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Research Article

POSSUM, P-POSSUM and O-POSSUM in Patients Undergoing Gastrectomy due to Gastric Cancer

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Abstract

Background: Gastric cancer is one of the most incident and deadliest worldwide, with surgery being the only curative treatment. Despite the existing models for surgical risk assessment, the ability to predict morbidity and mortality associated with gastric surgery in gastric cancer remains uncertain. The aim of this study is to assess the acuity in predicting mortality and morbidity of the scales POSSUM, P-POSSUM and O-POSSUM in patients undergoing gastrectomy due to gastric cancer.

Methods: Data from 146 patients submitted to curative gastrectomy between December of 2012 and December of 2016 were included. The predictive capacity of the scales was tested through the calibration, comparing the observed mortality to the expected one (O: E ratio) and discrimination, by accessing the analysis of the Receiver Operating Characteristic curve.

Results: This study included 86 men and 60 women, with a median age of 67 years. Mortality and morbidity observed at 30 days postoperative was 4.79% and 27.4%, respectively. In mortality, P-POSSUM presented the best calibration (O: E ratio = 1.41), underestimating mortality and the operative score was the only one that presented discriminative power, although reasonable (AUC = 0.763). In morbidity, POSSUM presented an O: E ratio of 0.496, overestimating the morbidity, especially in the higher risk groups (> 60%) and no scale/score presented discriminative capacity.

Conclusion: Therefore, no model predicted morbidity and mortality correctly, however, the P-POSSUM equation for mortality and POSSUM for morbidity may have potential in the Portuguese population, but further studies are needed.

Keywords: *Gastric Cancer; Morbidity; Mortality; POSSUM*

Introduction

Gastric cancer (GC) is the fifth more incident cancer worldwide [1]. Portugal remains a country with high rates of GC, with an estimated incidence of 19.1/100 000 and a mortality of 13.6/100 000, in 2012, being more incident in men (about 1.6 times) and in North part of

the country [1,2]. Although there is no current screening for gastric adenocarcinoma, this cancer is theoretically curable if it is in an initial state according to TNM staging. Most of CG in state I, II and some of the III are considered resectable and so potentially curable [3].

Despite the advances in multidisciplinary treatment, gastrectomy is still the best curative treatment, but it is linked to an elevated rate of complications and mortality. In the UK, the mortality and morbidity of this procedure, at 30 days postoperative has about 2.3% and 23.7%, respectively [4]. The majority of mortality is justified by respiratory and abdominal complications [4].

Some risk factors connected with post-surgical complications are well known and so their evaluation represents an accessible tool that allows the determination of surgical risk, allowing the distinguishing between the patients who will effectively benefit from the surgery and those in whom the surgical risks surpass the benefit in the short term [5].

Predicting surgical risk remains a challenge, however, with regard to GC some scoring systems have been used, namely models such as POSSUM, P-POSSUM and O-POSSUM.

The POSSUM (Physiological and Operative Severity Score for the enumeration of Mortality and morbidity) model was developed in 1991 to compare the morbidity and mortality of a variety of surgical procedures in elective and emergency surgeries. Subsequently it was validated for specific cancer pathologies. The POSSUM model uses 12 preoperative physiological parameters and 6 peri and postoperative surgical parameters [6].

The P-POSSUM (Portsmouth POSSUM) results from a review of the POSSUM logistic regression equation using the same data, in an attempt to overcome the fact that POSSUM overestimates mortality in the lower risk categories and underestimates the risk in elderly and urgent procedures [5,7].

The O-POSSUM model was created specifically for esophageal and gastric cancer. This method is based on a combination of patient's age, physiological score (with the same 12 parameters) and 3 surgical parameters.

These physiological and surgical parameters may improve the surgeon's ability to select patients who should have a tighter follow-up in the postoperative period, in order to reduce the morbidity and mortality associated with surgery. Thus, it is pertinent to evaluate the acuity of the POSSUM scales in patients submitted to gastrectomy, in Trás-os-Montes e Alto Douro Hospital Center, (CHTMAD), in order to determine which is best adapted to the reality of the patients treated there.

