

## REFERENCES

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2. Reja M, Mishra A, Tyberg A, et al. Gastric peroral endoscopic myotomy: a specific learning curve. *J Clin Gastroenterol* 2022;56:339-42.
3. Teitelbaum EN, Soper NJ, Arafat FO, et al. Analysis of a learning curve and predictors of intraoperative difficulty for peroral esophageal myotomy (POEM). *J Gastrointest Surg* 2014;18:92-9.
4. Liu XY, Cheng J, Chen WF, et al. A risk-scoring system to predict clinical failure for patients with achalasia after peroral endoscopic myotomy. *Gastrointest Endosc* 2020;91:33-40.

<https://doi.org/10.1016/j.gie.2022.07.006>

## Response:



We thank Zhang et al<sup>1</sup> for their interest in our study entitled “Gastroparesis peroral endoscopic myotomy outcomes after 4 years of follow-up in a large cohort of patients with refractory gastroparesis.”<sup>2</sup> In this study, our main aim was to evaluate the long-term outcomes of this fascinating third-space technique in patients with refractory gastroparesis (RG).

For this purpose, we decided to evaluate a large group of patients with RG of multiple causes: 141 diabetes (37.7%), 115 idiopathic (30.7%), 102 postsurgical (27.3%), and 16 other causes (4.3%). We found a general clinical success rate of 77.5% after 4 years of follow-up, patients with diabetes being those who showed the highest responses, with 86.5% (vs 72.5% idiopathic, vs 72.1% postsurgical, vs 68.8% other;  $P < .05$ ). Finally, long-term predictors of success were cause of diabetes (OR = 5.11 [1.64-5.98]); early diagnosis of <24 months (OR = 2.45 [1.12-5.52]); nausea/vomiting subtype (OR = 3.54 [1.88-5.51]); gastroparesis cardinal symptom index (GCSI) score between 1.5 and 2.5 at the 6-month evaluation (OR = 3.61 [2.12-5.31]), and a retention percentage at 4 hours (RP4H) of <10% at 6 months (OR = 2.18 [1.43-4.23]).

We have carefully read the concerns of Zhang et al<sup>1</sup> about the long-term predictors of clinical success that we found in our study, specifically the lack of consideration of the learning curve (LC) and the adverse events (AEs) of G-POEM as potentially contributory factors that could have affected our results and therefore that should have been considered in our multiple logistic regression model. Regarding the LC, we agree with Zhang et al<sup>1</sup> that G-POEM is a very complex technique, being the second third-space procedure reported after POEM for achalasia. As mentioned by Zhang et al,<sup>1</sup> information is scarce, and Reja et al<sup>3</sup> performed a retrospective study trying to determine the LC for G-POEM. They included 36 patients, most of them (44%) with idiopathic gastroparesis, and they determined a median procedure time of 60.5 minutes (35-136), with an increase in speed up to 45 minutes of total duration in their last cases. The cumulative sum control chart

showed that efficiency was reached after the eighteenth procedure, suggesting this as the potential cutoff in the LC for this procedure. However, there was no relationship among speed, lack of AEs during G-POEM, and clinical success. Therefore, the real effect of the LC of G-POEM on clinical success is not yet determined; however, it would be more appropriate to be based on a correct pyloric ring myotomy (PRM), which is supposed to be the most important objective when G-POEM is performed; or at least, this is the reason why this pyloric-targeted therapy was created. The same occurs with AEs during the procedure, in which their presence of course could affect not only the completion of G-POEM itself but also directly the clinical success, theoretically through 2 potential mechanisms: first, an incomplete PRM, or second, the formation of a consequently secondary scar at the surgical working area, potentially responsible for recurrence in these patients and also reported in patients with achalasia who have undergone POEM.<sup>4-7</sup>

