stable solid that can be tracked through the gastrointestinal system.

If the tracer is not firmly bound to the protein and separates, the emptying rate will vary because the meal is no longer a solid meal but partly liquid. Thus, attempts to radiolabel—such as squirting ^{99m}Tc-SC on previously cooked scrambled eggs or a peanut butter sandwich—that do not firmly attach the tracer to a protein by heat will produce inaccurate results because the tracer does not remain associated with the solid material. Consequently, if the ^{99m}Tc-SC is not bound to the egg whites, the study is basically a liquid gastric emptying study, in which liquid empties from the stomach more quickly. The normal gastric emptying time for a liquid is 30 min, compared with less than 10% of the solid meal left in the stomach at 4 h.

Standardized Solid Gastric Emptying Meal

- 18.5 - 37 MBq (0.5-1 mCi) ^{99m}Tc-sulfur colloid
- 118 mL (4 oz) liquid egg whites (e.g., Eggbeaters (ConAgra Foods, Inc))
- 2 slices of toasted white bread
- 30 g of jam or jelly
- 120 mL of water

To prepare: add the ^{99m}Tc-sulfur colloid to the liquid egg whites and beat well. Cook in a microwave or nonstick skillet, stirring once or twice during cooking, until firm texture.

FIGURE 2. Accuracy and reproducibility of gastric emptying study require strict adherence to SNMMI standardized protocol and meal. If different ingredients or preparation methods are used, reference values cited in GES guideline (*2*) cannot be used.

WHAT ARE OTHER LABORATORIES DOING?

Unfortunately, lack of compliance with the standardized SNMMI gastric emptying meal components is fairly common. A 2023 study by Tafti et al. examining the GES protocols from 118 laboratories found that only 62% of laboratories followed the exact standardized meal content and preparation (*9*). The good news is that the percentage is up from 31% in 2017.

Of those not using the standardized meal, 23% used whole eggs, which is problematic because ^{99m}Tc-SC does not bind to egg yolk. In addition, because egg yolk contains more fat than egg whites, gastric emptying can be artificially delayed. Tafti et al. also found that 6% of laboratories added other ingredients such as butter or peaches, further varying the caloric content, and 3% used inappropriate meals such as tuna sandwiches, peanut butter and jelly sandwiches, beef stew, or "the patient's favorite meal."

WHY DO LABORATORIES NOT USE THE GUIDELINE MEAL?

The next logical question is, "Why do laboratories not use the guideline meal?" The reason is not simply because people are lazy; the answer to that question is multifactorial. First, there are nonspecific reasons. For example, a laboratory may not be aware of the SNMMI procedure guideline (*2*). A study by Cabana et al. found a low rate of guideline awareness, in general, across medicine (*10*). Thus, it is unsurprising that some technologists and physicians may not know about the GES guideline, even though it was published in 2009. Additionally, even if a laboratory is aware of a guideline, it may not be familiar with the specific details or be able to apply them correctly.

Another barrier to guideline adoption is a lack of agreement. A laboratory protocol decision-maker may not agree with a specific guideline or parts of the guideline. Finally, inertia may be a factor in guideline adoption. We all know that change is difficult. In the Cabana et al. study, more than 20% of respondents reported inertia as a barrier to guideline adherence.

In addition to these general reasons, there are several specific reasons laboratories do not comply with the GES guideline. First, patients may require an alternate GES meal because of an egg allergy or gluten intolerance. Obviously, in these cases, the recommended standardized GES meal cannot be used. Similarly, patient preferences and lifestyle choices can affect willingness to consume the recommended meal. For example, the standardized meal will not work well with patients following vegan, keto, or Mediterranean diets and the run-of-the-mill picky eaters who hate eggs.

Another reason laboratories may not be able to comply with GES guidelines is a lack of equipment, such as microwaves, toasters, or refrigerators, necessary for radiolabeled egg preparation. Anecdotally, there have been reports of accreditation and state inspectors questioning how a technologist determines whether the radiolabeled eggs are thoroughly cooked (e.g., >170°) to prevent *Salmonella* or food poisoning (*11*). Several technologists have been told they must have food handler training (check state regulations, but food handler courses are relatively easy to obtain online). Finally, some technologists mistakenly believe radiolabeled egg preparation falls under the U.S. Pharmacopeia general chapter <825> regulations, which their laboratory may be unable to meet (*12*).

WHAT IS A NUCLEAR MEDICINE TECHNOLOGIST TO BELIEVE?

Distinguishing between low- and high-quality information on social media platforms can be challenging. And as we have preached, misinformation—defined as information that conflicts with the best scientific evidence available at the time—is plentiful (*13*). Therefore, we recommend using currency, reliability, authority, and purpose (CRAP) as a test to evaluate source trustworthiness (*14*).

Currency refers to the timeliness of the information. When was the information posted? *Reliability* relates to the accuracy of the information. Does the post include citations or references? Is the information linked to credible, peer-reviewed sources? Is the science sound? *Authority* is the source of the information. Who is the author of the information, and what are the author's credentials? Is the author qualified to direct patient care? Finally, *purpose* is the reason the information exists. Does the author seem to be pushing an agenda? Is the purpose of the post to sell, persuade, entertain, or inform? Is there any evidence of bias?

Let us apply the CRAP test to a real-life social media post. Earlier this year, a technologist queried an online nuclear medicine technologist group about acceptable solid-meal alternatives for a patient allergic to eggs. One person responded that macaroni and cheese could be substituted for the egg whites and referenced a 2020 article in the *Journal of Nuclear Medicine Technology*.

On face value, the recommendation might seem sound. The article was timely, having been published in 2020 (currency). The post referenced the *Journal of Nuclear Medicine Technology,* which is credible and peer-reviewed (reliability). Two nuclear medicine students wrote the cited reference (authority), and there was no bias from the social media poster (purpose). However, on further inspection of the reference, it was not a scientific research article but an abstract from the SNMMI annual meeting and, therefore, not peer-reviewed. Furthermore, the students' study included only 7 patients and compared the macaroni and cheese meal to 2 whole eggs and buttered toast. The students concluded that the emptying percentages did not vary between the 2 meals and fell within the reference limits specified by the SNMMI. These study results are problematic for 3 reasons: the small size of the sample, the comparison of macaroni and cheese to whole eggs and not the egg white standardized meal, and application of reference values from the standardized meal to a divergent meal.

The purpose of presenting this example is not to shame the students (we thought they were creative and look forward to reading their follow-up study). The aim is to show how recommendations found on social media must be scrutinized. In this case, the social media post appeared to satisfy the CRAP test parameters. However, on further inspection, the recommendation lacked reliability and authority.

CONCLUSION

Social media is a valuable tool that allows nuclear medicine technologists to network and learn from their peers. Social media content travels quickly, freely, and far. Technologists must recognize that most of the information found on social media is unvetted; thus, they must view it cautiously. Before implementing any suggestions from social media, especially if it involves changes to imaging protocols or something that could affect patient care, technologists must scrutinize and investigate the information thoroughly. The burden of evaluating the credibility and validity of content falls on the user.

One final plea to readers: unless your laboratory has validated the reference values and ensured firm binding of the ^{99m}Tc-SC to atypical ingredients, please follow the standardized solid gastric emptying meal and preparation method specified in the GES guideline (*2*). Stop squirting ^{99m}Tc-SC on whatever. Special-order meals using unvalidated reference values will not deliver accurate results and will serve up a buffet of confusion and irreproducible results.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Can solid-meal GES suggestions found on social media sites be trusted?

