GAVIN PUBLISHERS

Journal of Surgery

Sterbis E, et al. J Surg 2017: J110.

DOI: 10.29011/JSUR-110.000010

Research Article

Incidence of Gastrointestinal Stromal Tumors Is Drastically Increased In Patients with Morbid Obesity

Emily Sterbis, Jennifer Baker, Amy Rosenbluth, James Buwen, Alec C Beekley, David S Tichansky*, Michael R Kammerer

*Department of Surgery, Division of Minimally Invasive, Metabolic and Bariatric Surgery, Thomas Jefferson University, Philadelphia, Pennsylvania, USA

***Corresponding author:** David S Tichansky, Jefferson Bariatric and Metabolic Surgery 211 S. 9th Street, Suite 402, Philadelphia, PA 19107; Tel: 215-955-0020; Fax: 215-503-7577; E-mail: david.tichansky@jefferson.edu

Citation: Emily Sterbis, Jennifer Baker, Amy Rosenbluth, James Buwen, Alec C Beekley, David S Tichansky, Michael R Kammerer (2016) Incidence of Gastrointestinal Stromal Tumors Is Drastically Increased In Patients with Morbid Obesity. J Surg 2016. J110. DOI: 10.29011/JSUR-110.000010

Received Date: 06 December, 2016; **Accepted Date:** 04 January, 2017; **Published Date:** 11 January, 2017

Abstract

Introduction

While gastrointestinal stromal tumors (GIST) have not been directly associated with obesity, the observed incidence of these tumors is seemingly greater than previously reported. This study sought to determine the true incidence of GISTs in bariatric surgery patients.

Methods

A retrospective review was performed on prospectively collected data of consecutive laparoscopic bariatric procedures from August, 2012 to June, 2013. Thorough intra operative examination of the stomach to identify possible pathology was performed during each case, and the procedure was modified, if necessary, to resect suspicious lesions. All resected specimens were sent to pathology for microscopic examination.

Results

Two-hundred nine consecutive patients undergoing primary laparoscopic bariatric procedures at our institution were included in this study. All patients denied symptoms common to GIST in the preoperative period and no patients had GISTs definitively identified on pre-operative endoscopy. Five pathology-proven GISTs were found in 4 patients (1.9%). Half of these patients required modification of their procedure to achieve oncologically appropriate resection margin.

Conclusions

Bariatric surgery patients may have a dramatically greater incidence of GIST than the general population (1.9% vs. 0.002%). During bariatric surgery, meticulous examination of the stomach should be performed to facilitate resection of these tumors, even if asymptomatic, before they could become clinically relevant.

Introduction

Gastrointestinal stromal tumor (GIST) is a mesenchymal neoplasm of the gastrointestinal tract [1]. It has been proposed that interstitial cells of Cajal (ICC) and GIST share a common precursor cell as both share common immunohistochemical characteristics including c-KIT (CD117) and CD34 [2]. See (Figure 1-3).

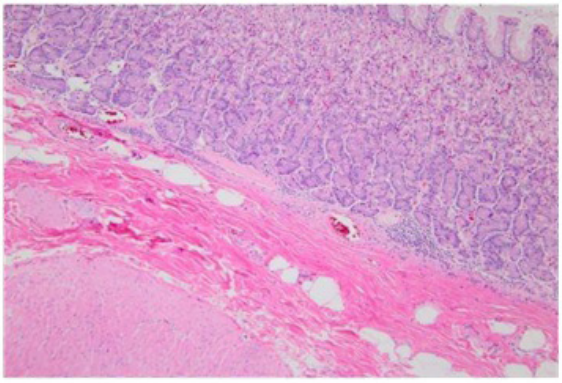

Figure 1: H and E Stain of stomach.

