4open 2022, **5**, 18

https://doi.org/10.1051/fopen/2022019

4open

Available online at:
www.4open-sciences.org

REVIEW ARTICLE OPEN ACCESS

Interconnection of severe obesity, gastric intestinal metaplasia, gastric cancer, bariatric surgery and the necessity of preoperative endoscopy

Mohammad Kermansaravi[1,2,*], Rohollah Valizadeh[3,**], and Behnood Farazmand[4]

[1] Department of Surgery, Minimally Invasive Surgery Research Center, Division of Minimally Invasive and Bariatric Surgery, School of Medicine, Iran University of Medical Sciences, 1445613131 Tehran, Iran
[2] Iran National Center of Excellence for Minimally Invasive Surgery Education, 1445613131 Tehran, Iran
[3] Department of Biostatistics and Epidemiology, School of Medicine, Urmia University of Medical Sciences, 5714783734 Urmia, Iran
[4] Minimally Invasive Surgery Research Center, Iran University of Medical Sciences, 1445613131 Tehran, Iran

Received 4 March 2022, Accepted 22 September 2022

Abstract – Obesity is a growing challenge around the globe accounting for approximately 1.7 billion adults with reduced life expectancy of 5–20 years and these patients are at greater risk for various cancers. Bariatric surgery is one efficient an approved treatment of severe obesity for losing weight and to decrease associated health complications. Besides correct indications and contraindications as well as the various risks of individual bariatric surgical procedures, many more variables influence decision-makings, such as patient's family history of diseases, as well as individual patient-specific factors, patient and family socioeconomic and nutrition status, and professionalism of a bariatric surgical unit and the presence of intestinal metaplasia that is the replacement of columnar epithelial cells by intestinal architecture and morphology. Patients with severe obesity undergoing esophagogastroduodenoscopy (EGD) and biopsy prior to bariatric surgery may present with gastric IM because regular follow-up to early diagnosis of any subsequent pathological changes is necessary and reveals the importance of addressing interconnections between pre-existing conditions and outcomes. However, there is currently no unified recommendation about preoperative EGD before bariatric surgery. With this short review, we point out the necessary knowledge that undermines why the responsibility for a patient with severe obesity cannot be divided across various disciplines, and why we recommend that EGD always be performed preoperatively.

Keywords: Bariatric surgery, Intestinal metaplasia, *Helicobacter pylori*, Gastric cancer, Intestinal metaplasia, Obesity

Introduction

Obesity is a chronic disease that is accompanied by increasing medical and socioeconomic problems. Its prevalence is growing across the world [1]. Moreover, it accounts for approximately 1.7 billion adults leading to lower life expectancies of 5–20 years [2] Obesity is related to several different diseases, consisting of gallstones, high blood pressure with insulin resistance and visceral fat hyperglycemia (metabolic syndrome), gastroesophageal reflux disease, type II diabetes mellitus, degenerative joint diseases, obstructive sleep apnea syndrome, fatty liver, and mental health issues [3]. Furthermore, the patients with severe obesity are at risk for various cancers, such as esophageal, gastric, pancreatic and colorectal cancer [4].

The available non-surgical treatments of severe obesity are effective only when they are actively used. On the other hand, weight regain usually occurs after cessation of this option [5]. Bariatric surgery is the mainstay treatment with respect to weight loss and remission of obesity associated medical problems [6]. Beyond the knowledge of the correct indications and contraindications as well as the various risks of individual bariatric surgery procedures, many more variables influence decision makings, such as the patient and family history of diseases, as well as individual patient and family socioeconomic and nutrition status, and professionalism of a bariatric unit [7]. One important variable is intestinal metaplasia.

Intestinal metaplasia

Replacement of columnar epithelial cells by intestinal architecture and morphology defines intestinal metaplasia (IM) as a conversion of the cells in the coating of the upper

*Corresponding author: mkermansaravi@yahoo.com, Kermansaravi.m@iums.ac.ir
**rohvali4@gmail.com

digestive tract, mostly the stomach or the esophagus as a precancerous gastric lesion with a 6-fold increased cancer risk [8, 9]. Although the risk of gastric cancer is increase in IM patients, the total risk is modest [10] and the reason is unknown.

Higher body mass index (BMI) in patients with severe obesity is shown to correlate with the presence of IM [11–14]. However, the literature refers to a gender and epidemiology differences as in Korea and that obesity and gastric cancer are more likely associated in men while women show gastric dysplasia regardless of *Helicobacter pylori* (*H. pylori*) infection [15].

Patients with obesity undergoing esophagogastroduodenoscopy (EGD) and biopsy prior to bariatric surgery, may have gastric IM [16, 17] and regular follow-up to early diagnosis of any subsequent pathological changes is recommended [4, 18].

IM is associated with age [19], smoking, alcohol consumption, and chronic biliary reflux [20, 21]. A cohort study with large sample size showed that obesity was independently related to an increased risk of new-onset IM [22].

A prospective, longitudinal and multicenter study from Singapore revealed that IM has an adjusted-HR 5.36-fold risk variable for early gastric neoplasia [23] which is in line with earlier reports of gastric carcinogenesis [10] and involves the influence of the microbiome [24] without the need to invoke somatic mutations [25–28].

The challenge of IM is that it is asymptomatic and it is assumed that it takes 4–7 years to develop gastric cancer [29]. Furthermore, IM is assumed to not be reversible ([8, 30, 31] *reviewed in* [29]) meaning that the precancerous niche (PCN) during the multistep carcinogenesis sequence [28] would have irreversibly passed.

Although the annual risk for IM transforming to gastric cancer is less than 1.8% [16],the presence of IM requires surveillance by EGD in high-risk populations, such as the patient with familial gastric cancer or Southeast Asian ethnicity [9]. In high-risk patients, surveillance EGD with mapping is necessary to have enough histologic specimens for a full evaluation [32].

