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Validation of the Estimation of Physiologic Ability and Surgical Stress (E-PASS) Score in Liver Surgery

Vanessa M. Banz · Peter Studer · Daniel Inderbitzin · Daniel Candinas

Abstract

Background The estimation of physiologic ability and surgical stress (E-PASS) has been used to produce a numerical estimate of expected mortality and morbidity after elective gastrointestinal surgery. The aim of this study was to validate E-PASS in a selected cohort of patients requiring liver resections (LR).

Methods In this retrospective study, E-PASS predictor equations for morbidity and mortality were applied to the prospective data from 243 patients requiring LR. The observed rates were compared with predicted rates using Fisher's exact test. The discriminative capability of E-PASS was evaluated using receiver-operating characteristic (ROC) curve analysis.

Results The observed and predicted overall mortality rates were both 3.3% and the morbidity rates were 31.3 and 26.9%, respectively. There was a significant difference in the comprehensive risk scores for deceased and surviving patients ($p = 0.043$). However, the scores for patients with or without complications were not significantly different ($p = 0.120$). Subsequent ROC curve analysis revealed a poor predictive accuracy for morbidity.

Conclusions The E-PASS score seems to effectively predict mortality in this specific group of patients but is a poor predictor of complications. A new modified logistic regression might be required for LR in order to better predict the postoperative outcome.

V. M. Banz · P. Studer · D. Inderbitzin · D. Candinas (✉)
Department of Visceral Surgery and Medicine, Inselspital, Bern University Hospital and University of Bern, CH-3010 Bern, Switzerland
e-mail: daniel.candinas@insel.ch

V. M. Banz
e-mail: vanessa.banz@gmx.ch

Introduction

The quality of medical care is being increasingly judged by hard facts and parameters that can be measured and compared, including the length of hospital stay, in-hospital mortality and morbidity, and the costs generated [1, 2]. If potential postoperative problems can be predicted in patient subgroups based on pre- and intraoperative measures, adequate preemptive steps can be taken to avoid these complications. Mortality and morbidity are, if well defined, readily measurable and objective parameters for monitoring the standard of care within a center while equally allowing for comparisons between different centers.

The estimation of physiologic ability and surgical stress (E-PASS) score was initially developed to predict adverse postoperative effects in a study population of approximately 300 patients requiring elective gastrointestinal surgery, ranging from laparoscopic cholecystectomy to transthoracic esophagectomy [3]. Based on their E-PASS score, patients are categorized into five groups, which then allows for risk stratification of the expected morbidity and mortality. The E-PASS score has already been validated and shown to be reproducible by other authors, not only for gastrointestinal surgery, but also for the elective repair of abdominal aortic aneurysms, thoracic surgery, and osteosynthesis for hip fractures [4–7]. A possible advantage of the E-PASS scoring system includes better overall assessment that not only permits the evaluation of a patient's preoperative reserve capacities, but also allows for a concise judgment of the surgical stress applied. Ideally, the surgeon can make a rough preoperative estimate of how much "surgical stress" the patient can tolerate in order to obtain a low E-PASS score, which is associated with a low expected morbidity and mortality.

The aim of the current study was to review whether the E-PASS scoring system could be used, without restrictions, in hepatic surgery as a means of correctly predicting morbidity and mortality.

Materials and methods

We carried out a retrospective analysis of prospective data collected between January 2002 and December 2006 and entered into a computer database system. All patients requiring hepatic resection for benign or malignant conditions treated in our unit were included for analysis. Exclusion criteria included patients who were initially seen for major hepatic surgery but only received liver biopsies due to disseminated, inoperable disease. All patients requiring emergency hepatic surgery were also excluded from further analysis; they may already have met, to an extent, the criteria for systemic inflammatory response syndrome (SIRS) [8], possibly confounding the E-PASS scores. The exclusion of patients requiring emergency surgery was in accordance with the initial guidelines developed by Haga et al. [3]. During the defined study period, a total of 243 patients were included for E-PASS analysis.

Postoperative complications were defined as all problems requiring medical, surgical, or other intervention and treatment [9–11]. Documented general and liver-specific complications included superficial infections in the form of erythema or discharge requiring opening of the wound or antibiotic therapy; deep infections in the form of intra-abdominal collections or an abscess confirmed radiologically or at laparotomy; pulmonary embolus or thrombosis confirmed radiologically by computed tomography or duplex sonography; pneumonia determined by typical clinical presentation, auscultatory findings, or positive chest X-ray; delayed gastric emptying requiring the placement of a nasogastric tube and intravenous fluids for more than 1 week with delayed patient discharge and hemorrhage or hematoma seen as a distinct drop in hemoglobin values confirmed clinically, radiologically, or at laparotomy; biliomas in the form of intra-abdominal fluid collection with clearly elevated bilirubin values requiring percutaneous drainage or surgical intervention.

