

Complication of Gastric Cancer Surgery: A Single Centre Experience

MARTA GOGLIA^{1,2,3}, SARA PEPE¹, MARCO PACE¹, LUDOVICA FATTORI¹,
ANDREA MINERVINI¹, DIEGO GIULITTI¹, DARIO SIRIMARCO¹, GAETANO GALLO⁴,
GIUSEPPE NIGRI¹, GIOVANNI RAMACCIATO¹ and PAOLO AURELLO⁴

¹Department of Medical and Surgical Sciences and Translational Medicine,
St. Andrea University Hospital, General Surgery Units, Sapienza University of Rome, Rome, Italy;

²Institute for Research Against Digestive Cancer (IRCAD), Strasbourg, France;

³IHU, Institute of Image-Guided Surgery, Strasbourg University Hospital, FMTS,
University of Strasbourg, Strasbourg, France;

⁴General Surgery Unit, Department of Surgery, Sapienza University of Rome, Rome, Italy

Abstract. *Background/Aim:* Gastric cancer surgery is still characterised by high morbidity and mortality. However, in 2018 an online platform, GASTRODATA has been proposed in Europe to standardize the recording of gastric surgery complications. The aim of the study was to present a single center experience regarding incidence and grading of acute postoperative complications in a population of patients treated surgically for gastric cancer on the basis of the gastrodata online platform. *Patients and Methods:* The present study was a single center, observational, retrospective trial held in the General Surgery Unit of the Sant'Andrea Hospital of Rome. The study included 181 consecutive patients who underwent gastric surgical resection for cancer from May 2004 to December 2020 with curative R0 purpose. *Results:* Thirty-three percent of patients reported at least one complication, while seventeen percent of the whole population reported a complication classified as at least grade 3 on the Clavien Dindo Classification. The most frequent complications were disorders of the respiratory system (13.3%), followed by bleeding (7.6%) and wound infections (6.2%). Deaths accounted for 3.7% of the population. *Conclusion:* A list of

defined complications of gastrectomy, if systematically adopted in the Literature, could lead to a reduction in the wide variation of proposals for treatment and assessment. Objectively evaluating the impact of complications on outcomes can lead to quality improvement project proposals.

Gastric cancer incidence and mortality decreased substantially over the last decades in most countries worldwide (1). However, it still represents a common malignant cancer with high mortality. According to the latest published global cancer data on (2), it represents the fifth diagnosed cancer (3) and the second cause of death worldwide (4).

Indeed, the number of newly diagnosed gastric cancer patients in 2019 was 1,270,000, which leaves an unsolved health problem that affects people all over the world. Furthermore, the prognosis of this pathology is still critical today. In fact, gastric cancer is characterized, especially in the Western countries, by a delay in diagnosis and therefore, the possibility of performing surgical endoscopy in T1 diagnosed cases and to treat this pathology with minimally invasive techniques, is rare. In addition, surgery is unfortunately characterized by frequent and severe postoperative complications. In 2015 the European chapter of the International Gastric Cancer Association (EGCA) proposed a project entitled "Complications after gastrectomy for cancer. European perspective" with the aim of collecting a list of perioperative complications associated with gastrectomy for cancer (5). Subsequently in 2018, an online platform for collecting clinical, oncological, and surgical data was launched with the name of www.gastrodata.org and it provided an excellent tool for the recording of complications specific for gastric surgery (6). The aim of the study was to present a single center experience regarding incidence and grading of acute postoperative complications

Correspondence to: Marco Pace, MD, Sapienza University of Rome, Department of Medical and Surgical Sciences and Translational Medicine, via di Grottarossa 1035, 00189 Rome, Italy. Tel: +34 55874837, email: marco.pace@uniroma1.it

Key Words: Gastric surgery, surgical complications, stomach neoplasms, GASTRODATA registry.



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Table I. *Clavien Dindo surgical complication classification.*

Grades	Definition
Grade 1	Any deviation from the normal post-operative course without the need of pharmacological treatment or surgical, endoscopic, or radiological intervention. Antiemetics, antipyretics, analgesics, diuretics, electrolytes, and physiotherapy are allowed
Grade 2	Requiring pharmacological treatment with drugs other than the ones allowed in grade 1
Grade 3	Requiring surgical, endoscopic, or radiological intervention with grade 3A under local anesthesia and grade 3B under general anesthesia
Grade 4	Life-threatening complication requiring intensive care management with grade 4A with single organ dysfunction and grade 4B multi-organ dysfunction
Grade 5	Patient demise

in a population of patients surgically treated for gastric cancer on the basis of gastrodata online platform.