Having a familial history is a risk factor for IM and gastric cancer according to recently updated European guidelines [33]. Based on the previous studies, patients whose first-degree relatives have gastric cancer are more prone to neoplastic progression after IM when compared to patients with no first-degree relatives with gastric cancer [34–36].

Some autoimmune disorders, such as autoimmune gastritis [37] and rheumatologic disorders [38] have been associated with risk for IM. Although the prevalence of IM is largely unknown, it is assumed to be related to regional gastric cancer incidence [39].

Types of gastric intestinal metaplasia

Gastric IM is divided into two complete (type-I) and incomplete (type-II) types. Type-I is described as small intestinal-type mucosa with goblet cells with a brush border and full absorptive cells. Type-II discharges sialo-mucins and is akin to colonic epithelium with intermediate cells in different phases of differentiation.

Mucin droplets are irregular and the brush border is absent [40]. The risk of developing gastric cancer in regard to IM is dependent on whether IM occurs completely or incompletely as "the risk significantly increases with IM over 20% of the gastric mucosa" and even *H. pylori* eradication seems to not influence regression of IM [8]. A recent analysis evaluated 10 studies in Asia, Europe, and Latin America with a follow up period of 10 months to 19 years and showed that incomplete IM led to the highest risk of gastric cancer [41].

Helicobacter pylori (*H. pylori*)

Helicobacter pylori is a known risk factor for IM [19, 42] and its eradication by Celecoxib for 8–12 weeks may lead to the regression of IM to normal mucosa [9, 43]. It is estimated that approximately 75% of IM cases are due to inflammation caused by *H. pylori* [44]. *H. pylori* migrates to the epithelial cells of the stomach and stimulate proteins that cause IM and eventually cancer. Although all subjects infected with *H. pylori* do not develop IM, chronic *H. pylori* infection is a known factor in the etiology of IM [45]. Also, it has long been known that *H. pylori*-related and non-related gastric cancers do not differ in regard to chromosomal aberrations [46]. *H. pylori* infected patients reveal a higher IM prevalence of 33.9% and at younger ages compared to 15.2% without *H. pylori* infection [47]. Phosphoglycerate kinase 1 (PGK1) was shown in 2010 to be crucial for peritoneal dissemination in gastric cancer [48] and for IM [49]. In addition, *H. pylori* infection is related to iron deficiency anemia [50–52] and iron deficiency anemia is associated with both IM [53] and gastric cancer [54].

Preoperative EGD recommendations

Today it is unquestioned that the appropriate bariatric surgical procedure needs to be chosen in an interdisciplinary and multifactorial manner.

However, worldwide there is no unified recommendation in regard to EGD before bariatric surgery [4, 18, 55–58].

Preoperative EGD as a routine diagnostic test prior to bariatric surgery was stated to be a conditional recommendation within the Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES) on bariatric surgery and its update in 2020 which was endorsed by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO-EC), the European Association for the Study of Obesity (EASO) and the European Society for the Peri-operative Care of the Obese Patient (ESPCOP) [59]. Otherwise, the American Gastrointestinal Endoscopy Association (AGEA) recommends endoscopy only for symptomatic patients scheduled for bariatric surgery [60, 61].

Personal opinion

It has been pointed out that

"Guidelines are and will continue to be an important scientific instrument to help physicians taking the best decisions according to the current state of science in many fields of medicine"

but in the same context it was also pointed out that

"there are not meant, however, to be absolute rules with legal implications because they may be the result of a complex drafting process involving schools of thought, conflicts of interest, industrial lobbying and dealing with areas of uncertainty and rapidly evolving concepts from research" [62].

Bariatric surgery is not just performing surgery at the highest technical quality. As discussed here a bariatric surgeon needs to minimize risk for the individual patient. In this regard, the patient's safety and needs are the most important ones. This includes from our perspective any kind of condition, which could result into an overlooked precancerous or cancerous lesion before bariatric surgery [4, 63, 64].

Due to this consideration, it seems to us to be logical to screen bariatric patients for *H. pylori* and other risk factors such as IM, preoperatively and attempt to eliminate them or even change the plan of surgery [65, 66] and to ensure that bariatric centers have full access for EGD after surgery in patients at the risk of gastric cancer [67]. However, independent from the bariatric surgical approach, there can be limitations for routine EGD after bariatric gastric bypass procedures. We are also aware; that there were associative findings between IM and *H. pylori* infection [68, 69] while in some studies, no association between *H. pylori* and IM was reported [70].

As the responsibility for a surgery patient cannot be divided across various disciplines, we recommend performing EGD before bariatric surgery in each patient.

Nomenclature of abbreviations

AGEA	American Gastrointestinal Endoscopy Association;
BMI	Body mass index;
EAES	European Association for Endoscopic Surgery;
EASO	European Association for the Study of Obesity;
EGD	Esophago-gastro-duodenoscopy;
ESPCOP	European Society for the Peri-operative Care of the Obese Patient;
GIM	Gastric intestinal metaplasia;
IFSO-EC	International Federation for the Surgery of Obesity and Metabolic Disorders;
IM	Intestinal metaplasia;
PCN	Precancerous niche;
PGK1	Phosphoglycerate kinase 1

Acknowledgments

The authors want to express their sincere gratitude to the enormous excellent efforts of the Editorial Board of ***4open*** for improving our manuscript significantly.

Conflict of interest

Mohammad Kermansaravi is Editorial Board member in Life Sciences-Medicine of *4open* by EDP Sciences. The authors alone are responsible for the content and writing of this Editorial. This manuscript contains original material that has not previously been published. Each author contributed equally to its contents and approved the manuscript.

