

Evaluation of Gastric Emptying Time in Patients with Subclinical Hypothyroidism and Euthyroid Goiter

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ABSTRACT

Objective: Upper gastrointestinal complaints are common in patients with euthyroid goiter and subclinical hypothyroidism for whom follow-ups are performed without treatment. This study evaluated gastroparesis using radionuclide imaging in patients with dyspepsia.

Methods: A total of 56 adult patients were included in this retrospective study. The average age of the patients was calculated as 70.88 ± 2.33 years. Euthyroid goiter was observed in 29 patients and subclinical hypothyroidism in 27 patients. A liquid gastric emptying scintigraphy test was performed on all patients, and thyroid function tests, thyroid ultrasonography, and body mass index evaluations were performed. Regions of interest, including the antrum and fundus, were drawn from anterior images. A time activity curve was obtained.

Results: The gastric emptying half-time was calculated using liquid gastric emptying scintigraphy. This value was found to be significantly higher in patients with subclinical hypothyroidism than in those with euthyroid goiter ($p=0.033$). Gastric emptying was prolonged in 17 subclinical hypothyroidism patients (63%) and 10 (34.5%) patients diagnosed with euthyroid goiter.

Conclusion: Liquid gastric emptying scintigraphy may be preferred in elderly patients with suspected gastroparesis because of its easy application and short duration. Detecting the prolongation of gastric emptying time due to the presence of gastroparesis in subclinical hypothyroidism and euthyroid goiter cases followed up without treatment may guide the prescription of treatment.

Keywords: Gastric emptying, goiter, dyspepsia, thyroid function tests, radionuclide imaging

INTRODUCTION

The presence of gastroparesis in patients with dyspepsia can be evaluated by gastric emptying scintigraphy. Gastric emptying scintigraphy can be applied to solid or liquid food (1). Solid gastric emptying scintigraphy (SGES) is considered to be the optimal test because it is a shorter study lasting for a bout 4 hours. There is a correlation between the results obtained by liquid gastric emptying scintigraphy (LGES) and those obtained by solid gastric emptying scintigraphy (2). Upper gastrointestinal complaints are frequently encountered in patients with euthyroid goiter (EG) and subclinical hypothyroidism (SH) with whom follow-ups are held in thyroid outpatient clinics without treatment. Treatment is controversial in patients with EG if there is no suspicion of malignancy or signs of compression (3). Goiter is an enlargement of the thyroid gland and is common in the elderly (4). Ultrasonography (USG) and thyroid function tests (TFTs) are primarily used for diagnosis and follow-up. If necessary, scintigraphy and biopsy can be performed (5). SH describes conditions in which free T4 (fT4) and fT3 values

are normal but the thyroid-stimulating hormone (TSH) value is above the upper limit. In these patients, treatment does not begin before TSH reaches a certain level or without obvious clinical symptoms, such as recurrent hypothyroidism symptoms (6,7). The present study evaluated gastric emptying time with LGES in elderly patients with a diagnosis of EG or SH with no use of thyroid hormone preparations and who suffered dyspeptic complaints. This study is expected to contribute to the literature to optimize treatment initiation in these patients.

METHODS

This retrospective study included 56 adult patients. The median age of the patients was 72 years (minimum 68, maximum 74). Of these, 49 (87.5%) were women. A total of 29 patients were diagnosed with EG and 27 with SH. LGES testing was performed on all patients. In addition, TFT, thyroid USG, and body mass index (BMI) evaluations were performed. Indigestion complaints were observed in all patients. Not included in the study were

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very underweight or obese patients, those with a thyroid volume of more than 40 mL, those with the presence of chronic disease and thyroid preparation, prokinetic drug use, chronic drug use, diabetes mellitus, smoking, stomach or bowel operation anamnesis, hiatal hernia, gastroesophageal reflux, or a diagnosed esophageal motility disorder. Those with 20 to 30 mL of thyroid volume were accepted as mild goiter, and those with 30 to 40 mL were accepted as moderate goiter. According to their BMI, the patients were evaluated as normal or overweight. Four to six hours of fasting were required before scintigraphy. Imaging was performed early in the morning when gastric emptying was faster. The study did not include patients with blood glucose levels of <40 mg/dL or >275 mg/dL. When liquid food enters the stomach, the fundus relaxes. The fluid takes approximately 30 min to empty from the relaxed stomach. For the test, 18.5-37 MBq (0.5-1 mCi) Tc-99m nanocolloid was added to 300 mL of water, which the patient was asked to swallow immediately. A low-energy multi-purpose collimator was used in a 128x128 matrix. The patient was seated at a 30-to 45-degree angle. Imaging started immediately after the patient drank the liquid. Late images were acquired at 30 min and 1 h. The patient was kept in a sitting position to reduce physical activity between the images. Regions of interest containing the antrum and fundus were drawn from the anterior images (Figure 1), and a time activity curve was obtained. LGES half-time was accepted as 23 ± 3 normal gastric emptying time (8). Our study was retrospective, and informed consent was obtained from all patients. Our study was approved by the University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee on 01.03.2023 with 28 decision numbers.