Classification using the criteria of the American Society of Anesthesiologists (ASA) was carried out by the attending anesthetist in charge prior to surgery. The operation time was defined as the time from the first skin incision to complete closure of all wounds. The E-PASS scoring system was used retrospectively with the computer database and supplemented by the patients' medical files if necessary, according to the defined criteria [3]. The comprehensive risk score (CRS) was calculated using the E-PASS equations and includes the calculation of the preoperative risk score (PRS) and the surgical stress score (SSS) (Table 1). Patients were divided into one of five groups [12] according to their final CRS: Group 1, CRS <0; Group 2, 0 to <0.5; Group 3, 0.5 to <1.0; Group 4,

Table 1 Equations for calculating the E-PASS score [12]

Preoperative Risk Score (PRS)

$-0.0686 + 0.00345X_1 + 0.323X_2 + 0.205X_3 + 0.153X_4 + 0.148X_5 + 0.0666X_6$

X_1 = age

X_2 = presence (1) or absence (0) of severe heart disease[a]

X_3 = presence (1) or absence (0) of severe pulmonary disease[b]

X_4 = presence (1) or absence (0) of diabetes mellitus[c]

X_5 = performance status index (range = 0–4)[d]

X_6 = American Society of Anesthesiologists (ASA) classification (1-5)

Surgical Stress Score (SSS)

$-0.342 + 0.0139X_1 + 0.0392X_2 + 0.352X_3$

X_1 = blood loss (ml)/body weight (kg)

X_2 = operation time (h)

X_3 = extent of skin incision; laparotomy plus thoracotomy (2), laparotomy (1), laparoscopy (0)

Comprehensive Risk Score (CRS)

$-0.328 + 0.936(\text{PRS}) + 0.976(\text{SSS})$

[a] Severe heart disease as defined by the New York Heart Association Class III and IV or severe arrhythmia requiring mechanical support

[b] Severe pulmonary disease as defined by a vital capacity less than 60% and/or a forced expiratory volume of less than 50%

[c] Diabetes mellitus as defined by the World Health Organization criteria

[d] Performance status index as defined by the Eastern Cooperative Oncology Group (ECOG) criteria

1.0 to <1.5; and Group 5, ≥1.5. Patients in Group 1 all have a CRS value below zero, i.e., only negative CRS numbers are included. Patients in Group 1 have the lowest risk of postoperative complications or death, whereas patients in Group 5 have the highest risk. Hospital mortality was defined as death during the same admission as the operation.

To avoid possible errors of observer-specific mistakes, all data were independently checked and compared by two staff members of our unit.

Statistical analysis

All variables were analyzed descriptively by the Fisher's exact test or Wilcoxon rank sum test; the Mann-Whitney U test was used to examine differences in CRS distribution of patients with and without complications. The same test was applied for the mortality group. Multivariate analysis was performed using the multiple logistic regression model. The ROC curves were plotted to assess the extent to which CRS, PRS, and SSS can accurately predict complications, where morbidity and mortality are combined, and the area under the curve (AUC) was used as a measure of overall diagnostic accuracy. A two-sided exact binomial test was used to compare CRS group-specific effective morbidity with expected morbidity. A *p* value of less than 0.05 was taken to be significant. Statistical calculations were carried out using R version 2.5 and SAS version 9.1 software. All statistical analyses were done with professional help from the Institute of Mathematical Statistics and Actuarial Science, University of Bern, Bern, Switzerland.

Results

Six of the initial 249 patients (2.4%) had to be excluded from analysis because they either had incomplete data or met SIRS criteria prior to surgery This resulted in a total of 243 patients receiving hepatic resections in our department who were analyzed. Patient demographics and admission data are summarized in Table 2. Table 3 lists the operative procedures performed. One hundred eighty-eight (77.4%) patients were operated on for malignant disease, with one third requiring hepatic resection for colorectal liver metastases (Table 4). Only a small percentage of our patients underwent surgery for hepatocellular carcinoma, with 21 patients (8.6%) of the total study population suffering from cirrhosis.