References

1. Lopez EKH, Helm MC, Gould JC, Lak KL (2020), Primary care providers' attitudes and knowledge of bariatric surgery. *Surg Endosc* 34, 5, 2273–2278. https://doi.org/10.1007/s00464-019-07018-z.
2. Deitel M (2003), Overweight and obesity worldwide now estimated to involve 1.7 billion people. *Obes Surg* 13, 3, 329–330. https://doi.org/10.1381/096089203765887598.
3. O'Brien PE, Hindle A, Brennan L, Skinner S, Burton P, Smith A, Crosthwaite G, Brown W (2019), Long-term outcomes after bariatric surgery: a systematic review and meta-analysis of weight loss at 10 or more years for all bariatric procedures and a single-centre review of 20-year outcomes after adjustable gastric banding. *Obes Surg* 29, 1, 3–14. https://doi.org/10.1007/s11695-018-3525-0.
4. Küper MA, Kratt T, Kramer MK, Zdichavsky M, Schneider JH, Glatzle J, Stüker D, Königsrainer A, Brücher BLDM (2010), Effort, safety, and findings of routine preoperative endoscopic evaluation of morbidity obese patients undergoing bariatric surgery. *Surg Endosc* 24, 8, 1996–2001. https://doi.org/10.1007/s00464-010-0893-5.
5. Ablett AD, Boyle BR, Avenell A (2019), Fractures in adults after weight loss from bariatric surgery and weight management programs for obesity: systematic review and meta-analysis. *Obes Surg* 29, 4, 1327–1342. https://doi.org/10.1007/s11695-018-03685-4.
6. Welbourn R, Hollyman M, Kinsman R, Dixon J, Liem R, Ottosson J, Ramos A, Våge V, Al-Sabah S, Brown W, Cohen R, Walton P, Himpens J (2019), Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the fourth IFSO Global Registry Report 2018. *Obes Surg* 29, 3, 782–795. https://doi.org/10.1007/s11695-018-3593-1.
7. Jennings NA, Small PK (2016), Procedure selection in bariatric surgery, in: S. Agrawal (Ed.), Obesity, Bariatric and Metabolic Surgery, Cham, Switzerland, Springer. https://doi.org/10.1007/978-3-319-04343-2_9, Print ISBN 978-3-319-04342-5.
8. Zullo A, Hassan C, Romiti A, Giusto M, Guerriero C, Lorenzetti R, Campo SM, Tomao S (2012), Follow-up of intestinal metaplasia in the stomach: When, how and why. World J Gastrointest Oncol 4, 3, 30–36. https://doi.org/10.4251/wjgo.v4.i3.30.
9. Jencks DS, Adam JD, Borum ML, Koh JM, Stephen S, Doman DB (2018), Overview of current concepts in gastric intestinal metaplasia and gastric cancer. Gastroenterol Hepatol (N Y) 14, 2, 92–101. PMID: 29606921.

