Is there a need for histopathological evaluation of sleeve gastrectomy specimens under the age of 40? Is macroscopic evaluation not enough?

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Citation

ABSTRACT

Background: Obesity is an increasing public health problem all over the world and laparoscopic sleeve gastrectomy (LSG) is the most common bariatric surgical method with sufficient weight loss. The need for histopathological evaluation of the stomach specimen removed is discussed all over the world. Materials and Methods: The aim of this study is to compare the pathology findings of LSG specimens in patients under and over 40 years old. Between January 2013 and June 2020, 1584 gastric resection material who had undergone LSG was evaluated. The patients were divided into two groups as those over and under 40 years of age, and their pathology results were compared. Results: Normal findings were identified in almost half of the specimen (46.6%) and the most common pathological alteration was chronic inactive gastritis (34.3%). There was an increased risk of intestinal metaplasia (%0.8; %11.5; p=0.00) and unexpected gastric pathologies in patients over 40 years of age. Conclusion: We believe that it would be more cost-effective not to evaluate LSG specimens routinely in patients under 40 years of age in the absence of macroscopically pathologies in low-income countries.

Keywords: Gastrectomy, Bariatric surgery, Granulomatous disease, gastrointestinal stromal tumor
1. INTRODUCTION

Obesity is a significant, preventable health problem, the worldwide prevalence of which has almost tripled since 1975. World Health Organization’s 2016 data reported that more than 1.9 billion adults aged 18 years and over were overweight, while 650 million of these individuals were obese. Morbid obesity has recently been listed as the fifth main cause of all mortality cases, while about 2.8 million mortality cases have annually been associated with obesity (Dumon & Murayama, 2011). Current weight loss attempts through non-surgical methods like dieting, exercise, and behavioral changes have also proven to be unsatisfactory for a great majority of morbidly obese patients (Buchwald et al., 2004). Studies have revealed that bariatric surgery was an efficient weight loss method in this patient group with its short and long-term results and helped such patients’ comorbid diseases recuperate or be completely eliminated. Laparoscopic sleeve gastrectomy (LSG) is the most commonly preferred bariatric surgery procedure worldwide due to its low morbidity and mortality rates (Stroh et al., 2012).

Most surgical clinics tend to drop upper gastrointestinal system (GIS) endoscopy and abdominal ultrasonography as standard exploration techniques prior to bariatric surgery as cost effectiveness has become a major concern (Petrick et al., 2015). There is also the tendency to avoid histopathology evaluation because of the same reasons when the macroscopic assessment of specimen resected during such commonly performed surgical procedures as appendectomy, cholecystectomy or hemorrhoidectomy proves to be normal. Today the same concerns are valid for bariatric surgery procedures as well (Lohsiriwat et al., 2009; Abdull Gaffar et al., 2016).

Although the number of LSG procedures gradually increases each year in our country, the spectrum of gastric histopathology findings in this patient sub-group has not been investigated on a large scale. The aim of this study, therefore, was to analyze the histopathology results of 984 morbidly obese patients who had received LSG at our center.

2. MATERIALS/PATIENTS AND METHODS

The General Surgery Clinic of Istanbul Fatih Sultan Mehmet Training and Research Hospital has been performing laparoscopic vertical sleeve gastrectomy procedure for the surgical treatment of morbid obesity since 2009. The records of all patients have been prospectively kept since 2013. The pathological evaluation of the gastric resection material of a total of 1584 patients, who had undergone laparoscopic vertical sleeve gastrectomy because of morbid obesity between January 2013 and June 2020, were retrospectively studied based on prospectively kept data within the scope of this study. The patients were divided into two groups as those over and under 40 years of age, and their pathology results were compared.

Study inclusion criterion was all patients with LSG. Patients with revision surgery due to obesity; partial gastric resection material delivered due to such reasons as peptic ulcer disease, trauma, benign or malign tumoral lesions were excluded from the study.