Materials and Methods

This study included patients who underwent surgical treatment with histological diagnosis of gastric adenocarcinoma between January 1st, 2012 and December 31st, 2016 in CHTMAD. Exclusion criteria included patients submitted to palliative surgical treatment; patients who had missing data and it was impossible to calculate the scores systems. Clinical and staging data collected include; age, gender, data needed to quantify the POSSUM scales, tumor location, histological type, tumor extension (T), lymph node involvement (N), neoadjuvant therapy or adjuvant therapy, tumor relapse, 30 day post-operative mortality and morbidity and overall mortality.

Tumor location was classified by the anatomical location as cardia, fundus, body and antrum.

Post-operative mortality was defined as the observed mortality attributed to surgery in the 30 days after the procedure. Morbidity is a change in a normal evolution in the postoperative period and were considered to occur within 30 days after surgery. For statistical purposes, it was only counted whether the patient presented operative complications, regardless of the number or type of complication.

The collected data were introduced and treated with Statistical Package for the Social Science® (SPSS®), version 22. A descriptive analysis of the variables under study was performed.

The physiologic and operative scores and the risk of morbidity and mortality estimated by POSSUM was calculated with use of the calculator tool https://www.mdcalc.com and for P-POSSUM and OPOSSUM was used the www.riskprediction.org.uk [8,9]. The POSSUM physiologic and operative scores were also analyzed [10,11].

The results of the scales were compared Mann Whitney Test. The models were analyzed for calibration and discrimination, global and in subgroups depending on: staging, histological type and surgery performed. P-value under 0.05 was considered significative.

Calibration is defined as the capacity of a scale to predict the correct probability of the outcome in a population [7,12], by comparing the observed events with the expected ones (O:E ratio and Hosmer-Lemeshow test). In the Hosmer-Lemeshow test, $P < 0.05$ implies that the scale has bad calibration [7].

Discrimination is the ability of the scale to distinguish the patients with or without the outcome in study by measuring the area under the ROC curve (AUC). An AUC under 0.70 implies low discrimination, between 0.70 - 0.80 medium discrimination and above 0.80 good discrimination [5,12].

Kaplan-Meier curves were used for survival analysis associated with Log-rank test for comparison of survival in groups of patients and Cox regression for identification of survival predictors in long term.

Results

Characterization of the population

This study included 146 patients, 86 men (58.9%) and 60 women (41.1%), aged between 30 and 84 years, with a median age of 67 years old at the time of diagnosis. Regarding the location, most of them had a tumor located in the antrum (63.7%), followed by the body (16.4%), cardia (13%), common to the body and antrum (3.4%), fundus (2.7%) and one case of neoplasm in the anastomosis zone after subtotal gastrectomy due to benign peptic disease (0.7%). 44.5% (n = 65) had an adenocarcinoma with characteristics of tubular type, 21.2% (n = 31) had an adenocarcinoma with signet ring cells and the remaining 34.2% (n = 50) showed little differentiation or were not classified by the anatomopathologist (n = 18, n = 32, respectively).

Primary and surgical treatment

Of the 146 patients included in the study, 139 (95.2%) had surgical treatment as the primary treatment. Of the remaining patients, 5 (3.4%) underwent neoadjuvant chemotherapy and 2 (1.4%) underwent neoadjuvant chemotherapy and radiotherapy.

A total of 91 (62.33%) subtotal gastrectomies with anastomosis in Billroth II were performed, 48 (32.88%) total gastrectomies with Roux-en-Y anastomosis, 4 (2.74%) subtotal gastrectomies with Roux-en-Y anastomosis, 2 (1.4%) total degastrectomies with Roux-en-Y anastomosis and one (0.7%) case of subtotal gastrectomy with anastomosis in Billroth type I.

