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Histologic and Cost-Benefit Analysis of Laparoscopic Sleeve Gastrectomy Specimens Performed for Morbid Obesity

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● **Context.**—Laparoscopic sleeve gastrectomy (LSG) has quickly become the bariatric surgical procedure of choice for patients with obesity who have failed medical management. Laparoscopic sleeve gastrectomy results in a gastric remnant that is routinely subject to pathologic examination.

Objective.—To perform a histologic and cost-benefit analysis of gastric remnants post-LSG.

Design.—All LSG cases performed at University Health Network, Toronto, Ontario, Canada, between 2010 and 2019 were reviewed. Specimens that underwent routine histopathologic assessment and ancillary immunohistochemical analysis were analyzed. Baseline patient characteristics and surgical outcomes were obtained from our internal database. The total cost of specimen gross preparation, examination, sampling, and producing and reporting a hematoxylin-eosin slide was calculated.

Results.—A total of 572 patients underwent LSG during the study period and had their specimens examined histologically. A mean of 4.87 blocks generating 4 hematoxylin-eosin slides was produced. The most common histologic findings reported in LSG specimens ranged from no

pathologic abnormalities identified together with proton pump inhibitor–related change. A minority of cases demonstrated clinically actionable histologic findings, of which *Helicobacter pylori* infection was the commonest. The total cost for the complete pathologic analysis of these cases amounted to CaD $66 383.10 (US $47 080.21) with a mean of CaD $116.05 (US $82.40) per case. A total of CaD $62 622.75 (US $44 413.30) was spent on full examination of cases that had no further postoperative clinical impact.

Conclusions.—There is a broad spectrum of pathologic findings in LSG specimens, ranging from clinically nonactionable to more clinically actionable. The vast majority of histologic findings had no clinical impact, with only a minority of cases being clinically significant. This study therefore recommends that LSG specimens be subject to gross pathologic examination in the vast majority of cases. However, sections should be submitted for microscopic analysis if grossly evident lesions are present and if there is a clinical/known history of clinically actionable findings.

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I nitial medical management of morbid obesity includes lifestyle and dietary modifications, failure of which results in treatment with adjunct pharmacotherapy or bariatric surgery.[1]

A variety of bariatric surgical procedures exist, including, but not limited to, Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy (LSG). In 2011, LSGs represented 17.8% of all metabolic and bariatric procedures performed in the United States; however, in 2016, the number of LSGs

represented 58.1% of all metabolic and bariatric procedures.[2] A recent meta-analysis demonstrated laparoscopic Roux-en-Y gastric bypass and LSG to be equivalent for excess weight loss.[3] However, patients with LSG experienced fewer postoperative complications and a lower reoperation rate than those who underwent laparoscopic Roux-en-Y gastric bypass.[4]

Laparoscopic sleeve gastrectomy involves taking down the greater curvature of the stomach with the subsequent division of the stomach, in turn creating a gastric remnant.[4] Currently, it is at the discretion of the institutions to determine whether LSG specimens undergo pathologic examination. In an era of severe fiscal constraint, we undertook a histologic and cost-benefit analysis of all LSG specimens seen at an academic center in Toronto, Ontario, Canada during a 9-year period.

MATERIALS AND METHODS

Patients

A total of 572 LSG cases performed at University Health Network Toronto, Canada, between September 2010 and Novem-

Table 1. Demographics			
Gender	No. (%)	Mean Age, y	Body Mass Index, kg/m²
Female	439 (76.8)	48.1 ± 11.5	50.5 ± 10.5
Male	133 (23.3)	48.7 ± 10.5	52.4 ± 11.5
Total	**572**	**48.2 ± 11.3**	**50.9 ± 10.7**

ber 2019 (inclusive) were reviewed. Institutional research ethics board approval was obtained, No. CAPCR-ID: 17-5578. Baseline demographics and preoperative investigations were obtained retrospectively from the bariatric surgery patient database (Table 1).

