Early Complications after Gastrectomies for Locally Advanced Gastric Cancer[#]

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Rezumat

Complicații precoce după gastrectomiile pentru cancer gastric avansat

Introducere: Rezultatele post-operatorii imediate, ca și evoluția pe termen scurt și mediu ale operațiilor pentru cancer gastric depind de condițiile generale și locale, în mod special de stadiul tumoral. Întârzierea diagnosticului și intervenției constituie cauze importante pentru o incidență ridicată a morbidității și mortalității post-operatorii.

Metodă: Am analizat retrospectiv o serie de 76 pacienți consecutivi, cărora li s-au efectuat gastrectomii pentru cancer în decursul a 5 ani (2015-2019), în secția Chirurgie generală I a Spitalului Clinic "Dr. I. Cantacuzino". Dintre acestea, 46 au fost gastrectomii sub-totale (distale), 12 gastrectomii totale D1 și 18 gastrectomii totale D2, unele cu rezecții multi-organ.

Rezultate: 50 pacienți au evoluat favorabil, 7 au prezentat complicații care au fost rezolvate prin tratament conservator, iar la ceilalți 19 au fost necesare una sau mai multe reintervenții. Am înregistrat 10 cazuri care au dezvoltat sepsis și MSOF, cu deces.

Concluzii: Tratamentul chirurgical al cancerului gastric avansat constituie o provocare, iar evoluția este adesea grevată de complicații post-operatorii severe și de un prognostic oncologic rezervat.

Cuvinte cheie: gastrectomie, cancer gastric

Abstract

Background: The post-operative results as well as the short and middle-term outcome of surgical procedures for gastric cancer

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depend on several general and local conditions, mainly on the stage of neoplasia. Delayed diagnosis and intervention are correlated with a high rate of postoperative morbidity and mortality.

Methods: 76 consecutive patients underwent surgical treatment for gastric cancer over a time span of 5 years (2015-2019), in the 1st Surgical Department of “Dr.I.Cantacuzino” Clinical Hospital. There have been 46 distal gastrectomies, 12 DI total gastrectomies and 18 DII total gastrectomies, 8 of them with multi-organ resection.

Results: Among them, 50 patients had a favorable evolution, 7 developed complications which were manageable through a conservative approach, while 19 needed one or more reinterventions. We encountered 10 cases of severe sepsis and MSOF, followed by exitus.

Conclusions: The surgical treatment of locally advanced gastric cancer poses many challenges both in terms of postoperative evolution and oncologic prognosis.

Key words: gastrectomy, gastric cancer

Introduction

Gastric malignancy has always been a challenging pathology, due to its high incidence and rather poor evolution (1). It was the most common neoplasia worldwide around 1980; nowadays it is the 5th most frequent cancer and the 3rd cause of cancer death (2). In Romania diagnosis is usually delayed, due to little willingness among patients to submit to endoscopic procedures and to the lack of systematic screening programs. The recent SARS-CoV-2 pandemic has reduced real-life access to health care facilities, thus making early diagnosis more difficult and augmenting the number of advanced gastric cancers. The middle- and long-term prognosis is dismal; even before that, severe complications often occur during the early post-operative evolution, due to technical difficulties, as well as the poor nutritional and biological status of these patients.

Material and Methods

We reviewed 76 consecutive patients who underwent surgical treatment for gastric cancer over a time span of 5 years (2015-2019) in the 1st Surgical Department of “Dr. I. Cantacuzino” Clinical Hospital. In most of these cases, diagnosis had been delayed for many months or even years and was achieved only when severe complications of gastric neo-

plasma became obvious: upper digestive bleeding, which caused chronic anemia or melena; digestive obstruction; severe weight loss. Therefore, the main objective of the surgical procedures was to address an emergency or life-threatening condition, while radical oncologic principles could not be realistically accomplished.

Our lot comprised 51 male and 25 female patients. The age group analysis shows a high prevalence among the 7th decade - 31 cases (41%), while those aged between 71 and 80 represented an added 23 cases (31%) (*Fig. 1*). Also, we noticed 5 patients (6.5%) which were over 81.

Severe preexisting conditions were frequently encountered: 21 patients had been diagnosed with severe cardiac and/or vascular disease (heart failure, atrial fibrillation, myocardial infarction, stroke), 12 - with diabetes mellitus, 8 - with chronic hepatitis or cirrhosis, and 6 - with respiratory diseases (asthma, chronic bronchitis); many of them had more than 1 associated conditions. Anemia and weight deficit were consequences of the neoplastic disease and of the nutritional difficulties (particularly in pyloric and cardial locations).