Tumor staging

Approximately 21.9% of patients (n = 32) had a stage I, 46.6% (n = 68) had a stage II and 31.5% (n = 46) had a stage III, according to the TNM classification of American Joint Committee on Cancer 7th edition.

Morbidity and mortality

Forty patients (27.4%) presented postoperative complications. The most common complications were anastomosis dehiscence, which occurred in 52% of the cases, and respiratory complications that occurred in 14 patients (41.18%), which are discriminated in table 1.

Complication		N*
Pulmonary	Respiratory infection	8
	Pleural effusion	3
	Atelectasis	1
	Pneumothorax	1
	Pulmonary Thromboembolism	1
Cardiovascular	Atrial fibrillation	3
	Acute myocardial infarction	1
Renal	Acute renal failure	3
Sepsis	Sepsis	8
Hemorrhage	Hypovolemic shock	3
Abdominal	Intestinal occlusion	2
	Paralytic ileus	1
	Peritonitis	4
	Abscess	6
	Hematoma	2
Others	Mediastinitis	1
	Deep venous thrombosis	1

Table 1: *Frequency of postoperative complications.*
**The total number of complications is greater than the number of patients presenting them, due to the occurrence of more than one complication in the same individual; N: Number of Patients.*

Mortality in the 30 days after surgery was 4.8%, corresponding to seven deaths. The main causes of mortality were respiratory or abdominal infection associated with septic shock.

Surgical risk assessment

The mortality risk predicted by POSSUM ranged between 3.8% and 75.80% with 71.2% (n = 104) with a predictive risk lower than 20%. The morbidity risk predicted by POSSUM ranged between 21.6% and 98.3%. Most patients had a risk between 40 - 59.9% (41.8%, n = 61).

The mortality risk predicted by P-POSSUM ranged between 1% - 59.4%, with 75.3% (n = 110) obtaining a risk under 10%.

The mortality risk predicted by O-POSSUM ranged between 0.20% - 3.4%, the majority of patients had a risk under 1% (84.9%, n = 124).

The physiologic score had a minimum of 17 and maximum of 42, with 104 patients having a score between 20 - 29. Operative score ranged between 10 - 26, with 89 patients having a score under 20.

Scale calibration

Scale calibration was calculated for mortality and morbidity using the O:E ratio and Hosmer-Lemeshow test.

Concerning mortality; the predicted 30 day post-operative mortality by POSSUM, P-POSSUM e O-POSSUM was 11.9%, 4.2% e 0.50% respectively (Table 2) and the observed 30 day post-operative mortality was 4.795% (n = 7) which gives a O:E ratio of 0.4, 1.41 and 9.59 in these order. P-POSSUM scale showed better calibration on most subgroups, except on patients with tumor stage I and III.

	N	n of deaths in 30 days (%)	POSSUM	P-POSSUM	OPOSSUM
Overall	146	7 (4.795)	11.9% (O:E 0.40)	4.2% (O:E 1.41)	0.5% (O:E 9.59)
Staging: I	32	0 (0)	8.65% (O:E 0)	2.6% (O:E 0)	0.4% (O:E 0)
Staging: II	68	3 (4.41)	13.4% (O:E 0.33)	4.95% (O:E 0.89)	0.5% (O:E 8.82)
Staging: III	46	4 (8.696)	13.55% (O:E 0.65)	4.95% (O:E 1.76)	0.5% (O:E 17.39)
Well differentiated adenocarcinoma	65	4 (6.15)	12.7% (O:E 0.48)	5% (O:E 1.23)	0.5% (O:E 12.3)
Signet-ring cell adenocarcinoma	31	1 (3.23)	9.4% (O:E 0.35)	3% (O:E 1.08)	0.5% (O:E 6.46)
Undifferentiated/unclassified adenocarcinomas	50	2 (4)	15.28% (O:E 0.26)	6.25% (O:E 0.64)	0.6% (O:E 6.67)
Total gastrectomy	50	2 (4)	12.65% (O:E 0.32)	4.5% (O:E 0.89%)	0.5% (O:E 8)
Subtotal gastrectomy	96	5 (5.2)	11.9% (O:E 0.44)	4.2% (O:E 1.24)	0.5% (O:E 10.4)