All patients underwent a multidisciplinary preoperative assessment through the bariatric program. *Helicobacter pylori* screening was performed on all patients using a combination of serology or C-14 breath test. Patients with a positive result were treated with dual or triple antibiotic therapy combined with a proton pump inhibitor as per programmatic policy.

Preoperative upper gastrointestinal endoscopy was performed selectively at the surgeon's discretion if patients complained of upper gastrointestinal symptoms, were suspected of having a hiatus hernia on unrelated preoperative imaging, or were thought clinically to be at increased risk of gastric malignancy.

Gross and Histologic Analysis

All pathology reports were reviewed, and the number of sections taken in each case, the gross descriptions, and the final diagnosis were noted. The number of blocks taken from each LSG specimen was calculated and hematoxylin-eosin slides from all cases were evaluated.

The final diagnoses were subdivided into 2 categories: clinically nonactionable or clinically actionable pathology. Clinically nonactionable findings were defined as those not requiring any further clinical intervention and included nonneoplastic and neoplastic conditions. Clinically actionable findings consisted of histologic findings that required a change in medical management of a patient, which were further subdivided into nonneoplastic, premalignant, and malignant conditions. Ancillary testing (mainly immunohistochemistry) was used in the setting of clinically actionable findings.

Cost-Benefit Analysis

The cost of each block of tissue sampled was based on the average time (approximately 20 minutes per case) for a pathologists' assistant to prepare and examine the gross specimen. This included patient chart review for indication of the surgery and to exclude comorbidity, inspection, measurement, sampling, and dictation of the gross report, which amounted to approximately CaD $3.50 (US $2.48). This, together with the cost of processing, cutting a block, and generating a hematoxylin-eosin–stained slide (CaD $12.00; US $8.51), totaled CaD $15.50 (US $10.99) per block/slide based on the hourly rates of pay and cost of consumables.

In terms of ancillary immunohistochemical stains, cost was based on the complexity of the test performed. In our study, most of the cases were of low complexity (tier 1), with only a few intermediate- and high-complexity (tiers 2 and 3) cases. The rates were CaD $14.30 (US $10.14) for tier 1 tests (tests ordered were CD3, CD20, CD117, DOG1, *H pylori*, MIB1, SMA, and synaptophysin), CaD $18.70 (US $13.26) for tier 2 tests (bcl-2, bcl-6, CD5, and CD23), and CaD $27.50 (US $19.50) for tier 3 tests (cyclin D1, MUM1, and polypeptide YY).

The mean time taken by the reporting pathologist was 15 minutes per case (mean range of 4–5 slides), with an additional 5 minutes added for interpretation of an ancillary stain(s). The hourly rate of salary for pathologists is CaD $135 (US $95.74) per hour.

Table 2. Patients with Preoperative Upper Gastrointestinal Endoscopy (UGIE)	
Histologic Finding(s) on UGIE	No. (%) of UGIE Patients[a]
Gastritis	20 (26.0)
Proton pump inhibitor related changes	16 (20.8)
No significant histologic abnormalities	17 (22.1)
Reactive gastropathy	9 (11.7)
Fundic gland polyp(s)	5 (6.5)
Helicobacter pylori	5 (6.5)
Hyperplastic polyp(s)	2 (2.6)
Esophageal candidiasis	1 (1.3)
Gastrointestinal stromal tumor	1 (1.3)
Low grade dysplasia	1 (1.3)
Total	**77 (100)**

[a] These patients represent 13.5% of all patients in the study.

RESULTS

A total of 572 patients underwent LSG during the study period and had their specimens submitted for full pathologic evaluation (Table 1).

Upper gastrointestinal endoscopy was performed in 77 of 572 patients (13.5%). The histologic findings of the biopsy specimens are summarized in Table 2.

The number of blocks taken from each LSG specimen ranged from 3 to 8, with a mean of 4.87 blocks from all cases. The total number of diagnoses rendered was 623. The most common histopathologic diagnoses were clinically nonactionable (n = 597 of 623; 95.8%). Abnormal findings warranting a change in postoperative management and/or follow-up were present in 26 of 623 specimens (4.2%).