Most of the tumours (41 of 76) were located in the antrum, 18 - in the corpus, 11 - near the gastroesophageal junction and 6 - in the fundus (*Fig. 2*). We emphasize that the extension of the

Figure 1. Age groups of the patients with gastric cancer

neoplastic process was usually important, so the precise location was difficult to establish. We counted the region which seemed to be the most affected. For instance, 13 of the 18 cases of cancer of the corpus were extended from nearby the fundus to the angle of His, while the remaining 5 were limited to the greater or lesser curvature.

All the tumours located in the antro-piloric region (distal third), as well as some of those of the corpus (middle third) were resected by distal subtotal gastrectomy (46 procedures), associated with lymphadenectomy and resection of the upper layer of the mesocolon. We were well aware of the improved oncological results of total gastrectomy with D2 lymphadenectomy (3), but in many cases the obstructive character of the lesions and/or heavy bleeding required a safer emergency procedure. Nevertheless, a recent study mentioned that subtotal gastrectomy may have a survival benefit in stage III gastric cancer (4) and provide better functional outcome (5).

We performed 30 total gastrectomies: 12 with D1 and 18 with D2 lymphadenectomy. 8 of them included multi-organ resections: 6 spleno-pancreatectomies, 1 hepatic resection and 1 hepatic resection, associated with spleno-pancreatectomy.

Results

The post-operative evolution was favourable in

Figure 2. Topographic location of the tumours

50 patients (66%) and included different complications in the other 26 (34%), pertaining to the complexity and difficulty of these cases. For increased clarity, we divided the complicated outcomes into three groups.

Firstly, we encountered 7 cases which were successfully managed through a conservative approach:

- 3 - diarrhea, caused by *C. difficile*
- 1 - fistula of the duodenal stump, which was thoroughly drained, thus avoiding a generalised peritonitis;
- 1 - external pancreatic fistula after distal pancreatectomy, with an initial daily outflow of 300 mL, which decreased significantly over the following 2 weeks;
- 1 - left pyothorax, which was drained (most probably caused by an esophageal fistula);
- 1 - myocardial infarction.

9 patients had complications which required 1 or more reinterventions, which led to a prolonged, but favourable evolution:

- 1 - early haemoperitoneum, which needed haemostasis;
- 1 - delayed pelvic abscess - drained 2 months later;
- 3 - surgical wound infection; in 2 of these cases, the cause was an insufficiently drained fistula of the duodenal stump and an osteitis of the appendix xiphoid, respectively;

- 2 - abdominal abscesses following acute necrotic pancreatitis, which were drained;
- 1 - pancreatic fistula, which occurred in day 4, leading to fistula of the esojejunal anastomosis (day 9) – a jejunostomy was performed;
- 1 - pleural fistula of the esojejunal anastomosis, which was drained; a jejunostomy was associated.

10 other cases ended in exitus. The average age was 72, 2 of which were over 80. All of them had had only partially corrected anemia and significant weight loss; 3 - diabetes mellitus, with chronic complications; 3 - cirrhosis and 2 - severe heart failure (NYHA III-IV), one of which had already had 2 episodes of myocardial infarction and had multiple coronary stents.

We consider useful a brief mention of the initial complication which led to the worsening of biological status, culminating in multiple system organ failure:

- 2 - fistulas of the gastro-jejunal anastomosis, associated with *C. difficile* infection;
- 1 - fistula of the duodenal stump, followed by fistula of the gastro-jejunal anastomosis and then by (possibly iatrogenic) fistula of the transverse colon;
- 1 - pancreatic fistula, followed by fistula of the gastro-jejunal anastomosis;
- 1 - delayed hemoperitoneum (day 15), through bleeding of the left gastric artery stump;
- 1 - fistula of the esojejunal anastomosis, which produced fasciitis of the abdominal and thoracic wall and required multiple reinterventions, including a skin graft;
- 1 - acute necrotic pancreatitis, which probably generated fistula of the esojejunal anastomosis;
- 1 - fistula of the duodenal stump, which produced fasciitis of the abdominal wall;
- 1 - recurrent myocardial infarction;
- 1 - severe *C. difficile* infection, with upper gastrointestinal bleeding.