**Preoperative upper gastrointestinal system endoscopy**

Preoperative upper gastrointestinal system endoscopy has been routinely performed prior to bariatric surgery at our clinic for all patients over 40 years of age and for patients under 40 years of age with symptomatic reflux disease, those with alarming symptoms like early onset dyspeptic complaint or weight loss, hematemesis, and familial gastric cancer history.

**Histopathology evaluation**

![Macroscopic evaluation of sleeve gastrectomy specimen.](image-url)
Vertical sleeve gastrectomy was performed using 34-36 French bougie, starting at 2-6 cm further from the pylorus. Further widening the initial port entry of 15 mm the specimen was taken out directly along the abdominal wall without using a specimen retrieval bag. Surgeons performing the procedures firstly evaluated the entire specimen in terms of stapler lines, gastric wall integrity, and serosal lesions etc.; then they were opened up along the stapler line for mucosal evaluation (Figure 1). The specimen was fixed for about 16-24 hours in 10% buffered formalin solution.

The samples were then macroscopically evaluated by pathologists in 3-mm-thick cross sections for any lesion presence from the mucosa to the serosa. If no pathology was identified, random samples were taken from four points (proximal and distal ends, greater and lesser curvatures) and were stained in hematoxylin-eosin and paraffin-embedded blocks were prepared. The mucosae of the specimen were assessed under the microscope and those that were identified to have findings other than normal histopathologic evaluation or those with detailed sampling subsequent to the identification of pathological findings in macroscopic assessment were stained in Giemsa and alcianblue dyes in order to look for microorganisms and to evaluate intestinal metaplasia. Immunohistochemical analysis was conducted for one case identified to have submucosal lesion. Histopathology data were collected for analysis.

### Statistical analysis

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS 21 Inc., Chicago, IL, USA). The recorded data were given as mean (± SD), minimum and maximum. Pearson Chi-Square test was performed to compare the difference between stomach pathologies of patients under 40 years old and older. \( p < 0.05 \) was considered significant.

### 3. RESULTS

While 1301 (82.1%) out of 1584 patients covered by the study were female, 283 (17.9%) were male (Table 1). The patients’ median body mass index was 44.9 kg/m² and their median age was 38.25 (18-66 years).

#### Table 1 Demographic information of the patients

<table>
<thead>
<tr>
<th>Total patient</th>
<th>1584</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>1301 (82.1%)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>283 (17.9%)</td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>44.9 (SD: ±5.77, 35-58)</td>
</tr>
<tr>
<td>Mean Age</td>
<td>38.25 (SD: ±10.4, 18-66 age)</td>
</tr>
</tbody>
</table>

Table 2 presents the number of patients and sex distribution according to age groups. Accordingly, when the patients who had had LSG at our clinic were divided into two groups as those over and under 40 years of age, it was seen that the numbers in both groups were close. When the male-female distribution was investigated, it was seen that the female sex was predominant in all age groups.

#### Table 2 The number of patients and distribution of sex according to age groups.

<table>
<thead>
<tr>
<th>Age Groups</th>
<th>No. of patients, n (%)</th>
<th>Male: Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-29 age</td>
<td>375 (23.7)</td>
<td>1:4.1 (73:302)</td>
</tr>
<tr>
<td>30-39 age</td>
<td>493 (31.1)</td>
<td>1:3.3 (114:379)</td>
</tr>
<tr>
<td>40-49 age</td>
<td>478 (30.2)</td>
<td>1:7.2 (58:420)</td>
</tr>
<tr>
<td>≥50 age</td>
<td>238 (15.0)</td>
<td>1:5.4 (37:201)</td>
</tr>
</tbody>
</table>