Statistical Analysis

SPSS version 21 software was used for statistical analysis. Normally distributed continuous variables were expressed as mean \pm standard deviation, non-normally distributed continuous variables were expressed as median (minimum and maximum values), and categorical variables were expressed as number of cases and percentage. Whether continuous variables were normally distributed or not was determined by visual (histogram and probability graphs) and analytical (Kolmogorov-Smirnov test) methods. Patients with SH and patients with EG were tested for categorical variables (gender, excess goiter volume, obesity, and length of gastric emptying time) using the chi-square test and for normally distributed continuous variables (TSH and fT4) using Student's t-test. It was compared with the Mann-Whitney U test for age and fT3, which is a non-normally distributed continuous variable. $P < 0.05$ value was considered statistically significant. The tests were evaluated as two-sided.

RESULTS

A total of 29 patients were diagnosed with EG. Of these, 25 (86.2%) were female. The thyroid gland size was between 30 and 40 mL in 16 of these patients (55.2%) and between 20 and 30 mL in 13 patients (44.8%). TFT was within normal limits in these

patients. In the 27 patients diagnosed with SH, TSH levels were higher than normal (7.47 ± 0.20 mIU/L). fT4 (1.09 ± 0.02 ng/dL) and fT3 [2.42 (2.17 - 2.73) pg/mL] values were within normal limits. These patients did not have any presence of goiter. The data for the patients are summarized in Table 1. The patients' upper gastrointestinal complaints were examined (patient assessment of upper gastrointestinal disorders-symptom severity index) (9,10). All patients complained of fullness of the stomach, early satiety, postprandial bloating, and frequent belching. Gastric emptying half-time (GEHT) was calculated using LGES. GEHT in SH cases was found to be significantly longer than that in EG cases ($p=0.033$). GEHT was prolonged in 17 of the SH patients (63%). Of the 10 patients whose GEHT was calculated as normal, three were male. TSH levels in these 10 patients ranged from 7.12 to 7.35 mIU/L. GEHT was prolonged in only 10 (34.5%) patients with a diagnosis of EG; all 10 were female. Goiter volume was between 30 and 40 mL in eight patients. BMI was within normal limits for seven of the 10 patients. TSH values were between 3.47 and 3.69 mIU/L in these 10 patients (Table 1).

DISCUSSION

Hypothyroidism and gastroparesis commonly coexist. Thyroid hormones play an important role in the regulation of metabolism (11). Gastroparesis is a disease in which gastric emptying is delayed in the absence of mechanical obstruction. Patient quality of life decreases because of upper gastrointestinal complaints (12,13). Levothyroxine (LT4) tablets are preferred for treating hypothyroidism. However, in patients with EG and SH, LT4 is prescribed in selected patients only if necessary (14). Approximately 10% of patients receiving LT4 therapy are euthyroid. Treatment is initiated for these patients because of



