

# The impact of patient-dependent risk factors on morbidity and mortality following gastric surgery for malignancies

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## ABSTRACT



Gastric cancer remains a leading cause of mortality worldwide. The treatment for gastric cancer is multimodal, in which gastrectomy remains the only curative approach. However, gastric resection is often associated with increased morbidity and mortality rates, depending on several factors. These factors can be attributed to the patient as comorbidities or effects of the disease upon him and, on the other hand, there are risk factors independent of the patient, such as aspects of the tumor (type, staging, location), experience of the surgical and anesthetic team, logistics of the hospital, yield of adjuvant therapies etc. We recognize the fact that patient-related risk factors are often overlooked and not taken into consideration prior to surgery, thus becoming a source of morbidity and mortality. These factors are more susceptible to modulating in order to better select candidates for gastric resection and thus create a better outcome. Therefore, identifying and modulating patient-related risk factors is paramount in order to decrease the incidence of morbidity and mortality following gastric resections.

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## Introduction

Gastric cancer represents a formidable malignant pathology, ranking the 5th in incidence worldwide and the first in mortality among digestive malignancies, according to GLOBOCAN 2020 data [1].

The treatment of gastric cancer is multimodal and gastric resection represents the sole curative treatment for this pathology. The early diagnosis and the early staging upon admission represent the best predictive factors for prolonged survival [2,3]. Apart from this, there are a multitude of factors which influence the postoperative course of surgical patients [4,5].

Morbidity associated with gastric resection in malignant pathologies varies wildly according to different studies, ranging from 9 to 46%. Mortality rates range from 2 to 8.5% [4-7]. It becomes obvious that apart from bias factors of different studies, there are a series of elements which influence these indices. There are patient-independent factors which correlate to the tumor type, the site of the tumor, the staging upon admission, the response to adjuvant therapies, the experience of the surgical and anesthetic team, the logistic capabilities of the oncologic

center and many more. On the other hand, there is a significant number of patient-dependent factors such as: bio-nutritional status (body mass index, serum levels of albumin and total proteins), hemoglobin level and associated comorbidities (such as diabetes mellitus, cardiovascular disease, hepatic disease, renal disease, pulmonary disease, etc.). These patient-dependent risk factors can be identified and controlled, up to a point, in the preoperative stage, in order to better prepare the body for the amplitude of the surgical procedure. In this way, we can assure the best possible outcome for the patient, both in terms of morbidity and mortality.

## Materials and Methods

This is an analytic retrospective study over a period of 6 years (between 2014 and 2019). The study was conducted in the Surgical Clinic of the Bucharest Emergency Hospital. A number of 114 patients with gastric cancer were operated on by a single team during this period and were included in the study. One important inclusion criterion was that all patients were operated on using mechanical staplers for resection and reconstruction.

The positive diagnosis of gastric cancer was performed through upper endoscopy with multiple biopsies and histopathological examination. The preoperative staging was performed using CT scans, endoscopic ultrasound or MRI.

The surgical procedure involved was gastric resection with adequate lymphadenectomy.

The aim of the study is to identify and evaluate patient-dependent risk factors that have an impact on the postoperative course, essentially influencing morbidity and mortality indices.

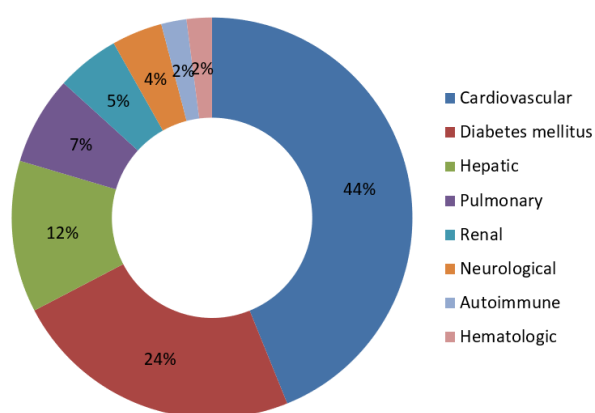
## Results

The majority of the patients included in the study were males (73.6%) from an urban area (74%). The mean age on admission was 66.5 years, ranging from 21 to 94 years of age.