Histopathology analyses were conducted for the LSG specimen of 1584 patients (Table 3). While normal findings were identified in almost half of the specimen (46.6%), the most common pathological alteration was chronic inactive gastritis characterized by chronic inflammatory cell presence in the lamina propria (34.3%). The second most frequent histopathological alteration was mild superficial chronic active gastritis (8.1%) characterized by the presence of chronic inflammatory cells and polymorphonuclear lymphocytes. This was followed by chronic active gastritis with chronic inflammatory cells and PMNLs in the lamina propria (5.5%), and lymphoid aggregate with plasma cells and lymphocytes in the lamina propria (5.2%). Two patients (0.1%) were identified to have a pathological finding consistent with gastrointestinal stromal tumor (GIST) of 11x10 mm and 16x12 mm in size, located in the fundus-corpus junction which revealed a positive result with CD (117) in immunohistochemical staining and one (0.1%) was diagnosed with granulomatous disease (Figure 2). Pathology consistent with accessory spleen of 15 x 9 mm in size resected with the
specimen in the gastrosplenic meso was found in another patient whose gastric specimen’s histopathology results were entirely normal.

Table 3 The types and prevalence of histopathology results of LSG specimen.

<table>
<thead>
<tr>
<th>Histopathologic evaluation</th>
<th>Normal Findings</th>
<th>Chronic Inactive Gastritis</th>
<th>Chronic Superficial Active Gastritis</th>
<th>Chronic Active Gastritis</th>
<th>Lymphoid Aggregate</th>
<th>GIST</th>
<th>Granulomatous Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>1584</td>
<td>739 (46.6%)</td>
<td>544 (34.3%)</td>
<td>128 (8.1%)</td>
<td>87 (5.5%)</td>
<td>2 (0.1%)</td>
<td>1 (0.1%)</td>
</tr>
<tr>
<td>&lt;40 age</td>
<td>868 (54.8%)</td>
<td>397 (45.7%)</td>
<td>278 (32.1%)</td>
<td>78 (8.9%)</td>
<td>61 (7.1%)</td>
<td>54 (6.2%)</td>
<td>0</td>
</tr>
<tr>
<td>≥40 age</td>
<td>716 (45.2%)</td>
<td>342 (47.8%)</td>
<td>266 (37.2%)</td>
<td>50 (6.9%)</td>
<td>26 (3.6%)</td>
<td>29 (4.1%)</td>
<td>1 (0.1%)</td>
</tr>
</tbody>
</table>

GIST: Gastrointestinal stromal tumor

Figure 2 Geographic necrosis area and granulomatous appearance (arrow) located in the submucosa (SM) under the auxintic type mucosa (M) in the stomach. H&E x40

When the patients were classified into two groups as those under and over than 40 years of age, the assessment revealed that their histopathology results were similar. The specimen of 845 patients, histopathology studies of whom revealed abnormal results, were stained in Giemsa and Alcian blue dyes in order to investigate microorganisms and intestinal metaplasia. The results revealed that 20.8% of the patients had Helicobacter pylori (H. pylori) positivity, while 5.5% patients had intestinal metaplasia. When the group covering patients under 40 years of age and the group with patients over 40 years of age were compared, it was observed that H. pylori positivity was similar in both (18.5%, 23.7% respectively, p=0.148) but intestinal metaplasia was found to be higher in the latter group (0.8%, 11.5% respectively, p=0.00) (Table 4).

Table 4 The prevalence of helicobacter pylori and intestinal metaplasia in patients with abnormal findings as revealed by histopathology results and their distribution according to age groups.

<table>
<thead>
<tr>
<th>No. of patients</th>
<th>H. Pylori Positivity</th>
<th>Intestinal Metaplasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;40 age</td>
<td>87/471 (18.5%)</td>
<td>4/471 (0.8%)</td>
</tr>
<tr>
<td>≥40 age</td>
<td>89/374 (23.7%)</td>
<td>43/374 (11.5%)</td>
</tr>
<tr>
<td>P value</td>
<td>0.148</td>
<td>0.00</td>
</tr>
</tbody>
</table>

*Pearson Chi-Square
4. DISCUSSION

The aim of this study was to evaluate the pathology results of a total of 1584 vertical sleeve gastrectomy specimen delivered between 2013 and 2020 at our clinic and to ascertain the patient group with abnormal histopathological alterations. The results of our study revealed that there was an increased risk of intestinal metaplasia and unexpected gastric pathologies in obese patients over 40 years of age. LSG as the surgical treatment of morbid obesity has been on the rise in our country as it is in all over the world. Consequently, data collected on gastric pathologies of obese patients have also improved through the histopathology evaluation of gastric specimen. While the results of histopathology evaluation of 46.6% of patients were found to be normal within the scope of our study, our figures were similar to those of Safaan et al., (2017) (n=1555, 52%) and Lauti et al., (2016) (n=976, 46%).

