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ORIGINAL ARTICLE

Retrospective Study

Is it necessary to stop glucagon-like peptide-1 receptor agonists prior to endoscopic procedure? A retrospective study

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Abstract

BACKGROUND

Glucagon-like peptide-1 receptor agonists (GLP-1 RA) are effective in diabetes and obesity, reducing hyperglycemia by increasing insulin release and delaying gastric emptying. However, they can cause gastroparesis, raising concerns about aspiration during procedures. Recent guidelines advise discontinuing GLP-1 RA before surgery to reduce the risk of pulmonary aspiration.

AIM

To evaluate the effect of GLP-1 RAs on gastric residual contents during endoscopic procedures.

METHODS

A retrospective chart review at BronxCare Health System, New York, from January 2019 to October 2023, assessed gastric residue and aspiration in GLP-1 RA patients undergoing endoscopic procedures. Two groups were compared based on dietary status before the procedure. Data included demographics, symptoms of gastroparesis, opiate use, hemoglobin A1c, GLP-1 agonist indication, endoscopic details, and aspiration occurrence. IBM SPSS was used for analysis, calculating means, standard deviations, and applying Pearson's chi-square and t-tests for associations, with $P < 0.05$ as being significant.

RESULTS
During the study, 306 patients were included, with 41.2% on a clear liquid/low residue diet and 58.8% on a regular diet before endoscopy. Most patients (63.1%) were male, with a mean age of 60 ± 12 years. The majority (85.6%) were on GLP-1 RAs for diabetes, and 10.1% reported digestive symptoms before endoscopy. Among those on a clear liquid diet, 1.5% had residual food at endoscopy compared to 10% on a regular diet, which was statistically significant (P = 0.03). Out of 31 patients with digestive symptoms, 13% had residual food, all from the regular diet group (P = 0.130). No complications were reported during or after the procedures.

CONCLUSION
The study reflects a significant rise in GLP-1 RA use for diabetes and obesity. A 24-hour liquid diet seems safe for endoscopic procedures without aspiration. Patients with upper gastrointestinal symptoms might have a higher residual food risk, though not statistically significant. Further research is needed to assess risks based on diabetes duration, gastroparesis, and GLP-1 RA dosing, aiming to minimize interruptions in therapy during procedures.

Key Words: Glucagon-like peptide-1 agonists; Gastroparesis; Endoscopic procedures; Residual food; Complications

Core Tip: This retrospective study assessed the impact of glucagon-like peptide-1 receptor agonists (GLP-1 RA) on gastric residual contents during endoscopy. Patients on a clear liquid diet had significantly lower residual food rates (1.5%) compared to those on a regular diet (10%, P = 0.03). Among patients with digestive symptoms, 13% had residual food, all from the regular diet group (P = 0.130). No complications occurred during or after the procedures. The study suggests that a 24-hour liquid diet is safe for endoscopic procedures. However, further research is needed to understand residual food risks in patients with upper gastrointestinal symptoms and to evaluate risks based on diabetes duration, gastroparesis presence, and GLP-1 RA dosing.

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INTRODUCTION

There has been a recent increase in the use of glucagon-like peptide-1 receptor agonists (GLP-1 RA) in diabetes and obesity[1]. GLP-1 RA includes human analogues (Albiglutide, Dulaglutide, Liraglutide, Semaglutide) and exendin-4 derivatives (Exenatide, Lixisenatide) are effective in reducing postprandial hyperglycemia[2]. GLP-1 RAs lead to increased insulin release, reduced glucagon release, delayed gastric emptying, and induce a sense of fullness[3].

Gastroparesis is defined as delayed gastric emptying in the absence of any mechanical obstruction. The etiology of gastroparesis can be categorized as idiopathic or secondary to diabetes, iatrogenic (due to medication), post-surgical, autoimmune condition, neurological condition, and viral infection[4]. A systemic review of the literature concluded that the prevalence of gastroparesis in the general population ranged from 13.8 to 267.7 per 100000 adults, and the incidence varied from 1.9 to 6.3 per 100000 person-years[5]. In a United States study, gastroparesis prevalence was 4.6% in type 1 diabetes and 1.3% in type 2 diabetes[6]. Gastroparesis presents with a variety of symptoms which include nausea, vomiting, and abdominal pain. Once the mechanical obstruction is excluded, the diagnosis of gastroparesis can be confirmed by the presence of delayed gastric emptying on scintigraphy[7].