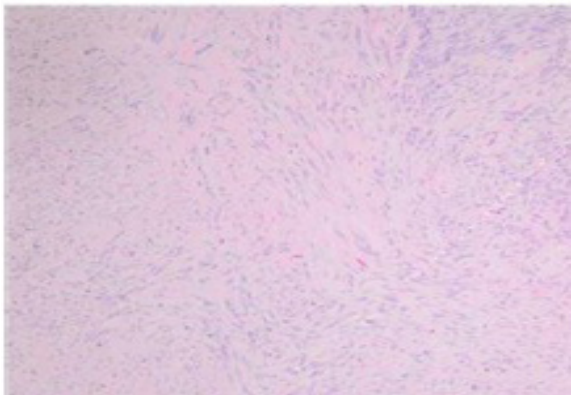

Figure 2: H and E stain of incidental asymptomatic GIST resected during bariatric surgery.

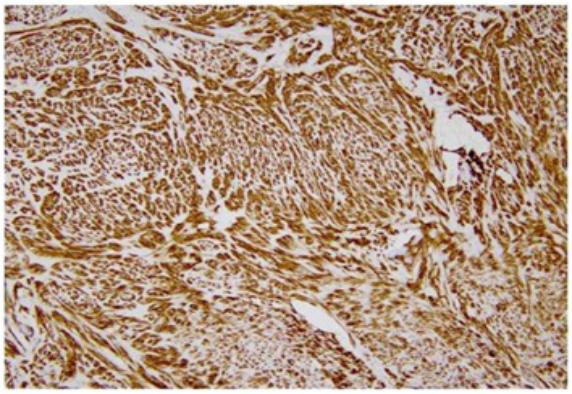

Figure 3: cKit stain of incidental asymptomatic GIST resected during bariatric surgery.

It is this precursor cell that is probably the origin of GISTs which likely arise due to KIT proto-oncogene activation. Immunohistochemical studies have shown that most GIST are c-KIT positive (80-100%), CD34 positive (50-80%), and Desmin negative [3]. GIST most often arises in the stomach (39-50%), small intestine (25-36%), colon (5-10%), rectum (5-10%), and esophagus (1-5%) [1,4]. There is a reported incidence of 7-20 new cases per million per year in the general population [1,5-8]. Currently, the mainstay of treatment remains surgical excision of the tumor with adequate negative margin [9-10].

Obesity has been implicated as a risk factor for many cancers, including esophageal, endometrial, thyroid, colon, and renal [11-12]. The unexpected finding of pathology in the course of a bariatric procedure has been described and in most cases the initial procedure could be completed with little to no alteration [13]. GISTs are some of the more common incidentally discovered neoplasms in these cases. The first incidental GIST found during bariatric surgery was described in 2005 [14]. There have since been recent retrospective analyses and case series looking more closely at the increased incidence in this patient population. Several sources propose that bariatric patients may have an increased incidence of GIST, estimated at 0.31-0.8% [9, 14-17].

The combination of previous retrospective reports of unexpected pathology and the experience at our institution led to active prospective intra operative inspection of the stomachs of patients undergoing laparoscopic bariatric surgery for any incidental pathology, but specifically for lesions likely to be small asymptomatic GISTs. To date, there has been no prospective study on the incidence of GIST during bariatric procedures. The purpose of this study was to determine if the true incidence of GIST in patients undergoing obesity surgery is indeed even greater than previously reported when these lesions are prospectively sought. It is expected that the incidence should be higher as we are actively searching for GIST pathology instead of pas-

sively recording pathologic incidence. The larger question of whether morbid obesity increases incidence of GIST remains unanswered. However, this investigation proposes use of an opportunistic safety net for these patients to avoid more complicated resections or disease that would certainly be caused by passively waiting for lesions to become symptomatic.

