Evaluation of P-POSSUM Risk Scoring System in Prediction of Morbidity and Mortality after Pancreaticoduodenectomy

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Abbreviations:

PD: Pancreaticoduodenectomy;
ERAS: Enhanced Recovery After Surgery;
PVR: Portal Vein Resection;
POPF: Postoperative Pancreatic Fistula;
DGE: Delay Gastric Emptying;
PPH: Postpancreatectomy Hemorrhage;

Rezumat

Evaluarea scorului P-POSSUM în predicția morbidității și a mortalității după duodenopancreatectomia cefalică

Introducere: Societatea ERAS (Enhanced Recovery After Surgery) recomandă folosirea scorurilor POSSUM și P-POSSUM în chirurgia abdominală majoră, pentru estimarea riscului de apariție a complicațiilor și a decesului postoperator.

Material și metodă: Studiul include 113 duodenopancreatectomii cefalice consecutive efectuate într-un singur centru în perioada iulie 2013-decembrie 2015. Datele pacienților au fost introduse prospectiv într-o bază de date și ulterior analizate utilizând R v3.2.4 software. Scorul statusului biologic, scorul operator și scorurile asociate morbidității și mortalității au fost calculate accesând <http://www.riskprediction.org.uk/index-pp.php>.

Rezultate: Rata de apariție a complicațiilor a fost de 61,95%: 19,47% complicații generale, 14,16% supurații de plagă și 28,32% complicații specifice duodenopancreatectomiei cefalice (11,5% fistule pancreatice; 8,85% evacuare gastrică întârziată și 6,19% hemoragii). Comparând morbiditatea și mortalitatea observate cu cele estimate de scorul P-POSSUM, am obținut diferențe statistice semnificative ($p=0,05$ și $p=0,03$). Aceste diferențe nu au mai existat dacă am comparat complicațiile specifice duodenopancreatectomiei cefalice și mortalitatea consecutivă lor, cu cele estimate de scor ($p=0,8$, respectiv $p=0,86$). Aria de sub curbă a avut valori de 0,61 pentru morbiditate, 0,64 pentru morbiditatea specifică operației, respectiv 0,61 pentru mortalitate și 0,68 pentru mortalitatea consecutivă complicațiilor specifice.

Concluzie: P-POSSUM este un instrument util, dar nu suficient, de

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apreciere a riscului de complicații și deces după duodenopancreatectomia cefalică. Rezultate mai bune pot fi obținute dacă analizei i se asociază și factorii de risc specifici intervenției.

Cuvinte cheie: duodenopancreatectomie cefalică, scor P-POSSUM, morbiditate postoperatorie, mortalitate

Abstract

Background: POSSUM and P-POSSUM are risk scores recommended by ERAS Society for the preoperative evaluation of patients undergoing major surgery.

Methods: This study includes 113 consecutive pancreaticoduodenectomy performed in a single centre between July 2013-December 2015. Patients data were prospectively collected using Excel 2009 and retrospectively analysed with R v3.2.4 software. Biological status score, surgical severity score and risk scores for complications and death were calculated using: <http://www.riskprediction.org.uk/index-pp.php>.

Results: Morbidity rate was 61,95%: 19,47% general complications, 14,16% wound infections and 28,32% PD specific complications (11,5% POPF; 8,85% DGE and 6,19% PPH). Comparing the observed and estimated morbidity and mortality, we obtained statistical significant results ($p=0,05$ and $p=0,03$, respectively). When we considered only specific PD complications and subsequent mortality, there was no longer significant difference between observed and estimated values ($p=0,8$ and $p=0,86$). The under ROC curve area was 0,61 for morbidity and 0,64 for specific PD morbidity, respectively 0,61 for mortality and 0,68 for specific PD complications related mortality.

Conclusion: P-POSSUM represents a useful tool for appreciating the complication and death risk after PD, but better results could be obtained by considering also specific PD risk factors.

