

## Joint TIGERS-EUREOS call for EoE cases undergoing bariatric surgery

---

### TITLE

#### **Bariatric Surgery in Patients with Eosinophilic Esophagitis: Disease course and surgical outcomes**

### BACKGROUND

Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder of the esophagus characterized clinically by symptoms of esophageal dysfunction and histologically by an eosinophil-predominant infiltration of the esophageal mucosa.<sup>1</sup> Since its first description in the 1990s,<sup>2,3</sup> incidence and prevalence of EoE have been rapidly increasing.<sup>4</sup> In North America and Europe, it is currently estimated that 1 individual among 2000 inhabitants is affected by EoE. Chronicity is a predominant feature of the disease: observational studies and clinical experience accordingly show that in the vast majority of patients both symptoms and eosinophilic inflammation persist over years. Delay in diagnosis and inadequate treatment may result in development of disease complications such as stricture formation and bolus impactions, which may warrant endoscopic removal.<sup>5,6</sup> However, despite EoE possibly interfering with food intake, weight loss is rarely observed in adult patients. In fact, even (severe) obesity may occur.<sup>13</sup>

Bariatric surgery has been demonstrated to be an effective treatment for morbid obesity and its comorbidities.<sup>7-9</sup> In fact, and despite emerging medical options, it represents the most effective long-term treatment and is increasingly common in the US and Europe.<sup>10</sup> The two most often performed surgical techniques are sleeve gastrectomy and gastric bypass which result in a mean weight loss of 20-25%.<sup>11,12</sup> Ongoing gastrointestinal inflammatory diseases, particularly Crohn's disease, have long been considered (relative) contraindications to such surgery. However, it appears to be safe for CD patients to undergo bariatric surgery if indicated and if the disease is under control.<sup>10</sup> Theoretically, EoE as another chronic inflammatory disorder affecting the esophagus could negatively impact bariatric surgery and vice versa. Ongoing inflammation in the lower esophagus could complicate healing of the gastro-jejunosomy after gastric bypass, while increased reflux after sleeve gastrectomy could worsen the eosinophil infiltration. However, no published data are available. Currently, clinicians are puzzled how to deal with EoE patients requiring bariatric surgery and it remains

elusive whether or not such surgery can be safely recommended. This is particularly challenging given considerable rates of obesity in EoE.<sup>13</sup>

Given these uncertainties, we aim to evaluate EoE patients undergoing bariatric surgery with regards to EoE-related and surgery-related outcomes.

## RESEARCH QUESTIONS

With this retrospective study, we seek to answer the following research questions:

- What are patient and disease characteristics of EoE patients undergoing bariatric surgery?
- What is the disease-related outcome of patients with EoE undergoing bariatric surgery?
- How is the procedural outcome of bariatric surgery affected by the presence and the activity of EoE at the timepoint of surgery?

## SIGNIFICANCE

This study will be the first study to systematically assess the impact of EoE on bariatric surgery and vice versa.

## RESEARCH HYPOTHESIS

We hypothesize that

- In most of the patients undergoing bariatric surgery EoE is clinically and histologically well-controlled at the time of surgery, either by dietary or medical treatment.
- In contrast, bariatric surgery is rarely performed in EoE patients with active disease.
- EoE disease activity does not increase after bariatric surgery.
- EoE does not negatively affect the surgical outcome of bariatric surgery.
- The inflammatory activity at the time-point of surgery may affect the post-procedural outcome.

## OBJECTIVES

The primary objective of this study is to evaluate the natural history of EoE after bariatric surgery and the effect of EoE on surgical outcomes

We will:

- *Investigate* baseline patient and disease characteristics of EoE patients undergoing bariatric surgery;
- *Assess* the natural history of EoE after bariatric surgery;
- *Analyze* surgical outcome after bariatric surgery;

- *Evaluate* thereby the effect of EoE on bariatric surgery and vice versa

## **RESEARCH TEAM**

- Anne Godat, GZO Zurich Regional Health Center, Wetzikon, Switzerland
- Alex Straumann, University Hospital Zurich, Zurich, Switzerland
- Thomas Greuter, University Hospital Zurich, University Hospital Lausanne – CHUV, and GZO – Zurich Regional Health Center, Wetzikon, Switzerland

## **AUTHORSHIP RULES**

All researchers contributing at least one single case to this series will be mentioned as a co-author (in alphabetical order). First position Anne Godat. Last position: Thomas Greuter.

## **METHODS**

### **Study Design**

This is an observational, retrospective multicenter case series involving EoE patients undergoing bariatric surgery.

### **Study Population**

#### **Inclusion and exclusion criteria**

All EoE patients undergoing bariatric surgery will be included. Patients will be excluded if EoE has not been established according to international guidelines and if follow-up after bariatric surgery is too short (< 4 weeks). Only patients >16 years will be included.

### **Outcomes**

The following outcome parameters will be assessed:

- Clinical EoE activity: Presence of dysphagia on a visual analogue scale (VAS) from 0-10
- Endoscopic EoE activity: Assessed by EREFS<sup>14</sup>
- Histological EoE activity: assessed by peak eosinophil counts (and if applicable the EoE-HSS<sup>15</sup>).
- Outcome of bariatric surgery: mean weight loss after surgery

- Postsurgical complications: presence of early vs late complications

### **Recruitment of the Study Population**

Patients will be recruited through a joint call for cases among EoE experts involved in the US (TIGERS) and Europe (EUREOS). The project will be presented at virtual meetings (TIGERS, EUREOS) and members will thereafter be contacted through email. The call will be open between Nov 15 and Jan 15.

### **Data collection**

Structured data collection is performed by means of a standardized spreadsheet. All data are anonymized.