Discussions

The pathogenesis of gastric malignant tumours is yet incompletely known; however, recent studies emphasize the importance of *H. pylori* infection, which seems to be involved in as many as 90% of all the cases, while in the remaining 10% the Epstein Barr virus might be responsible (6).

The diagnosis of gastric neoplasms should not pose great issues in the era of endoscopy. In Japan, which is the world-leader in the diagnosis of early gastric cancer, the 5-year survival rate is as high as 81% (7). This has undoubtedly been achieved in part through an extensive screening program, using both radiographic and endoscopic methods (8). However, in Romania most patients first present with late complications of the neoplastic disease: bleeding (anemia ± melena), digestive obstruction, weight loss up to cachexia. The age groups distribution may offer an explanation, as older patients are harder to persuade to accept a medical examination, especially an invasive one (endoscopy), even in countries with advanced health care systems and higher levels of compliance to medical recommendations. A recent Japanese study found that mortality related to gastric cancer in people in their 80s was twice that in people in their 70s; revealingly, the rate of endoscopies was half among patients in the first category (9).

In Europe and North America, the standard treatment for locally advanced gastric is either perioperative adjuvant chemotherapy or postoperative adjuvant chemoradiation (10). In Japan, D2 total gastrectomy with postoperative adjuvant chemotherapy is preferred. However, there are ongoing studies on the efficacy of preoperative neoadjuvant chemotherapy, which could lead to better outcomes for this stage of neoplasia (3). Unfortunately, the time for a radical oncological approach, as recommended by the international guidelines, had past for most of our patients. More importantly, the severity of the presenting symptoms did not allow for extensive preoperative correction of nutritional and volemic deficits. These life-threatening complications required emergency

operations, which were performed on patients with a substandard biological status and could only partially observe the principles of radical oncological surgery.

This might be the main explanation for our high overall morbidity (34.2%) and post-operative mortality rates (13%). Unsurprisingly the main life-threatening complication was the fistula of the eso/gastro-jejunal anastomosis. The 5 cases (4 - documented and 1 - supposed) of eso-jejunal fistula represent 6.5%, which is on a par with the data in literature. The surprisingly high incidence of fistula of the gastro-jejunal anastomosis (4 cases) might be explained by the severely altered biological status of our patients; its poor outcome is also well-known (11). Fistulas of the duodenal stump had a better evolution. In some of the cases in which an anastomotic fistula occurred, jejunostomy was the life-saving solution, as nutritional support is of the utmost importance in the case of digestive fistulas, in order to prevent excessive catabolism and multiple system organ failure (12).

Many attempts have been made to identify unfavourable prognostic factors (13). Body weight seems to play a part, as low BMI has been associated with more severe postoperative complications among patients with stages III or IV gastric cancer (14). Kidney function is also an independent predictive factor for complications: the incidence of anastomotic leaks is significantly higher in patients with estimated glomerular filtration rate under 63.2 mL/min/1.73 m² (15). Also, some studies have found a clear relationship between hypercoagulation and the incidence of post-operative complications (16). As previously mentioned, most of our patients had chronic anemia and, in some cases, acute gastric bleeding with melena. It has been widely reported - most recently by a meta-analysis involving more than 13,000 patients - that both overall survival and disease-free survival are significantly lower in patients with preoperative anemia (17).

Looking towards the future, the SARS-CoV-2 pandemic will likely worsen these issues (18). For over a year, screening and early detection

of neoplastic diseases, insufficient as they might have been, have all but disappeared. The new social distancing rules have cut off the elderly, rural dwelling-population from their families; they have been once again left behind. The oncological consequences of the decisions taken during the pandemic are yet to be exposed. It is reasonable to expect a new wave of delayed diagnosis of all types of cancer and subsequent deaths.

Conclusion

Gastric cancer remains a public health problem with high mortality rate, despite its essential pathogenic mechanism (*H. pylori* infection) being well-known and relatively simple to eradicate. The diagnosis requires endoscopic and radiological examinations, which are widely accessible and inexpensive. Early diagnosis should therefore become the rule; nowadays it is still the exception. Significant improvements in the evolution and prognosis of this neoplasm can only be achieved through a proactive approach. An endoscopy can be performed almost everywhere in Romania, but few patients are willing to accept it.

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Conflict of Interests

The authors have no conflict of interests to disclose.

Ethics of Approval

All procedures performed were in accordance with the ethical standards of the 1964 Helsinki Declaration and its later amendments.

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