PERTINENT FINDINGS: Although social media sites provide a valuable resource and forum for technologists to interact, any recommendations, especially those regarding patient care, should be carefully scrutinized and evaluated on the basis of scientific merit. The CRAP test, a method to evaluate the information source's trustworthiness, can be used to weigh social media recommendations and avoid the use of unsupported solid-meal GES ingredients.

IMPLICATIONS FOR PATIENT CARE: GES solid-meal ingredients suggested on social media are unvetted and must be scrutinized before implementation.

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The Efficacy of Radiolabeling the Albumin in Egg Whites with ^{99m}Tc-Sulfur Colloid

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In 2009, the Society of Nuclear Medicine and Molecular Imaging published a standardized protocol guideline for gastric emptying scintigraphy that contains specific instructions on the exact meal and preparation procedure. Previous research has shown that the standardized meal and proper preparation of the meal for gastric emptying scintigraphy are not being adopted by some facilities. This research explores the differences of radiolabeling in the method of preparation of ^{99m}Tc-sulfur colloid (SC)–radiolabeled eggs. **Methods:** Liquid egg whites were mixed with ^{99m}Tc-SC before cooking in conjunction with the standardized protocol. A second sample set was prepared by adding the ^{99m}Tc-SC to eggs after they were cooked. Each sample set was placed in a solution of HCl and pepsin to simulate gestation. Radiolabeling efficacy was tested on each sample set at 2 and 4 h after gestating in HCl and pepsin. **Results:** ^{99m}Tc-SC added to the liquid egg whites before microwave cooking yielded radiolabeling efficacy of 70% ^{99m}Tc-SC after 2 and 4 h of simulated gastric fluid gestation. In contrast, radiolabeling after cooking the egg whites yielded 50% radiolabeling after simulated gestation. **Conclusion:** The results from this experiment showed that the method of mixing the ^{99m}Tc-SC with liquid egg whites before microwave cooking has higher binding efficacy than when adding ^{99m}Tc-SC onto already cooked egg whites. These results highlight the importance of following the standardized protocol for the meal preparation of a gastric emptying study.

Key Words: gastrointestinal; radiopharmaceuticals; gastric emptying scintigraphy; radiolabeling; meal preparation; standardized meal

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Gastric emptying scintigraphy is the gold standard for evaluating gastric motility (*1*). The reliability of gastric emptying studies is dependent on careful adherence to the procedure guidelines, especially the standardized meal. However, previous literature has demonstrated that wide variations from the standard protocol exist (*2–4*). A common divergence from the standardized protocol is to add the ^{99m}Tc-sulfur colloid (^{99m}Tc-SC) to the egg whites after they have been cooked rather than before (*2*,*5*). This research evaluates and contrasts the radiolabeling efficacy of adding ^{99m}Tc-SC to egg whites before and after cooking.

A gastric emptying study is performed by radiolabeling the solid or liquid meal and measuring the radioactivity in the stomach for 1 min every hour up to 4 h (*1*,*5*). In 2009, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) sought to reduce any variations that may occur in the preparation of a meal for a gastric emptying study by publishing a standardized procedure guideline for solid-meal gastric emptying (*1*,*3*). The SNMMI gastric emptying study protocol contains precise instructions for patient preparation, meal ingredients and preparation, radiopharmaceutical dose, camera acquisition, and image processing (*5*). According to the gastric emptying study protocol, the meal consists of 118 mL of liquid egg whites, 2 slices of toasted white bread, 30 g of jam or jelly, and 120 mL of water (*1*,*5*). The meal preparation consists of adding 18.5–37 MBq (0.5–1 mCi) of ^{99m}Tc-SC to the eggs, which are then mixed well and cooked in a microwave oven or nonstick skillet. The eggs are stirred a couple of times during cooking until they are firm. It is essential to add the ^{99m}Tc-SC to the eggs before cooking to increase binding efficiency between the ^{99m}Tc-SC and the albumin in the eggs (*2*,*4*,*5*).

The standardized meal and meal preparation guidelines must be followed because normalized gastric emptying values depend on the contents of the meal (*4*,*5*). The emptying rate of the stomach depends on whether the meal is liquid or solid, whether it is high in fats or in carbohydrates and proteins, its digestibility and caloric density, and the amount consumed. For example, vegetables will stay in the stomach longer than foods that are more digestible (*3*), a liquid meal will empty from the stomach much more quickly than a solid meal, and a meal high in fat will stay in the stomach longer than a meal high in carbohydrates or proteins.

The standardized protocol includes instructions for preparation set by the SNMMI, but research has shown that the protocol is not always followed (*2*,*4*). Manipulating the method of preparation can result in variability, decrease comparison ability, and decrease the credibility of the gastric emptying results (*2*). In 2013–2015, the Intersocietal Accreditation Commission evaluated 129 accreditation-seeking facilities for compliance with the standardized protocol (*3*). Of those facilities, 69% were not compliant with meal preparation (*3*). Farrell et al. also noted that several nuclear medicine laboratories

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were following the standardized meal but not the preparation guidelines and were instead adding the ^{99m}Tc-SC by squirting it onto cooked eggs (*2*). Although the most recent data show that adherence to the standardized protocol has improved, variations in meal and meal preparation are still widespread (*4*).

It is also essential that the meal preparation protocol be followed to ensure complete binding of the eggs (*4*). The ^{99m}Tc-SC should be added before or during cooking of the eggs (*5*). When ^{99m}Tc-SC is cooked together with liquid egg whites, the albumin protein in the egg whites denatures because of the heat and forms a stable bond with the ^{99m}Tc-SC (*4*,*6*). However, when ^{99m}Tc-SC is added to cooked eggs, it will not have a stable bond with the egg. The result is disintegration of the tagging between the albumin and the ^{99m}Tc-SC during digestion, with at least a portion of the quantitative analysis being ^{99m}Tc-SC not bound to eggs. If the ^{99m}Tc-SC does not remain bound to the albumin, the quantitative analysis will reflect transit not of a solid meal but of a mixture of solid and liquid (*6*). It has become common practice to add ^{99m}Tc-SC to eggs after they are cooked. This research examines the labeling efficacy of ^{99m}Tc-SC added to liquid egg whites before and after cooking in a microwave oven.

MATERIALS AND METHODS

The materials and methods for this research are similar to those of previous research examining the radiolabeling efficacy for gastric emptying studies (*7*,*8*). This research was performed in the Hillsborough Community College Nuclear Medicine Technology Program laboratory under supervision. The research methods were reviewed and approved by the Nuclear Medicine Technology Program, and it was determined that Institutional Review Board approval was not needed.

TABLE 1
Materials Used for This Research

Material	Quantity
^{99m}Tc-SC	5.92 MBq (160 μCi)
1% bovine serum albumin	0.5 mL
NaCl	15 mL
HCl and pepsin	3.5 mL
Distilled water	50 mL
Sterile gauze pack	1
Test tubes	24
Test tube rack	1
1,000-mL beakers	2
Hot plate with stirrer	1
Food scale	1
3-mL syringes	12
Liquid egg whites	118 mL
Paper cup	2
Square disposable plastic scale-tray	2
Metal laboratory spatula	1
Foam cup	2
Microwave	1
Dose calibrator	1
Well counter	1
Survey meter	1

Several materials were used for this research (Table 1). The ^{99m}Tc-SC was purchased from a licensed radiopharmacy following radiation safety guidelines and department protocol. A survey meter was used to measure the package before it was opened. A dose calibrator was used to measure the dose before it was added to the egg whites, which were transferred to foam cups for cooking in the microwave oven. A metal laboratory spatula was used to chop the egg whites and transfer them to the test tubes after they had been weighed. A square disposable plastic scale-tray was used to weigh the egg whites on the food scale. NaCl, HCl, pepsin, and distilled water were used to simulate the environment inside the human stomach (Fig. 1). A hot plate with a stirrer was used to warm distilled water inside a beaker, within which the test tubes were submerged. Bovine serum albumin, gauze, syringes, and NaCl were used to separate the simulated gastric fluids from the egg whites. A well counter was used to measure the radioactivity in each sample.