10. Correa P (2004), The biological model of gastric carcinogenesis. IARC Sci Publ 2004157, 301–310. PMID: 15055303.
11. Kim N, Park YS, Cho SI, Lee HS, Choe G, Kim IW, Won YD, Park JH, Kim JS, Jung HC, Song IS (2008), Prevalence and risk factors of atrophic gastritis and intestinal metaplasia in a Korean population without significant gastroduodenal disease. *Helicobacter* 13, 4, 245–255. https://doi.org/10.1111/j.1523-5378.2008.00604.x.
12. Joo YE, Park HK, Myung DS, Baik GH, Shin JE, Seo GS, Kim GH, Kim HU, Kim HY, Cho SI, Kim N (2013), Prevalence and risk factors of atrophic gastritis and intestinal metaplasia: a nationwide multicenter prospective study in Korea. Gut Liver 7, 3, 303–310. https://doi.org/10.5009/gnl.2013.7.3.303.
13. Kim N, Youn CH, Kim AS, Ko HJ, Kim HM, Moon H, Park S (2017), Associations between body mass index and chronic atrophic gastritis and intestinal metaplasia. *Korean J Gastroenterol* 70, 2, 81–88. https://doi.org/10.4166/kjg.2017.70.2.81.
14. Kim K, Chang Y, Ahn J, Yang HJ, Jung JY, Kim S, Sohn CI, Ryu S (2019), Body mass index and risk of intestinal metaplasia: a Cohort study. *Cancer Epidemiol Biomarkers Prev* 28, 4, 789–797. https://doi.org/10.1158/1055-9965.EPI-18-0733.
15. Kim HJ, Kim N, Kim HY, Lee HS, Yoon H, Shin CM, Park YS, Park DJ, Kim HH, Lee KH, Kim YH, Kim HM, Lee DH (2015), Relationship between body mass index and the risk of early gastric cancer and dysplasia regardless of *Helicobacter pylori* infection. Gastric Cancer 18, 4, 762–773. https://doi.org/10.1007/s10120-014-0429-0.
16. Falkeis-Veits C, Vieth M (2019), Non-malignant *Helicobacter pylori*-Associated Diseases. Adv Exp Med Biol 1149, 121–134. https://doi.org/10.1007/5584_2019_362.
17. Huang RJ, Choi AY, Truong CD, Yeh MM, Hwang JH (2019), Diagnosis and management of gastric intestinal metaplasia: current status and future directions. Gut Liver 13, 6, 596–603. https://doi.org/10.5009/gnl19181.
18. Cheng YL, Elli EF (2022), Management of gastric intestinal metaplasia in patients undergoing routine endoscopy before bariatric surgery. *Updates Surg* 74, 4, 1383–1388. https://doi.org/10.1007/s13304-021-01181-6.
19. Uno Y (2019), Prevention of gastric cancer by *Helicobacter pylori* eradication: A review from Japan. *Cancer Med* 8, 8, 3992–4000. https://doi.org/10.1002/cam4.2277.
20. Leung WK, Lin SR, Ching JY, To KF, Ng EK, Chan FK, Lau JY, Sung JJ (2004), Factors predicting progression of gastric intestinal metaplasia: results of a randomised trial on *Helicobacter pylori* eradication. *Gut* 53, 9, 1244–1249. https://doi.org/10.1136/gut.2003.034629.
21. Raghavendra RS, Kini D (2012), Benign, premalignant, and malignant lesions encountered in bariatric surgery. *JSLS* 16, 3, 360–372. https://doi.org/10.4293/108680812X13462882736457.
22. Kocarnik JM, Compton K, Dean FE, Fu W, Gaw BL, Harvey JD, Henrikson HJ, Lu D, Pennini A, Xu R, Ababneh E, Abbasi-Kangevari M, Abbastabar H, Abd-Elsalam SM, Abdoli A, Abedi A, Abidi H, Abolhassani H, Adedeji IA, Adnani QES, Advani SM, Afzal MS, Aghaali M, Ahinkorah BO, Ahmad S, Ahmad T, Ahmadi A, Ahmadi S, Ahmed Rashid T, Ahmed Salih Y, Akalu GT, Aklilu A, Akram T, Akunna CJ, Al Hamad H, Alahdab F, Al-Aly Z, Ali S, Alimohamadi Y, Alipour V, Aljunid SM, Alkhayyat M, Almasi-Hashiani A, Almasri NA, Al-Maweri SAA, Almustanyir S, Alonso N, Alvis-Guzman N, Amu H, Anbesu EW, Ancuceanu R, Ansari F, Ansari-Moghaddam A, Antwi MH, Anvari D, Anyasodor AE, Aqeel M, Arabloo J, Arab-Zozani M, Aremu O, Ariffin H, Aripov T, Arshad M, Artaman A, Arulappan J, Asemi Z, Asghari Jafarabadi M, Ashraf T, Atorkey P, Aujayeb A, Ausloos M, Awedew AF, Ayala Quintanilla BP, Ayenew T, Azab MA, Azadnajafabad S, Azari Jafari A, Azarian G, Azzam AY, Badiye AD, Bahadory S, Baig AA, Baker JL, Balakrishnan S, Banach M, Bärnighausen TW, Barone-Adesi F, Barra F, Barrow A, Behzadifar M, Belgaumi UI, Bezabhe WMM, Bezabih YM, Bhagat DS, Bhagavathula AS, Bhardwaj N, Bhardwaj P, Bhaskar S, Bhattacharyya K, Bhojaraja VS, Bibi S, Bijani A, Biondi A, Bisignano C, Bjørge T, Bleyer A, Blyuss O, Bolarinwa OA, Bolla SR, Braithwaite D, Brar A, Brenner H, Bustamante-Teixeira MT, Butt NS, Butt ZA, Caetano Dos Santos FL, Cao Y, Carreras G, Catalá-López F, Cembranel F, Cerin E, Cernigliaro A, Chakinala RC, Chattu SK, Chattu VK, Chaturvedi P, Chimed-Ochir O, Cho DY, Christopher DJ, Chu DT, Chung MT, Conde J, Cortés S, Cortesi PA, Costa VM, Cunha AR, Dadras O, Dagnew AB, Dahlawi SMA, Dai X, Dandona L, Dandona R, Darwesh AM, das Neves J, De la Hoz FP, Demis AB, Denova-Gutiérrez E, Dhamnetiya D, Dhimal ML, Dhimal M, Dianatinasab M, Diaz D, Djalalinia S, Do HP, Doaei S, Dorostkar F, Dos Santos Figueiredo FW, Driscoll TR, Ebrahimi H, Eftekharzadeh S, El Tantawi M, El-Abid H, Elbarazi I, Elhabashy HR, Elhadi M, El-Jaafary SI, Eshrati B, Eskandarieh S, Esmaeilzadeh F, Etemadi A, Ezzikouri S, Faisaluddin M, Faraon EJA, Fares J, Farzadfar F, Feroze AH, Ferrero S, Ferro Desideri L, Filip I, Fischer F, Fisher JL, Foroutan M, Fukumoto T, Gaal PA, Gad MM, Gadanya MA, Gallus S, Gaspar Fonseca M, Getachew Obsa A, Ghafourifard M, Ghashghaee A, Ghith N, Gholamalizadeh M, Gilani SA, Ginindza TG, Gizaw ATT, Glasbey JC, Golechha M, Goleij P, Gomez RS, Gopalani SV, Gorini G, Goudarzi H, Grosso G, Gubari MIM, Guerra MR, Guha A, Gunasekera DS, Gupta B, Gupta VB, Gupta VK, Gutiérrez RA, Hafezi-Nejad N, Haider MR, Haj-Mirzaian A, Halwani R, Hamadeh RR, Hameed S, Hamidi S, Hanif A, Haque S, Harlianto NI, Haro JM, Hasaballah AI, Hassanipour S, Hay RJ, Hay SI, Hayat K, Heidari G, Heidari M, Herrera-Serna BY, Herteliu C, Hezam K, Holla R, Hossain MM, Hossain MBH, Hosseini MS, Hosseini M, Hosseinzadeh M, Hostiuc M, Hostiuc S, Househ M, Hsairi M, Huang J, Hugo FN, Hussain R, Hussein NR, Hwang BF, Iavicoli I, Ibitoye SE, Ida F, Ikuta KS, Ilesanmi OS, Ilic IM, Ilic MD, Irham LM, Islam JY, Islam RM, Islam SMS, Ismail NE, Isola G, Iwagami M, Jacob L, Jain V, Jakovljevic MB, Javaheri T, Jayaram S, Jazayeri SB, Jha RP, Jonas JB, Joo T, Joseph N, Joukar F, Jürisson M, Kabir A, Kahrizi D, Kalankesh LR, Kalhor R, Kaliyadan F, Kalkonde Y, Kamath A, Kameran Al-Salihi N, Kandel H, Kapoor N, Karch A, Kasa AS, Katikireddi SV, Kauppila JH, Kavetskyy T, Kebede SA, Keshavarz P, Keykhaei M, Khader YS, Khalilov R, Khan G, Khan M, Khan MN, Khan MAB, Khang YH, Khater AM, Khayamzadeh M, Kim GR, Kim YJ, Kisa A, Kisa S, Kissimova-Skarbek K, Kopec JA, Koteeswaran R, Koul PA, Koulmane Laxminarayana SL, Koyanagi A, Kucuk Bicer B, Kugbey N, Kumar GA, Kumar N, Kumar N, Kurmi OP, Kutluk T, La Vecchia C, Lami FH, Landires I, Lauriola P, Lee SW, Lee SWH, Lee WC, Lee YH, Leigh J, Leong E, Li J, Li MC, Liu X, Loureiro JA, Lunevicius R, Magdy Abd El Razek M, Majeed A, Makki A, Male S, Malik AA, Mansournia MA, Martini S, Masoumi SZ, Mathur P, McKee M, Mehrotra R, Mendoza W, Menezes RG, Mengesha EW, Mesregah MK, Mestrovic T, Miao Jonasson J, Miazgowski B, Miazgowski T, Michalek IM, Miller TR, Mirzaei H, Mirzaei HR, Misra S, Mithra P, Moghadaszadeh M, Mohammad KA, Mohammad Y, Mohammadi M, Mohammadi SM, Mohammadian-Hafshejani A, Mohammed S, Moka N, Mokdad AH, Molokhia M, Monasta L, Moni MA, Moosavi