Methods

Patients undergoing weight loss surgery at our institution (laparoscopic Roux-en-Y gastric bypass or laparoscopic sleeve gastrectomy) are determined to meet National Institute of Health criteria and then participate in a comprehensive work-up including routine pre-operative outpatient upper endoscopy. Informed consent was obtained from study participants and no stipend was offered. Thorough intra-operative examination of the stomach to identify possible pathology was performed during each case, with a high index of suspicion for small mural lesions representing GISTs. The procedure was modified, if necessary, to provide oncologically adequate resection of any lesion found. All resected specimens were sent to pathology for microscopic examination. All sleeve resection specimens were also routinely sent to pathology for review. In sleeve gastrectomy cases where suspicious lesions were identified and resected as part of the sleeve specimen, the pathology department was alerted to specifically examine the relevant area of the sleeve resection specimen.

A retrospective review was performed on prospectively collected pathology data of consecutive laparoscopic bariatric procedures from August 2012 to June 2013 to quantify the presence of GIST in these patients. Statistical comparison of the incidence of GIST with proactive examination of the stomach for GIST during bariatric surgery (our data) to retrospective reports of GIST in bariatric surgery patients in the literature was performed using Fisher's exact test (GraphPad Software, Inc. La Jolla, CA, USA).

Results

Between August 2012 and June 2013, 209 patients underwent weight loss surgery at our institution. No patients complained of symptoms associated with GIST (abdominal pain, nausea, vomiting, palpable mass, or blood in the stool/vomit) in the preoperative period. There were no GISTs definitively identified on pre-operative endoscopy in any patient. Four patients (1.9%) were found to have suspicious lesions at operation which were resected. Two of the four patients required modification of their procedure to achieve oncologically appropriate resection margins. There were no complications post-operatively as a result of these modifications. Five pathology-proven GISTs were found in these 4 patients (1.9%).

One patient had two nodules of 4 mm in diameter located on the fundus of the stomach. A second patient had a tumor of 0.9 cm in diameter though the tumor was fragmented and may have been larger than measured. This tumor was located on the posterior stomach near the gastroesophageal junction. The third patient had a tumor with a diameter of 1.1 cm. This tumor was from the anterior wall of a sleeve gastrectomy specimen. The fourth patient had two tumors of 0.4 cm and 0.3 cm located within a sleeve gastrectomy specimen. Both tumors had involved the muscularis propria of the wall of the stomach. All tumors were spindle cell GIST subtypes, c-KIT (CD117) positive (when tested), low grade mitotic rate, and the margins of the resection for the tumors were negative (Table 1).

	Patient 1	Patient 2	Patient 3	Patient 4
Size	4 mm	0.9 cm	1.1 cm	0.4 cm, 0.3 cm
Location	Fundus	Posterior stomach near GE junction	Anterior wall of sleeve specimen	Sleeve specimen
c-KIT Positive?	N/A	Yes	Yes	Yes
CD-34 Positive?	N/A	Yes	No	Yes
S100 Positive?	N/A	No	No	No

Microscopic Features	While not stained, the microscopic features of this tumor were consistent with a diagnosis of GIST	Consistent with GIST	Consistent with GIST	Consistent with GIST

Table 1: Found GIST Characteristics

Table 1. Shows a summary of the tumor characteristics.The collective data of the four largest reports [9, 14-16] includes 29 patients with incidental GISTs found at the time of bariatric surgery in 5362 patients (0.5%). Comparison of the data from our study to these reported data shows a statistically significant increase in the incidence of GIST detection through active inspection for GIST (p=0.0336) (Table 2).

	GIST	No GIST
Our Study	4	205
Other Studies	29	5333

Table 2: Contingency Table for Fisher Exact Test.

Shows the contingency table we used for our Fisher's exact test.