The method to determine radiolabeling efficacy used a simulated digestion process applied in previous research examining radiolabeling for gastric emptying studies (*7*,*8*). Two radiolabeling methods were used to tag the radiotracer to the egg whites. Egg whites for each sample were measured to 118 mL in a beaker and transferred to a foam cup for both preparation methods. For the precooking method, 2.59 MBq (70 μCi) of ^{99m}Tc-SC were added to the egg whites and mixed well before they were cooked in the microwave. For the postcooking method, 3.1 MBq (84 μCi) of

FIGURE 1. Materials used to simulate gastric environment and examine radiolabeling: simulated gastric fluid with HCl and pepsin. Bovine serum albumin was used to evaluate radiolabeling efficacy.

FIGURE 2. Twelve test tubes with radiolabeled cooked egg whites separated from simulated gastric fluid.

^{99m}Tc-SC were added to the egg whites after they were cooked in the microwave. For both methods, the egg whites were cooked to a firm consistency on high for 50 s, stirred for 5 s, and then cooked on high for another 15 s to ensure thorough cooking.

Two digestive processes inside the stomach had to be simulated: mechanical and chemical (*9*). After the egg whites had been cooked and allowed to cool for 10 min, they were chopped into small pieces with a metal laboratory spatula to mimic the mechanical process of chewing. Half of the 12 test tubes were labeled "precooked" and the other half "postcooked." Three test tubes in each set were labeled "2 h," and the other 3 were labeled "4 h." Both sets were then placed into square disposable plastic scale-trays, and 0.5-g samples were weighed out on a food scale and placed into each test tube.

During the chemical process, HCl and pepsin help break the food down to the macronutrients (*7*,*8*). To simulate the environment inside a human stomach, 3.5 mL of HCl and pepsin, 15 mL of NaCl, and 50 mL of distilled water were added to the egg whites in the test tubes, which were then placed in a water bath at 98.6°F to simulate the internal temperature of the human body. Stirrers at 125 rpm were used to simulate churning in the stomach. One timer was set for 2 h and another for 4 h, at which times the tubes were removed from the water bath.

Sterile gauze was moistened with 1% bovine serum albumin to prevent ^{99m}Tc-SC from sticking to the gauze (*7*,*8*). The gauze was then folded and packed into the tubes so that the simulated gastric fluid rose above it. The simulated gastric fluid was then removed from the egg whites using a 3-mL syringe (Fig. 2) and transferred to another test tube, leaving just the egg whites tagged with the radiotracer. The egg whites were rinsed with 1 mL of NaCl, which was then filtered out and added to the simulated gastric fluid.

TABLE 2
Radiolabeling Efficacy Results for Precooked Sample

Time	Simulated gastric fluid	Precooked egg whites	Radiolabeling efficacy
2 h	5,784	12,656	(12,656/18,440) × 100 = 69%
	5,676	12,689	(12,689/18,365) × 100 = 69%
	5,974	12,679	(12,679/18,653) × 100 = 68%
4 h	4,542	12,628	(12,628/17,170) × 100 = 74%
	5,200	12,630	(12,630/17,830) × 100 = 71%
	5,467	12,659	(12,659/18,126) × 100 = 70%

Mean of precooked sample set is 70%. All measurements are in counts per minute.

RESULTS

The activity of the egg white samples in each test tube was counted using the well counter. The simulated gastric fluid with the rinse activity was also counted using the well counter. Each was recorded in counts per minute. To determine the radiolabeling efficacy percentage, the total counts of the egg whites and the gauze was divided by the total counts of the egg whites, gauze, simulated gastric fluid, and rinse and then multiplied by 100.

The mean percentage for each method was calculated by adding the radiolabeling efficacy percentages and then dividing by 6 (the number of samples in each set). At both time points for the precooking method, most activity was still tagged to the egg whites in all 6 samples. At both time points, the precooking method had a higher radiolabeling efficacy, at an average of 70% (Table 2), versus 50% for the postcooking method (Table 3).

DISCUSSION

This study examined the labeling efficacy of ^{99m}Tc-SC added to egg whites before and after cooking in a microwave oven. Some limitations to the study include the lack of actual

TABLE 3
Radiolabeling Efficacy Results for Postcooked Sample

Time	Simulated gastric fluid	Postcooked egg whites	Radiolabeling efficacy
2 h	12,548	12,176	(12,176/24,724) × 100 = 49%
	11,666	10,954	(10,954/22,620) × 100 = 48%
	11,165	11,358	(11,358/23,023) × 100 = 49%
4 h	10,903	11,478	(11,478/22,381) × 100 = 51%
	11,729	12,572	(12,572/24,301) × 100 = 52%
	12,196	11,973	(11,973/24,169) × 100 = 50%

Mean of postcooked sample set is 50%. All measurements are in counts per minute.

human gastric fluid, the measuring of samples only at 2 and 4 h instead of the full protocol time length, and the limited sample size. Evaluation of labeling efficiency before digestion would also be useful. Despite these limitations, this research found that the radiolabeling efficacy of ^{99m}Tc-SC was much higher when added to the egg whites before they were cooked.

Our findings support previous findings in similar research on meal preparation methods. Knight et al. determined binding efficacy to be much better when ^{99m}Tc-SC was added to whole eggs before they were cooked (*7*). Similarly, McKee et al., who used a simulated digestion method to examine the radiolabeling of whole eggs before and after microwave cooking, found that labeling before cooking yielded 73% binding whereas labeling after cooking yielded 43% binding (*8*). Our current study yielded slightly higher binding for egg whites using similar methods but supported the same outcome that adding ^{99m}Tc-SC before cooking yields a much higher binding efficacy. Tafti et al. reported that variations in gastric emptying study protocols are still widespread but are lessening (*4*). Future research should be done with larger sample sizes and other meal preparation methods.

CONCLUSION

Gastric emptying scintigraphy remains the gold standard for evaluating gastric motility. The reliability of the examination depends strongly on adherence to the standardized meal and meal preparation. However, there is a lack of consistency across facilities, with a common variation being to add the ^{99m}Tc-SC to cooked scrambled egg whites. This study documented the efficacy of ^{99m}Tc-SC radiolabeling of egg whites according to the SNMMI protocol guidelines (i.e., before cooking) versus after cooking. The precooking method had higher efficacy than the postcooking method. These results highlight the importance of following the standardized protocol in preparing the meal for a gastric emptying study.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

KEY POINTS

QUESTION: Is radiolabeling of egg whites with ^{99m}Tc-SC as effective after cooking as before cooking?

PERTINENT FINDINGS: The bond between ^{99m}Tc-SC and the albumin in egg whites is not as strong when the ^{99m}Tc-SC is added after the egg whites are cooked and is more likely to disintegrate during digestion.

IMPLICATIONS FOR PATIENT CARE: Gastric emptying scintigraphy results may be less accurate when the ^{99m}Tc-SC is added to the egg whites after they are cooked.