Table 2: *Calibration of POSSUM scales in mortality. Mortality observed 30 days postoperatively both overall and by subgroups, and the mortality expected by each one of the scales, as well as the respective O: E. n.: Number of Patients; POSSUM: Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity; P-POSSUM: Portsmouth Physiologic and Operative Severity Score for the enumeration of Mortality and morbidity; O-POSSUM: Oesophagogastric Physiologic and Operative Severity Score for the enumeration of Mortality and morbidity.*

Every scale had $p > 0.05$ on the Hosmer-Lemeshow test, so they all showed good calibration [18].

In morbidity, observed post-operative morbidity was 27.4% (n = 40) and the expected morbidity by POSSUM was 55.20%, with an O:E ratio 0.496. In the group of patients with morbidity risk above 60.0%, POSSUM had poorer correlation between the observed and estimated morbidity (Table 3).

	n	n with morbidity within 30 days (%)	POSSUM
Overall	146	40 (27.397)	55.2% (O:E 0.496)
Staging: I	32	11 (34.38)	42.55% (O:E 0.81)
Staging: II	68	17 (25)	59.1% (O:E 0.42)
Staging III	46	12 (26.09)	59.5% (O:E 0.44)
Well differentiated adenocarcinoma	65	20 (30.77)	57.7% (O:E 0.53)
Signet-ring cell adenocarcinoma	31	4 (12.9)	47.3% (O:E 0.27)
Undifferentiated/unclassified adenocarcinomas	50	16 (32)	61.83% (O:E 0.52)
Total gastrectomy	50	14 (28)	57.15% (O:E 0.49)
Subtotal gastrectomy	96	26 (27.08)	55.2% (O:E 0.49)

Table 3: *Calibration of the POSSUM scale, regarding morbidity. Morbidity observed 30 days postoperatively both overall and by subgroups, and the expected morbidity, as well as the respective O: E. n.: Number of Patients; POSSUM: Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity; P-POSSUM: Portsmouth Physiologic and Operative Severity Score for the Enumeration of Mortality and Morbidity; O-POSSUM: Oesophagogastric Physiologic and Operative Severity Score for the enumeration of Mortality and Morbidity.*

Scale discrimination

The discriminative power for morbidity and mortality was assessed by the AUC of ROC curve. For mortality, only the operative score presented statistical significance with an AUC of 0.763 (p = 0.019). O-POSSUM had an AUC of 0.627 (p = 0.259) followed by physiological score (AUC = 0.632, p = 0.239), P-POSSUM (AUC = 0.661 p = 0.15) and POSSUM (AUC = 0.682, p = 0.104) (Figure 1).

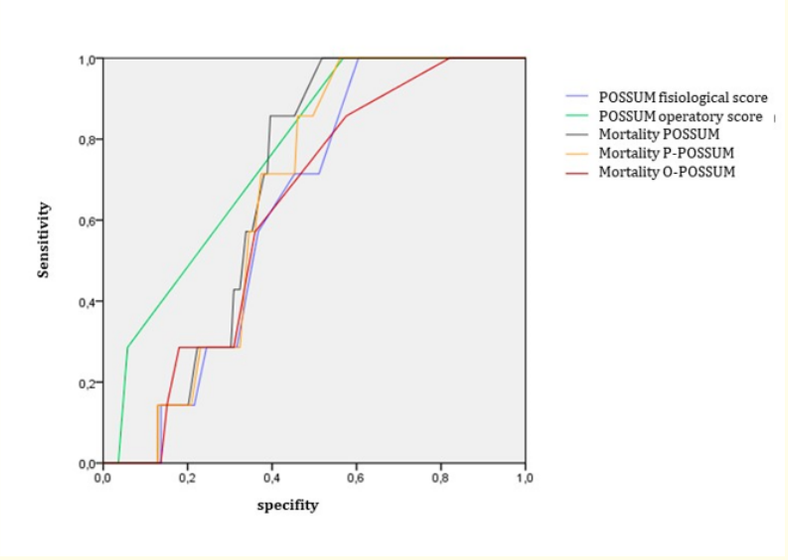

Figure 1: *ROC curve for mortality.*

Any scale showed statistically significant results in none of the subgroups.