Discussion

It is well known that GIST most often arises in the stomach [1,4]. There is a reported incidence in the literature of 7-20 new cases per million per year in the general population [1, 5-8]. At most, this amounts to an incidence of 0.002%. The remarkable increase in bariatric procedures in the last decade has allowed over 100,000 people per year to undergo examination of their asymptomatic stomach intra operatively. This phenomenon has led to the realization that the previously reported and generally accepted incidence of GIST is much lower than what is actually seen in the bariatric surgery population. Multiple retrospective reports have reported the incidence of GIST in bariatric surgery patients to be 0.3-0.8% [9, 14-16]. In 2005, Sanchez et al, reported a 0.8% incidence of gastric GIST in 4 out of 517 patients undergoing laparoscopic Roux-en-Y gastric bypass [14]. Yuval et al found an incidence of 0.6% in 5 out of 827 patients undergoing laparoscopic sleeve gastrectomy [15]. The recent study published by Chiappetta et al in 2015 demonstrated GIST in 8 out of 2,603 patients undergoing laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass (incidence 0.31%) [9]. Another recent study by Crouthamel et al in 2015 found 12 GIST out of 1,415 patients undergoing sleeve gastrectomies [16]. It is understandable that the incidence of found GISTs is higher as bariatric surgery allows one a closer look at the stomach to identify suspicious lesions. Our study took this concept a step further by prospectively looking for GIST intraoperatively in patients with morbid obesity. Our data within this study reveal that actively seeking these lesions during bariatric surgery yields a significantly higher incidence of 1.9%. It is uncertain if these data reflect an increased incidence in the entire population or just bariatric surgery patients. While it is fairly well known that minute asymptomatic GISTs are likely more common than previously reported, it is not clear what the conversion rate from clinically non-significant to clinically significant is. Previously, researchers have not actively searched for GISTs in a population as one is capable of doing within the bariatric population. By actively searching for GISTs, we were able to find a higher incidence than previously noted in studies which noted only incidental findings of GIST, usually through postoperative review of pathology reports. All of the tumors in our investigation were considered benign and unstageable by pathology. Whether they would have become clinically significant later on, we could not determine. However, the natural evolution of GISTs implies that at least some of them would have.

While GIST has not been directly found to have an increased risk in obesity, obesity has been implicated as a risk factor for many cancers, as previously stated [11-12]. It is not completely clear why this correlation exists. Some hypothesize that part of this increased incidence is due to a chronic inflammatory state from excess adipose tissue. Increased IL-6, TNF-α, IGF-1, IL-1β, insulin, and bio available estrogen has all been implicated in this process. These cytokine effects have been demonstrated on a local and systemic basis and are thought to be the driving forces of the obesity-cancer link [18]. Regardless of cause, it is clear that the rates of death from many cancers, and specifically stomach cancer in men, are associated with increased body weight and obesity [19]. It has been shown that bariatric surgery reduces cancer mortality by 60% during a 7-year follow-up [20].

Conclusion

It is clear from the data within this study that asymptomatic GISTs are present in bariatric surgery patients at a much higher rate than previously reported. With greater than 100,000 bariatric procedures being performed annually, a great number of lesions can be found and adequately resected before becoming clinically significant if they are actively sought as a matter of standard care during the initial bariatric procedure.

The limitations of our study are the small number of patients and that it is essentially observational, except for the two patients who had modification of their procedure to resect their GIST. Further, our data do not elucidate whether the resected GISTs would ever have become clinically significant, nor is it powered enough to recommend significant changes in the current practices for detection and treatment of GIST. Thus, it would be useful to see future studies with more prospective searches of GIST incidence in the bariatric population to confirm our data.

However, what if not all of these lesions become clinically significant, statistically at least some of them will. When actively sought during bariatric surgery, removal of these lesions often does not require significantly more effort. Proactive action to remove these tumors may prove to help prevent the clinical development of the few GISTs that do occur.