We have ascertained in our study that H. pylori positivity was 20.8% with a small increase in the patient group over 40 years of age (23.5%), however, it did not have a statistically significant relationship with age. While the rate of intestinal metaplasia was 5.5% in all age groups, it showed a pronounced increase in the over 40 years of age patient group (11.5%, p=0.000). Moreover, we observed that 34(72.3%) out of 47 patients with intestinal metaplasia also had H. pylori positivity.

Studies in literature that evaluated the H. pylori positivity of sleeve gastrectomy specimen of obese patients have reported results ranging between 0% and 91.9%. Onzi et al. (Onzi et al., 2014) in their small study group (n=12), reported no H. pylori positivity in the specimen due to the fact that all patients had been receiving eradication therapy but found 66.7% positivity in the preoperative endoscopic biopsy results in the same study. Adali et al. (2019), on the other hand, reported that 91.9% of 37 obese patients had H. pylori positivity, while 21.6% had intestinal metaplasia. The authors underlined that there was a statistically significant relationship between high BMI and intestinal metaplasia. Safaan et al. (2017) indicated in their study involving 1,555 patients that 40.9% of the patients were found to have H. pylori positivity, while 1.4% had intestinal metaplasia.

Yardimci et al. (2018) reported in their study conducted in our country that the routine preoperative endoscopic biopsy results of 755 patients revealed 23.5% H. pylori positivity and this rate was similar to that of our study. The histopathology evaluation results in the same study were found to be normal in 23.9% of the patients, while chronic gastritis unrelated to H. pylori was observed in 64.9% of the patients and H. pylori-related chronic gastritis was seen in 9.1% of the patients. Although all the patients in the study received endoscopic biopsy and accordingly treated, the fact that normal specimen rates were low in the histopathology assessment of sleeve gastrectomy material suggests patients’ non-adherence to treatment. The difference in H. pylori infection between preoperative endoscopy and specimen evaluation was associated with the fact that all patients found to have H. pylori positivity as revealed by preoperative endoscopic biopsy had been receiving triple eradication therapy.

In another study conducted in our country (Öner & Özdaş, 2018), the authors found H. pylori positivity in 64% of 161 patients, followed by intestinal metaplasia in 5%. The authors also reported a statistically significant relationship between patients with H. pylori positivity and chronic gastritis and chronic active gastritis. Lee et al. (Lee et al., 2017) stated in their study on preoperative endoscopy that patients under 40 years of age without any reflux symptoms and NSAID administration comprised the low-risk group and reported 18.9% to be the rate of abnormal endoscopy finding in such patients. The authors, however, underlined the necessity that all patients should receive preoperative endoscopy evaluation because 27.2% of 268 patients were found to have significant endoscopic alterations that would change or delay plans for obesity surgery.

Parikh et al. (2016) argued in their meta-analysis assessing the results of 6,616 patients in 28 studies that preoperative endoscopy delayed or changed surgical procedures merely in 7.6% of the cases. The authors, therefore, suggested that preoperative endoscopy would better be performed depending on symptom presence, risk factors and the type of planned bariatric surgery rather than performing routine preoperative endoscopy. Although the cost of healthcare services is rather low in our country (ie, the cost of histopathologic evaluation is 33,7$, preoperative endoscopy evaluation is 84,3$), physicians tend to opt out of performing upper endoscopy for asymptomatic patients in preoperative evaluation prior to morbid obesity surgery because of the limited budget allocated to healthcare spending (about 5% of the total annual budget). Whether detailed histopathology analysis is required for macroscopically normal gastric specimen is a controversial issue in our country due to the same reasons as is the case all over the world.