GLP-1 RAs have been shown to reduce cardiovascular mortality in patients with type 2 diabetes. Despite benefits, there is a growing concern about gastroparesis leading to aspiration in some patients taking GLP-1 RA while undergoing procedures requiring general anesthesia or deep sedation[8]. Various studies have shown that GLP-1 RAs can lead to delayed gastric emptying[9-11]. The underlying mechanism is inhibition of peristalsis of stomach while increasing tonic contraction of pyloric region and suppressing gastric emptying[9]. According to a case-control study, 5.8% of the patients on GLP-1 RA had gastric residue as compared to 0.49% in patients who were not on GLP-1 RA[12]. Studies have also shown that the effect of GLP-1 RAs on gastric emptying decreases over time due to tachyphylaxis at the level of vagal nervous activation[13]. GLP-1 RAs have been shown to cause gastroparesis by slowing down gastric emptying *via* its effect on antral and duodenal motility and increasing pyloric pressures[14-16]. GLP-1 RAs also increase the duodenal-small bowl emptying time[9].

Recently the American Society of Anesthesiologists (ASA) recommended holding GLP-1 RA one week prior to surgical and endoscopic procedures because of GLP-1 RAs' effect on gastric emptying[17]. The reason for this recommendation was due to the increased risk of pulmonary aspiration of gastric contents in patients taking GLP-1 RA. This recom-

mendation was based on a case report of a 42-year-old patient on GLP-1 RA who had pulmonary aspiration after an esophagogastroduodenoscopy (EGD)[18]. These recommendations have led to some confusion and cancellation of elective procedures. The purpose of this study is to assess the impact of GLP-1 RAs on gastric residual contents found while performing endoscopic procedures.

MATERIALS AND METHODS

Study design

We conducted a retrospective chart review of patients on GLP-1 RAs who underwent endoscopic procedures at BronxCare Health System, New York during the study period January 2019 to October 2023 to assess gastric residue contents and aspiration. All patients who were on GLP-1 RAs and who underwent EGD with or without colonoscopy during the study period were included in the study. Patients who only underwent colonoscopy were not included in the study. In our study, only presence of food was considered to reduce interobserver variability in quantification of food residue. Residual food estimation was done primarily to determine the completeness of the assessment and the risk of aspiration during the procedure. This solely was the estimate of experienced gastroenterologists. All the endoscopic procedures were done by 6 board certified gastroenterologists with more than 7 years of experience. The patients received monitored anesthesia care utilizing mainly intravenous propofol during the endoscopic procedure. No other anesthetic agents were used. We compared two groups of patients who were placed on a liquid diet 24 h prior to procedure *vs* those who were kept only Nothing by Mouth/*nil per os* (NPO) after midnight without dietary restrictions prior to the procedure. The liquid diet comprised of clear juices like apple juice, lemonade or broth. Low reidue diet included foods like mashed potatoes and boiled eggs. Patients who were only getting EGD done were asked to continue regular diet as they would do at their baseline one day before the procedure and be NPO on the day of the procedure. Patients who were planned for both colonoscopy and EGD were placed on a clear liquid diet/low residue diet one day before the procedure and be NPO on the day of the procedure. Patients underwent EGD and Colonoscopy to determine the cause of anemia or obscure gastrointestinal bleeding. Medical records were reviewed for demographics and clinical data including age, gender, signs or symptoms of gastroparesis, history of opiate use, hemoglobin A1c (HbA1c) value (within last 6 months), indication for the GLP-1 agonist use, history of gastric emptying study, type of endoscopic procedure, the findings of EGD especially studies of residual food in the stomach, and if the patient developed any aspiration after the procedure.

Statistical analysis

Data was analyzed using the Statistical Package for the Social Sciences (SPSS), version 21.0 (IBM, Armonk, NY, Unites States). The mean and the standard deviation were calculated for continuous variables like age and HbA1C. Variables including gender, digestive symptoms present prior to endoscopy, history of cannabis use, and history of opiate including methadone use were analyzed. Pearson's χ^2 test was used to find an association between the presence of residual food at endoscopy in patients who were on a clear liquid diet/low residue diet as compared to patients who were on a regular diet one day prior to the endoscopic procedure. Independent *t*-test was applied to assess if there was any significant difference in age and HbA1c in patients who had residual food in the stomach as compared to patients who did not have any residual food in the stomach. *P* value of less than 0.05 was considered as significant.