Figure 1. Region of interest drawing in functional gastric emptying scintigraphy

recurrent hypothyroidism symptoms (15). Hormone therapy can be used in patients with EG and SH in the presence of clinical conditions such as unexplained fatigue, resistant obesity despite a low-calorie diet, severe hypercholesterolemia, depression resistant to antidepressant drugs, infertility in women with high TPO, and simple goiter that grows over time (16). There was no history of LT4 in the patients included in this study. Among the surveyed patients, gastric emptying delay was more pronounced in patients with SH. These findings may be due to the relative hypothyroid state of the patients. Insufficient production of peripheral LT4 and LT3 may have occurred because of intracellular hypothyroidism and variations in LT4 transfer (17). TSH suppression can cause osteoporosis and cardiac mortality. As such, some studies caution against prescribing LT4 therapy to elderly patients with EG or SH (18). Although the use of LT4 to treat goiter is still preferred, additional treatments, such as selenium and iodine, are not recommended (19). EG and SH are quite common in the general population. In the Pomeranian Population-Based Health Study, which included 4310 participants without known thyroid disease, 5.9% had goiter and 20.2% had thyroid nodules (20). Goiter is usually asymptomatic until the thyroid volume is 40 mL (19). In 85% of asymptomatic goiter cases, compression occurs on the trachea or esophagus at a rate of 30% (19). The patients surveyed in this study had a goiter volume between 20 and 40 mL. Patients with goiter exhibited less GEHT prolongation than patients without goiter. If patients with goiter present signs of malignancy, such as a hypoechoic nodule, microcalcification, intra-nodular vascularization, or a lesion with irregular borders, a biopsy should be performed (21). Thyroid USG was performed in all patients in this study. The sensitivity and specificity of USG were 83-99% and 85-56%, respectively. None of the patients had any signs of malignancy. Currently, there is no generally accepted approach to the drug treatment of goiter in euthyroid patients (22). Some large-scale studies have indicated goiter volume reduction after treatment with levothyroxine iodide (22). These studies report that with radioactive iodine treatment, a 35-40% reduction in thyroid volume can be achieved in the first year (22). Even large goiters (100-300 mL) have been reported to reduce in volume by 40-60% in two years (23). None of the 56 patients in this study received radioactive iodine treatment before the study.

Many studies do not recommend LT4 treatment for SH and EG disease until certain clinical findings occur. In elderly patients, this is due to TSH suppression, which can put the patients at risk of atrial fibrillation and metabolic bone disorder (3). If the aim is to reduce the euthyroid nodular goiter size, surgery or radioactive iodine treatment can be applied (3). Surgery is mandatory in the presence of cancer. A single measurement is not sufficient to diagnose TFT at follow-up. The present study's patients were followed up from 6 months to one year, at least three months apart. Thyroid disease is generally more common in women (11). Female gender was also more common in the present study's patients. Some male patients were excluded from the study because of smoking, which is more common among males in the country of study. Dyspeptic complaints in patients who received follow-ups without treatment may have resulted from gastroparesis. To evaluate gastroparesis, LGES and SGES results are correlated (2). SGES testing is lengthy and complex; therefore, it can be difficult to apply in the elderly population. LGES, in contrast, is very easy to apply and to obtain cooperation from elderly patients. Existing studies indicate that the correlation between GEHT and dyspeptic complaints lack statistical power (2). The present study, which evaluated GEHT by scintigraphy, found that more than one-third of the patients had normal gastric emptying (9). GEHT was within the normal limits for 29 patients with dyspeptic complaints. However, scintigraphic GEHT calculations may not fully represent the digestive process and gastrointestinal neuroendocrine events (9). A meta-analysis study that examined 25 studies in which GEHT was calculated using scintigraphy reported a relationship between delayed gastric emptying and dyspepsia complaints (24). In this study, prolonged GEHT was more common in patients with SH. Another study using wireless motility reported a relationship between gastroparesis and duodenal contractility severity (24), and a further study reported that gastroparesis symptoms are associated with small bowel dysmotility (25). In this study, LGES testing was completed within 1 h, and the standard method was used for all patients (9). As stated, there is no reliable method to evaluate mixed solid-liquid food and liquid gastric emptying (9). LGES may be preferred over SGES in the elderly population to evaluate gastroparesis apart from specific diseases. LGES, unlike

Table 1. Data on subclinical hypothyroidism and euthyroid goiter cases

	Subclinical hypothyroidism (n=27)	Euthyroid goiter (n=29)	p-value
Age [med (min-max)]	72 (68-74)	72 (68-74)	0.584
Gender (female/male)	24 (88.9%)	25 (86.2%)	1
TSH (mIU/L) (mean ± standard deviation)	7.47±0.20	3.30±0.24	<0.001
ft4 (ng/dL) (mean ± standard deviation)	1.09±0.02	1.28±0.08	<0.001
ft3 (pg/mL) [med (min-max)]	2.42 (2.17-2.73)	3.15 (2.53-3.29)	<0.001
Liquid gastric emptying T1/2 (prolonged/normal)	17 (63%)	10 (34.5%)	0.033
BMI (overweight/normal)	9 (33.3%)	10 (34.5%)	0.928
Goiter size (mild/moderate/normal)	0/0/27 (0/0/100%)	13/16/0 (44.8%/55.2%/0)	0.005

min-max: minimum-maximum, med: median, TSH: thyroid-stimulating hormone, ft4: free T4, BMI: body mass index