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An Evaluation of Gastric Emptying Scintigraphy Protocols in Health Care Institutions When Compared with the Society of Nuclear Medicine and Molecular Imaging Procedure Guidelines

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This study aimed to analyze the compliance of health care institutions with the Society of Nuclear Medicine and Molecular Imaging (SNMMI) procedure guidelines for gastric emptying scintigraphy (GES). **Methods:** A 19-question survey on demographics and the GES protocol was conducted using a Google form. The demographic questions covered position, number of technologists in the department, location, type of health care institution, and number of GES studies per month. The protocol questions included patient preparation, meal preparation, withholding of scheduled medications, radiopharmaceutical type, and radiopharmaceutical dose. The survey was sent to 7 nuclear medicine Facebook groups and a list of clinical affiliates provided by the Indiana University School of Medicine Nuclear Medicine Program. Descriptive statistics were compiled for most questions. A Fisher exact test with a significance level of 0.05 was used to compare the type of health care institution with compliance with the SNMMI GES protocol regarding radiolabeling time, meal preparation, and meal components, as well as to compare the type of health care institution with the number of GES studies performed per institution. **Results:** In total, 240 people responded to the survey. Most were nonsupervisory nuclear medicine technologists (72%) in nonacademic institutions (72%) and groups with 4 or more technologists (62%). Of the respondents, 72% followed the SNMMI guideline of adding the radiopharmaceutical before cooking, but only 37% followed the meal component guideline. There was no significant association between the type of institution or the number of GES studies and compliance with radiolabeling time or with meal preparation or components. Most respondents asked patients to withhold medications per SNMMI guidelines and used the recommended radiopharmaceutical (^{99m}Tc-sulfur colloid, 95%) at the recommended dose (18.5–37 MBq, 84%). **Conclusion:** Although most respondents followed most aspects of the SNMMI guidelines for GES, more than half did not use the recommended meal of liquid egg whites. Compliance did not vary between academic and nonacademic institutions or between groups performing a large or a small number of GES studies.

Key Words: gastric emptying scintigraphy; SNMMI; egg whites; compliance

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Gastric emptying scintigraphy (GES) is a diagnostic test to assess gastric motor function (*1*). GES was first developed in 1966, using "a standard breakfast of ordinary food" labeled with ^{51}Cr (*2*). The radiolabeling of the meal allowed quantitative measurement of radioactivity in the stomach at specific time points and the percentage remaining of the meal, often allowing for diagnosis and treatment (*3*). Since then, there have been trials of which radiopharmaceutical and meal components are best used to obtain accurate results (*3*).

In 2013, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) published a procedure guideline for adult solid-meal GES (*4*). The standardized meal recommended by the SNMMI protocol includes 118 mL (4 oz) of liquid egg whites, 2 slices of toasted bread, 30 g of jam or jelly, and 120 mL of water (*4*). The ^{99m}Tc-SC is added to the liquid egg whites, stirred, and then cooked in a microwave oven or skillet until the egg whites reach the consistency of an omelet (*4*). Oatmeal may be radiolabeled with ^{99m}Tc-SC as an alternative for patients with an albumin allergy, but radiolabeling efficiency has been shown to be much lower with oatmeal, causing inaccurate reference values (*5*). Research on alternative meals results in a lack of standardization and inconsistent results (*5*).

To achieve optimal radiolabeling efficiency and reproducible outcomes, the liquid egg whites must be cooked together with the ^{99m}Tc-sulfur colloid (SC) (*1*) because ^{99m}Tc-SC binds to the egg white protein as it becomes denatured during the cooking process (*6*). Thus, the egg whites must be cooked with the ^{99m}Tc-SC for the procedure to be considered a solid-meal GES. The study will be regarded as a liquid GES and provide exponentially different results if the egg whites are not cooked with the ^{99m}Tc-SC.

Health care institutions that have established their own protocols for GES may need to adhere to the guidelines set by the SNMMI (*4*). If the standardized meal and preparation for solid GES are not followed (*1*), published reference values are inaccurate and cannot be used, making it difficult to compare results between different health care institutions that use different meals or imaging protocols (*4*). Standardization of the GES protocol eliminates this problem and also

TABLE 1
Survey Questions

Category	Question
Demographic	1. What is your position?
	2. How many technologists work in your department (all positions: as needed, part-time, full-time)?
	3. Is your institution outside Indiana?
	4. If you answered yes to previous question, in which state/country is your institution?
	5. What type of facility is your institution?
	6. On average, how many GES studies are ordered/performed per month?
Patient preparation	7. Which pharmaceuticals must patients stop using before GES (check all that apply)?
	8. What is withholding time for pharmaceuticals listed in previous question?
	9. Are serum glucose levels tested before patients undergo GES?
Meal components and preparation	10. What protocol is used for patients who have albumin/egg allergy?
	11. What is used to radiolabel GES meal?
	12. Please list anything else that is part of meal (toast, jelly, butter, salt pepper, milk, etc.).
	13. Is GES meal radiolabeled before or after cooking?
	14. Which radiopharmaceutical is used for GES?
	15. What dose range is used for GES?
	16. Are patients required to eat their GES meal within a time limit?
Imaging protocol	17. What are the imaging interval times and total examination time (e.g., images at 1, 2, and 4 h and total time of 4 h)?
	18. Are patients allowed to drink water or fluids during intervals between imaging?
	19. What imaging views are required?

allows the patient's progress to be tracked over time (*7*). The primary objective of this study was to analyze health care institutions' compliance with SNMMI procedure guidelines for GES.

MATERIALS AND METHODS

Institutional Review Board approval for this prospective study was sought, and the study was deemed exempt from the requirement for written informed consent.

A survey of 19 questions was created using a Google form, made available for 4 wk on 7 different nuclear medicine technologist Facebook (Meta) groups, and emailed to 10 nuclear medicine technologist supervisors whose names were provided by the Nuclear Medicine Program of the Indiana University School of Medicine. All participants were notified that the survey would be anonymous and conducted exclusively for research and educational purposes. Demographics, patient preparation, and meal preparation were the topics of the survey (Table 1). The demographic questions included the position of the respondent, the number of technologists in the department, the location and type of facility (nonacademic, Veterans Administration/military, academic, outpatient), and the number of GES studies performed per month. The patient preparation questions included which medications were withheld before the examination and for what duration. The meal preparation questions included the meal chosen for the GES study, the alternatives for patients with an albumin or egg allergy, any additional meal components, the radiopharmaceutical and dose, and the eating time limit.

Descriptive statistics were compiled for most questions: a Fisher exact test with a significance level of 0.05 was used to compare the type of health care institution with compliance with the SNMMI GES protocol regarding radiolabeling time and meal preparation/components, as well as to compare the type of health care institution with the number of GES studies performed per month. A P value of less than 0.05 allowed rejection of the null hypothesis that GES protocols in health care institutions comply with SNMMI procedure guidelines. The alternate hypothesis was that GES protocols in health care institutions are not compliant with SNMMI procedure guidelines.

RESULTS

Table 2 summarizes demographics. Hospitals with no academic affiliation were the most common type of health care institution (57.0%), and nuclear medicine technologists were the most common type of position (72%). Most respondents were in nuclear medicine departments that had 4 or more technologists (62.0%). Health care institutions performed an average of 9.5 GES studies monthly (range, 0–60) (Table 2).

Of the 240 respondents, 218 were from the United States; the remaining 22 were from Canada, Pakistan, Australia, Croatia, the United Kingdom, Kosovo, and Ethiopia. The most represented states were Texas, Florida, and Indiana (Fig. 1).

