

A COMPARATIVE ANALYSIS OF THE IMMEDIATE POST-OPERATIVE COMPLICATIONS OCCURRING AFTER SUBTOTAL GASTRECTOMY IN PATIENTS WITH GASTRIC CARCINOMA

Samantha Mc Kenzie Stancu¹, Bogdan Popescu²

¹ Carol Davila University of Medicine and Pharmacy, Bucharest, ROMANIA

² Department of General Surgery, Bucharest Clinical Emergency Hospital, Bucharest, ROMANIA

ABSTRACT

Aims: The aims of this study were to scrutinize the immediate post-operative complications encountered after different subtotal gastrectomy procedures and to identify the safest surgical variant.

Methods: In this retrospective, observational study data of 54 patients, of whom 32 were male and 22 were female, with a mean age of 65.7 years diagnosed with gastric carcinoma underwent a variant of subtotal gastrectomy in the Surgery Department of the Bucharest Clinical Emergency Hospital between January 2010 and December 2012 were recorded. The categorical statistical data was obtained with Chi-square method using GraphPad Prism and statistical significance was set at a p-value <0.05.

Results: A total of 73 immediate post-operative complications were encountered in 23 (41.8%) patients classified into local in 14 (19.2%) patients and general in 59 (80.8%) patients. The most common complication classified as local was leakage found in 5 (6.9%) patients, while the most frequent ones in general complications were secondary anemia presented in 17 (23.3%) patients and pulmonary compromise: pleural effusion in 3 (4.1%) patients. Ten associated surgical procedures were necessary, the most common being omentectomy (30%). Re-operation was deemed imperative in 5 (9.1%) cases, 4 (80%) of which were after Billroth I and 1 (20%) case was subsequent to Roux-en-Y Side-End Esophagojejunostomy. Three (5.6%) deaths were reported, 2 (66.7%) of which occurred after Roux-en-Y Side-End Esophagojejunostomy and 1 (33.3%) after the Billroth I variant.

Conclusion: Billroth I yielded the highest number of complications, both local and general, compared to Hofmeister-Finsterer which generated the lowest number. The same pattern was noted with respect to the length of hospital stay. The longest operative time was recorded in Hofmeister-Finsterer and the shortest in Billroth I. A statistically significant chi-square analysis between the type of subtotal gastrectomy procedure and anastomotic leakage was obtained.

Keywords: Gastrectomy, gastric cancer, post-operative complications

INTRODUCTION

Despite of the steady decrease in the incidence and mortality rate of gastric carcinoma, it is still the fourth most common cancer worldwide (1). Being the second most lethal cancer in the world, preceded only by lung cancer, its prognosis is poor (2). The five-year survival rate in patients with advanced gastric cancer remains 10-15%. In 2012, gastric carcinoma had an estimated incidence of 139.000 new cases and 107.000 deaths in Europe alone (3). Gastric cancer is endemic in Japan, exhibiting a 20-fold incidence comparing with the United

States. In the 1960's, this outstanding epidemiological variance gave rise to a mass screening program since the 1960s, with the subsequent publication of the international guidelines for surgical resection of gastric carcinoma (4).

Subtotal gastrectomy (SG), also called distal gastrectomy, is defined as the surgical removal of two-thirds to four-fifths of the stomach (5). It entails diverse procedures with numerous complications. The four main procedures are Billroth I gastroduodenostomy (B-I), Billroth II gastrojejunostomy (B-II) with the Hofmeister-

ter-Finsterer (H-F) and Richter-Polya subtypes, Roux-en-Y Gastrojejunostomy (R-Y) and double tract jejunal interposition with no clear benefit of one technique over the other (6).

Ever since the first successful pylorotomy was performed by Billroth in 1881, surgical resection still remains the only treatment offering hope for cure (7). SG is the treatment choice in an attempt at curative resection of tumors located in the middle and inferior two-thirds of the stomach (8). The most important surgical prognostic factor for both early and advanced gastric cancer is adequate lymph node clearance. More precisely, lymphatic clearance beyond the perigastric stations is of paramount importance for offering patients a chance for cure. Lymphadenectomy is also the most technically challenging part of any gastrectomy procedure (9).

Consensus concerning the best method of reconstruction following resection is still lacking, which led us to define the parameters and aims of this study as identifying the safest variant (6). In order to accomplish this task, a thorough analysis of the immediate post-operative complications was pursued.

Therefore, the objectives of this study were to analyze the immediate post-operative complications after SG occurring in patients diagnosed with gastric carcinoma and subsequently to identify the safest variant.