The most common type of tumor was gastric carcinoma (84%) followed by gastrointestinal stromal tumors (14%) and lymphoma (2%). Tumor staging was, unfortunately, advanced in the majority of the cases, with 71% of the patients having stage III or IV of the disease.

The most utilized type of gastric resection was total gastrectomy (65%), followed by distal resections (20%) and limited wedge resections (15%). The digestive reconstruction was performed consequently, using esophageal anastomosis, gastroduodenal anastomosis or gastrojejunal anastomosis.

At the moment of admission, 60 patients (52.6%) presented at least one comorbidity. The most common comorbidities found in patients were cardiovascular disease (44%), diabetes mellitus (24%) and hepatic pathologies (12%) (Figure 1).

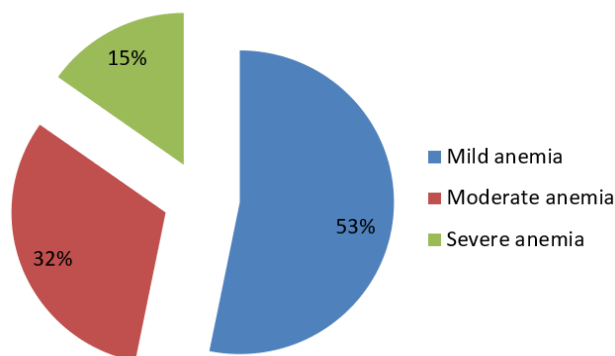


**Figure 1.** Associated comorbidities on admission

Other pathologies included pulmonary, renal, hematologic and autoimmune diseases. The nutritional status of the patient was also noted: 16 patients (14%) presented with neoplastic cachexia (objectified by BMI<20 or unintentional loss of weight >10% regardless of the time period or unintentional weight loss >5% in the last 3

months) and 17 patients (15%) presented with obesity (BMI>30).

Another factor analyzed was the hemoglobin level upon admission. A number of 70% of patients presented different degrees of anemia preoperatively. About half of these patients presented with mild anemia (53%), but also 15% presented with severe forms of anemia (Figure 2).

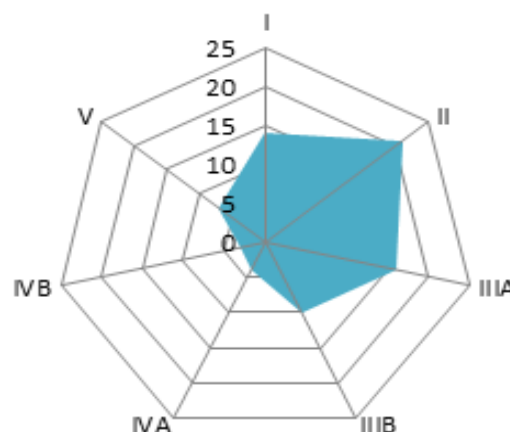


**Figure 2.** The severity of anemia upon admission

The patients were monitored using a specific protocol in the postoperative period and all the common and specific complications were noted and analyzed. Specifically, for this study we are going to focus on three major types of postoperative complications: anastomotic leak, infectious complications, pancreatic complications and also the mortality rates.

The statistical analysis was performed using IBM SPSS version 19 and Microsoft Excel, using Fischer test, Student t-test and Pearson correlation.

Morbidity and mortality events were classified according to the Clavien Dindo scale. Figure 3 shows that the majority of the complications were part of grade I-III.



**Figure 3.** Postoperative complications according to Clavien Dindo scale

The anastomotic leak is perhaps the most fearful complication following gastric surgery. The incidence of the anastomotic leak was 7% and because of the wide range of resections performed, the site of the leak ranged from esophageal to gastrojejunal and the duodenal stump.

The main risk factors associated with the anastomotic leak were poor nutritional status ( $p < 0.035$ ) and advanced staging ( $p < 0.019$ ).

The infectious complications were far more numerous with an incidence of 39%. However, the vast majority were extra-peritoneal (88.8%) and were included in grade I or II according to Clavien Dindo scale. These comprised common infections following abdominal surgery, such as: surgical site infection ( $n=18$ ), urinary infection ( $n=8$ ), pulmonary infection ( $n=5$ ), Clostridium difficile colitis ( $n=8$ ). The intraperitoneal infectious complications which manifested as peritoneal abscesses had an incidence of 11.2% ( $n=5$ ).