RESULTS

We compared two groups of patients who underwent EGD and were either on a regular diet with NPO after midnight or had a clear liquid/low residue diet with NPO after midnight. A total of 306 patients met the inclusion criteria during the study period. There were 126 (41.2%) patients who were on a clear liquid/low residue diet the day prior to the procedure, while 180 (58.8%) patients were on a regular diet the day prior to the procedure. Overall, 63.1% (193) were males and 36.9% (113) were females. The mean age of the patients was 60 ± 12 years. Only 10.1% of the patients complained of digestive symptoms prior to the endoscopy. About 10.8% of patients had a history of cannabis use and 5.2% of patients had a history of Opioid use. The mean HbA1c value was 8 ± 2%. Most of the patients (85.6%) were on GLP-1 RAs because of diabetes. Only 12 (3.9%) patients had a gastric emptying study done prior to endoscopy. Five patients had a delayed gastric emptying study. Out of the 5 patients who were diagnosed with gastroparesis; one was on a clear liquid diet/low residue diet and four were on a regular diet the day prior to the procedure. Out of these 5 patients with gastroparesis, only one patient who was on a regular diet one day prior to the procedure was found to have residual food at endoscopy (Table 1).

There was no significant difference in age and level of HbA1c between the two groups, although the duration of diabetes in these patients was unknown. Out of 126 patients who were on a clear liquid diet/low residue diet; only 2 patients (1.5%) had residual food at endoscopy, whereas 18 out of 180 (10%) patients who were on a regular diet one day prior to the procedure were noted to have residual food. This was found to be statistically significant ($P = 0.03$) (Figure 1).

Out of 31 patients who had digestive symptoms prior to endoscopy, 3 were on clear liquid/low residue diet one day prior to procedure whereas 28 were on regular diet. Four out of 31 patients (13%) were noted to have residual food at endoscopy ($P = 0.130$) and all of them were on regular diet. None of the patients developed any complications during or after the procedure.

Table 1 Association of type of gastrointestinal procedure done with gender, presence of digestive symptoms prior to endoscopy, history of cannabis use, history of opioids or methadone use, and presence of residual food

Parameter		Type of diet one day prior to the procedure		*P* value
		Regular diet	Clear liquid/low residue diet	
Gender	Female	112	81	0.713
	Male	68	45	
Nausea, vomiting, dyspepsia, bloating (digestive symptoms) prior to endoscopy	No	152	123	< 0.001
	Yes	28	3	
History of cannabis use	No	165	108	0.099
	Yes	15	18	
History of opioids or methadone use	No	172	118	0.461
	Yes	8	8	
Presence of residual food	No	162	124	0.03
	Yes	18	2	

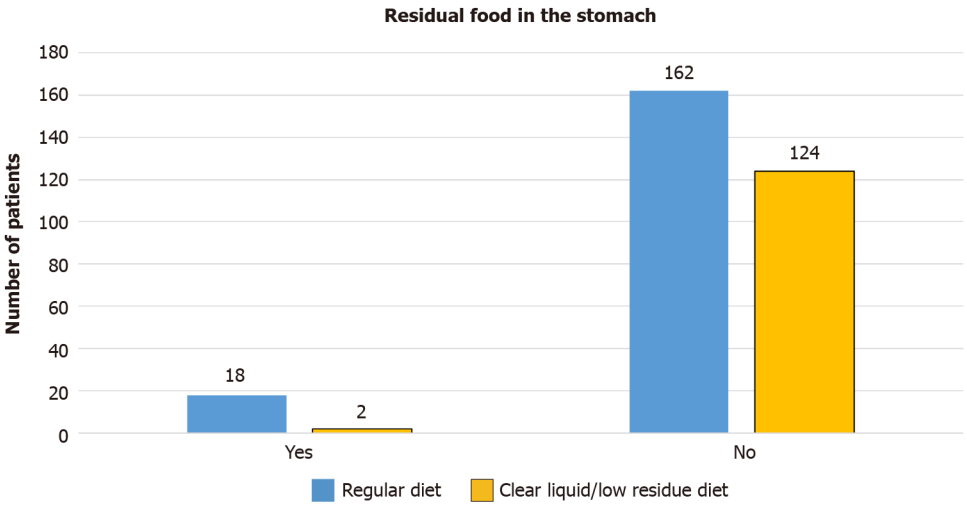

Figure 1 Residual food in the stomach after regular diet and clear liquid/low residue diet.