Clinically Nonactionable Histologic Findings

Clinically nonactionable histologic findings represented the vast majority of all reported histologic findings. "No significant pathologic abnormalities" (n = 263 of 623; 42.2%), proton pump inhibitor related changes (n = 155 of 623; 24.9%), and non–*H pylori* chronic gastritis (n = 95 of 623; 15.2%) were amongst the most common made diagnoses. These findings are summarized in Table 3.

Clinically Actionable Histologic Findings

Clinically actionable histologic findings are summarized in Table 4 and included nonneoplastic conditions such as active *H pylori* infection (n = 11 of 623; 1.8%); premalignant conditions such as intestinal metaplasia (n = 7 of 623; 1.1%), enterochromaffin cell–like (ECL) hyperplasia (n = 4 of 623; 0.6%), and neuroendocrine microadenoma (n = 1 of 623; 0.2%); and malignancies or tumors such as gastrointestinal stromal tumor (GIST; n = 1) measuring greater than 2 cm in greatest dimension, intramucosal signet ring carcinoma (n = 1), and a well-differentiated neuroendocrine tumor, grade 1 (n = 1).

Clinically actionable histologic findings that were not appreciated on gross examination or that were clinically unknown consisted of nonmalignant, nonneoplastic conditions: *H pylori* (n = 1) and premalignant (but indolent) conditions such as ECL hyperplasia (n = 3) and intestinal metaplasia (n = 2).

Enterochromaffin cell–like hyperplasia, along with intestinal metaplasia, remnant parietal cell pseudohypertrophy,

Table 3. Summary of Clinically Nonactionable Histologic Findings					
Histologic Findings	No. (% of All Histologic Findings)	Grossly Identified Lesions, No./Total (%)	Total Blocks	No. of Blocks/Specimen	No. of Ancillary Tests
Nonneoplastic					
No significant histologic abnormalities	263 (42.2)	4/263 (1.5)	1207	4.6 ± 1.5	19
PPI-related change	155 (24.9)	54/155 (34.8)	687	4.8 ± 1.8	2
Non-*Helicobacter* gastritis	95 (15.2)	40/95 (42.1)	385	4.6 ± 1.5	56
Fundic gland polyp	23 (3.7)	20/23 (87.0)	142	6.4 ± 3.6	2
Lymphoid aggregates	45 (7.2)	7/45 (15.6)	80	3.8 ± 1.1	1
Reactive gastropathy	3 (0.5)	1/3 (33.3)	13	4.3 ± 1.2	0
Focal ischemic changes	2 (0.3)	0/2 (0.0)	6	3.0 ± 0.0	0
Granulomatous inflammation	1 (0.2)	0/1 (0.0)	4	4.0 ± 0.0	2
Hyperplastic polyp	2 (0.3)	2/2 (100.0)	4	2	0
Neoplastic					
Gastrointestinal stromal tumor (<2 cm)	6 (1.0)	4/6 (57.1)	36	6 ± 3.6	38
Leiomyoma	1 (0.2)	1/1 (100.0)	13	13 ± 0.0	6
Lipoma	1 (0.2)	1/1 (100.0)	10	0 ± 0.0	0
Total	**597**	**134/597 (22.4)**	**2587**	**64.5 ± 3.0**	**126**

Abbreviation: PPI, proton pump inhibitor.

atrophy of the oxyntic mucosa, and dense lymphoplasmacytic inflammation, is a characteristic feature of autoimmune metaplastic atrophic gastritis.

One case of the 4 that demonstrated ECL hyperplasia was associated with *Helicobacter* gastritis. Another was associated with intestinal metaplasia, and follow-up biopsies post-LSG confirmed autoimmune metaplastic atrophic gastritis. The third case of ECL hyperplasia was not associated with intestinal metaplasia and could potentially be explained by the use of proton pump inhibitors. The fourth case of ECL hyperplasia was associated with a well-differentiated neuroendocrine tumor, grade 1.