For morbidity, neither the POSSUM scale nor the physiological/operative score presented a statistically significant result. The physiological score had the biggest AUC with 0.596 (p = 0.074) (Figure 2).

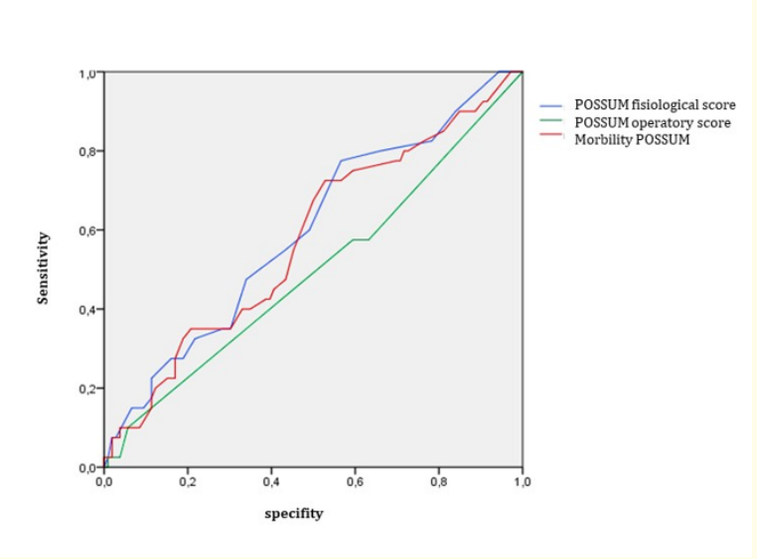

Figure 2: *ROC curve for morbidity.*

When patients are subdivided, there is still no statistical significance for any of the groups depending on the stage, type of adenocarcinoma or surgical type.

Long term survival predictors

Patients were divided in two groups for each scale based on the median of that specific scale (patients with result inferior to the median and those with result equal or superior to the median) and overall survival was assessed. Cox regression was used to identify survival predictors. Operative score and POSSUM were statically significance as a survival predictor (p = 0.025 and hazard ratio (HR) = 2.085, p = 0.049 and HR = 9.357, respectively). Patients with an operative score below 12 had a mean survival of 45,18 months different (p = 0.03 in the Long Rank test) from the patients with an operative score equal or superior to 12, which had a mean survival of 33,66 months (Figure 3).

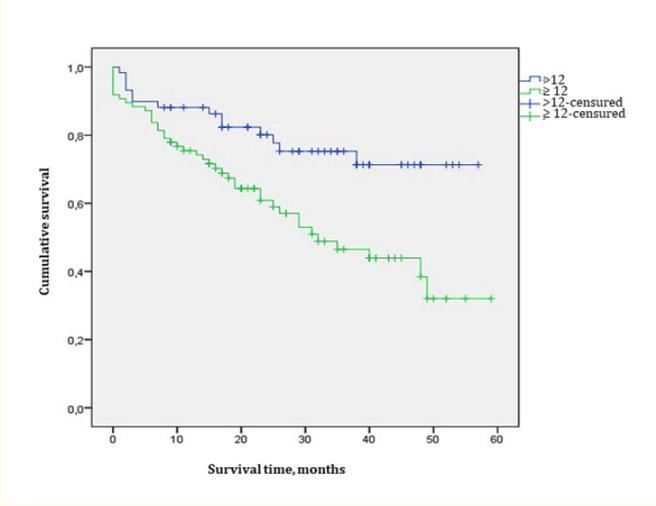

Figure 3: *Cumulative survival curve comparing patients with an operative score below 12 (in blue) and patients with a score greater than or equal to 12 (in green) in months.*

In POSSUM, patients with a value under 11.9% had a mean survival of 44,29 months significantly different (p = 0.011) than those who had a value greater or equal to 11.9%, which had a mean survival of 31,4 months. (Figure 4).