Key words: cephalic pancreaticoduodenectomy, P-POSSUM score, postoperative morbidity, mortality

Introduction

During preoperative morbidity and mortality evaluation of the patient for a major surgery, risk scores can be used due to their ability to offer numeric or percentage results, which may allow an objective evaluation of risks and a fair discussion with the patient himself or his family. For pancreaticoduodenectomy (PD), we can find several risk scores, proposed by different surgical centres, one of them being P-POSSUM score, recommended by ERAS (Enhanced Recovery After Surgery) Society. Both POSSUM and P-POSSUM are risk prediction tools for complications or postoperative deaths, based on patient biological status and surgical severity scores. Due to some authors observation that POSSUM

overestimates mortality, Whitley (1), using logical regression, modified mortality risk formula, so coming into existence P-POSSUM risk score. For biological status score, both POSSUM and P-POSSUM take into consideration twelve parameters (age, cardiac, respiratory, ECG, systolic BP, pulse rate, haemoglobin, leucocytes, urea, sodium, potassium, Glasgow score) and for surgical severity score, six parameters (operation type, number of procedures, operative blood loss, peritoneal contamination, malignancy status, elective/urgent surgery).

Objectives

The aim of this study is to evaluate the capacity of P-POSSUM risk scores concerning the morbidity and mortality following standard

pancreaticoduodenectomy and pancreaticoduodenectomy associated with portal vein resection (PVR-PD). Validation of the score enables afterwards a preoperative identification of risk patients and prevents the risk of undesirable consequences by both preparing the patient properly before the procedure and a closer postoperative monitoring.

Material and Methods

In this study we included 113 consecutive pancreaticoduodenectomy performed for periampullary malignant tumors in Surgical Clinic no. 3 Cluj Romania, during July 2013-December 2015. Demographic, clinical, imaging and operative data were prospectively collected in a database and retrospectively analysed.

Biological status score, surgical severity score as well as risk scores for complications and death were calculated using online link address: <http://www.riskpredictionorg.uk/index-pp.php>. We considered standard PD as "major operation", but it became a "complex major operation" if portal vein resection was added. Also, to "number of procedures" parameter we fill in: "one" if we performed only the PD, or "two", if PD was preceded by biliary drainage. All surgeries were elective.

For postoperative pancreatic fistula (POPF) we used the International Study Group for Pancreatic Fistula definition (2), including three degrees: A- no clinical impact, just high amylase level in a drainage tube; B- high amylase level in a drainage tube and clinical symptoms, or need for drainage maintenance for more than three weeks, or endoscopic/imagistic drainage of an intra-abdominal collection; C- hemodynamic instability and need for reoperation. Delay gastric emptying (DGE) (3) is the patient incapacity for resuming oral feeding by the 7th postoperative day due to important gastric stasis, imposing prolonged nasogastric tube maintenance. It has also three degrees: A-maintaining the nasogastric tube for more than seven days or reinsertion of the tube after 4th postoperative day, with or without nausea or vomiting or prokinetics; B-maintaining the nasogastric

tube for 8-14 days or reinsertion the tube after postoperative day 7, with vomiting and prokinetics, the patient being unable to eat the first 14 days; C- maintaining the nasogastric tube for more than 14 days or reinsertion of the tube after postoperative day 14, with vomiting and prokinetics, the patient being unable to eat for the first 21 days. For postpancreatectomy hemorrhage (PPH) we used the International Study Group of Pancreatic Surgery definition (4), which recognize three categories: mild, moderate and severe. Mild hemorrhage means a haemoglobin loss under 1,5g/dl, which stops spontaneously, without needing blood transfusion. Moderate hemorrhage refers to a haemoglobin loss between 1,5-3 g/dl, with minor hemodynamic impact, which don't need endoscopic or surgical intervention. A severe bleeding involves a haemoglobin loss more than 3 g/dl, which dictate an endoscopic or surgical approach. We consider as general complications: respiratory (broncho-pulmonary infections or inflammations, pleurisy, respiratory insufficiency), circulatory (cerebrovascular stroke, myocardial ischemia, cardiac failure), hepatic (hepatic failure) or renal ones (acute renal failure).

The data were collected using Excel 2009 and the statistical analysis was done with R v3.2.4 software. Kolomogorov-Smirnov test was the first step in analysis. For continuous data we used T-tests and the results were reported as median± standard deviation. For nominal data we used chi-square test and the results were presented as frequencies. The $p < 0,05$ values were considered statistically significant.

Results

This study involved 113 patients, including 64 males (56,64%) and 49 females (43,36%), age between 22-81 (median of 64).