Patients and Methods

Study design. This study was a single center, observational, retrospective trial held in the General Surgery Unit of the Sant’Andrea Hospital of Rome. The study included 181 consecutive patients who underwent gastric surgical resection for cancer from May 2004 to December 2020 with curative R0 purpose. All patients had a diagnosis of adenocarcinoma of the stomach or of the esophago-gastric junction type III Siewert histologically documented and staged by total body CT scan.

Gastrodata online platform. The web-based platform www.gastrodata.org was developed by a specialized software form, able of ensuring the anonymity of patient data. The gastrodata web platform was already approved for data harvesting and collection in 13 European countries; only the data of patients having had a post-operative complication after gastrectomy are collected in the gastrodata platform.

Operative technique. The whole population underwent elective surgical treatment at the Sant’Andrea Hospital of Rome by an experienced general surgeon. All patients with stage II disease or higher were treated with adjuvant therapy, as indicated by the guidelines proposed by the Journal of National Comprehensive Cancer Network (JNCCN) according to their progressive update (7). Patients underwent partial or total gastrectomy, possibly associated with partial distal esophagectomy, based on tumor characteristics such as extension, grading, Lauren classification, and localization (8). Routine lymphadenectomy was modified D2, D1 in case of low performance status.

Resection of other organs, such as the spleen, distal pancreas, or colon, was performed only in the case of tumor invasion of these organs. All standard clinical-pathological data, such as sex, age, type of surgery, tumor location, were collected following the guidelines of the Japanese Gastric Cancer Association (9), histological type, depth of invasion, number of lymph nodes removed, number of metastatic lymph nodes, LNR, grading, LVI, PNI and stage, following the TNM system described by the AJCC of the VIII edition of 2017 (10). The study considers peri-operative surgical complication arising within 30 days from the operation. Complications were classified through the Clavien Dindo classification which stratifies the postoperative course into 5

categories (Table I) (11). On the basis of the Clavien-Dindo classification, the Comprehensive Complication Index (CCI) was subsequently calculated as the weighted sum of the different degrees of complications, with a final score between 0 (no complication) and 100 (death due to a complication) (12). Patients under 18 years old or having surgery for non-oncological reasons were excluded from the study. All patients gave their written informed consent for data analysis (in some cases the patients have been contacted telephonically waiting for the next control visit and written consent form) and procedure. The primary endpoints were incidence and frequency of surgical complication in the early post-operative period. Data were collected and preserved in the General Surgery Unit of Sant’Andrea Hospital. This study was conducted according to STROBE checklist and guidelines (13).

Statistical analysis. Descriptive statistics were performed. Categorical variables were analyzed and reported as counts and percentages, and as the mean±SD (range) for continuous normally distributed variables, whereas ordinal categorical variables and continuous nonnormally distributed variables were reported as median [interquartile range (IQR)].

Results

Patient characteristics. A total of 181 patients who underwent gastric resection for cancer were enrolled in the present study. Among the entire population, there was a slight predominance of males who were 100 out of total (55.3%) while the females were 81 out of 181 (44.8%). Mean age of the population was 69.93±10.71 (range=34-88).

Characteristics of gastric cancer. The majority of cancers were localized in the lower third of the stomach, being present in 85 patients out of 181 (47%). On the contrary, the tumor was localized in the medium third in 57 cases out of 181 (31.5%), while in 36 cases out of total population it was found in the upper third of the stomach (19.9%) (Table II). According to Lauren’s classification, intestinal cancer was the most frequent (64.6%), followed by the diffuse type (26.5%) and the mixed/undifferentiated type (7.2%); 1.7% of patients, on the other hand, presented adenocarcinoma of the gastroesophageal junction, classified as Siewert III (Table II). The mean dimension was of 4.8 cm±2.42 (range=1-8.5

Table II. Patient surgical characteristics.