Patient-dependent risk factors were found to be associated with an increase in infectious complications were anemia with hemoglobin  $< 8\text{g/dl}$  ( $p=0.002$ ), poor nutritional status with cachexia ( $p=0.03$ ), diabetes mellitus ( $p < 0.0001$ ) and cardiac failure ( $p=0.003$ ) as shown in Table 1.

A stand apart category of complications related especially to the patients included in our study because of their advanced staging were pancreatic complications. These complications comprised postoperative acute pancreatitis and pancreatic leak, thus representing an independent risk factor for morbidity and mortality. These complications are somehow specific to this cohort because of the need for multivisceral resection, which included the pancreas. The incidence of pancreatic complications

following gastric resection was influenced by poor nutritional status ( $p=0.03$ ) and preoperative anemia ( $p=0.004$ ).

**Table 1.** Patient-dependent risk factors and infectious complications

Correlation	Pearson	Statistical significance
Anemia $< 8\text{g/dl}$	$r = 0.3288$	$p = 0.002$
Diabetes mellitus	$r = 0.5102$	$p < 0.0001$
Poor nutritional status	$r = 0.4018$	$p = 0.03$
Cardiac failure	$r = 0.2315$	$p = 0.003$

As suspected, patients with a high incidence of morbidity had an increase in the length of hospital stay and implicitly the costs were significantly higher (Table 2). Patients without complications following surgery had a mean hospital stay of 7 days with average costs around 1,800 euros, as opposed to patients who developed complications during their postoperative course. These patients had a prolonged hospital stay of approximately 21 days with average costs of 4,200 euros. The poor nutritional status ( $p=0.01$ ) and anemia ( $p < 0.001$ ) were the primary contributors, in terms of patient-dependent factors, of prolonged hospital stay (Table 3).

**Table 2.** The length of the hospital stay and consequent costs for patients with and without postoperative complications

Patients without postoperative complications			Patients with postoperative complications		
Variable	Length of the hospital stay (days)	Costs (RON)	Variable	Length of the hospital stay (days)	Costs (RON)
Average	7	8,950	Average	21	21,935
Standard deviation	2.4	3,450	Standard deviation	11.5	18,419

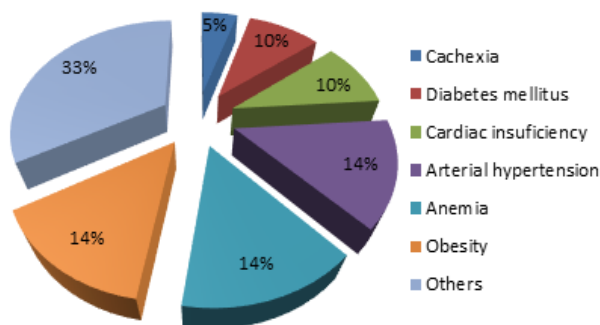
**Table 3.** Correlations between albumin and hemoglobin levels and the length of the hospital stay

		Hemoglobin	Albumin	Length of stay
Hemoglobin	Pearson Correlation	1	.301**	-.104
	Sig. (2-tailed)		.001	.269
	N	114	114	114
Albumin	Pearson Correlation	.301**	1	.044
	Sig. (2-tailed)	.001		.643
	N	114	114	114
Length of hospital stay	Pearson Correlation	-.104	.044	1
	Sig. (2-tailed)	.269	.643	
	N	114	114	114

The mortality rates in the study were 5.98% ( $n=7$ ). Following statistical analyses, we were able to determine a possible correlation between infectious complications ( $p < 0.0001$ ), the anastomotic leak ( $p < 0.03$ ), pancreatic complications ( $p=0.01$ ) and an increased mortality rate.

All of these factors were influenced, in turn, by the patient-dependent risk factors examined in this study. Furthermore, all the patients who deceased had at least two comorbidities which were diagnosed at the time of admission.

The most frequent comorbidities encountered in deceased patients were represented by several cardiac pathologies (24%), moderately or severely affected nutritional status (19%), anemia (14%), and diabetes mellitus (10%) (Figure 4).