Morbidity rate was 61,95%: 19,47% general complications, 14,16% wound infections and 28,32% PD specific complications. Pancreatic fistula had a 11,5% incidence (two cases grad A, four cases grad B and seven cases grad C).

Table 1. Complications following pancreaticoduodenectomy

Type	PD	PVR-PD
POPF	11/103 (9,73%)	2/10 (20%)
Biliary fistula	1/103 (0,97%)	0/10
Digestive fistula	1/103 (0,97%)	0/10
Pancreatic stump hemorrhage	6/103 (5,82%)	0/10
Intraabdominal hemorrhage	1/103 (0,97%)	0/10
DGE	8/103 (7,77%)	2/10 (20%)
General complications	19/103 (18,45%)	3/10 (30%)
Total	47/103 (45,63%)	7/10 (70%)
Mortality	6/103 (5,83%)	2/10 (20%)

Delay gastric emptying, without following a fistula, appeared in ten patients (8,85%), none needing relaparotomy. Postpancreatectomy hemorrhage was manifested in seven patients (6,19%) (six with upper digestive hemorrhage from intragastric pancreatic stump and one with intraperitoneal hemorrhage), relaparotomy being mandatory for two patients with upper digestive hemorrhage and for the patient with intraperitoneal hemorrhage. There was one external biliary fistula which spontaneously healed and one gastro-jejunal anastomotic fistula, which needed relaparotomy. *Table 1* include patients complications.

Totally, there were eleven relaparotomies (9,7%), three deaths (2,65%) following general complications and five deaths (4,24%) following specific PD complications (five pancreatic fistulas, one pancreatic stump hemorrhage and one intraperitoneal hemorrhage).

It should be noticed that the more frequent rate of pancreatic fistula and gastric stasis occur in portal vein resection group, without being able to achieve statistical significance, due to the reduced number of cases.

Both biological status and surgical severity scores, and morbidity and mortality risk scores for the all the patients can be found in *Table 2*.

There is no statistical difference between patients with standard PD and those with portal resection PD regarding biological status score. Also, adding portal vein resection to standard PD did not increased the estimated risk for complications (31,7% versus 40%, $p=0,75$). Instead, having more cases with

Table 2. P-POSSUM values

	PD	PVR-PD	p
Biological status score	19,15±4,98	17±4,52	0,97
Surgical severity score	15,5±4,23	27,3±2,63	0,03
Morbidity	31,7	40	0,75
Mortality	4,53	16,4	0,002

Table 3. Validation of P-POSSUM score considering all complications

	PD (103)	PVR-PD (10)	TOTAL (113)
O Morb/E Morb	1,44	1,75	1,66
O Mort/E Mort	1,29	1,22	0,69

O Morb=observed morbidity; E Morb=estimated morbidity;
O Mort=observed mortality; E Mort=estimated mortality

Table 4. Validation of P-POSSUM score considering PD specific complications

	PD (103)	PVR-PD (10)	TOTAL (113)
O Morb/E Morb	0,86	1,0	0,89
O Mort/E Mort	0,86	0,61	0,72

O Morb=observed morbidity; E Morb=estimated morbidity;
O Mort=observed mortality; E Mort=estimated mortality

intraoperative of over 500 ml blood loss cases and due to superior score granted to portal vein resection PD, we obtained significant increase of operative score (from $15,5 \pm 4,23$ to $27,3 \pm 2,63$, $p=0,03$), with mortality increased 3,5 times.

In order to determine the value of P-POSSUM score in evaluating postoperative complications and death, we compared the observed values for morbidity and mortality with the estimated ones. The results of this comparison can be found in *Table 3* and *Table 4*.

First, we noticed that the predictive power of P-POSSUM score was higher in PD specific complications and subsequent mortality compared to the whole morbidity and mortality rates.

When to specific complications, wound infections and general complications occur, the score underestimates risk. If we take into consideration only PD specific complications, P-POSSUM overestimates it.

Comparing the observed morbidity and estimated morbidity, we obtained statistical significant results (61,95% versus 37,2%;

$p=0,03$). The same situation appeared when evaluating the observed mortality and estimated mortality (7,08% versus 12,9%; $p=0,05$).

However, when we considered only specific PD complications and subsequent mortality, there was no longer significant difference between observed and estimated values (28,32% versus 33,1%; $p=0,8$ for morbidity and 4,24% versus 5,6%; $p=0,86$ for mortality).