SGES, is an easy and short-term test. Solid foods are broken down into small pieces by enzymes and gastric juice. While solid food must be broken down to pass through the pyloric sphincter, liquids pass directly. No cause is found in 50% of patients with dyspeptic complaints (9). Patients with upper gastrointestinal symptoms may have antrypyloroduodenal contraction disorder (24). Scintigraphic GEHT calculation is superior to barium studies because LGES is a physiological test (24). Small intestinal dysmotility may be associated with gastroparesis symptoms. Normally, 12% of antral contractions cause duodenal spread (25). Gastroparesis is common in diabetic patients. The prevalence of gastroparesis in diabetic patients is 64% (25). Some studies involving diabetic patients have reported a correlation between dyspeptic complaints and prolonged GEHT. Furthermore, acute changes in blood sugar affect gastric emptying (24). Diabetic patients were not included in this study; the included patients did not have hypoglycemia or hyperglycemia. Rapid gastric emptying may also be a consequence of autonomic dysfunction (25). There was no evidence of rapid gastric emptying in the present study. Although SGES is the gold standard method for calculating GEHT, dynamic imaging for 90 min and imaging late at 4 h make it difficult to apply, especially in the elderly population. Dynamic imaging places significant strain on the SPECT system; therefore, static imaging is more advantageous. In this study, GEHT was calculated using LGES and static images. The radiation dose required for LGES imaging is very low and the test time is short; therefore, it fulfilled the requirement of a practical test. Dyspepsia complaints may accompany many chronic diseases, such as diabetes, neuromuscular disorders, and endocrine disorders. However, with appropriate precautions, dyspeptic complaints can be prevented. In cases of SH, minor changes in thyroid hormone levels may delay gastric emptying. In this study, patients with gastroparesis who were prolonged in GEHT were referred to the endocrinology outpatient clinic for treatment prescription.

Study Limitations

A retrospective approach is a weakness of our study.

CONCLUSION

LGES may be preferred in elderly patients with suspected gastroparesis because of its easy application and short duration. Detecting the prolongation of gastric emptying time due to the presence of gastroparesis in SH and EG cases followed up without treatment may guide the prescription of treatment.

Ethics Committee Approval: Our study was approved by University of Health Sciences Türkiye, Gaziosmanpaşa Training and Research Hospital Clinical Research Ethics Committee on 01.03.2023 with 28 decision numbers.

Informed Consent: Informed consent was obtained from all participants of this study.