DISCUSSION

In our study, only 2 out of 126 patients (1.58%) on a clear liquid/low residue diet had residual food in the stomach at EGD as compared to 18 patients out of 180 patients (10%) who were on regular diet ($P = 0.03$). Although a significant number of patients (13%) who had digestive symptoms had residual food in the stomach, it was not statistically significant ($P = 0.130$). None of the patients in our study had aspiration. We hypothesize that patients who were on a clear liquid/low residue diet were less likely to have residual food as this diet has a shorter gastric emptying time compared to regular diet. The presence of symptoms suggestive of gastroparesis also appears to predict the presence of residual food, although this association did not reach statistical significance.

GLP-1 RA have been classified as short-acting or long-acting based on their duration of action and administration frequency. Short-acting GLP-1 RA like Exenatide and Lixisenatide need to be taken once or two times a day. The short-acting GLP-1 RA reduce the postprandial hyperglycemia by delaying gastric emptying and decreasing endogenous glucose production by 50%[19]. Long-acting GLP-1 RA such as Liraglutide, Exenatide, Lemaglutide, and Dulaglutide activate the GLP-1 RA continuously and only needs to be taken once weekly. According to a randomized controlled trial done by Maselli *et al*[20], Liraglutide leads to a significant delay in gastric emptying ($P < 0.001$)[20]. A study done by Kalas *et al*[21], in patient who were on Semaglutide initially and were diagnosed as diabetic gastroparesis, discontinuation of the GLP-1 RA resulted in symptom alleviation and the resolution of delayed gastric emptying[21]. Limited literature exists on GLP-1 RA in individuals with preexisting gastroparesis. A study done by Beti *et al*[22], revealed that 75% of participants with normal gastric emptying developed delayed gastric emptying after GLP-1 RA treatment, while 30% with preexisting gastroparesis experienced worsening of gastric emptying[22]. A case is reported by Rai *et al*[23], on acute gastroparesis induced by Liraglutide in a patient with type 2 diabetes[23]. According to studies done by Little *et al*[24], and Ishihara *et al*[25], even a low dose of GLP-1 RA can lead to gastroparesis[24,25].

Table 2 Impact of glucagon-like peptide-1 receptor agonist on colonoscopy preparation

Ref.	Selected population	Type of study	Patients (*n*)	Endpoint	Significant results
Yao *et al* [26]	Patients on GLP-1 RAs (cases) and patients not taking GLP-1 RAs (controls)	Retrospective cohort study	446	Comparing bowel prep quality using the BBPS between diabetic patients taking GLP-1 RAs (case group) and diabetic patients not on GLP-1 As (control group)	BBPS score of < 5 was 15.5% in the case group *vs* 6.6 in the control group. 18.9% of the case group needed repeat colonoscopy as compared to 11.1% in the control group
Tong *et al*[27]	Patients on liraglutide *vs* patients on sitagliptin *vs* patients not on GLP-1 RAs	Prospective observational study	360	Assess the incidence of inadequate bowel cleaning using the BBPS, in patients taking GLP-1 RAs *vs* DPP-4i *vs* patients not taking GLP-1 RA	No statistical significance in the incidence of inadequate bowel cleaning was found between the liraglutide group, the sitagliptin group, and the control group $P = 0.927$. Patients with Type 2 Diabetes and peripheral neuropathy taking GLP-1 RA did have a significant increase in inadequate bowel cleaning when compared to the sitagliptin group (61.3% *vs* 32.1%, $P = 0.022$) and control group (61.3% *vs* 32.8%, $P = 0.025$)
Sharma *et al*[28]	Patients aged 45-75 who had an outpatient elective colonoscopy between 2012 and 2015, took one of the following drugs–Byetta, Victoza, or Bydureon	Retrospective medical record analysis	255	Comparing bowel prep quality using high-volume polyethylene glycol electrolyte lavage solution among two groups, one taking a GLP-1 RA and other group not taking a GLP-1 RA	The percentage of satisfactory bowel preparations in the group taking a GLP-1 RA was 92.06% and 92.25% in the group not taking a GLP-1 RA

GLP-1 RAs: Glucagon-like peptide-1 receptor agonists; DPP-4i: Dipeptidyl peptidase-4-inhibitor; BBPS: Boston Bowel Preparation Scale.

