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Association of Age with the Detection of Gastrointestinal Stromal Tumor During Surgical Repair of Hiatal Hernia

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Introduction

Gastrointestinal Stromal Tumors (GISTs) are mesenchymal neoplasms that arise along the gastrointestinal tract, most frequently at the gastric fundus [1-5]. Pathology series of gastric or Gastroesophageal Junction (GEJ) resections have found the incidence of GIST to range between 7.8% and 17.4% [6-8]. These described lesions are often small in size and benign in nature, however one study reported a 1.9% occurrence of high-risk GIST lesions [8].

The incidence of GIST in patients undergoing Hiatal Hernia (HH) repair for intractable Gastroesophageal Reflux Disease (GERD) or paraesophageal hernia has yet to be thoroughly evaluated. Despite the known occurrence of incidental tumors in the surgical vicinity, there are only a few case reports of GIST associated with HH repair [9-16]. The location of these neoplasms within the stomach wall is not well described. Abraham et al. found that 44% of GIST occur at the outer muscularis propria, 39% at the innermost muscularis, and 17% between the muscle layers [7]. At this time, only one study has identified and briefly described GIST in a subserosal location [17].

Abstract

Background and Objectives: Gastrointestinal Stromal Tumors (GISTs) are neoplasms that arise along the gastrointestinal tract. The incidence of GIST during Hiatal Hernia (HH) repair is not well delineated.

Methods: A retrospective study of 183 HH surgeries was performed at an outpatient surgery center. Several patient data was documented including, but not limited to, age, gender, race, BMI, preoperative diagnosis, surgery type, smoking history, and GIST detection and characteristics.

Results: The 183 HH patients were a mean age of 55.7 years, 70.5% female, and 94.0% Caucasian. The group had an average BMI of 28.9 kg/m², 44.3% had a history of smoking, and 8.2% were current smokers. A majority (71.0%) of the patients underwent surgery for GERD. Age at surgery was strongly associated with gender ($p=0.007$). Patients > 60 years old had a higher incidence (8.9%) of GIST ($p=0.002$). Most incidental GISTs were subserosal (71.4%) and all were located at the proximal stomach.

Conclusions: GIST was detected only among patients ≥ 60 years old with an incidence of 8.9%, indicating a strong association between age and presence of GIST during HH surgery. They were most commonly subserosal and located at the proximal stomach. These tumors should be noted, appreciated, and removed appropriately.

Keywords: Hiatal hernia surgery; Gastrointestinal stromal tumor; Hiatal hernia; Paraesophageal hernia

The objective of this study was to determine the incidence of subserosal GIST discovered during HH repair for both paraesophageal hernia and GERD and to evaluate for patient characteristics and comorbidities associated with such discovery. This study presents a three-year analysis of anti-reflux and paraesophageal hernia procedures performed laparoscopically and robotically by a single surgeon.

Materials and Methods

Study Design and Population

This is a retrospective, single surgeon study of HH surgeries during three consecutive calendar years. The study was reviewed and exempted from approval by the Institutional Review Board at Tacoma General Hospital in Tacoma, Washington. HH surgery was performed primarily for intractable GERD manifestations or paraesophageal hernia. Patient data, pathology, and tumor characteristics were collected by chart review for both outpatient and inpatient precedes.

The following variables were collected for each patient: age, gender, race, Body Mass Index (BMI), pre-operative diagnosis (GERD versus paraesophageal hernia), laparoscopic versus robotic approach, history of cancer, smoker versus non-smoker, and presence of GIST during surgery. Previous medical histories of hypertension, diabetes, anemia, or chest pain were also documented. The anatomical and histological location, size, grade, and mitoses per high powered field were included for incidental GIST. Confirmatory testing was done using C-Kit analysis.

Statistical Analysis

The data were analyzed using SPSS for Windows version 26.0 (IBM SPSS Inc, Chicago, IL). For this study, the surgical patients were grouped based on age (< 60 years or ≥60 years).

Continuous data (e.g. BMI) of the two groups were analyzed using *t* test, and categorical data (e.g. gender) associations were evaluated using χ^2 test. Pearson correlation coefficient (*r*) was used for analysis of associations between age and continuous data. Results are presented as Mean (M) ± Standard Deviation (SD) or as number (n) and percentage (%). Statistical significance for all tests was established at *P*<.05.