Seven GISTs were identified in the entire study; however, only 1 of the 7 GISTs was considered to be clinically actionable, as it measured greater than 2 cm in dimension and required postoperative follow-up. This diagnosis was known prior to surgery and was also easily identified upon gross inspection. The 6 remaining GISTs, 3 of which were detected at gross examination, were less than 2 cm in diameter. The case with intramucosal signet ring cell carcinoma was grossly evident as a diffusely thickened, polypoid, rigid, and congested stomach wall.

Cost-Benefit Analysis

The total cost was CaD $42 113.50 (US $29 867.73) for the study period, excluding pathologists' time was calculated by taking into account the average number of blocks taken and the average cost of CaD $15.50 (US $10.99) per block/slide. Additional ancillary immunohistochemical testing resulted in a further cost of CaD $2624.60 (US $1861.42). Finally, factoring in the pathologists' time (looking at electronic patient records, assessing all slides thoroughly, and generating a pathologic report) at an average of 20 minutes per case, the total cost during the study period was CaD $66 383.10 (US $47 080.21), with a mean cost of CaD $116.05 (US $82.30) per LSG specimen. Of this total cost, specimens with clinically nonactionable findings cost CaD $63 162.75 (US $44 796.28; 95.1%) and cases with clinically actionable findings cost CaD $3760.35 (US $2666.91).

Cost-benefit analysis was also performed if 2 blocks were submitted for LSG that had no grossly identifiable lesions or concerning clinical history. An average of 10 minutes was spent on microscopic examination by the pathologist, resulting in an overall cost of CaD $38 137.35 (US $27 047.77). Of this total cost, specimens with clinically nonactionable findings cost CaD $34 377.00 (US $24 380.85;

Table 4. Summary of Clinically Actionable Histologic Findings					
Histologic Findings	No. (% of All Histologic Findings)	No. identified on UGIE	Grossly Identified Lesions, No./Total (%)	Total Blocks	No. of Ancillary Tests
Helicobacter pylori	11 (1.8)	3	10/11 (90.9)	52	10
Intestinal metaplasia	7 (1.1)	0	5/7 (71.4)	33	11
ECL hyperplasia	4 (0.6)	0	1/4 (25.0)	11	9
Neuroendocrine microadenoma[a]	1 (0.2)	0	1/1 (100.0)	NA	NA
Gastrointestinal stromal tumor (≥2 cm)	1 (0.2)	1	1/1 (100.0)	10	5
Intramucosal signet ring carcinoma[a]	1 (0.2)	0	1/1 (100.0)	72	15
Well-differentiated neuroendocrine tumor, G1	1 (0.2)	0	1/1 (100.0)	28	14
Total	**26 (4.2)**	**4**	**20/26 (76.9)**	**206**	**64**

Abbreviation: ECL, enterochromaffin cell–like; G1, grade 1; NA, not applicable; UGIE, upper gastrointestinal endoscopy.

[a] Represent the same case.