### **Statistics**

For statistical analyses, GraphPad Prism software version 8.3.0 and R version 3.6.0 will be used. Metric data are presented as medians with IQR (if data is not normally distributed) or means +/- SD (in case of normal distribution). Categorical data are depicted as percentage of the group total. For comparisons between continuous variables, two-sample t-test and Wilcoxon rank-sum test will be used depending on whether data is normally distributed or not. Comparison between categorical data will be performed by using Chi-square test or Fisher`s exact test, if sample size is less than 10. Multivariate regression models will be computed by first taking into account all covariates with an univariate p-value of < 0.1, removing insignificant covariates, and then adding remaining covariates one by one, checking the model significance and consistency at each step. For the purposes of this study, a p-value of < 0.05 is considered statistically significant.

### **FUND RAISING**

The intellectual work is performed by the members of the research team for free. Fund raising for additional costs is the task of TG and AS.

### **ETHICAL CONSIDERATIONS**

- **Informed Consent:** Informed written consent (a general consent for data collection is sufficient) is needed from every patient.
- **IRB-Submission:** IRB approval has been approved in Switzerland for the collection of EoE patient data within our database (EKNZ 2015-388/CER-VD 148-15)
- **ClinicalTrials.gov Registration:** A registration in clinicaltrials.gov is not required because this is an observational study and not a clinical trial.

## REFERENCES

1. Liacouras CA, Furuta GT, Hirano I, et al. Eosinophilic esophagitis: updated consensus recommendations for children and adults. *J Allergy Clin Immunol*. Jul 2011;128(1):3-20.e6; quiz 21-2. doi:10.1016/j.jaci.2011.02.040
2. Attwood SE, Smyrk TC, Demeester TR, Jones JB. Esophageal eosinophilia with dysphagia. A distinct clinicopathologic syndrome. *Dig Dis Sci*. Jan 1993;38(1):109-16.
3. Straumann A, Spichtin HP, Bernoulli R, Loosli J, Vögtlin J. [Idiopathic eosinophilic esophagitis: a frequently overlooked disease with typical clinical aspects and discrete endoscopic findings]. *Schweiz Med Wochenschr*. Aug 1994;124(33):1419-29.
4. Hruz P, Straumann A, Bussmann C, et al. Escalating incidence of eosinophilic esophagitis: a 20-year prospective, population-based study in Olten County, Switzerland. *J Allergy Clin Immunol*. Dec 2011;128(6):1349-1350.e5. doi:10.1016/j.jaci.2011.09.013
5. Schoepfer AM, Safroneeva E, Bussmann C, et al. Delay in diagnosis of eosinophilic esophagitis increases risk for stricture formation in a time-dependent manner. *Gastroenterology*. Dec 2013;145(6):1230-6.e1-2. doi:10.1053/j.gastro.2013.08.015
6. Kuchen T, Straumann A, Safroneeva E, et al. Swallowed topical corticosteroids reduce the risk for long-lasting bolus impactions in eosinophilic esophagitis. *Allergy*. Sep 2014;69(9):1248-54. doi:10.1111/all.12455
7. Buchwald H, Avidor Y, Braunwald E, et al. Bariatric surgery: a systematic review and meta-analysis. *JAMA*. Oct 13 2004;292(14):1724-37. doi:10.1001/jama.292.14.1724
8. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. *Am J Med*. Mar 2009;122(3):248-256.e5. doi:10.1016/j.amjmed.2008.09.041
9. Sjöström L, Gummesson A, Sjöström CD, et al. Effects of bariatric surgery on cancer incidence in obese patients in Sweden (Swedish Obese Subjects Study): a prospective, controlled intervention trial. *Lancet Oncol*. Jul 2009;10(7):653-62. doi:10.1016/S1470-2045(09)70159-7
10. Wise J, Plescia T, Cummings BP, Lyo V. Exploring the Relationship Between Bariatric Surgery and Inflammatory Bowel Disease: A Systematic Review. *Crohns Colitis 360*. Apr 2022;4(2):otac013. doi:10.1093/crocol/otac013
11. Courcoulas AP, King WC, Belle SH, et al. Seven-Year Weight Trajectories and Health Outcomes in the Longitudinal Assessment of Bariatric Surgery (LABS) Study. *JAMA Surg*. May 01 2018;153(5):427-434. doi:10.1001/jamasurg.2017.5025
12. Peterli R, Wölnerhanssen BK, Peters T, et al. Effect of Laparoscopic Sleeve Gastrectomy vs Laparoscopic Roux-en-Y Gastric Bypass on Weight Loss in Patients With Morbid Obesity: The SM-BOSS Randomized Clinical Trial. *JAMA*. Jan 16 2018;319(3):255-265. doi:10.1001/jama.2017.20897
13. Ketchem CJ, Ocampo AA, Xue Z, et al. Higher Body Mass Index Is Associated With Decreased Treatment Response to Topical Steroids in Eosinophilic Esophagitis. *Clin Gastroenterol Hepatol*. Aug 2023;21(9):2252-2259.e3. doi:10.1016/j.cgh.2022.11.004

14. Hirano I, Moy N, Heckman MG, Thomas CS, Gonsalves N, Achem SR. Endoscopic assessment of the oesophageal features of eosinophilic oesophagitis: validation of a novel classification and grading system. *Gut*. Apr 2013;62(4):489-95. doi:10.1136/gutjnl-2011-301817
15. Collins MH, Martin LJ, Alexander ES, et al. Newly developed and validated eosinophilic esophagitis histology scoring system and evidence that it outperforms peak eosinophil count for disease diagnosis and monitoring. *Dis Esophagus*. 02 2017;30(3):1-8. doi:10.1111/dote.12470