Only 37% of health care institutions follow the SNMMI consensus meal guidelines (Fig. 2). Those that do not comply with the guidelines use ingredients such as whole eggs, grits, macaroni and cheese, sausage, and oatmeal for their main radiolabeling meal.

TABLE 2
Summary of Demographic Data (n = 240) such as Institution Type, Position Type, and Number of Technologists in Department

Variable	Category	Frequency (n)	%
Institution type	Hospital (nonacademic)	137	57.0
	Academic	66	27.5
	Veterans Administration/military	8	3.3
	Outpatient	22	9.1
	Other	7	2.9
Position type	NMT	173	74.1
	Supervisor NMT	56	24
	Nuclear medicine physician	3	1.3
	NMT program director	1	0.4
	PET/CT technologist	2	0.8
	NMT instructor	1	0.4
	Student	3	1.3
	Other	1	0.4
Number of staff in department	1	18	7.5
	2	18	7.5
	3	55	22.9
	≥4	149	62.0

NMT = nuclear medicine technologist.
GES monthly volume has mean of 9.58, median of 7.5. and range of 0–60.

Additionally, 4.5% of health care institutions use fatty or high-caloric drinks such as Ensure (Abbott Laboratories) or Boost (Nestlé) for their main meal. Around 14.5% of health care institutions use ingredients not recommended in the guidelines, including butter, saltine crackers, and—instead of water—juice or milk. Furthermore, 5% of health care institutions do not require patients to finish consuming the radiolabeled meal within 10 min.

Figures 3 and 4 compare how many survey participants follow the SNMMI guidelines for medication withholding and radiopharmaceutical doses; 174 of 240 participants (72.5%) withhold the pharmaceuticals listed in Table 3, whereas 66 (27.5%) do not. Forty-seven of 240 respondents (19.5%) require patients to withhold the pharmaceuticals for 2 d before the procedure, whereas 193 (80.4%) do not.

As shown in Figure 4, 95% of participants radiolabel using ^{99m}Tc-SC, and 83.7% use the recommended dose range (18.5–37 MBq). Five percent of participants use other radiopharmaceuticals for radiolabeling (^{111}In-diethylenetriamine pentaacetic acid or ^{99m}Tc-macroaggregated albumin), and 16.3% use doses outside the recommended range (all >37 MBq).

The survey was completed by 240 participants. Table 4 shows a Fisher exact test on the relational data between the demographics, such as the type of health care institution and compliance with the SNMMI GES protocol regarding when the meal was radiolabeled. Forty-three responses (17.9%) did not apply to this Fisher exact test. The P value was 0.39, making the results not statistically significant. From the statistical analysis, since the P value is larger than

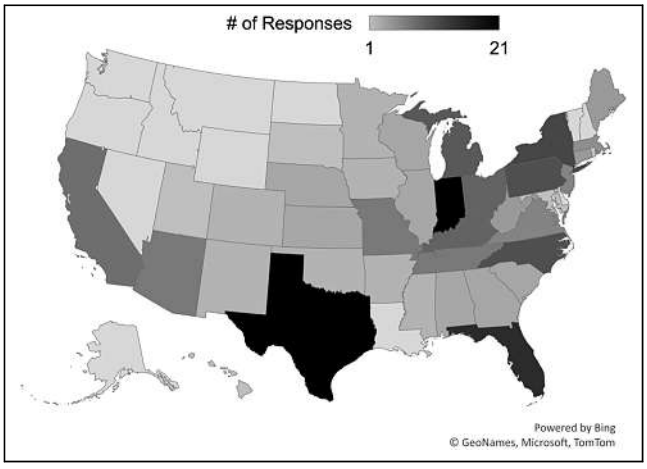

FIGURE 1. Map of participant locations in United States.

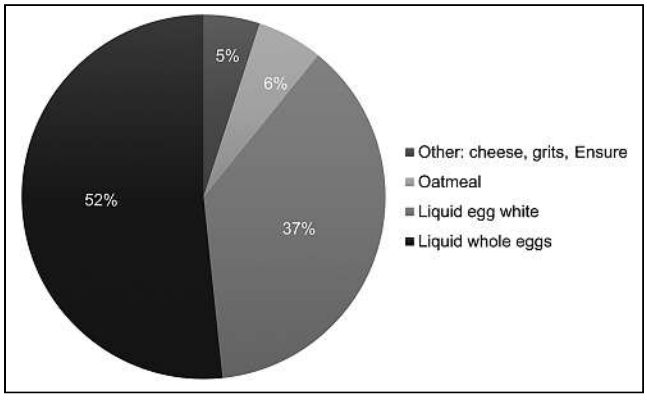

FIGURE 2. Frequency of radiolabeled meal component.

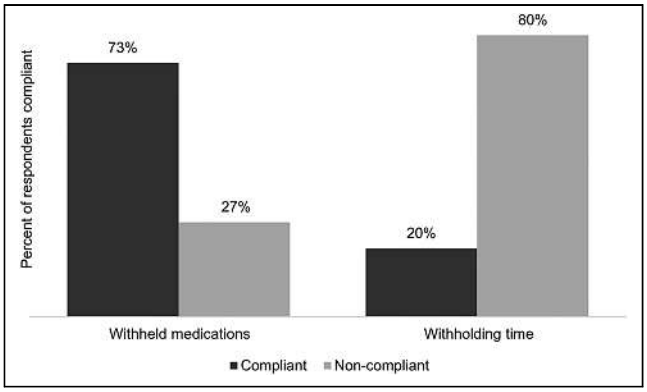

FIGURE 3. Compliance with pharmaceutical and withholding time.

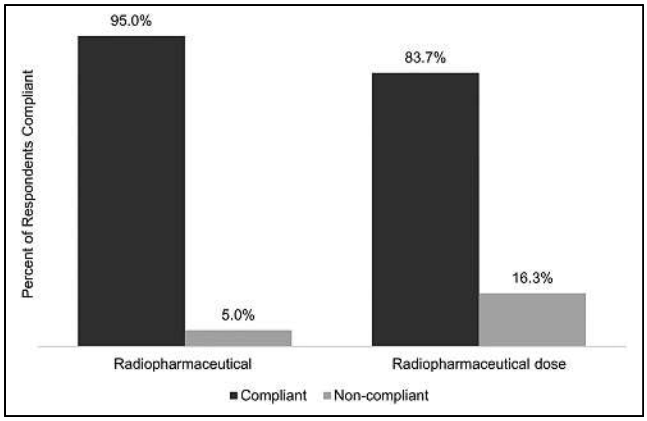

FIGURE 4. Compliance with radiopharmaceutical and dose.

the significance level of 0.05, we fail to reject the null hypothesis. This indicates that there is no significant difference in radiolabeling before or after cooking based on the type of institution.

The comparison between use of the meal components recommended by the SNMMI (liquid egg whites) and the number of GES studies performed by each health care institution is analyzed in Table 5. The patient volume was divided into 2 groups: less than or more than 40 monthly examinations. The *P* value was 0.63; thus, there was no association between the number of studies and compliance with meal components. Sixteen of 240 respondents were not applicable for this Fisher exact test.

DISCUSSION

The SNMMI recommends that health care institutions follow the standardized protocol for GES. This ensures consistency in examination outcomes and decreases variation in practice, resulting in patients' receiving the same protocols and treatment regardless of where they undergo GES. This study aimed to assess compliance with the SNMMI recommendations for the GES protocol. We surveyed practicing technologists and found that 52% are not compliant with the SNMMI guidelines, and the most significant areas of noncompliance are the meal components and the time of radiolabeling (before or after cooking).