To validate or invalidate P-POSSUM score in assessing risk after PD, we used ROC curves. The results showed that under ROC curve area was 0,61 for morbidity and 0,64 for specific PD morbidity, respectively 0,61 for mortality and 0,68 for specific PD complications related mortality.

We tried to find a cut-off, a point from which the test accomplished good predictive value and we chose the biological status score of 18. For morbidity, the results were: sensibility 0.65 [CI95% (0.562, 0.735)] and specificity 0.5 [CI95% (0.388, 0.606)], under ROC curve area being 0,63. For PD specific morbidity, sensibility was 0.733 [CI95% (0.611, 0.837)], specificity was 0.515 [CI95% (0.434, 0.583)] and under ROC curve area was 0,7.

Discussions

P-POSSUM score involves parameters regarding biological status of the patient and intraoperative aspects. Of those, only few were unanimously recognised as risk factors for pancreaticoduodenectomy complications: anaemia, leucocytosis and intraoperative blood loss. But, the P-POSSUM does not consider some well-established risk factors, as pancreatic texture, Wirsung diameter, pancreatic stump anastomosis, surgical expertise. An important fact regarding PD is that despite significant decreasing of mortality rates in pancreatic tertiary centres (under 5%) (5, 6, 7), morbidity remains high and constant, being considered one of the most important postoperative care indicators (8).

Our first result indicates a significantly difference between surgical severity scores ($p=0,03$) and mortality scores ($p=0,002$) between patients with portal vein resection PD and those with standard PD. The difference is due to more

cases with blood loss over 500 ml in portal vein resection PD group and a superior score granted for a "complex major operation", as venous resection PD was classified. The result, "ad litteram" seen, indicates that the venous resection is a risky moment. Actually, in all cases, the vein resections were tangentially and prepared by the surgeon, without significant blood loss. Confronting those data, we decided, further on, to evaluate the score including all patients in one group, trying to avoid errors. Same kind of errors were reported by Tamijmarane (9), who recommends that standard PD and portal vein resection PD to be consider either "major operation" or "complex major operation".

Ratio between observed and estimated morbidity was 1,66, meaning that the score underestimates morbidity risk. However, an important percentage, over 50%, was represented by wound infections and temporary organ failure immediately after surgery. Excluding those, the ratio became subunitary and close to 1 (0,89).

The fact that P-POSSUM is more valuable in predicting specific complications after PD is also indicated by the significant difference between observed and estimated morbidity when all complications are considered ($p=0,03$), difference which is no longer statistically significant when only specific complications are analysed ($p=0,8$).

Regarding mortality, P-POSSUM overestimates death risk both when all complications were analysed (0,69) and when only specific ones were evaluated (0,72).

For assessing P-POSSUM efficiency in estimating morbidity and mortality risks, we calculate under ROC curve area. For morbidity and PD specific morbidity, the area was 0,61 and 0,64, respectively. For mortality and PD specific complications related mortality, the under ROC curve area was 0,61 and 0,68, respectively. These results may be interpreted as "fair", which indicates that the P-POSSUM score may be used as prediction tool for PD morbidity and mortality, but not alone.

We tried to determine some conditions which, once obtained, are capable to offer

valuable results for risk prediction. We chose biological status score, the less liable to bias, due to the fact that, from all twelve parameters involved in this score formula, only one, meaning "ECG" is subjective (10). From 18 upwards of the biological status score value, under ROC curve area is 0,63 for all complications and 0,7, meaning "good", for PD specific morbidity.

Reviewing the literature, after the first studies enthusiasm (11, 12), beginning with 2013 there are publications whose authors are more reserved, admitting though that P-POSSUM can be used, but in addition to the recognised PD risk factors (13, 14, 15) and some more studies with larger study on patients are needed (9, 16).

Conclusions

P-POSSUM represents a useful tool, but not complete, for appreciating the complication risk or death risk after PD. The importance of the information P-POSSUM gives may become relevant whether it takes into consideration a larger number of patients, cut-offs that provide sensibility, specificity and graphic connection between them (under ROC curve area) become statistically significant. The cut-off should include the least subjective score, namely the biological status score. Early prediction of some specific risk factors for the patient scheduled for a PD may be more valuable information.

Conflict of Interest: none declared.

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