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REFERENCES

- Maurer AH, Yu D, Lu X, Dadparvar S, Kamat BH, Shahsavari D, et al. Addition of small-bowel transit scintigraphy to gastric emptying for assessment of patients with upper gastrointestinal symptoms. *Neurogastroenterol Motil* 2021; 33: e13987.
- Ceylan S, Yilmaz N. Evaluation of Dyspepsia with Optimal and Suboptimal Gastric Emptying Tests in Patients with Euthyroid Goiter. *Curr Med Imaging* 2023; 19: 1665-74.
- Dietlein M, Dressler J, Grünwald F, Leisner B, Moser E, Reiners C, et al. Guideline for radioiodine therapy for benign thyroid diseases (version 4). *Nuklearmedizin* 2007; 46: 220-3.
- Führer D, Bockisch A, Schmid KW. Euthyroid goiter with and without nodules--diagnosis and treatment. *Dtsch Arztebl Int* 2012; 109: 506-15.
- Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedüs L, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: Executive Summary of recommendations. *J Endocrinol Invest* 2010; 33: 287-91.
- Garber JR, Cobin RH, Gharib H, Hennessey JV, Klein I, Mechanick JI, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Thyroid* 2012; 22: 1200-35.
- Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al. Guidelines for the treatment of hypothyroidism: Prepared by the American thyroid association task force on thyroid hormone replacement. *Thyroid* 2014; 24: 1670-751.
- Abell TL, Camilleri M, Donohoe K, Hasler WL, Lin HC, Maurer AH, et al. Consensus recommendations for gastric emptying scintigraphy: a joint report of the American Neurogastroenterology and Motility Society and the Society of Nuclear Medicine. *J Nucl Med Technol* 2008; 36: 44-54.
- Bonapace ES, Maurer AH, Davidoff S, Krevsky B, Fisher RS, Parkman HP. Whole gut transit scintigraphy in the clinical evaluation of patients with upper and lower gastrointestinal symptoms. *Am J Gastroenterol*. 2000; 95: 2838-47.
- Rentz AM, Kahrilas P, Stanghellini V, Tack J, Talley NJ, de la Loge C, et al. Development and psychometric evaluation of the patient assessment of upper gastrointestinal symptom severity index (PAGI-SYM) in patients with upper gastrointestinal disorders. *Qual Life Res* 2004; 13: 1737-49.
- Chaudhary SC, Ahmad T, Usman K, Sawlani KK, Gupta KK, Verma AK, et al. Prevalence of thyroid dysfunction in chronic obstructive pulmonary disease patients in a tertiary care center in North India. *J Family Med Prim Care* 2018; 7: 584-8.
- Parkman HP, Hasler WL, Fisher RS; American Gastroenterological Association. American Gastroenterological Association technical review on the diagnosis and treatment of gastroparesis. *Gastroenterology* 2004; 127: 1592-622.
- Yu D, Ramsey FV, Norton WF, Norton N, Schneck S, Gaetano T, et al. The burdens, concerns, and quality of life of patients with gastroparesis. *Dig Dis Sci* 2017; 62: 879-93.
- Wiersinga WM, Duntas L, Fadeyev V, Nygaard B, Vanderpump MP. 2012 ETA Guidelines: The Use of L-T4 + L-T3 in the Treatment of Hypothyroidism. *Eur Thyroid J* 2012; 1: 55-71.
- Petersen M, Knudsen N, Carlé A, Andersen S, Jørgensen T, Perrild H, et al. Increased Incidence Rate of Hypothyroidism After Iodine Fortification in Denmark: A 20-Year Prospective Population-Based Study. *J Clin Endocrinol Metab* 2019; 104: 1833-40.
- Wang X, Zhang Y, Tan H, Bai Y, Zhou L, Fang F, et al. Effect of levothyroxine on pregnancy outcomes in women with thyroid autoimmunity: A systematic review with meta-analysis of randomized controlled trials. *Fertil Steril* 2020; 114: 1306-14.
- Perros P, Van Der Feltz-Cornelis C, Papini E, Nagy EV, Weetman AP, Hegedüs L. The enigma of persistent symptoms in hypothyroid patients treated with levothyroxine: A narrative review. *Clin Endocrinol (Oxf)* 2023; 98: 461-8.
- Lillevang-Johansen M, Abrahamsen B, Jørgensen HL, Brix TH, Hegedüs L. Duration of Hyperthyroidism and Lack of Sufficient Treatment Are Associated with Increased Cardiovascular Risk. *Thyroid* 2019; 29: 332-40.
- Hegedüs L, Bonnema SJ, Bennedbæk FN. Management of simple nodular goiter: Current status and future perspectives. *Endocr Rev* 2003; 24: 102-32.

20. Völzke H, Lüdemann J, Robinson DM, Spieker KW, Schwahn C, Kramer A, et al. The prevalence of undiagnosed thyroid disorders in a previously iodine-deficient area. *Thyroid* 2003; 13: 803-10.
21. Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-time elastography for the differentiation of benign and malignant thyroid nodules: a meta-analysis. *Thyroid* 2010; 20: 1145-50.
22. Grussendorf M, Reiners C, Paschke R, Wegscheider K; LISA Investigators. Reduction of thyroid nodule volume by levothyroxine and iodine alone and in combination: a randomized, placebo-controlled trial. *J Clin Endocrinol Metab* 2011; 96: 2786-95.
23. Fast S, Hegedüs L, Grupe P, Nielsen VE, Bluhme C, Bastholt L, et al. Recombinant human thyrotropin-stimulated radioiodine therapy of nodular goiter allows major reduction of the radiation burden with retained efficacy. *J Clin Endocrinol Metab* 2010; 95: 3719-25.
24. Vijayvargiya P, Jameie-Oskooei S, Camilleri M, Chedid V, Erwin PJ, Murad MH. Association between delayed gastric emptying and upper gastrointestinal symptoms: a systematic review and meta-analysis. *Gut* 2019; 68: 804-13.
25. Cogliandro RF, Rizzoli G, Bellacosa L, De Giorgio R, Cremon C, Barbara G, et al. Is gastroparesis a gastric disease? *Neurogastroenterol Motil* 2019; 31: e13562.