MATERIAL AND METHODS

Using a prospectively collected database, we performed a retrospective analysis of all patients undergoing SG from January 1st 2010 to December 31st 2012. The study design was retrospective observational in nature and consisted of 54 consecutive patients with gastric carcinoma who underwent SG at the University Emergency Hospital in Bucharest. The variables recorded and analyzed were the variants of SG performed and the immediate post-operative complications encountered. Immediate post-operative complications were considered as those occurring in the hospital until 30 days after surgery.

The including criteria were histopathological diagnosis of gastric carcinoma and having underwent a variant of SG between Jan 1st, 2010 and Dec 31st, 2012 while patients with non-epithelial cell derived gastric tumors were excluded. Patient data was retrieved from patient charts and hospital's computer software "Hippocrate".

Patient data was collected and organized into a Microsoft Excel 2010 database. Descriptive statistical analysis was applied to the study sample using the GraphPad Prism 6 program. Descriptive statistical parameters such as numbers, percentages mean \pm standard deviation, median (minimum-maximum) were used to analyze the post-operative follow-up; namely length of stay (LOS), number of post-operative days and time until resumption of oral alimentation and intestinal transit. Two different statistical tests were applied to patient age: Student t-test and standard deviation which were used to reveal whether a statistically significant difference existed between the ages of the participants based on gender. P-values were calculated using the Chi-square test for categorical data and statistical significance was set at a p-value < 0.05 .

In order to identify the safest SG procedure in addition to analyzing the complications that occurred, chi-square analysis between the type of SG procedure and a variety of factors such as tumor staging, the type of lymphadenectomy, type of anastomosis performed (manual or mechanical), associated surgical procedures performed as well as average operative time was reported statistically.

RESULTS

During the study period, 54 patients with gastric carcinoma underwent SG. Of these, 32 (60%) were male and 22 (40%) were female. The age range was between 32-86 years, with an average age of 65.7 ± 11.64 years in both genders. Mean age was 63.9 years for males and 68.5 years for females. However, a statistically insignificant result was obtained from the Student t-test ($p=1.43$).

Three types of SG procedures were analyzed in this study: 31 cases of B-I, 14 cases of R-Y and 9 cases of H-F which is a subtype of B-II.

Regarding staging, advanced disease was observed, shown by 42 (80%) of the patients having a stage III or IV tumor. Out of which, stage IIIC was the most prevalent with 16 (29.6%) cases. The distribution of advanced disease (stage III and IV tumor) among SG procedures is as follows: 24 (77.1%) in B-I, 11 (78.6%) in R-Y and 9 (100%) in H-F.

Overall, 40 (74.1%) of the patients underwent D1 lymphadenectomy and 14 (25.9%) D2 lymphadenectomy. A preponderance of D1 lymphadenectomies were per-

formed with the following distribution among procedures: 27 (87.1%) in B-I, 6 (42.9%) in R-Y and 8 (77.8%) in H-F.

With respect to the type of anastomosis performed, mechanical anastomosis was employed in all SG procedures studied except H-F. Mechanical anastomosis was carried out in a total of 13 (24.1%) patients, with the following breakdown: 8 (61.5%) cases in B-I and 5 (38.5%) cases in R-Y.

A total of 10 associated procedures were performed, the most common being omentectomy (30%). Splenectomy was the only combined procedure that was performed in all 3 types of the SG procedures studied. The B-I variant was associated with the highest number of combined procedures: 3 procedures compared to one each in R-Y and H-F.

The average operative time ranged from 156 to 231 minutes in all variants. The time range of each procedure was as follows: 150-275 minutes in B-I, 110-360 minutes in R-Y and 60-360 minutes in H-F. The average operative times with standard deviation obtained were the following: 231 ± 75.49 minutes in B-I, 198 ± 72.29 minutes in R-Y and 156 ± 69.52 minutes in H-F. The duration of the H-F procedure was 75 minutes longer than B-I and 33 minutes longer than that of R-Y.

A total of 73 complications occurred in 23 (41.8%) patients. Complications were dichotomized into local in 14 (19.2%) patients and general in 59 (80.8%) patients. Local and general complications were further subclassified into local, general and life-threatening, as well as pulmonary compromise.

The local complications encountered were: leakage, abdominal wall abscess, seroma, ascites, urinary tract infection (UTI) and surgical site infection (SSI). Leakage was the most frequent local complication, encountered in 5 cases, accounting for 7% of all complications (Table 1).