		Clinically Nonactionable Histologic Findings	Clinically Nonactionable Histologic Findings (2 Blocks Only)	Clinically Actionable Histologic Findings
Table 5. Cost-Benefit Analysis of Laparoscopic Sleeve Gastrectomy (LSG) Specimens				
	Currency[a]			
Frequency in all LSG specimens		597	597	26
Total No. of blocks		2583	1194	134[b]
Total No. of ancillary tests		126	126	49[b]
Total cost of gross examination	CaD $	9040.50	4179.00	469.00
	US $	6411.70	2963.83	332.62
Total cost of histology processing	CaD $	30 996.00	14 328.00	1608.00
	US $	21 982.98	10 161.70	1140.42
Total cost of gross inspection and processing of a block	CaD $	40 036.50	18 507.00	2077.00
	US $	28 394.68	13 125.53	1473.05
Total cost of ancillary tests	CaD $	1897.50	1897.50	727.10
	US $	1345.74	1345.74	515.67
Total cost of examination by pathologist	CaD $	20 148.75	13 432.50	776.25
	US $	14 289.89	9526.60	550.53
Total cost of examination of ancillary tests	CaD $	540.00	540.00	180.00
	US $	382.98	382.98	127.66
Total cost of pathologic examination of LSG specimens	CaD $	62 622.75	34 377.00	3760.35
	US $	44 413.30	24 380.85	2666.91
Mean cost of examination of LSG specimen	CaD $	114.07	57.58	163.49
	US $	80.90	40.83	115.95
Overall total cost of examination of LSG specimens	CaD $	66 383.10		
	US $	47 080.21		
Overall total cost of examining 2 blocks for LSG specimens	CaD $	38 137.35		
	US $	27 047.77		
Overall mean cost of examination of LSG specimens	CaD $	116.05		
	US $	82.30		
Overall mean cost of examining 2 blocks for LSG specimens	CaD $	66.67		
	US $	$ 47.28		

[a] US $1 = CaD $1.41.
[b] Excluding signet ring carcinoma in situ and neuroendocrine microadenoma case.

90.1%) and cases with clinically actionable findings cost CaD $3760.35 (US $2666.91) of the total costs. The overall mean cost per block, if 2 blocks were submitted for LSG that had no grossly identifiable lesions or concerning clinical history, was CaD $66.67 (US $47.28). The results are summarized in Table 5.

An important caveat to these calculations is the exclusion of the intramucosal signet ring carcinoma and neuroendocrine microadenoma, both of which were a part of the same case and were grossly apparent with linitis plastica and polyps. This case required a total of 72 blocks and 15 ancillary immunohistochemical stains; consequently, it was excluded from cost-benefit analysis, as it represented an outlier and would have skewed the results of the study.

DISCUSSION

As health budgets come under ever-increasing pressure, careful scrutiny of operations and evaluation of return on investment are important and integral to efficient practice. Redirection of limited resources into high-yield, clinically impactful practice is an important facet of efficient resource management. In Toronto, the Hospitals Act of Ontario mandates that specimens removed at surgical procedures have pathologic assessment. This assessment is very much left to the discretion of the individual pathology department and ranges from gross examination to full microscopic histopathologic evaluation. Several specimens that are deemed clinically nonactionable, or thought to have a low pathology yield with little to no impact on patient care, fall within this remit. Nail clippings, teeth, and prostheses and other implants/devices are examples of such specimens. Careful gross examination is conducted on all specimens, and submission of tissue sections is based on grossly observed/detected abnormalities and pertinent clinical information. Recently, within the Division of Anatomical Pathology at University Health Network, hernia sac evaluation became a gross examination–only activity on a routine basis. Caveats to this routine policy were grossly observed lesions and clinical indications for histologic evaluation. Furthermore, all so-called gross-only specimens are retained within the grossing room for a period of 30 days after the issuance of a pathologist-sanctioned report. This allows clinicians the ability to contact the pathologist requesting sections to be taken because of a valid clinical indication.

In this study, clinically nonactionable histologic findings represented a total of 95.8% of all histopathologic evaluations made in LSG specimens. These findings are consistent with reports from other such series evaluating the histologic findings in LSG specimens.[5–27] Indeed, "no pathologic abnormality" is the most frequent histologic diagnosis rendered in LSG specimens. Another common diagnosis is non–H pylori-associated gastritis, and this is thought to be associated with decreased levels of adiponectin in obese patients; there is also an association of obesity with endoscopically detected gastritis and gastric ulcers.[5]

Neoplastic but clinically nonactionable histologic findings from our study included 7 GISTs (6 with no risk of progression), 1 leiomyoma, and 1 lipoma. The GIST with a low risk of progression, measuring 3.5 cm, was easily identified on gross inspection of the specimen, and the diagnosis of GIST was known prior to surgery.