Hansen et al. (2017), for instance, argued that routine histopathology evaluation was not necessary as it failed to deliver any significant clinical pathology and cost between 500$ and 1500$ per specimen in their study assessing 351 LSG specimen. Abdulgaffar et al. (2016) too, reported that the probability of finding an unexpected pathological finding was low, unnecessary histopathology assessments cost their center about 18,500$ per annum while costing pathologists 1,440 working hours adding that macroscopic evaluation should certainly be conducted and, only after this, physicians should decide whether additional evaluation was called for or not. The authors also stated that the cost of preoperative endoscopy evaluation at their clinic was about 1400-2100$, while offering eradication therapy without prior endoscopy was a cost efficient method due to the fact that the cost of
routine *H. pylori* eradication therapy was quite low (51$). Safaan (2017) reported that the rate of abnormal findings was higher in the elderly and female patient groups and routine pathological evaluation would be appropriate in a selective patient group.

Yardımcı et al. (Yardımcı et al., 2018), on the other hand, stated that they found neoplasia in 0.5% of 755 patients while Canil et al. (2018) did so in 0.3% of 925 patients and underlined that both preoperative endoscopy and routine histopathology evaluation was necessarily called for because of these reasons. Moreover, Kopach et al. (2017) reported in their study involving 511 patients that they ascertained incidental pathologies other than chronic gastritis in 12% of their patients while 5.7% of these had clinical significance along with the fact that these lesions with clinical significance could not be revealed by macroscopic evaluation. The authors argued that the cost of pathological evaluation of sleeve gastrectomy specimen was 883$ which further increased by 314$ when immunohistochemical analyses were performed adding routine histopathology evaluation should nevertheless be carried out.

In another study on costs conducted in France, the authors reported that the cost of specimen evaluation was low (34€) arguing that such evaluation for all patients would not burden the country’s economy (Uguen et al., 2018). To end such controversy, Waledziak et al. (2019) reported in their 2018 prospective study that the evaluation of outer gastric layer during laparoscopic examination and macroscopic specimen assessment in patients with preoperative endoscopy proved to be a good method in revealing incidental pathologies (sensitivity 75%, specificity 98.2%, negative predictive value 99.1%).

5. CONCLUSION
Consequently, we would like to suggest that physicians perform routine histopathology evaluation for patients over 40 years of age while this routine would be appropriate for patients under 40 years of age only if they were found to have pathologies in the macroscopic evaluation of their specimen in countries like ours where the cost of histopathology evaluation was low and the budget allocated to healthcare spending was limited.

Limitations of study
The fact that the study was planned retrospectively along with the absence of data on patients with preoperative endoscopy constitutes the limitations of the study. Although there is an ample number of studies on the subject in literature, our study is the one with the highest number of patients and is the first of its kind to compare gastric pathologies in patients over and under 40 years of age.

Ethical Statement
The ethical committee of Fatih Sultan Mehmet Training and Research Hospital declared ethical approval for the current study (No: 17073117-050.06-E.22; Date: 03.02.2020)

Conflict of Interest
There is no conflict of interest with any financial organization. The authors have not received funding for research of the article.

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All authors have contributed to the paper, met criteria of authorship and are familiar with the contents of the final draft.

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Author Contributions
Hüseyin Çiyiltepe: Study conception and design, acquisition of data, analysis and interpretation of data, drafting of manuscript.
Anıl Ergin, Ali Cihan Bilgili, Mehmet Mahir Fersahoglu: Acquisition of data, drafting of manuscript.
Nuriye Esen Bulut, Mehmet Timuçin Aydin: Study conception and design, analysis and interpretation of data.
Aziz Bora Karip, Adnan Somay: Acquisition of data, analysis and interpretation of data, critical revision.
Kemal Memişoğlu: Critical revision, language.

Data and materials availability
All data associated with this study are present in the paper.
REFERENCES AND NOTES