Table 1: Immediate Local Post-Operative Complications Encountered According to SG Procedure

SG variant	Leakage	Abdominal wall abscess	Seroma	Ascites	Urinary tract infection	SSI
Billroth I	-	1	-	1	-	2
Roux-en-Y gastrojejunostomy	5	2	-	-	1	1
Hofmeister-Finsterer	-	-	1	-	-	-
Total	5	3	1	1	1	3
Percentage	6.9%	4.1%	1.4%	1.4%	1.4%	4.1%
p-value	0.0003	0.23	0.07	0.68	0.23	0.72

The general and life-threatening complications recorded were secondary anemia, febrile syndrome, peritonitis, pulmonary thromboembolism (PTE), multisystem organ failure (MSOF) and cardiac arrest. Secondary anemia was not only the most common general complication with 17 (23.3%) cases, but it also proved to be the most frequent complication encountered in the study (Table 2).

Table 2: General and Life-Threatening Complications According to SG Procedure

SG variant	Febrile syndrome	Secondary anemia	Cardiac arrest	MSOF	Peritonitis	Pulmonary embolism
Billroth I	8	8	1	1	1	-
Roux-en-Y gastrojejunostomy	6	7	1	-	-	1
Hofmeister-Finsterer	2	2	-	-	-	-
Total	16	17	2	1	1	-
Percentage	21.9%	23.3%	2.7%	1.4%	1.4%	1.4%
p-value	0.44	0.21	0.66	0.68	0.68	0.23

In terms of pulmonary compromise, the recorded complications were pneumonia and pleural effusion which was the most prevalent form of pulmonary compromise that occurred in 3 (4.1%) cases (Table 3).

Table 3: Pulmonary Compromise According to SG Procedure

SG variant	Pleural effusion	Pneumonia
Billroth I	2	1
Roux-en-Y gastrojejunostomy	2	1
Hofmeister-Finsterer	-	-
Total	4	2
Percentage	5.5%	2.7%
p-value	0.42	0.66

Re-operations were deemed imperative in 5 (9.1%) cases, 4 (80%) after B-I and 1 (20%) after R-Y, the reasons being 3 cases of leakage, and 1 case each of hemoperitoneum and evisceration. Hemoperitoneum was the result of an acute necrotic pancreatic process that eroded the middle colic artery. The course of treatment was lavage of the peritoneal cavity upon exploratory laparotomy on the 9th post-operative day.

Three (5.6%) deaths were recorded during the period studied, 2 (66.7%) after R-Y and 1 (33.3%) after B-I. The causes of death were PTE, diffuse peritonitis secondary to leakage and anesthetic complications in a patient with atrial fibrillation. Of these 3 patients, all had advanced disease (stage III and IV tumors) and were elderly: aged 60-86 years. Furthermore, 2 deaths occurred after

manual anastomosis and 1 after mechanical. 2 (66.7%) deaths occurred in patients who underwent D2 lymphadenectomy.

Post-operative follow-up was evaluated using length of stay (LOS), number of post-operative days and the number of days until resumption of oral alimentation and intestinal transit. The results were expressed in median and range, respectively, as presented in Table 4.

Table 4: Post-Operative Follow-Up

SG variants	Length of stay (LOS) (day) (median, min-max)	post-operative days (median, min- max)	Resumption of oral alimentation (day) (median, min-max)	Resumption of intestinal transit (day) (median, min-max)
Billroth I	16 (10-37)	11 (6-27)	5 (2-10)	3 (2-11)
Roux-en-Y gastrojejunostomy	16 (12-32)	11 (8-25)	4 (0-13)	3 (0-11)
Hofmeister- Finsterer	16 (13-19)	11 (7-13)	4 (2-9)	3 (2-5)

Complications were assigned to 1 of 5 classes after applying the Clavien-Dindo Classification of Surgical Complications. Sixty percent of the complications encountered after Hofmeister-Finsterer were local complications (class 1), and the remaining 40% were class 2. R-Y and B-I had the highest number of class 2 complications, which were presented in 6 (50%) patients and in 8 (47.1%) patients, respectively. Moreover, R-Y had the highest number of class 4 and class 5 (death) complications as may be observed in Table 5.

Table 5: Clavien-Dindo Classification of Complications According to SG Variant

SG variant	Clavien-Dingo Classification of Complications				
	I	II	III	IV	V
Billroth I	3	8	4	1	1
Roux-en-Y gastrojejunostomy	1	6	1	2	2
Hofmeister-Finsterer	6	4	-	-	-
Total	10	18	5	3	3
Percentage	25.6%	46.1%	12.8%	7.7%	7.7%

DISCUSSION

Gastric cancer is the second most lethal cancer worldwide, rendering it a major public health issue (2). Distal tumors are the most numerous in terms of location and necessitate resection by means of a SG (8). SG is a complex procedure with abundant potential complications. Therefore, an improved surgical technique, even of pre-existing procedures, is of paramount

importance due to the fact that surgeon's experience is the most important non-TNM prognostic factor in gastric cancer (5).