Gastrointestinal stromal tumors represent 0.1% to 1% of all malignant neoplasms of the gastrointestinal tract,[28] and a review of literature demonstrated that the incidence of GISTs in LSG specimens ranged from 0.6% to 0.8%.[29–32] The vast majority of gastric GISTs encountered in LSG specimens are less than 2 cm in maximal diameter, are considered benign, and are treated adequately by surgical resection (in these particular cases LSG being deemed adequate surgical intervention). This is in accordance with the National Comprehensive Cancer Network guidelines on GISTs.[33] If selective tissue sampling had been routine and if the diagnosis had not been known preoperatively, this case would have been detected, sampled, and appropriately reported with current standard of patient care maintained.

Clinically actionable findings represented a total of 4.2% (26 of 623 diagnoses) of all histologic diagnoses rendered. Of the 26 patients, 3 were known to have active *H pylori* infection and another patient had a preoperative diagnosis of GIST. If one then considers these known diagnoses, the number of clinically actionable diagnoses is reduced from 26 to 22 of 623 (3.5%). If grossly identified, clinically actionable lesions are also accounted for, then unexpected clinically actionable histologic findings further decrease to only 6 of 26, with an overall rate of unexpected clinically actionable histologic findings of only 0.96% of a total of 623 diagnoses.

The clinically actionable histologic findings that were not detected on gross examination or not clinically known were all nonmalignant/nontumor conditions: *H pylori* infection, ECL hyperplasia, and intestinal metaplasia, all of which are not appreciated at gross examination.

With regard to *H pylori* infection and LSG, it does not influence perioperative complications, postoperative outcomes, or weight loss.[34,35] It is also known that *H pylori* is a major risk factor for the development of gastric adenocarcinoma[36,37] and extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue.[38]

Helicobacter pylori infection represented 42.3% of all clinically actionable histologic findings (11 out 26 cases), but only 1.8% (11 of 623 cases) of all histologic diagnoses made in this study. The incidence of *H pylori* in our study was lower than the rate of 2.5% to 43% reported in literature.[7–27] The difference between our study and the literature can be explained by geographic variation,[39] and all patients in this study underwent preoperative *H pylori* screening and treatment if warranted. It should also be noted that the American Society for Gastrointestinal Endoscopy has not deemed necessary upper gastrointestinal endoscopy prior to LSG or testing and eradication of *H pylori* prior to bariatric surgery.[40]

The diagnosis of intestinal metaplasia was made 7 times in a total of 623 diagnoses (1.1% of all LSG specimens from our study) and is in keeping with the quoted range of 0% to 9.9% in literature.[7–27]

Malignant clinically actionable histologic findings included a low-risk GIST, a well-differentiated neuroendocrine tumor, and an intramucosal signet ring carcinoma. All of these lesions were visible at the time of gross inspection.

CONCLUSIONS

There is a broad spectrum of pathologic findings in LSG specimens, ranging from clinically nonactionable to clinically actionable. The vast preponderance of histologic findings in LSG specimens are clinically nonactionable, with only a small portion of diagnoses being clinically actionable. Based on the extremely low yield of unexpected clinically actionable diagnoses from our cohort, we suggest that LSG specimens should fall into the category of specimens with gross examination only. However, sections should be submitted for microscopic analysis if grossly evident lesions are present and if there is a clinical/known history of clinically significant findings or other valid clinical indication warranting histologic examination.

An institution wishing to adopt this "gross-only" approach should amend its surgical pathology operating manuals, stating that these specimens will be gross only, that sections will be taken if lesions are seen at gross examination and/or there is a clinical indication to do so, and that specimens will be retained for a period of not less than 30 days, allowing for reevaluation and sectioning of the specimen should the clinical scenario warrant it.

Although the overall dollar cost savings accomplished during the 9-year study period are modest, the time saving by pathologists' assistants, medical laboratory technologists, administrative assistants, and pathologists makes a compelling case for LSG specimens being triaged by gross pathologic evaluation only, as this would allow staff members to focus on more clinically pertinent activities.

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