	N (%)
Age (mean±σ)	69.93±10.71
Sex (F/M)	81/100
Localization of the tumor	
Superior third	36 (19.9)
Middle third	57 (31.5)
Inferior third	85 (47.0)
Gastric stump/anastomosis	3 (1.7)
Type of surgery	
Total gastrectomy	89 (49.2)
Subtotal gastrectomy	72 (39.8)
Distal gastrectomy	16 (8.8)
Degastrogastrectomy	4 (2.2)
Lauren classification	
Intestinal	117 (64.6)
Diffuse	48 (26.5)
Mixed/undifferentiated	13 (7.2)
Gastro-esophageal junction	3 (1.7)

F: Female; M: male; N: number.

cm). A total gastrectomy was performed in 89 patients out of 181 (49.2%), a sub-total gastrectomy was chosen in 72 patients out of total (39.8%), while a distal gastrectomy was performed in 16 patients out of 181 (8.8%) and a de-gastro gastrectomy was performed in 4 patients out of total (2.2%) (Table II). In addition, 48 of 181 patients (26.5%) underwent resection of adjacent organs, in most cases by performing a distal splenopancreatectomy, due to the infiltrative processes involving the contiguous organs.

Postoperative morbidity and mortality. A total of 122 patients (67.4%) did not report any surgical complication at 30 days from the procedure, while 59 patients out of 181 (32.6%) reported at least one complication. Indeed, 45 patients (24.9%) reported just one complication, whereas the rest had more than one surgery-related sequelae (14 patients). Thirty-one patients out of total (17.1%) reported a complication classified as 3 or more in the Clavien Dindo (CD) classification as reported in Table III. As well as, among the 59 patients who experienced at least one post-operative complications, the mean Comprehensive Complication Index resulted to be 47.7, with a median value of 40. This score indeed enables the calculation of the overall morbidity of a patient after any surgical intervention based on the complication grading by the Clavien-Dindo Classification. The CCI reflects the gravity of this overall complication burden on the patient on a scale from 0 (no complication) to 100 (death).

The most frequent postoperative complication, comprehending any grade of CD classification, belongs to the 13.3% of total population (24 patients out of 181) and involves, also in this case, disorders of the respiratory system

Table III. Postoperative complications.

CD of 59 patients* (32.6%)	N (%)	Mean	Median
Overall complications	84	–	–
Grade 1	4 (2.2)	–	–
Grade 2	40 (22.1)	–	–
Grade 3a	12 (6.6)	–	–
Grade 3b	12 (6.6)	–	–
Grade 4a	9 (5.0)	–	–
Grade 4b	0 (0)	–	–
Grade 5	7 (3.9)	–	–
CCI		47.68	40

*Fifty-nine patients (32.6%) experienced at least one complication, while some more than one. The number of overall registered complications was 84. CD: Clavien Dindo; N: number; CCI: comprehensive complication index.

going from pneumonia to respiratory insufficiency and pleural effusion. Respiratory system complications are followed by bleeding (13 patients out of 181, being the 7.2% of total population) and wound infections (12 patients out of 181 with 6.6%) (Table IV). The majority of the registered complications were mild, staged as grade 2 of the CD classification, present in 40 cases (22%), while grade 4a was registered 9 times (5.0%) and grade 5, death, was reported for 7 patients (3.9%).

Among the patients who reported at least one major complication, classified as CD>3, the 38.7% of them was due to a respiratory system complication, while the 19.4% of them (6/31 patients) was due to post-operative bleeding, followed by bowel occlusion and anastomotic leak in 12.9% (4/31), respectively (details are reported in Table V). Details regarding the causes of death are reported in Table VI. The rest of the population had a minimum of 8-month survival after surgery.

Discussion

Despite its declining incidence, gastric cancer is still the third most common cancer-related cause of death after lung and liver (14). The reasons are certainly to be found in the screening programs, in the diagnostic modalities and also in both medical and surgical therapeutic management. Early and reliable assessment of the risk for developing postoperative complications serves as an important contributor to pre-operative, intra-operative, and postoperative decision making (15). Indeed, surgery still shows a high percentage of complications and mortality. In our population, seven patients died of perioperative surgical complications (3.9%). All seven patients had systemic multicomorbidities in anamnesis which probably influenced the post-operative course (such as diabetes, arterial hypertension, previous ischemic heart

Table IV. Incidence of complication and median Clavien Dindo (CD) classification.