MA, Moradi Y, Moraga P, Morgado-da-Costa J, Morrison SD, Mosapour A, Mubarik S, Mwanri L, Nagarajan AJ, Nagaraju SP, Nagata C, Naimzada MD, Nangia V, Naqvi AA, Narasimha Swamy S, Ndejjo R, Nduaguba SO, Negoi I, Negru SM, Neupane Kandel S, Nguyen CT, Nguyen HLT, Niazi RK, Nnaji CA, Noor NM, Nuñez-Samudio V, Nzoputam CI, Oancea B, Ochir C, Odukoya OO, Ogbo FA, Olagunju AT, Olakunde BO, Omar E, Omar Bali A, Omonisi AEE, Ong S, Onwujekwe OE, Orru H, Ortega-Altamirano DV, Otstavnov N, Otstavnov SS, Owolabi MO, Padubidri Jr PAM, Pakshir K, Pana A, Panagiotakos D, Panda-Jonas S, Pardhan S, Park EC, Park EK, Pashazadeh Kan F, Patel HK, Patel JR, Pati S, Pattanshetty SM, Paudel U, Pereira DM, Pereira RB, Perianayagam A, Pillay JD, Pirouzpanah S, Pishgar F, Podder I, Postma MJ, Pourjafar H, Prashant A, Preotescu L, Rabiee M, Rabiee N, Radfar A, Radhakrishnan RA, Radhakrishnan V, Rafiee A, Rahim F, Rahimzadeh S, Rahman M, Rahman MA, Rahmani AM, Rajai N, Rajesh A, Rakovac I, Ram P, Ramezanzadeh K, Ranabhat K, Ranasinghe P, Rao CR, Rao SJ, Rawassizadeh R, Razeghinia MS, Renzaho AMN, Rezaei N, Rezaei N, Rezapour A, Roberts TJ, Rodriguez JAB, Rohloff P, Romoli M, Ronfani L, Roshandel G, Rwegerera GM, Manjula S, Sabour S, Saddik B, Saeed U, Sahebkar A, Sahoo H, Salehi S, Salem MR, Salimzadeh H, Samaei M, Samy AM, Sanabria J, Sankararaman S, Santric-Milicevic MM, Sardiwalla Y, Sarveazad A, Sathian B, Sawhney M, Saylan M, Schneider IJC, Sekerija M, Seylani A, Shafaat O, Shaghaghi Z, Shaikh MA, Shamsoddin E, Shannawaz M, Sharma R, Sheikh A, Sheikhbahaei S, Shetty A, Shetty JK, Shetty PH, Shibuya K, Shirkoohi R, Shivakumar KM, Shivarov V, Siabani S, Siddappa Malleshappa SK, Silva DAS, Singh JA, Sintayehu Y, Skryabin VY, Skryabina AA, Soeberg MJ, Sofi-Mahmudi A, Sotoudeh H, Steiropoulos P, Straif K, Subedi R, Sufiyan MB, Sultan I, Sultana S, Sur D, Szerencsés V, Szócska M, Tabarés-Seisdedos R, Tabuchi T, Tadbiri H, Taherkhani A, Takahashi K, Talaat IM, Tan KK, Tat VY, Tedla BAA, Tefera YG, Tehrani-Banihashemi A, Temsah MH, Tesfay FH, Tessema GA, Thapar R, Thavamani A, Thoguluva Chandrasekar V, Thomas N, Tohidinik HR, Touvier M, Tovani-Palone MR, Traini E, Tran BX, Tran KB, Tran MTN, Tripathy JP, Tusa BS, Ullah I, Ullah S, Umapathi KK, Unnikrishnan B, Upadhyay E, Vacante M, Vaezi M, Valadan Tahbaz S, Velazquez DZ, Veroux M, Violante FS, Vlassov V, Vo B, Volovici V, Vu GT, Waheed Y, Wamai RG, Ward P, Wen YF, Westerman R, Winkler AS, Yadav L, Yahyazadeh Jabbari SH, Yang L, Yaya S, Yazie TSY, Yeshaw Y, Yonemoto N, Younis MZ, Yousefi Z, Yu C, Yuce D, Yunusa I, Zadnik V, Zare F, Zastrozhin MS, Zastrozhina A, Zhang J, Zhong C, Zhou L, Zhu C, Ziapour A, Zimmermann IR, Fitzmaurice C, Murray CJL, Force LM (2022), Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life years for 29 cancer groups from 2010 to 2019: a systematic analysis for the global burden of disease study 2019. JAMA Oncol 8, 3, 420–444. https://doi.org/10.1001/jamaoncol. 2021.6987.