Currently, consensus concerning the best method of reconstruction following resection is still lacking (6). There is, however, a clear preference according to geographic location. The Billroth procedures are preferred methods of reconstruction in Asia, whereas R-Y is more opted for in Europe and North America (10). In our study, the preference of technique is not consistent with the trend in Europe: out of 54 patients, 31 (57.4%) of them underwent B-I and only 14 (25.3%) of them had a R-Y reconstruction.

Complications are especially prone to occur after gastrectomy due to the necessity of a durable anastomosis which is technically challenging to perform due to the frailty of cancerous gastric tissue and the subsequent high fluid flow through the afferent jejunal loop in the case of R-Y and B-II (11). Lymphadenectomy preceded by lymph node dissection still remain the most challenging parts of gastrectomy operations (9).

In this study we examined the immediate post-operative complications that occurred after different SG procedures. The fact that general complications accounted for 80% of all complications in our study demonstrated the crucial necessity that an improved technique is urgently needed. Regarding demographics, our findings of male preponderance and in terms of the age distribution being confined to the 6th decade and above, proved to be consistent with literature (1).

Despite the "Roux-en-Y stasis syndrome" being described as the most common complication occurring after R-Y, our study identified leakage as a complication exclusive to R-Y at our facility (11). Furthermore, this variant was associated with far more serious complications than stasis syndrome such as PTE and cardiac arrest which resulted in the highest death rates among the procedures analyzed. It also yielded the longest hospital stay.

Attempts to chi-square analysis between mortality and factors such as the type of SG procedure, type of lymphadenectomy and type of anastomosis resulted insignificant.

The B-I procedure cumulated the highest number of complications, both local and general, needed one re-operation secondary to leakage and resulted in one death. Regarding the post-operative follow-up, the lon-

gest interval until resumption of oral alimentation and resumption of intestinal transit was noticed.

Leakage is known to be the most common complication occurring after gastrectomy operations. Pedrazzani et al. (12) performed a prospective study on the post-operative complications that occurred in a cohort of 310 patients that underwent B-II SG. Only 2% of the study sample developed post-operative leakage. This data is concordant with our finding: a complete absence of leakage after B-II. A statistically significant chi-square analysis between the type of SG procedure and leakage was obtained ($p=0.0003$) (Table 1).

However, the chi-square analysis between SG procedure and other local complications such as abdominal wall abscess, seroma, ascites, UTI and SSI were statistically insignificant (Table 1).

Furthermore, the statistical analysis failed to reveal any significant chi-square analysis between the type of SG procedure and general complications: febrile syndrome, secondary anemia, peritonitis, cardiac arrest, MSOF and PTE (Table 2). This was also the case with pulmonary compromise: pleural effusion ($p=0.42$) and pneumonia ($p=0.66$) (Table 3).

Although 8 (88.9%) of H-F tumors being stage III and IV, this procedure still had the best post-operative outcome (lack of negative outcomes and shortest hospital stay), in comparison with the B-I procedure in which only 45.1% of patients had advanced disease, but a dramatically detrimental outcome (4 re-operations, 1 death).

Another interesting point that arose throughout the process of analyzing the H-F technique was the longest operative time even with the simplest associated procedures performed (i.e. cholecystectomy), which could be explained by greater technical complexity.

The limitations of this study were its retrospective nature, a limited patient number and an unequal distribution among SG procedures. Future research could thrive to conduct a prospective multicenter study with a larger patient number and an equal distribution among SG procedures with a perfected, multivariate statistical analysis. The culmination of such a concerted, broad-based study would be to establish an improved surgical technique or the nomination of a new "golden standard" procedure. This concerted effort would lay foundation for improving the efficacy of the health care system as

well as increasing the post-operative survival of patients as individuals with gastric cancer. Achieving consistency in the surgical approach of SG will attenuate economic burden on hospitals and go a long way towards improving the life expectancy of gastric cancer patients.

Consequently, we identified the H-F technique as the safest SG procedure based on the lack of negative outcomes, having only class 1 in 6 (60%) patients and class 2 in 4 (40%) patients Clavien-Dindo complications and having the shortest hospital stay with the only disadvantage of its long operative time. The statistically significant chi-square analysis between the type of SG procedure and leakage found in our study demonstrated consistency with the literature (12). Further studies with larger group of population would contribute to determine safest SG procedure.

Ethics Committee Approval: This study was approved by Bucharest Emergency Hospital Research Ethics Committee.

Informed Consent: Written informed consent was obtained from the participants of this study.

Conflict of Interest: The authors declared no conflict of interest.

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