Results

A total of 183 surgical patients were evaluated for the presence of GIST during HH surgery. Table 1 summarizes the characteristics of the surgical patients partitioned by their age group (<60 years or ≥60 years). The mean age at surgery was 55.7 years. Most patients were female (70.5%) and Caucasian (94.0%). Overall, the group was overweight, with an average BMI of 28.9 kg/m², 44.3% had a history of smoking, and 8.2% were current smokers. A majority (71.0%) of the patients underwent HH surgery for intractable GERD and 92.9% of the surgeries were performed laparoscopically. Of the concomitant diseases prevailing in the group, 35% had a history of hypertension, 18.6% anemia, 13.1% cancer, and 6.6% diabetes. Among the other clinical symptoms and manifestations of the study group, 30.6% experienced occasional chest pain. Incidental GIST was identified in 3.8% of the patients undergoing HH surgery.

Variable	Entire Group M±SD / n (%)	Age Group < 60 years M±SD / n (%)	Age Group ≥ 60 years M±SD / n (%)	P
Number of Patients (n)	183 (100.0)	104 (56.8)	79 (43.2)	----
Age (years)	55.7 ± 14.4	45.9 ± 10.6	68.6 ± 6.0	----
Gender				0.007*
Female	129 (70.5)	65 (62.5)	64 (81.0)	
Male	54 (29.5)	39 (37.5)	15 (19.0)	
Ethnicity				0.875
Caucasian	172 (94.0)	98 (94.2)	74 (93.7)	
Other ^a	11 (6.0)	6 (5.8)	5 (6.3)	
Body Mass Index (Kg/m ²)	28.9 ± 5.0	28.8 ± 5.0	29.1 ± 5.0	0.751
Tobacco Use				
History	81 (44.3)	41 (39.4)	40 (50.6)	0.130
Current	15 (8.2)	10 (9.6)	5 (6.3)	0.422
Indication for HH Surgery				0.001*
Gastroesophageal Reflux Disorder	130 (71.0)	91 (87.5)	39 (49.4)	
Paraesophageal	53 (29.0)	13 (12.5)	40 (50.6)	
Surgery Type				0.349
Laparoscopic	170 (92.9)	95 (91.3)	75 (94.9)	
Robotic	13 (7.1)	9 (8.7)	4 (5.1)	
Concomitant Diseases				
Diabetes	12 (6.6)	7 (6.7)	5 (6.3)	0.913
Hypertension	64 (35.0)	25 (24.0)	39 (49.4)	0.001*
Cancer	24 (13.1)	11 (10.6)	13 (16.5)	0.243
Anemia	34 (18.6)	11 (10.6)	23 (29.1)	0.001*
Presence of				
Chest Pain	56 (30.6)	31 (29.8)	25 (31.6)	0.789
Gastrointestinal Stromal Tumor (GIST)	7 (3.8)	0 (0.0)	7 (8.9)	0.002*

Note: M=Mean; SD=Standard Deviation.

^a(Other includes African American, Asian and Hispanic).

acteristics of the surgical patients partitioned by their age group (<60 years or ≥60 years). The mean age at surgery was 55.7 years. Most patients were female (70.5%) and Caucasian (94.0%). Overall, the group was overweight, with an average BMI of 28.9 kg/m², 44.3% had a history of smoking, and 8.2% were current smokers. A majority (71.0%) of the patients underwent HH surgery for intractable GERD and 92.9% of the surgeries were performed laparoscopically. Of the concomitant diseases prevailing in the group, 35% had a history of hypertension, 18.6% anemia, 13.1% cancer, and 6.6% diabetes. Among the other clinical symptoms and manifestations of the study group, 30.6% experienced occasional chest pain. Incidental GIST was identified in 3.8% of the patients undergoing HH surgery.

In this study, a larger proportion (56.8%) of the patients were under the age of 60. Age at which surgery was performed was strongly associated with gender (*p*=0.007), with females making up 81% of the older age group. The prevailing indication for HH surgery among the younger age group (< 60 years) was GERD (87.5%, *p*=0.001), whereas the older age group (≥ 60 years) showed a similar proportion between the two indications, with 49.4% seeking surgical management for GERD and 50.6% for paraesophageal hernia. Older patients had a higher prevalence of hypertension (*p*=0.001) and anemia (*p*=0.001). The presence of GIST was strongly associated with older age (*p*=0.002), with an incidence of 8.9% among older patients and 0% among younger patients. A majority (85.7%) of the GISTs were discovered in female patients.

C-kit mutation analysis accurately confirmed the 7 cases of GIST encountered. Patients with GIST had a history of hypertension (100%) and chest pain (57.1%); none of the patients had a history of diabetes or cancer. All encountered GISTs were identified at the proximal stomach, specifically the fundus (71.4%) or GEJ (28.6%). A majority of the tumors (71.4%) were declared subserosal in location on pathology review. Size of tumors were between 0.3 and 1.0 cm and removed by either wedge (71.4%) or excision (28.6%) resection. Four of the seven GISTs (57.1%) were found in patients undergoing HH surgery for GERD, whereas the remaining GISTs were found in those with a paraesophageal hernia (Table 2).