How meals are composed and prepared can significantly impact the accuracy of GES (*7*). Carbohydrates are processed more quickly than foods high in fat and protein, and liquids pass through the stomach more rapidly than semisolid foods, which, in turn, are digested more quickly than solid ones (*8*). Additionally, the quantity of food and the stress it puts on the stomach wall also influence how quickly the stomach empties (*9*). Consequently, if an alternative meal with varying nutrients and volume is used without enough research to standardize reference values (baseline results), unreliable interpretations can result (*9*). Only 37% of respondents use the SNMMI-recommended egg whites, and institutions performing a high volume of GES studies are less compliant than those performing a low volume.

TABLE 3
Standard Protocol Guidelines for Patient Preparation, Meal, and Radiolabeling of Meal

Category	Variable	Definition
Patient preparation	Withheld medications	Prokinetic agents: metoclopramide, tegaserod (Zelnorm; Alfasigma USA), domperidone, erythromycin, and cisapride; opiates; anticholinergic and antispasmodic agents; atropine, nifedipine, progesterone, octreotide, theophylline, benzodiazepine, and phentolamine
	Withholding time	2 d
	Blood glucose testing	Measurement of level before GES and inclusion in final report
Meal	Consensus meal*	118 mL (4 oz) of liquid egg whites, 120 mL of water, 2 slices of toast, 30 g of jam or jelly
	Meal ingestion time	<10 min
Radiolabeling of meal	Radiopharmaceutical	^{99m}Tc-SC
	Radiopharmaceutical dose	18.5–37 MBq (0.5–1.0 mCi)
	Radiolabeling method	Mixing of ^{99m}Tc-SC with liquid egg whites before cooking

*All 4 listed ingredients and no other ingredients (e.g., no butter or juice).

TABLE 4
Relationship Between Time of Radiolabeling and Type of Health Care Institution (Questions 5 and 13)

Institution type	Before cooking (142/240 respondents [59.1%])	After cooking (55/240 respondents [22.9%])
Hospital (nonacademic)	93	40
Academic	49	15

Radiolabeling efficiency for GES studies is significantly higher when ^{99m}Tc-SC is added to liquid egg whites before cooking rather than being injected onto cooked egg whites (*10*). The study also found that even when whole eggs are used, ^{99m}Tc-SC has a much higher radiolabeling efficiency when applied before cooking than after cooking (*10*).

Of the 240 institutions, 162 (92 nonacademic, 49 academic, 15 Veterans Administration or military, and 5 outpatient) follow the SNMMI guidelines by radiolabeling the meal before cooking. This indicates that 32.5% of health care institutions label their meal after cooking, regardless of whether they use the standard meal. The accuracy of results may be affected by the use of alternative meals, making reference values for solid-meal GES inapplicable and requiring a liquid-meal GES study. Compliance did not vary between academic and nonacademic institutions.

Other factors, such as medications, can also significantly impact the results (*1*). Many pharmaceuticals (Table 3) can alter the gastric emptying rate and should be withheld 48 h before the examination (*1*). About 75% of our respondents follow the guidelines regarding withholding of medications.

This study had limitations. Because the survey was posted on nuclear medicine technologist Facebook groups, multiple technologists from the same department may have taken the survey. Additionally, some participants who wished to portray their department as following the SNMMI standards may have given inaccurate responses.

TABLE 5
Relationship Between Number of GES Studies Performed and Meal Component (Questions 9 and 11)

Meal component	>40 GES/mo (51/249 respondents [21.1%])	<40 GES/mo (173/240 respondents [72%])
Recommended liquid egg whites	19	73
Nonrecommended ingredients*	32	101

*For example, whole eggs, oatmeal, grits, or cheese.

CONCLUSION

Although most respondents follow most aspects of the SNMMI guidelines for GES, more than half do not use the recommended meal of liquid egg whites. Compliance did not vary between academic and nonacademic institutions or between groups performing a large or small number of GES studies.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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KEY POINTS

QUESTION: How compliant are GES protocols in health care institutions with the SNMMI procedure guidelines?

PERTINENT FINDINGS: Only 37% of respondent laboratories follow the SNMMI GES guidelines regarding meal components.

IMPLICATIONS FOR PATIENT CARE: The lack of standardization for GES protocols highlights the importance of following standardized procedures, such as those outlined by the SNMMI, to ensure accurate and consistent results.

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Gastric Metastasis from Invasive Lobular Breast Cancer, Resembling Primary Gastric Cancer

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Invasive lobular carcinoma (ILC) is the second most common subtype of invasive breast cancer and sometimes presents with an unusual metastatic pattern. Its gastric metastasis is difficult to differentiate from primary adenocarcinoma. This report presents a case of breast ILC for which the initial presentation was gastric metastasis. A 62-y-old woman presented with gastric outlet obstruction secondary to a gastric mass that had been diagnosed on upper gastrointestinal endoscopy and biopsy. The patient had been referred for ^{18}F-FDG PET/CT for staging. The baseline ^{18}F-FDG PET/CT scan demonstrated extensive axillary nodal and gastric metastases with a breast mass, which raised suspicion of a primary breast carcinoma. Distinguishing primary gastric adenocarcinoma from metastatic breast ILC is essential, considering that the 2 diagnoses lead to divergent treatments. Therefore, this entity needs to be considered in the differential diagnosis in clinical practice.

Key Words: gastric metastasis; ^{18}F-FDG PET/CT; lobular breast carcinoma; primary gastric carcinoma

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Breast carcinoma is the most common malignancy in women, accounting for 25.1% of all cancers in women and being the leading cause of cancer-related death among women worldwide (*1*). Despite early recognition by screening and the efficacy of new treatment modalities, many patients eventually develop metastatic disease either by locoregional recurrence or distant metastases. Metastatic disease to the gastrointestinal tract is rare and poses a clinical problem in both diagnosis and management. The primary malignancies that most commonly metastasize to the stomach include breast cancer (27.9%), lung cancer (23.8%), esophageal carcinoma (19.1%), renal cell carcinoma (7.6%), and malignant melanoma (7.0%) (*2*).

Based on clinical and autopsy findings, the reported incidence of gastric metastasis is 0.2%–0.7%. The postmortem frequency of gastric metastasis from breast carcinoma is estimated to be 0.8%–18%. Most cases originate from invasive lobular carcinoma (ILC) (*3*).

According to the National Comprehensive Cancer Network 2018 guidelines, ^{18}F-FDG PET/CT may be performed as an alternative to a contrast-enhanced CT scan of the chest, abdomen, and pelvis and ^{99m}Tc-methylene diphosphonate bone scanning for evaluation of distant metastatic disease in patients with newly diagnosed stage III breast cancer. ^{18}F-FDG PET/CT is usually not performed for stage I or stage II breast cancer because a change in patient management is rare (*4*). ^{18}F-FDG PET/CT may be more appropriate as an alternative to CT and bone scanning for patients with invasive ductal carcinoma rather than ILC, because ^{18}F-FDG demonstrates comparatively reduced sensitivity for ILC metastases (*5*). Compared with invasive ductal carcinoma, ILC is more often occult on mammography, ultrasound, and ^{18}F-FDG PET/CT, which is of importance for clinical management because ILC is more often multifocal and bilateral than invasive ductal carcinoma (*6*).