References

1. Tran T, Davilla JA, El-Serag HB (2005) The epidemiology of malignant gastrointestinal stromal tumors: an analysis of 1,458 cases from 1992 to 2000. Am J Gastroenterol 100: 162-168.
2. Min KW and Leabu M (2006) Interstitial Cells of Cajal (ICC) and Gastrointestinal Stromal Tumor (GIST): facts, speculations, and myths. J Cell and Mol Med 10: 995-1013.
3. J F G. van Roggen, M L F van Velthuysen, P Hogendoorn (2001) The histopathological differential diagnosis of gastrointestinal stromal tumors. J Clin Pathol 54: 96-102.
4. Emory TS, Sobin JH, Lukes L, Lee DH, O'Leary TJ (1999) Prognosis of Gastrointestinal Smooth-Muscle (Stromal) Tumors: dependence on anatomic site. Am J Surg Pathol 23: 82-87.
5. Nilson B, Bumming P, Meis-Kindblom JM, Anders Ode´ n, Aydin Dortok, et al (2005) Gastrointestinal stromal tumors: the incidence, prevalence, clinical course, and prognostication in the preimatinib mesylate era-a population based study in western Sweden. Cancer 103: 821.
6. Trygvason G, Gislason HG, Magnusson MK, Jonasson JG (2005) Gastrointestinal stromal tumors in Iceland, 1990-2003: the Icelandic GIST study, a population-based incidence and pathologic risk stratification study. Int J Cancer 117: 289-293.
7. Goettsch WG, Bos SD, Breekveidt-Postma N, Casparie M, Herings RM, et al (2005) Incidence of gastrointestinal stromal tumors is underestimated: results of a nation-wide study. Int J Cancer 41: 2868-2872.
8. Tzen CY, Wang JH, Huang YJ, Wang MN, Lin PC, et al (2007) Incidence of gastrointestinal stromal tumor: a retrospective study based on immunohistochemical and mutational analysis. Dig Dig Sci 52: 792-797.
9. Chiappetta S, Theodoridou S, Stier C, Weiner RA (2015) Incidental finding of GIST during obesity surgery. Obes Surg 25: 579-583.
10. Eisenberg BL and Judson I (2004) Surgery and Imatinib in the Management of GIST: Emerging Approaches to Adjuvant and Neoadjuvant Therapy. Ann Surg Onc 11: 465-475.
11. Wolin KY, Carson K, Colditz GA (2010) Obesity and Cancer. Oncologist 15: 556-565.
12. Renehan AG, Tyson M, Egger M, Heller RF, Zwahlen M (2008) Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet 371: 569-578.
13. Finnell CW, Madan AK, Ternovits CA, Menachery SJ, Tichansky DS (2007) Unexpected pathology during laparoscopic bariatric surgery. Surg Endosc 21: 867-869.
14. Sanchez BR, Morton JM, Curet MJ, Alami RS, Safadi BY (2005) Incidental finding of gastrointestinal stromal tumors (GISTs) during laparoscopic gastric bypass. Obes Surg15: 1384-1388
15. Yuval JB, Khalaileh A, Abu-Gazala M, Shachar Y, Keidar A, et al (2014) The true incidence of Gastric GIST- a study based on morbidly obese patients undergoing sleeve gastrectomy. Obes Surg 24: 2134-2137.
16. Crouthamel MR, Kaufman JA, Biling JP, Biling PS, Landerholm RW (2015) Incidental gastric mesenchymal tumors identified using laparoscopic sleeve gastrectomy. Surg Obes Relat Dis 11: 1025-1028.
17. Roshanravan R, Esfahani MH, Moslemi S, Hosseini SV, Gabash KM (2014) Gastric Gastrointestinal Stromal Tumor (GIST) Incidentally Found After Laparoscopic Sleeve Gastrectomy: A Case Report. Ann Colorectal Res 2: e24855.
18. Iyengar NM, Hudis CA, Dannenberg AJ (2015) Obesity and Cancer: Local and Systemic Mechanisms. Annu Rev Med 66: 297-309.
19. Calle EE, Rodriguez C, Walker-Thurmond K, Thun MJ (2003) Overweight, obesity, and mortality from cancer in a prospectively studied cohort of U.S. adults. N Engl J Med 348: 1625-1638.
20. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, et al (2007) Long-term mortality after gastric bypass surgery. N Eng J Med 357: 753-761.