Therefore, we consider that in spite of the fact that LC and AEs must be important points that should be considered when G-POEM is offered as an alternative option for RG in these patients, we doubt its role regarding a potential change in the results of our study. We mean that in our study, if LC could have had a potential effect on CS, we should have found different outcomes in the first G-POEM cases (at least in the first 20); however, this was not so. Of the 141 patients with diabetes included, with 15 recurrences, only 1 was part of the first 20. Of the 155 patients with idiopathic RG, with 25 recurrences, none of them were part of the first 20. Of the 102 patients with postsurgical gastritis, with 28 recurrences, none of them were part of the first 20 cases, and from the 4 recurrences in the other group, none of them were part of this group of first cases. Similar results were found in failures. Therefore, a clinical relationship between LC and CS seems unlikely. The same occurs with AEs, in which technical success was reached in 100% (we mean that all steps were completely performed, including the PMR), and all AEs were minor and endoscopically controlled during G-POEM. If AEs had been related to CS, we would have seen a relationship with failures or recurrences in our cohort, but this did not occur.

We have to remember that when a multiple logistic regression model is built, first a univariate analysis must be performed, including all of the potential clinical factors that we consider to be potentially related to the final binary outcome, in this case long-term success. From all included factors, even in our primary analysis, we did not find any relation between LC and AEs in our model, nor in either the univariate analysis or the multivariate analysis. This is not new; Gonzalez et al,<sup>8</sup> Ragi et al,<sup>9</sup> Mekaroonkamol et al,<sup>10</sup> Abdelfatah et al,<sup>11</sup> Xu et al,<sup>12</sup> and Vosoughi et al<sup>13</sup> have performed similar analyses searching for the potential predictive factors of CS. In general, gender, cause of RG, early CS (measured as a change in CSI or RP4H in the first months after G-POEM), duration of disease, RG subtype, body mass index, and age have been related to CS, and

no relationship with LC or AEs has been found. In achalasia, for example, there is an abnormal relaxation of the lower esophageal sphincter combined with esophageal aperistalsis. Of both, POEM throughout the myotomy of the lower esophageal sphincter can generate the expected CS. However, the lack of experience in the performance of third-space procedures in the early years of POEM could potentially have affected the outcomes of this procedure in the first patients treated with this technique. This has been confirmed by several authors throughout the role of LC in early and midterm outcomes.<sup>14-16</sup> This could be explained by the lack of the endoscopist's experience with third-space procedures, translated in the potential absence of an adequate rupture of the lower esophageal sphincter myotomy, besides which the endoscopist thought that this was adequately performed, mostly in difficult cases such as those with submucosal fibrosis. AEs have similar behavior. However, in RG, this is completely different, first, because most of the endoscopists who perform these procedures have previous good experience in POEM (as in our case); therefore, the third space is a well-known territory, meaning that the operator can correctly identify different structures including the pyloric muscle ring, and therefore its myotomy can be performed adequately, minimizing or avoiding AEs during the procedure; and second, because the pathophysiology of RG is very complex. Besides that, the rationale of CS is based on the indirect improvement in gastric emptying throughout an adequate PRM, whereas no homogeneous response is observed among different causes of subtypes of RG. In our case, we obtained the best results in patients with diabetes with nausea and vomiting, early diagnosis, and good improvement in early-term measures (GCSI and RP4H), probably explained by the major proportion of patients with pylorospasm in this population; however, this has not been observed in all causes of RG. In conclusion, although there is no universal criterion standard of treatment for this disease, G-POEM represents a potential first-line therapy in some patients, such as those with diabetes; however, efforts for clarification of the real role of G-POEM in RG must be continued.

## DISCLOSURE

*All authors disclosed no financial relationships.*

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<https://doi.org/10.1016/j.gie.2022.08.010>

## Artificial intelligence–assisted cholangioscopy for automatic detection of malignant biliary strictures



To the Editor:

We read with great interest the article by Mascarenhas Saraiva et al<sup>1</sup> regarding optimal diagnosis of malignant biliary strictures by using an artificial intelligence (AI) algorithm. We concur with their findings and agree that the introduction of AI algorithms such as convolutional neural network (CNN) imaging may significantly increase our