23. Lee JWJ, Zhu F, Srivastava S, Tsao SK, Khor C, Ho KY, Fock KM, Lim WC, Ang TL, Chow WC, So JBY, Koh CJ, Chua SJ, Wong ASY, Rao J, Lim LG, Ling KL, Chia CK, Ooi CJ, Rajnakova A, Yap WM, Salto-Tellez M, Ho B, Soong R, Chia KS, Teo YY, Teh M, Yeoh KG (2022), Severity of gastric intestinal metaplasia predicts the risk of gastric cancer: a prospective multicentre cohort study (GCEP). *Gut* 71, 5, 854–863. https://doi.org/10.1136/gutjnl-2021-324057.
24. Brücher BLDM, Jamall JS (2019), Microbiome and morbid obesity increase pathogenic stimulus diversity. 4open 2, 10, 1–16. https://doi.org/10.1051/fopen/2018007.
25. Brücher BLDM, Jamall IS (2014), Epistemology of the Origin of Cancer: A New Paradigm. *BMC Cancer* 14331, 1–15. https://doi.org/10.1186/1471-2407-14-331.
26. Brücher BLDM, Jamall JS (2016), Somatic Mutation Theory – Why it's Wrong for Most Cancers. Cell Physiol Biochem 38, 5, 1663–1680. https://doi.org/10.1159/000443106.
27. Brücher BLDM, Jamall JS (2019), Chronic inflammation evoked by pathogenic stimulus during carcinogenesis. 4open 2, 8, 1–22. https://doi.org/10.1051/fopen/2018006.
28. Brücher BLDM, Jamall JS (2019), Precancerous niche (PCN), a product of fibrosis with remodeling by incessant chronic inflammation. 4open 2, 11, 1–21. https://doi.org/10.1051/fopen/2018009.
29. Lam SK, Lau G (2020), Novel treatment for gastric intestinal metaplasia, a precursor to cancer. *JGH Open* 4, 4, 569–573. https://doi.org/10.1002/jgh3.12318.
30. Liu KS, Wong IO, Leung WK (2016), *Helicobacter pylori* associated gastric intestinal metaplasia: Treatment and surveillance. World J Gastroenterol 22, 3, 1311–1320. https://doi.org/10.3748/wjg.v22.i3.1311.
31. Kiriyama Y, Tahara T, Shibata T, Okubo M, Nakagawa M, Okabe A, Ohmiya N, Kuroda M, Sugioka A, Ichinose M, Tatematsu M (2016), Tsukamoto Z (2016) Gastric-and-intestinal mixed intestinal metaplasia is irreversible point with eradication of *Helicobacter pylori*. Open J Pathol 6, 93–104. https://doi.org/10.4236/ojpathology.2016.62012.
32. Kishikawa H, Ojiro K, Nakamura K, Katayama T, Arahata K, Takarabe S, Miura S, Kanai T, Nishida J (2020), Previous *Helicobacter pylori* infection-induced atrophic gastritis: A distinct disease entity in an understudied population without a history of eradication. Helicobacter 25, 1, e12669. https://doi.org/10.1111/hel.12669.
33. Pimentel-Nunes P, Libânio D, Marcos-Pinto R, Areia M, Leja M, Esposito G, Garrido M, Kikuste I, Megraud F, Matysiak-Budnik T, Annibale B, Dumonceau JM, Barros R, Fléjou JF, Carneiro F, van Hooft JE, Kuipers EJ, Dinis-Ribeiro M (2019), Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy 514, 365–388. https://doi.org/10.1055/a-0859-1883.
34. Safaee A, Moghimi-Dehkordi B, Fatemi SR, Maserat E, Zali MR (2011), Family history of cancer and risk of gastric cancer in Iran. Asian Pac J Cancer Prev 1211, 3117–3120. PMID: 22394000.
35. Yaghoobi M, Bijarchi R, Narod SA (2010), Family history and the risk of gastric cancer. Br *J Cancer* 102, 2, 237–242. https://doi.org/10.1038/sj.bjc.6605380.
36. Oliveira C, Pinheiro H, Figueiredo J, Seruca R, Carneiro F (2015), Familial gastric cancer: genetic susceptibility, pathology, and implications for management. *Lancet Oncol* 16, 2, e60–e70. https://doi.org/10.1016/S1470-2045(14)71016-2.
37. Minalyan A, Benhammou JN, Artashesyan A, Lewis MS, Pisegna JR (2017), Autoimmune atrophic gastritis: current perspectives. *Clin Exp Gastroenterol* 10, 19–27. https://doi.org/10.2147/CEG.S109123.
38. Brito-Zerón P, Kostov B, Fraile G, Caravia-Durán D, Maure B, Rascón FJ, Zamora M, Casanovas A, Lopez-Dupla M, Ripoll M, Pinilla B, Fonseca E, Akasbi M, de la Red G, Duarte-Millán MA, Fanlo P, Guisado-Vasco P,

Pérez-Alvarez R, Chamorro AJ, Morcillo C, Jiménez-Heredia I, Sánchez-Berná I, López-Guillermo A, Ramos-Casals M, SS Study Group GEAS-SEMI (2017), Characterization and risk estimate of cancer in patients with primary Sjögren syndrome. *J Hematol Oncol* 10, 1, 90. https://doi.org/10.1186/s13045-017-0464-5.