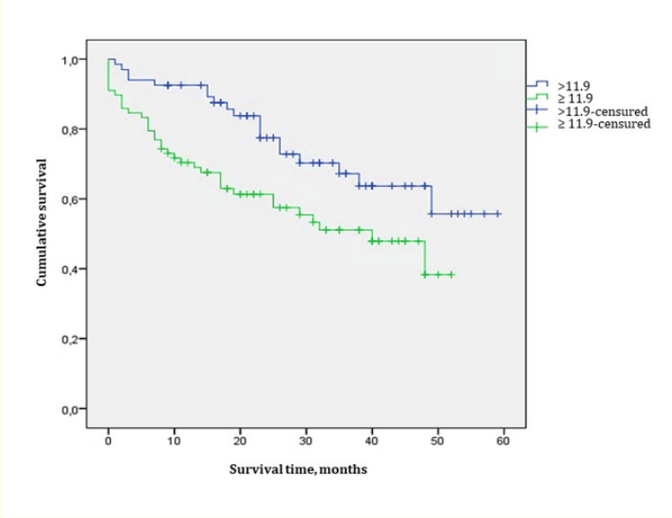

Figure 4: *Cumulative survival curve comparing patients with POSSUM risk below 11.9% (in blue) and patients with a POSSUM greater than or equal to 11.9% (in green) in months.*

Discussion

Gastric cancer continues to be one of the most incident and fatal worldwide and Portugal remains one of the European countries with the highest incidence of this tumor [1,13]. Surgery is the only potentially curative treatment, but it is essential to understand which patients may benefit from this treatment [3,5].

In the current study, most of the patients were male, aged over 60 years and with tumors mostly located in the antrum, which corresponds to the literature described [4,14,15].

The mortality rate was 4.79% and the postoperative morbidity was 27.4%, equivalent to other published studies, namely values between 2 - 12% for mortality and 20 - 35% for morbidity [4,7,16,17]. Most of the morbidity was justified by abdominal and pulmonary complications, also consistent with the literature [4,7].

The 30-day survival was 95% and the one-year survival was 79.6%. The 30-day survival was similar to the literature (97.7% in the United Kingdom) [4] and the one-year survival was superior (44% in the United Kingdom and 51% in Shanghai), which may be justified by the fact that patients with advanced stage of disease were not included in this study [4,18].

The POSSUM scales were first developed in the United Kingdom, but have already been applied and validated in other countries [19,20]. However, predict morbidity and mortality associated with gastric surgery remains difficult [5,7].

This study evaluated the calibration and discrimination of the POSSUM scale and its variants P-POSSUM and O-POSSUM in patients submitted to surgical intervention for curative purposes in Trás-os-Montes e Alto Douro Hospital Center.

Regarding the scores and scales, there was not significantly differences between patients who developed mortality or morbidity and those who did not, implying that patients who develop postoperative complications or mortality do not score disproportionately to those who develop.

Regarding calibration of the scales, POSSUM overestimated mortality in general and in all subgroups, while P-POSSUM and O-POSSUM underestimated. The P-POSSUM presented the best O: E ratio overall, with 1.41, which is higher than the values described in the literature (0.5 - 0.91) [5,7,16]. POSSUM predicted mortality about 2.5 times higher than the observed one and a 2-fold morbidity, which makes the ratio O: E 0.4 and O: E 0.496, respectively. These are relatively similar to others described in the literature with O: E of 0.34 for mortality [16] and O: E of 0.5 for morbidity [7]. The O-POSSUM scale underestimated the overall mortality by 10%, with an O: E ratio of 9.59, much higher than that described, ranging from 0.6 - 1.26 [5,16,21,22].