Complications (CD>1) N=84	Adverse event (N)	Adverse event (%)	Clavien Dindo (median)
Anastomotic leak	6	3.3	3a
Wound infection	12	6.6	2
Stenosis of the anastomosis	2	1.1	3a
Bowel occlusion	5	2.8	3b
Delayed gastric emptying	4	2.2	2
Bleeding	13	7.2	2
Biliary fistula	3	1.7	2
Acute pancreatitis	4	2.2	2
Respiratory complications (PNX, pneumonia, pleural effusion, respiratory insufficiency)	24	13.3	3a
Pulmonary embolism	2	1.1	4a
Cardiovascular complications	6	3.3	2
Liver insufficiency	3	1.7	3a
Overall	84	-	-

N: Number; PNX: pneumothorax.

disease, COPD, obesity, and smoking). However, even though in the Literature the reported rate of mortality after total gastrectomy varies from 9.1% at 0 post-operative day to 4.7% at 30-day from the operation according to Shannon *et al.* (17) and 12.4% according to the last report coming from the GASTRODATA registry, postoperative mortality rate is still high and deserves further investigations to be decreased (18).

A strong correlation between post-operative complications and poor long-term outcome has been reported for esophageal and esophagogastric junction cancer. In addition, postoperative intraabdominal infectious complications adversely affect overall survival and relapse-free survival (16).

Accurate identification and detailed description, according to a standardized registry, of surgical complications may represent a starting point to provide a risk stratification before surgery. Indeed, it has the potential to improve several aspects of overall patient care, including more accurate informed consent, improved selection of procedures, better estimates of the likelihood of early and safe discharge, and more appropriate targeting of postoperative critical care services. Our population was a common Western oncological population, in which 70-year-old patients, with various comorbidities were predominant. More than half of the patients experienced weight loss, almost half of them underwent neoadjuvant chemotherapy, and around the 70% of the entire population had a T3/T4 cancer. The majority of them underwent open surgery and D2 lymphadenectomy. Baiocchi *et al.* in their consecutive articles, accounting for a wider population than ours, reported that the most frequently registered complications were non-surgical infections. They collected the presence of urinary, pulmonary, and gastrointestinal infection signs or symptoms associated with

microbiological isolations in a percentage ranging from 23% to 29% (according to the different papers). The most frequently registered complications in our population were disorders of the respiratory system going from pneumonia to respiratory insufficiency and pleural effusion, in 13.3% of the population. Similarly, other studies registered as the most important and clinically relevant post-operative complication the pulmonary infection, sometimes needing pleural drainage and re-intubation (18). The consensus guidelines on Enhanced Recovery After gastric Surgery (ERAS) (19) recommended perioperative multidisciplinary assessment in order to limit the appearance of respiratory disorders. They recommend mid-thoracic epidurals especially in cases of major open abdominal surgery because they showed superior pain relief and fewer respiratory complications compared with use of intravenous opioids. Moreover, they insist, with a strong level of recommendation, on the administration of a dedicated preoperative counselling routinely to patients who are going to face a gastric surgery. Indeed, detailed explanations of procedure and specific daily targets for the postoperative period may facilitate eating, mobilization, pain control and respiratory function, thus reducing the risk of complications. As well as, one month of abstinence from smoke before surgery, is reported to be beneficial with a moderate level of evidence and a strong grade of recommendation (20).

However, anastomotic/staple line leak following any type of gastrectomy remains one of the most severe complications that can lead to significant delays in recovery, worse short-term quality of life, and delays in initiating adjuvant chemotherapy (16). Concerning our rate of anastomotic leak, we registered a 3.3% of dehiscence and the grade of severity

Table V. Incidence of complications (CD>3).

Complications (CD>3) N 31 (17%)	Adverse event (N)	Adverse event (%)
Anastomotic leak	4	12.9
Wound infection	3	9.7
Stenosis of the anastomosis	2	6.5
Bowel occlusion	4	12.9
Delayed gastric emptying	0	0
Bleeding	6	19.4
Biliary fistula	1	3.2
Acute pancreatitis	1	3.2
Respiratory complications (PNX, pneumonia, pleural effusion, respiratory insufficiency)	12	38.7
Pulmonary embolism	1	3.2
Cardiovascular complications	2	6.5
Liver insufficiency	3	9.7
Overall	31	-

CD: Clavien-Dindo; N: number; PNX: pneumothorax.

of the complication was high. We registered three cases of conservative management that then evolved into percutaneous drainage, and three patients who needed major urgent surgical re-intervention with one death in the end. All of them were at the esophago-jejunal anastomosis and occurred after total or extended total gastrectomy.