According to a retrospective study conducted by Yao *et al*[26], 15.5% of patients receiving GLP-1 RA had a Boston Bowel Preparation Scale (BBPS) score of less than 5, compared to 6.6% of patients not receiving GLP-1 RA[26]. An observational study done by Tong *et al*[27] did not notice a significant difference in the incidence of inadequate bowel preparation on colonoscopy in patients taking Liraglutide, Sitagliptin, and patients not on GLP-1 RA. In the subgroup analyses it was shown that type 2 diabetes patients with diabetic neuropathy on Liraglutide were more likely to have inadequate bowel prep (61.3%) as compared to patients in Sitagliptin group (32.1%; $P = 0.022$) and control group (32.8% $P = 0.025$)[27]. A retrospective medical record analysis done by Sharma *et al*[28], on type 2 diabetes patients in GLP-1 RA showed no significant difference between the groups. A summary of these studies has been presented in Table 2.

There is limited literature available on the impact of GLP-1 RA on gastric food retention in patients undergoing EGD. A retrospective study done by Stark *et al*[12] concluded that 6.8% of the patients taking GLP-1 RA had food retention as compared to 1.7% of the patients in the control group, but it was not statistically significant. None of the patients in the study required a repeat EGD due to 2 poor visualization[13]. A case-control study done by Kobori *et al*[29] reported that patients on GLP-1 RA had a significantly high gastric residue as compared to patients not taking GLP-1 RA ($P = 0.004$). A single-center retrospective study done by Silveira *et al*[30] reported that patients taking Semaglutide were 5.15 times more likely to have gastric residue as compared to patients not on Semaglutide[30]. The study also concluded that patients with digestive symptoms before EGD were more likely to have increased residual gastric content. In our study, 13% of the patients who had digestive symptoms had food residue in the stomach. However, it was not statistically significant ($P = 0.130$). A study done on 20 participants by Sherwin *et al*[11], shows that GLP-1 RAs has a significant impact on gastric emptying and can lead to an increased risk of aspiration in patients requiring anesthesia[11]. A summary of these studies has been presented in Table 3.

Currently, there are limited studies addressing this issue. To the best of our knowledge, this is one of the first studies assessing if a clear liquid/low-residue diet prior to the endoscopic procedure requiring deep sedation had any impact on gastric emptying in patients taking GLP-1 RA. We believe that the current recommendations by the ASA based on anecdotal reports require further examination. Despite the limitations of our retrospective study, it demonstrated that it was unnecessary to discontinue GLP for one week. Discontinuation of therapies for one week often leads to poor glycemic control requiring multiple visits to the primary care provider.

Limitations

This is a retrospective study, and we are unable to assess if the patients were adherent to our dietary recommendations. We were also unable to assess the adherence of the patient use of GLP-1 RA due to the retrospective nature of the study. The duration of diabetes was not available, and this may have an impact on the presence of gastroparesis. Additionally, due to retrospective nature of the study, evaluation of quantity of food residue was limited. Also, the quantity of regular food that the patients were eating at baseline could not be defined given the retrospective nature of the study.