39. Sonnenberg A, Lash RH, Genta RM (2010), A national study of Helicobactor pylori infection in gastric biopsy specimens. *Gastroenterology* 139, 6, 1894–1901.e2; quiz e12. https://doi.org/10.1053/j.gastro.2010.08.018.
40. Toyoshima O, Nishizawa T, Yoshida S, Watanabe H, Odawara N, Sakitani K, Arano T, Takiyama H, Kobayashi H, Kogure H, Fujishiro M (2022), Brown slits for colorectal adenoma crypts on conventional magnifying endoscopy with narrow band imaging using the X1 system. World J Gastroenterol 28, 24, 2748–2757. https://doi.org/10.3748/wjg.v28.i24.2748.
41. González CA, Sanz-Anquela JM, Companioni O, Bonet C, Berdasco M, López C, Mendoza J, Martín-Arranz MD, Rey E, Poves E, Espinosa L, Barrio J, Torres MÁ, Cuatrecasas M, Elizalde I, Bujanda L, Garmendia M, Ferrández Á, Muñoz G, Andreu V, Paules MJ, Lario S, Ramírez MJ; Study group, Gisbert JP (2016), Incomplete type of intestinal metaplasia has the highest risk to progress to gastric cancer: results of the Spanish follow-up multicenter study. J Gastroenterol Hepatol 31, 5, 953–958. https://doi.org/10.1111/jgh.13249.
42. Turan G, Kocaöz S (2019), *Helicobacter pylori* infection prevalence and histopathologic findings in laparoscopic sleeve gastrectomy. Obes Surg 29, 11, 3674–3679. https://doi.org/10.1007/s11695-019-04052-7.
43. Canil AM, Iossa A, Termine P, Caporilli D, Petrozza V, Silecchia G (2018), Histopathology findings in patients undergoing laparoscopic sleeve gastrectomy. *Obes Surg* 28, 6, 1760–1765. https://doi.org/10.1007/s11695-017-3092-9.
44. Amieva M, Peek RM Jr (2016), Pathobiology of *Helicobacter pylori*-Induced Gastric Cancer. Gastroenterology 150, 1, 64–78. https://doi.org/10.1053/j.gastro.2015.09.004.
45. Nieuwenburg SAV, Mommersteeg MC, Eikenboom EL, Yu B, den Hollander WJ, Holster IL, den Hoed CM, Capelle LG, Tang TJ, Anten MP, Prytz-Berset I, Witteman EM, Ter Borg F, Burger JPW, Bruno MJ, Fuhler GM, Peppelenbosch MP, Doukas M, Kuipers EJ, Spaander MCW (2021), Factors associated with the progression of gastric intestinal metaplasia: a multicenter, prospective cohort study. Endosc Int Open 9, 3, E297–E305. https://doi.org/10.1055/a-1314-6626.
46. van Grieken NC, Weiss MM, Meijer GA, Hermsen MA, Scholte GH, Lindeman J, Craanen ME, Bloemena E, Meuwissen SG, Baak JP, Kuipers EJ (2000), *Helicobacter pylori*-related and -non-related gastric cancers do not differ with respect to chromosomal aberrations. *J Pathol* 192, 3, 301–306. https://doi.org/10.1002/1096-9896(2000)9999:9999<::AID-PATH697>3.0.CO;2-F.
47. Craanen ME, Dekker W, Blok P, Ferwerda J, Tytgat GN (1992), Intestinal metaplasia and *Helicobacter pylori*: an endoscopic bioptic study of the gastric antrum. Gut 33, 1, 16–20. https://doi.org/10.1136/gut.33.1.16.
48. Zieker D, Königsrainer I, Tritschler I, Löffler M, Beckert S, Traub F, Nieselt K, Bühler S, Weller M, Gaeddcke J, Taichman RS, Northoff H, Brücher BLDM, Königsrainer A (2010), P Phosphoglycerate kinase1 a promoting enzyme for peritoneal dissemination in gastric cancer. Int J Cancer 126, 6, 1513–1520. https://doi.org/10.1159/000129635.
49. Huang B, Cai W, Wang Q, Liu F, Xu M, Zhang Y (2018), Gankyrin drives malignant transformation of gastric cancer and alleviates oxidative stress via mTORC1 activation. Oxid Med Cell Longev 2018, 9480316. https://doi.org/10.1155/2018/9480316.
50. Blecker U, Renders F, Lanciers S, Vandenplas Y (1991), Syncopes leading to the diagnosis of a *Helicobacter pylori* positive chronic active haemorrhagic gastritis. Eur J Pediatr 150, 8, 560–561. https://doi.org/10.1007/BF02072207.
51. Marignani M, Angeletti S, Bordi C, Malagnino F, Mancino C, Delle Fave G, Annibale B (1997), Reversal of long-standing iron deficiency anaemia after eradication of *Helicobacter pylori* infection. Scand J Gastroenterol 32, 6, 617–622. https://doi.org/10.3109/00365529709025109.
52. Noto JM, Piazuelo MB, Shah SC, Romero-Gallo J, Hart JL, Di C, Carmichael JD, Delgado AG, Halvorson AE, Greevy RA, Wroblewski LE, Sharma A, Newton AB, Allaman MM, Wilson KT, Washington MK, Calcutt MW, Schey KL, Cummings BP, Flynn CR, Zackular JP, Peek RM Jr (2022), Iron deficiency linked to altered bile acid metabolism promotes *Helicobacter pylori*-induced inflammation-driven gastric carcinogenesis. J Clin Invest 132, 10, https://doi.org/10.1172/JCI147822.
53. Zlatewa M, Manewska B (1976), Histological and histochemical changes in stomach mucosa in sick people with iron deficiency anemia. *Zentralbl Allg Pathol* 120, 4, 310–314. PMID: 136851.
54. Hershko C, Vitells A, Braverman DZ (1984), Causes of iron deficiency anemia in an adult inpatient population. Effect of diagnostic workup on etiologic distribution. Blut 49, 4, 347–352. https://doi.org/10.1007/BF00320209.
55. de Vries AC, Kuipers EJ (2007), Epidemiology of premalignant gastric lesions: implications for the development of screening and surveillance strategies. Helicobacter 12, Suppl 2, 22–31. https://doi.org/10.1111/j.1523-5378.2007.00562.x.
56. Rugge M, Genta RM, Fassan M, Valentini E, Coati I, Guzzinati S, Savarino E, Zorzi M, Farinati F, Malfertheiner P (2018), OLGA gastritis staging for the prediction of gastric cancer risk: a long-term follow-up study of 7436 patients. Am J Gastroenterol 113, 11, 1621–1628. https://doi.org/10.1038/s41395-018-0353-8.
57. Magouliotis DE, Tasiopoulou VS, Tzovaras G (2019), One anastomosis gastric bypass versus roux-en-y gastric bypass for morbid obesity: an updated meta-analysis. Obes Surg 29, 9, 2721–2730. https://doi.org/10.1007/s11695-019-04005-0.
58. Gudaityte R, Kavaliauskaite A, Maleckas A (2021), Mid-term outcomes of laparoscopic gastric greater curvature plication versus Roux-en-Y gastric bypass: weight loss, gastrointestinal symptoms, and health-related quality of life. Medicina (Kaunas) 58, 1, 64. https://doi.org/10.3390/medicina58010064.
59. Di Lorenzo N, Antoniou SA, Batterham RL, Busetto L, Godoroja D, Iossa A, Carrano FM, Agresta F, Alarçon I, Azran C, Bouvy N, Balaguè Ponz C, Buza M, Copaescu C, De Luca M, Dicker D, Di Vincenzo A, Felsenreich DM, Francis NK, Fried M, Gonzalo Prats B, Goitein D, Halford JCG, Herlesova J, Kalogridaki M, Ket H, Morales-Conde S, Piatto G, Prager G, Pruijssers S, Pucci A, Rayman S, Romano E, Sanchez-Cordero S, Vilallonga R, Silecchia G (2020), Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES) on bariatric surgery: update 2020 endorsed by IFSO-EC. EASO and ESPCOP, Surg Endosc 34, 6, 2332–2358. https://doi.org/10.1007/s00464-020-07555-y.
60. ASGE STANDARDS OF PRACTICE COMMITTEE, Anderson MA, Gan SI, Fanelli RD, Baron TH, Banerjee S, Cash BD, Dominitz JA, Harrison ME, Ikenberry SO, Jagannath SB, Lichtenstein DR, Shen B, Lee KK, Van Guilder T, Stewart LE (2008), Role of endoscopy in the bariatric surgery patient. Gastrointest Endosc 68, 1, 1–10. https://doi.org/10.1016/j.gie.2008.01.028.