**Figure 4.** Associated comorbidities of deceased patients upon admission

## Discussions

Gastric cancer remains a pathology with a high index of morbidity and mortality worldwide. Gastric resection with lymphadenectomy continues to be the sole curative treatment for this formidable pathology [8-10]. But, in order for the surgical procedure to have the desired effect in terms of outcome, it needs to be performed on selected patients. Surgical and medical innovations have managed or eliminated some patient-independent risk factors which contribute to an increase in morbidity and mortality rates, such as operating time, blood loss, anesthetic drug usage and septic time of surgeries using stapling technology, electrosurgical and tissue heat sealing devices, minimal invasive surgery, increasing surgical team experience by training specific teams for this pathology, etc. The careful preoperative evaluation of the digestive tract, through endoscopic examination and barium enema, is important to exclude the concomitant colorectal tumor [11]. Moreover, efforts must be done to determine the preoperative staging in order to better select patients.

However, there are still the patient-dependent risk factors which need to be taken into consideration when preparing a patient for gastric resection. These risk factors are more difficult to manage, but the first step is to recognize them and to try to bring them into balance prior to surgery.

The factors identified in this study are poor nutritional status (objectified by BMI<20 or serum albumin <3g), anemia (hemoglobin levels < 8g/dl), the presence of different comorbidities, the most significant being poorly controlled diabetes mellitus and cardiovascular disease. In other studies, diabetes mellitus and the poor nutritional status expressed in the form of cachexia were associated with both increased surgical related and cardiovascular postoperative morbidity, requiring closer perioperative care [12]. All these factors contribute significantly to an increase in morbidity and mortality and consequently to a poor quality of life for the patients, decreased overall survival and increase in hospital stay and associated costs [13,14].

For this reason, the optimal control of the patients' comorbidities and nutritional and volemic balance are important aspects which need to be taken into consideration preoperatively in order to have the best possible postoperative outcome.

Furthermore, we noticed that the presence of these unchecked patient-dependent risk factors usually leads to a plethora of other complications. All these factors lead to an increase in the incidence of complications, such as the anastomotic leak, infectious complications (both intra and extraperitoneal) and pancreatic complications. These complications, in turn, lead to secondary complications, which can be lethal: single or multiple organ failure, sepsis, pulmonary complications, thromboembolic disease and others [15-17]. Moreover, the initial complications tend to potentiate each other: leakage-related complications and pancreatic complications lead to infectious complications and vice versa. Looking at this intricate context in which complications potentiate each other in a negative way, it becomes all the more important to identify and balance the patient-dependent risk factors in the preoperative stage and thus, perform a patient selection for the surgical procedures in order to have the best outcome. Informing patients is particularly important, as they will become an active partner in the patient-physician relationship in the preoperative training and postoperative care [18].

Exerting a better control on patients' comorbidities requires a higher confidence of patients in addressing medical facilities and also screening programs for different pathologies. In this way, we can start to better control or even eliminate patient-dependent risk factors, which often undermine the surgical effort in gastric malignancies.

## Conclusions

Gastric resection in malignant pathologies remains the only curative treatment available. Knowing and identifying the risk factors which lead to increased morbidity and mortality rates is paramount in order to correctly select patients for the surgical procedure and obtain the best mid- and long-term results. Patient-independent risk factors are more difficult to control and require nationwide strategies, such as screening procedures for the early detection of cancer, sanitary education, elimination of etiological risk factors of cancer, proper logistics of hospitals, training and promoting tertiary oncological centers dedicated to specific malignant pathologies etc. Patient-dependent risk factors, however, are relatively easy to identify in the preoperative stage and are more susceptible to managing until the surgical procedure.

Patient-dependent risk factors were found to significantly contribute to the increased rates of morbidity and mortality in this study, i.e. the poor nutritional status (cachexia), anemia (hemoglobin levels beneath 8 g/dl),

diabetes mellitus and cardiac failure. Taking into account the fact that gastric resections have innate increased morbidity and mortality rates, all efforts must be done in order to better select and prepare the patients in order to minimize the incidence of these indices and to give the patient the best chance of survival.

## Conflict of interest disclosure

There are no known conflicts of interest in the publication of this article. The manuscript was read and approved by all authors.

## Compliance with ethical standards

Any aspect of the work covered in this manuscript has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

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