CASE REPORT

A 62-y-old woman presented with gastrointestinal symptoms including abdominal swelling, loss of appetite, dysphagia, and gastroesophageal reflux, which had developed over a 20-d period. A contrast-enhanced CT scan of the abdomen was done and revealed circumferential polypoidal thickening involving the pyloric and antral parts of the stomach, with fat stranding. It was associated with a distended body and fundus of the stomach, findings highly suggestive of a neoplastic lesion with partial gastric outlet obstruction. The patient underwent upper gastrointestinal endoscopy, which demonstrated a thickened, hard gastric mucosa involving predominantly the distal two thirds of the gastric body with pyloric narrowing, suggestive of gastric outlet obstruction with severe distal diffuse esophagitis. An initial histopathologic study revealed a small focus of infiltrating carcinoma. PET/CT showed ^{18}F-FDG–avid circumferential mural thickening of the antrum and pylorus along with hypermetabolic lymphadenopathy involving the right axillary and mediastinal lymph nodes, the porta hepatis, and widespread bone lesions (Fig. 1A). PET/CT also showed a nonavid soft-tissue-density nodule with slightly speculated margins in the superolateral quadrant of the right

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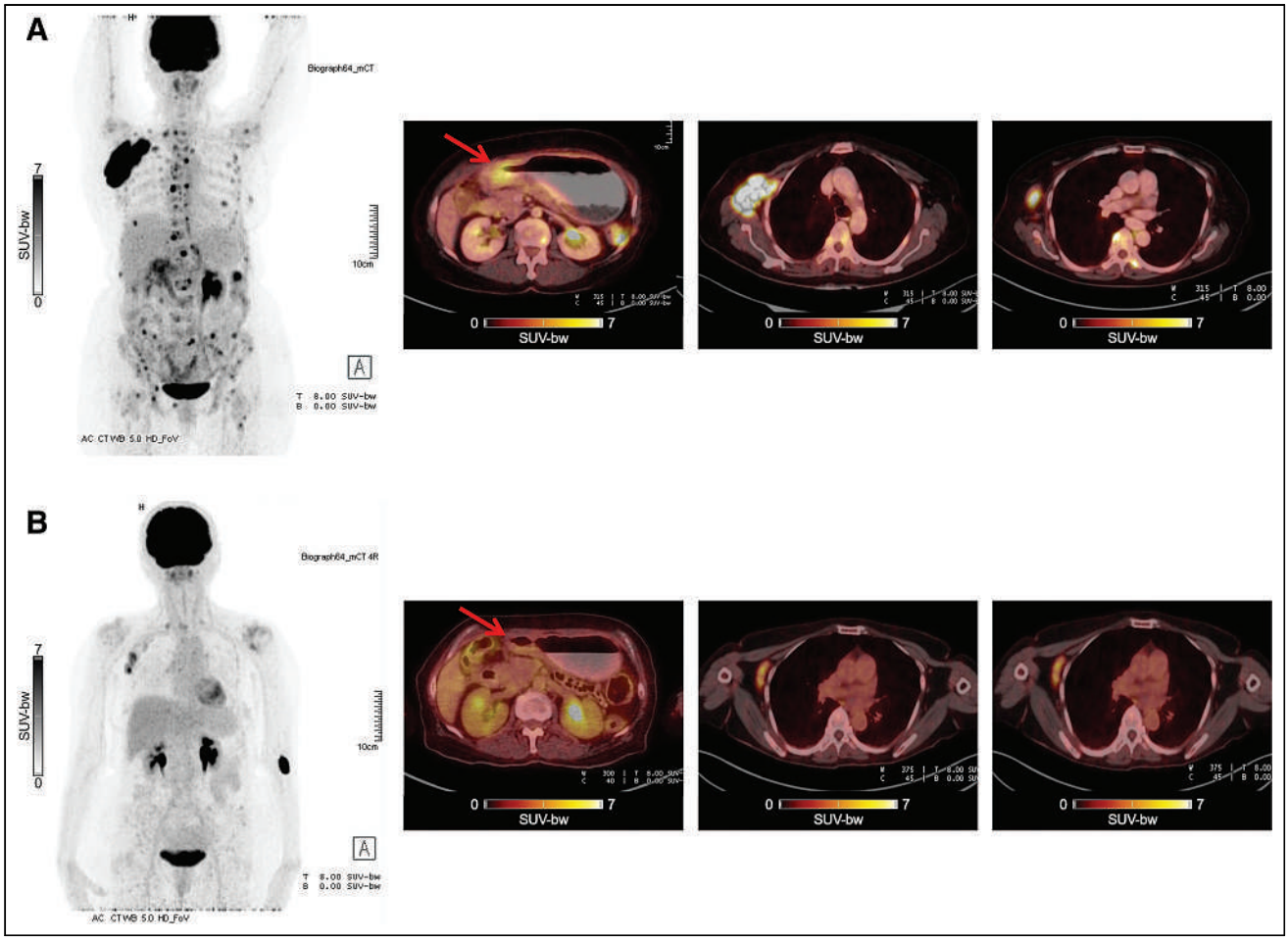

FIGURE 1. (A) Baseline ^{18}F-FDG PET/CT showed gastric, nodal, and osseous metastases. Arrow depicts ^{18}F-FDG–avid lesion involving gastric antrum and pylorus in baseline PET scan, corresponding with uptake over biopsy-proven infiltrative gastric carcinoma. (B) Follow-up scan showed regression of disease. Arrow depicts reduction of ^{18}F-FDG uptake over same site. PET imaging was done on Siemens PET-CT hybrid system equipped with 64-slice CT scanner, with 185 MBq of ^{18}F-FDG intravenously administered; scan was done 60 min after injection with 2 min/bed and 6 imaging beds used for acquisition. Maximum-intensity projection images are shown in baseline and follow-up along with hybrid (PET + CT) images shown in transaxial planes.

breast. Ultrasound with additional mammography showed a highly suggestive mass involving the right breast with extensive axillary lymphadenopathy, features suggestive of category V on the Breast Imaging Reporting and Data System—highly suggestive of malignancy. A core biopsy was performed from the right breast, and the histopathologic study revealed ILC, grade II. The tumor show positive staining for immunohistochemical marker GATA-3 and was negative for CDX2. Similarly, another biopsy from the stomach showed a small focus of infiltrating carcinoma that was also positive for GATA-3, confirming involvement of the stomach by carcinoma of breast origin. Additionally, the metastatic focus in the right axillary lymph nodes showed negative E-cadherin staining, confirming the involvement of this node by ILC originating in the right breast. After comparison of the samples, the final diagnosis was a metastasis of breast carcinoma.

Posttherapy follow-up PET/CT showed a significant interval reduction in lesion size and metabolic activity at the antrum, pyloric canal, and right axillary lymph nodes but no significant interval change in the size or appearance of the right breast lesion, suggestive of overall disease regression. (Fig. 1B).

DISCUSSION

ILC is the second most common subtype of invasive breast cancer, accounting for about 5%–15% of cases (*6*,*7*). In the reported case, the main symptoms were indigestion and upper abdominal pain resulting from pyloric obstruction caused by the gastric mass. The patient underwent upper gastrointestinal endoscopy and biopsy, which revealed a thickened, hard gastric mucosa predominantly involving the distal two thirds of the gastric body with pyloric narrowing, suggestive of gastric outlet obstruction with severe distal diffuse esophagitis. Histopathologic examination revealed a small focus of infiltrating carcinoma. This pattern of metastasis mimics primary adenocarcinoma because it has similar symptoms, imaging and endoscopic features, and histopathologic findings (*8*).