A retrospective observational study (6) including a wider population than ours, reported a 30.3% of adverse events in the perioperative period with anastomotic leak, abdominal collections unrelated to leaks, postoperative bleeding, and other major postoperative issues as the most frequent surgical complications. An invasive procedure was necessary to treat these 4 complications in 68.9%, 31.9%, 100%, and 100% of cases and a surgical reintervention was necessary in 42.6%, 13.7%, 57.1%, and 62.8% of cases. Similarly, Gertsen *et al.*, in a wider population sample, reported a 15% of pulmonary complications, 7% of anastomotic leakage, and 6% of cardiac complications as the most common postoperative complications. They experienced a 5% of postoperative mortality, and 11% of reoperations (21).

An identified risk factor which plays a negative prognostic role on the post-operative outcomes in patients undergoing gastric surgery accompanied by D2 lymphadenectomy for neoplastic pathology is the administration of blood transfusion in the peri-operative/intra-operative period (22). Ohtani *et al.* reported a significant difference in intraoperative blood loss with a laparoscopic approach *vs.* open approach (23). In comparison to their population, even though we did not record any intraoperative complication nor need of intraoperative blood transfusion, we registered a higher rate of post-operative bleeding (7.2% *vs.* 1.6%) with 5 patients requiring blood transfusion and one reintervention.

Table VI. Postoperative mortality (30-day after surgery) and cause of deaths.

Patients died in 30-day after surgery	N (%)
Deaths	7 (3.9)
Age	83 (IQR=12)
Cause of death	
Cardiovascular complications	2
Pulmonary embolism	1
Respiratory complications	1
Acute pancreatitis	1
Biliary fistula	1
Anastomotic leak	1

N: Number; IQR: interquartile range.

However, Grasso *et al.* concluded in their paper that, when talking about surgery for gastric neoplasia, transfusions should be avoided when not strictly necessary and in particular the intraoperative ones should be avoided because the immunomodulation effect would enhance the one already linked to the surgical stress, hence worsening the patient's prognosis (24). We decided to include in our analysis of the complications the CCI system being a wide continuous scoring variable that is able to combine both the number and severity of complications providing additional accuracy to the CD classification. Indeed, a limitation of the CD classification is that events of lesser severity may not be considered, leading to an underestimation of the true overall postoperative morbidity. In our cohort we registered a mean CCI value of around 48 and a median score of 40, representing with an easier comparison of patients with more than one complication, as all postoperative events including their respective severity are taken into account for its calculation (25). However, another interesting factor that has always to be taken into account is the peculiar geographical incidence of gastric cancer. In fact, it is more frequent identified in eastern countries with the highest incidence rates observed in East Asia, Central Asia, Eastern Europe, and the Pacific Coast of South and Central America, whereas the lowest incidence rates found in Northern Europe and North America. The reason for this geographical distribution probably lies in the different lifestyle of the population, but the search for risk factors associated with geographical location is still ongoing and rapidly changing over time (26). One of the questions that may arise from data analysis is: is it possible that the complication rate could be indirectly influenced by the patient's geographic location? Has the frequency of this pathology in our country, influenced the medical approach to the patient, the timing of the screening and, last but not least, the surgical technique? In other words, is it possible to prevent the surgical complications obtained in our study that, however, are in line with the percentage

currently reported in Literature? This field of study certainly deserves further investigations on the epidemiology and its correlation with the clinical assessment and the surgical approach related to gastric neoplasia. However, the absence of a standardized system for recording perioperative complications associated with radical gastrectomy generates wide variations in evaluating the impact of complications on outcomes among the different studies reported in Literature (18). This point should be addressed in future to seek standard methods of evaluation. In conclusion, we must underline that our analysis unfortunately has many limitations that mainly lay in the retrospective nature of the study and in the limited sample of patients.

In conclusion, surgery for gastric cancer still involves high morbidity and mortality rates. Gastrodata is a useful tool to understand and discover the factors mostly associated with these rates of mortality and morbidity. Moreover, a standardized register in which collect all surgical complications could be a relevant tool in order to plan future plans of prevention.

Conflicts of Interest

The Authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author's Contributions

PA and GR approved the final version to be published, MG, SP and MP conceived, designed, and wrote the study, AM and LF provided data, GN collected data, DG, DS analyzed data, GG critically revised the article.

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