61. Kanat BH, Doğan S (2022), Is gastroscopy necessary before bariatric surgery? World J Gastrointest Endosc 141, 29–34. https://doi.org/10.4253/wjge.v14.i1.29.
62. Sitges-Serra A (2014), Clinical guidelines at stake. J Epidemiol Community Health 6810, 906–908. https://doi.org/10.1136/jech-2014-203862.
63. Csendes A, Burgos AM, Smok G, Beltran M (2007), Endoscopic and histologic findings of the foregut in 426 patients with morbid obesity. Obes Surg 17, 1, 28–34. https://doi.org/10.1007/s11695-007-9002-9.
64. Dittler HJ, Pesarini AC, Siewert JR (1992), Endoscopic classification of esophageal cancer: correlation with the T stage. Gastrointest Endosc 38, 6, 662–668. https://doi.org/10.1016/s0016-5107(92)70561-6.
65. Jouet P, Barbieri J, Coffin B, Msika S, Duboc H, Grossin M, Merrouche M, Ledoux S, Coupaye M, Castel B, Sghiouar N, Sabate JM (2011), Results of routine endoscopy performed in patients with morbid obesity before bariatric surgery and prevalence of *helicobacter pylori*: a single center study in 288 patients. Gastroenterology Mo1123, S563. Website: https://www.gastrojournal.org/article/S0016-5085(11)62329-9/pdf?referrer=https%3A%2F%2Fwww.researchgate.net%2F. Access: Apr 2022.
66. Kermansaravi M, Kabir A, Pazouki A (2020), 1-year follow-up of Single Anastomosis Sleeve Ileal (SASI) bypass in morbid obese patients: efficacy and concerns. Obes Surg 30, 11, 4286–4292. https://doi.org/10.1007/s11695-020-04781-0.
67. Yang P, Chen B, Xiang S, Lin XF, Luo F, Li W (2019), Long-term outcomes of laparoscopic sleeve gastrectomy versus Roux-en-Y gastric bypass for morbid obesity: Results from a meta-analysis of randomized controlled trials. Surg Obes Relat Dis 154, 546–555. https://doi.org/10.1016/j.soard.2019.02.001.
68. Safaan T, Bashah M, El Ansari W, Karam M (2017), Histopathological changes in laparoscopic sleeve gastrectomy specimens: prevalence risk factors, and value of routine histopathologic examination. Obes Surg 27, 7, 1741–1749. https://doi.org/10.1007/s11695-016-2525-1. ERRATUM IN DOI: https://doi.org/10.1007/s11695-017-2819-y.
69. Komaei I, Currò G, Mento F, Cassaro G, Lazzara C, Barbera A, Ammendola M, Alibrandi A, Navarra G (2020), Gastric histopathologic findings in South Italian morbidly obese patients undergoing laparoscopic sleeve gastrectomy: Is histopathologic examination of all resected gastric specimens necessary? Obes Surg 30, 4, 1339–1346. https://doi.org/10.1007/s11695-019-04272-x.
70. Corsini DA, Simoneti CA, Moreira G, Lima SE Jr, Garrido AB (2006), Cancer in the excluded stomach 4 years after gastric bypass. Obes Surg 167, 932–934. https://doi.org/10.1381/096089206777822313.

Cite this article as: Kermansaravi M, Valizadeh R & Farazmand B 2022. Interconnection of severe obesity, gastric intestinal metaplasia, gastric cancer, bariatric surgery and the necessity of preoperative endoscopy. 4open, **5**, 18.