The patient was considered to have primary gastric cancer and was referred to our hospital for ^{18}F-FDG PET/CT for staging. The PET scan showed mild ^{18}F-FDG avidity in the pyloric antrum with circumferential mural thickening. The sensitivity of PET is reported to be relatively lower for the diagnosis of gastric cancer than for other cancer types, as is attributed to physiologic absorption of ^{18}F-FDG and involuntary movements by the gastric wall. Gastric cancer morphology is also associated with the sensitivity of PET. Although the sensitivity of PET is high for papillary or ductal carcinoma and poorly differentiated solid adenocarcinoma, high false-negative rates are reported for signet ring cell carcinoma and poorly differentiated nonsolid adenocarcinoma (*9*).

Apart from the gastric metastasis, the PET scan also showed extensive right-sided lymphadenopathy and osseous metastases. The right breast parenchyma showed a superolateral quadrant nodule that was of soft-tissue density and was not ^{18}F-FDG–avid. The patient underwent a workup for primary breast carcinoma, and histopathology revealed ILC, grade II, with right axillary tumor metastasis. Immunohistochemistry findings confirmed the primary breast carcinoma with axillary and gastric metastases. Importantly, gastric metastasis from invasive lobular breast carcinoma is reported to occur at a higher rate than the metastasis from invasive ductal carcinoma. A detailed immunohistochemical analysis can be of great help. O'Connell et al. compared immunohistochemical results between gastric metastases from breast cancer and gastric metastases from primary gastric cancer (*10*).

Posttherapy follow-up PET/CT showed a significant reduction in nodal, gastric, and osseous metastases.

CONCLUSION

Cases such as the reported one—ILC of the breast with nodal, gastric, and osseous metastases—can be misdiagnosed as primary gastric cancer. Accurate diagnosis and patient-tailored treatment can be achieved through clinical suspicion, repeated endoscopy, and accurate histologic examination, including disease-specific immunohistochemical analysis. Distinguishing primary gastric adenocarcinoma from metastatic breast ILC is essential, considering that the 2 diagnoses lead to divergent treatments.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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Scintigraphic Detection of Abdominal Pseudocyst: A Complication of Ventriculoperitoneal Shunt

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We report a case of a large abdominal pseudocyst detected on scintigraphy in a patient with a history of ventriculoperitoneal shunt placement who presented with headache and suspected shunt malfunction.

Key Words: abdominal CSF pseudocyst; VP shunt malfunction; ^{111}In-DTPA shunt study

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Abdominal pseudocyst is an uncommon complication of ventriculoperitoneal shunting. It should be considered a differential diagnosis in patients with a ventriculoperitoneal shunt who complain of abdominal symptoms such as distention and pain. Early diagnosis improves clinical outcomes.

CASE REPORT

A 41-y-old man with a history of communicating hydrocephalus and ventriculoperitoneal shunt placement 11 y previously presented with headache. Shunt malfunction was suspected. A radionuclide cerebrospinal fluid shuntogram was done after injection of 106.93 MBq (2.89 mCi) of ^{111}In-diethylenetriaminepentaacetic acid into the shunt reservoir on the left scalp. Dynamic images of the head and chest and static image of the abdomen were acquired. Injected activity was noted in the shunt reservoir. Tracer activity in the lateral ventricles suggested patent proximal tubing, and activity along the distal tubing suggested patent distal tubing (Fig. 1). However, there was a large area of well-defined loculated activity in the abdomen (Fig. 2). Further evaluation with SPECT/CT confirmed that the activity in the abdomen correlated with a large pseudocyst occupying the abdomen and pelvis. The distal tip of the shunt was seen within the pseudocyst. Excision of the pseudocyst was planned for the patient.

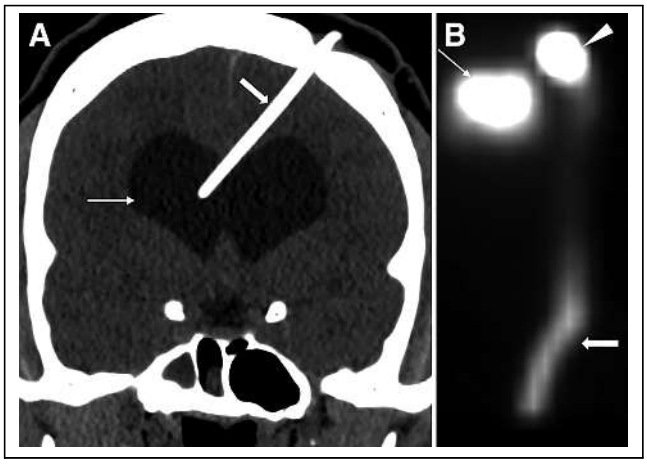

FIGURE 1. (A) Coronal CT of head shows hydrocephalus (thin arrow) and left frontal approach ventricular shunt catheter terminating in right ventricle (thick arrow). (B) Planar scintigraphy in anterior projection shows injected activity in shunt reservoir on left scalp (arrowhead). Activity is seen in lateral ventricles (thin arrow) suggestive of patent proximal tubing. Activity is seen tracking through distal tubing along chest and upper abdomen (thick arrow).

DISCUSSION

Ventriculoperitoneal shunting is the common treatment for hydrocephalus, with the cerebrospinal fluid being absorbed into the peritoneal cavity. When cerebrospinal fluid is not adequately absorbed, there can be focal peritonitis with inflammatory pseudocyst formation. Other etiologies for pseudocyst include adhesions from previous abdominal surgeries or silicone allergy (*1*,*2*). Symptoms include abdominal pain, distension, and constipation. There can be signs of increased intracranial pressure such as headache, nausea, vomiting, and fatigue due to shunt malfunction. Sometimes the pseudocyst can get infected. Ultrasonography is the initial method to diagnose a pseudocyst and can be confirmed with CT. Routine radiography can detect other shunt complications, such as kinking or disconnection. With persisting suspicion, cerebrospinal fluid shunt scintigraphy aids to further assess shunt patency. In our case, the pseudocyst was incidentally detected on the scintigram done to evaluate shunt patency. Excision of the cyst and shunt relocation is the definitive treatment. Percutaneous drainage can be therapeutic and diagnostic.

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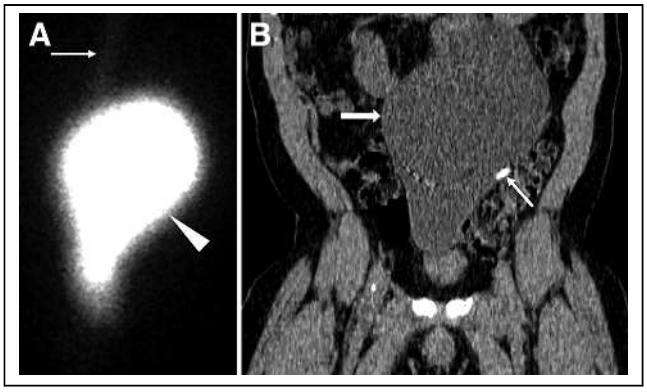

FIGURE 2. (A) Planar scintigraphy of abdomen demonstrates well-defined loculated activity in abdomen (arrowhead), as well as part of distal tubing in upper abdomen (arrow). (B) Coronal CT depicts correlating large pseudocyst occupying abdomen and pelvis (thick arrow) with fluid density and thin wall, as well as distal end of shunt catheter tip terminating within pseudocyst (thin arrow).

CONCLUSION

Though ultrasonography is the method of choice for the initial diagnosis, we report initial detection of a large abdominal pseudocyst incidentally on scintigraphy in a patient with a history of ventriculoperitoneal shunt placement and headache. An abdominal pseudocyst has to be suspected, especially if there are abdominal symptoms. Timely diagnosis and management can alleviate the patient's symptoms.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

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