Table 3 Summary of the studies assessing the impact of glucagon-like peptide-1 receptor agonists on patients undergoing esophagogastroduodenoscopy

Ref.	Selected population	Type of study	Patients (*n*)	Endpoint	Significant results
Stark *et al*[12]	Patients undergoing EGD with the use of GLP-1 RA and patients without GLP-1 RA	Retrospective cohort study with matched controls	177	Odds of retained food documented during EGD and incidence of lavage and need for repeat EGD due to poor visualization	Food retention present in 6.8% in the GLP-1 group versus 1.7% in the control group, but it was not statistically significant [OR: 4.22 (95%CI: 0.87-20.34)]. None of the patients in the study required repeat EGD due to poor visualization
Kobori *et al*[29]	Patients with diabetes undergoing EGD with the use of GLP-1 RA and patients without GLP-1 RA	Matched pair case-control study	410	Assess the association between GLP-RA treatment and gastric residue in patient's undergoing EGD	The proportion of gastric residue was significantly higher in the GLP-1 RA group when compared to the group without GLP-1 RA treatment (5.4% *vs* 0.49%; $P = 0.004$)
Silveira *et al*[30]	Patients with diabetes undergoing EGD with the use of GLP-1 RA and patients without GLP-1 RA	Single-center retrospective electronic chart review	404	To determine if the use of GLP-1 RA is associated with delayed gastric emptying and increased residual gastric content despite adequate pre-procedure fasting before EGD	The use of Semaglutide was associated with 5.15-fold increase in residual gastric content (24% *vs* 5.1%; $P < 0.001$). The presence of digestive symptoms was associated with increased residual gastric content [3.56 (95%CI: 2.2-5.78)]
Sherwin *et al*[11]	Volunteers who were taking Semaglutide for weight loss and volunteers who were not on Semaglutide	Prospective observational study	20	To evaluate the presence of gastric content using gastric ultrasound in patients taking GLP-1 RA compared with controls, after 8 hours of fasting	Patients using Semaglutide had solid gastric content in 70% of the cases in the supine position as compared to 10% in control (RR: 3.50; $P = 0.02$). In the lateral position solid content was found in 90% of the cases *vs* 20% in controls (RR: 7.36; $P = 0.005$)

EGD: Esophagogastroduodenoscopy; GLP-1 RAs: Glucagon-like peptide 1 receptor agonists; OR: Odds ratio; RR: Relative risk.

CONCLUSION

The use of GLP-1 RAs has significantly increased in managing diabetes and obesity. In our study, a 24-hour liquid diet appears to be adequate to safely perform endoscopic procedures (including both EGD and Colonoscopy) in patients who are on GLP-1 RA without risk of aspiration. Discontinuation of GLP-1 RAs is unnecessary in most patients without signs of gastroparesis. Patients with upper gastrointestinal symptoms appear to have a higher risk of residual food even though it did not reach statistical significance. Further studies are needed to determine the risk based on the duration of diabetes, the presence of gastroparesis, and the dosing of GLP-1 RAs. The goal would be to have minimal interruptions of these essential therapeutic agents while safely performing endoscopic procedures.

FOOTNOTES

Author contributions: Ghazanfar H, Patel H, Makker J, Balar B, Dev A and Chilimuri S conceptualized the study; Javed N, Qasim A, Sosa F, Altaf F, Khan S, Mahasamudram J, Kandhi SD and Hanumanthu S were involved in data curation; Ghazanfar H, Kandhi SD, Jyala A, Shin D, Mantri N, Sun H and Hanumanthu S were involved in data analysis and investigation; Ghazanfar H, Kandhi SD, Jyala A, Shin D, Mantri N, Sun H, Patel H, Makker J, Balar B, Dev A and Chilimuri S designed the methodology of the study; Ghazanfar H, Patel H, Makker J, Balar B, Dev A and Chilimuri S were involved in project administration; Patel H, Makker J, Balar B, Dev A and Chilimuri S provided resources; Javed N, Sosa F, Khan S, Hanumanthu S and Shin D were involved in software acquisition; Patel H, Makker J, Balar B, Dev A and Chilimuri S were involved in supervision; Data validation was performed by Javed N, Qasim A, Altaf F, Khan S, Hanumanthu S and Shin D; Visualization was done by Javed N, Qasim A and Altaf F; The first draft of the study was written by Ghazanfar H, Javed N, Qasim A, Sosa F, Altaf F, Khan S, Mahasamudram J, Kandhi SD and Shin D; The draft was revised by Ghazanfar H, Javed N, Kandhi SD, Shin D, Mantri N, Sun H, Patel H, Makker J, Balar B, Dev A and Chilimuri S. All authors agreed to be responsible for all aspects of the final version of the manuscript.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of the BronxCare Health System.

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data.

Conflict-of-interest statement: We have no financial relationships to disclose.

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