Table S2: Incidental GIST: Patient and Tumor Characteristics.

Age	Gender	Indication for Surgery	Pathological Location	Anatomical Location	Size (cm)
76	Male	GERD	Subserosal	Fundus	0.4
63	Female	GERD	Subserosal	Fundus	0.6
72	Female	Paraesophageal Hernia	Subserosal	GEJ	0.8
75	Female	Paraesophageal Hernia	Muscularis Propria	Fundus	0.4
63	Female	GERD	Subserosal	Fundus	0.3
62	Female	Paraesophageal Hernia	Submucosal	Fundus	1.0
80	Female	GERD	Subserosal	GEJ	0.6

Discussion

Aside from a few case reports of large GIST associated with HH, the incidence of GIST discovered during HH repair has not been previously reported [9-16]. The purpose of our study was to evaluate the incidence of GIST during HH surgical repair, identify associated patient demographics and comorbidities, and highlight common anatomical and pathological locations of the tumors. Prior reports have demonstrated malignant transformation of GIST, emphasizing the importance of the identify-

ing and removing these tumors while in the surgical vicinity of high-risk patients [11,12].

The overall incidence of GIST in our study was 3.8%, which is higher than previous studies examining the incidence of GIST during Roux-en-Y gastric bypass (0.8%) and sleeve gastrectomy (0.5%) [18,19]. Abraham et al. conducted a study similar to ours on patients who underwent esophagectomy for esophageal or GEJ carcinoma and found an incidence rate of 10% [7]. Our results pertaining to HH surgery add to the previously established rates of GIST for surgeries in a similar anatomical region. When stratifying our patients with GIST into two age groups, we discovered a strong correlation between older age and incidental GIST during HH surgery. While the majority of patients were less than 60 years old (56.8%), there were no identified GIST in this age group. A systematic review of the epidemiology of GIST concluded a median age of diagnosis in the mid-60's, with several studies confirming an increased risk with increased age [20,22]. Our findings further support and strengthen the conclusion of age being a dominant predictor for GIST discovery during surgery.

It has been well established that a majority of these tumors, whether incidental or symptomatic, are found in the stomach [1-5]. The anatomical location within the stomach, as well as pathological location, are less well-delineated. Interestingly, all GISTs in our study were found and biopsied around the proximal stomach, specifically at the fundus or GEJ. These findings are unique to our study, as previous investigations have found GIST in a variety of locations within the stomach [1]. On pathological review, a majority of tumors resected were identified as subserosal. The subserosal occurrence of GIST in this study is concerning due to the possibility of the tumor being a metastatic lesion. This metastatic potential was the driving force for biopsy on each of the discovered lesions. The extensive testing which accompanies these surgeries, including endoscopy, CT scan, and barium swallow, is likely to uncover a GIST within the submucosal layer of the stomach [23,24]. In contrast, extrinsic or subserosal tumors are difficult to identify with these testing modalities, thus highlighting the importance of identification during surgery itself. Lastly and not surprisingly, these incidental and asymptomatic GISTs were small in size, contrary to the larger size of symptomatic GISTs found in other cases [9-16]. Similar studies evaluating incidental GIST found sizes ranging from 0.2 to 3.7 cm [19,25]. Although the GISTs were small in size, we do not believe this downplays the importance of their discovery and removal as malignant GISTs have been discovered in the surgical vicinity [11,12].

Our study highlights important findings in regard to the incidence of GIST encountered during HH surgery, common anatomical and pathological locations around the stomach, as well as the association of age and tumor presence. It is best that surgeons are aware of this entity and recognize that GISTs are small, not intramural, and are unlikely to be diagnosed preoperatively. Incidental tumors found during HH surgery should be suspicious for malignancy and removed. The resection of these tumors, even if benign, is a safe and reasonable plan of action when encountered during laparoscopic or robotic HH surgery [6,26]. Although our results are significant and relevant to the surgical care of HH patients, especially those age 60 years or older, there are some limitations to our study. The retrospective nature of this study sets limitations to the data collected and analyzed. It would be beneficial to further investigate the incidence of GIST in HH patients in a prospective nature. Secondly,

the patients analyzed in this study are from a single, private practice experience in a suburban setting, therefore there is a lack of diversity among patient demographics, including gender and race. With this in mind, there are limitations to the generalizability of our results. Nevertheless, our study is unique, introduces an awareness of GIST during HH surgery, and warrants further discussion.

Author Statements

Disclosures

Dr. Hallie Wwst, Dr. Kyler Perry, Dr. Julia Wright, Dr. Anil Aranha, and Dr. Robert Wright have no conflicts of interest or financial ties to disclose.

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