The discriminative capacity of the scales and scores was evaluated through the ROC curve and the respective AUC, and only the operative score showed significance in mortality, with an AUC of 0.763 ($p = 0.019$), which had a discriminative capacity considered reasonable, concordant with Nagablushan., *et al*. (2007) [5], where P-POSSUM and O-POSSUM failed to discriminate patients, however, contradictory to other studies in which O-POSSUM was the most discriminating [16,17].

In the morbidity, the POSSUM scale and physiological and operative scores failed to discriminate patients with or without morbidity, and the literature states that the POSSUM scale is a reasonable predictor of morbidity [16].

There are several published studies on the best scale for predicting the risk of morbidity and mortality in individuals undergoing gastrectomy, although these are also ambiguous, where some demonstrate the feasibility of a scale and others do not [16,17,22]. In this study, in relation to mortality, the P-POSSUM scale presented a better calibration, followed by the POSSUM scale. O-POSSUM underestimated the

expected mortality. Nevertheless, none of these scales presented a significant discriminative capacity, the only one that reached significance was the operative score, but only with a reasonable discrimination [5].

Mortality, although more frequent than mortality, was overestimated by the POSSUM scale, especially in those with high risk (greater than 60%), which agrees with the study by Bernardo., *et al*. (2016) in which the results were similar [7]. This scale, as well as the operative and physiological score, did not discriminate patients with and without complications. Thus, since POSSUM was created for several types of surgery, it entails complications that are often neglected in the case of gastric surgery. In this sense, the morbidity equation should be revised to fit this type of major intervention [7,16,23].

In the long term, the POSSUM scale ($p = 0.049$) and the operative score ($p = 0.025$) were predictors of survival, with patients who scored below 11.9% and 12 points, respectively, presenting different survival rates ($p = 0.011$ and $p = 0.03$, in this order) of those with values greater or equal to those mentioned above. The fact that the operative score, together with POSSUM (which may be justified by the operative score having more impact in its equation for mortality), enhances the importance of surgery in the general prognosis of the patient. Some studies have demonstrated the importance of the physiological score in long-term survival, but not in the operative score [24].

In this study, O-POSSUM was the one that obtained worse results, which can be partly explained by the differential evaluation that this scale does of the operative parameters. The POSSUM and P-POSSUM scales use 6 parameters instead of O-POSSUM which only accesses three. Assuming the importance that the operative score had in this population, this difference of evaluation can be a contribution to a worse performance of this scale.

Limitation of the Study

This study has several limitations. Primarily, because it is a retrospective study, the collection of data specific to the physiological state and the intraoperative course was conditioned. Another factor that is not negligible and intrinsic to the different scales is that they do not take into account the surgical type performed, that is, they do not include the extent of lymphadenectomy, nor the type of anastomosis performed. In addition, the physiological score fails to, for example, take into account the recent history of acute myocardial infarction or the nutritional status of the patient.

Conclusion

Several scales were developed with the aim of predicting surgical risk in patient's submitted to surgery for GC but in the present there isn´t yet one that answers this need accurately.

In mortality, P-POSSUM was the one that presented better calibration in general and in several subgroups. POSSUM overestimated mortality while O-POSSUM underestimated mortality. Regarding discrimination, only the operative score had discriminative ability, although only reasonable one. Regarding morbidity, the POSSUM scale overestimated the number of complications, especially in the higher risk groups (> 60.0%) and, together with the operative and physiological scores, did not have discriminative capacity. Thus, no risk scale predicted correctly morbidity and mortality in this population; however, P-POSSUM together with operative score appear to play a role in mortality prediction. In the morbidity, no model presented a good acuity; however, the POSSUM model may have some applicability in the categories of lower risk.

Conflict of Interest

The authors declare no financial interest or any conflict of interest.

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