Both the observed and predicted overall mortality rates were 3.3% (8 and 8.03 patients, respectively); the observed and predicted overall morbidity rates were 31.3% (76 patients) and 26.9% (65.4 patients), respectively. Overall group-specific (Groups 1-5) predictive correlation was good with a correlation coefficient of 0.96. Complications were observed in 76 patients (Table 5) of which 10 (13.2%) required operative intervention, including four abdominal lavages for biliomas and one for an abscess, one revision for a biliary-cutaneous fistula and one for a hematoma, one redo hepaticojejunostomy for persistent biliary leakage, one closure of a small duodenal perforation, and one ileostomy for a colonic anastomotic leakage in a patient who had received a combined liver and colon segment resection. Of the eight deceased patients, five died of multiple-organ failure, one of postoperative liver failure, and two of acute cardiac failure.

Table 6 summarizes the mean CRS, PRS, and SSS values for the study population, specifically comparing those with and without mortality or morbidity. Expected

Table 2 Demographics of the 243 patients included in the E-PASS study

Variable	*N* (243)
Median age (range) (years)	61 (19-82)
Sex ratio (M:F)	131:112
ASA classification (I:II:III)	14:115:114
Mean (range) BMI (kg/m^2)	24 (16.8-40.6)
Severe heart disease (%)[a]	32 (13.2)
Severe pulmonary disease (%)[b]	31 (12.8)
Diabetes mellitus (%)[c]	29 (11.9)
Observed hospital morbidity (%)	76 (31.3)
Observed hospital mortality (%)	8 (3.3)
Observed 30-day mortality (%)	6 (2.5)

ASA American Society of Anesthesiologists; *BMI* body mass index

[a] Severe heart disease as defined by the New York Heart Association Class III and IV or severe arrhythmia requiring mechanical support

[b] Severe pulmonary disease as defined by a vital capacity less than 60%

[c] Diabetes mellitus as defined by the World Health Organisation criteria

Table 3 Extent of liver resection in 243 patients

Type of hepatic resection	*N* (%)
Hemihepatectomy left	17 (7)
Extended hemihepatectomy left	13 (5.4)
Hemihepatectomy right	62 (25.5)
Extended hemihepatectomy right	18 (7.4)
Atypical segment[a] resection (≥1)	23 (9.5)
Typical segment[a] resection (≥1)	106 (43.6)
Laparoscopic resection	4 (1.6)
≥2 segments[a]	185 (76)
<2 segments[a]	58 (24)

[a] Liver segments are based on Couinaud's classification

Table 4 Indications for hepatic resection

Underlying liver pathologies	$N = 243$ (%)	Patients with cirrhosis (Child score)
Colorectal liver metastases	78 (32.1)	1 (Child A)
Other liver metastases	40 (16.5)	0
Benign liver tumors	38 (15.6)	0
Cholangiocarcinoma	34 (14.0)	1 (Child A)
Hepatocellular carcinoma	24 (9.9)	19 (13 Child A, 6 Child B)
Echinococcal cysts	17 (7.0)	0
Other primary malignant tumors	12 (4.9)	0

Table 5 Postoperative complications requiring medical, surgical, or other intervention

Type of complication	N (%)[a]
Bilioma/ascites	36 (14.8)
Superficial infection	16 (6.6)
Pneumonia	11 (4.5)
Deep infection	10 (4.1)
Pulmonary embolus	8 (3.3)
Hemorrhage	7 (2.9)
Delayed gastric emptying	5 (2.1)
Deep vein thrombosis	2 (0.8)
Other (including myocardial infarction, percutaneous bile fistula, duodenal perforation, leakage of colon anastomosis, urosepsis, and portal vein thrombosis)	6 (2.5)
Number of complications	101
Number of patients with complications	76 (31.3)
Complications requiring operative intervention	10 (13.2)

[a] Out of a total 243 patients

morbidity (or mortality) was calculated by examining each of the five possible CRS groups individually and multiplying the number of patients in each group (as observed in this patient population) by the percentage probability of a complication (or death) occurring according to the values given by Haga's study population [12].

As might be expected, deceased patients had a significantly higher CRS than surviving patients ($p = 0.043$). The CRS revealed no significant difference between the rounded expected and observed in-hospital mortality ($p = 0.804$), indicating that it might effectively predict the outcome. However, there was no significant difference in the CRS of patients with or without morbidity ($p = 0.120$). The lack of power of CRS for predicting postoperative complications is also demonstrated by the low AUC (0.574) (Fig. 1a). Similar results were obtained by a separate analysis of PRS and SSS (Fig. 1b and c, AUC = 0.521 and 0.571, respectively).

When comparing the group distribution of our 243 patients to that of the 5215 patients in Haga's study population [12], our study population exhibits a highly significant right shift ($p < 0.001$), with more patients belonging to a higher CRS group (Fig. 2). If group-specific morbidity is evaluated, comparing actual, i.e., observed, morbidity with expected morbidity (Table 7), we found that significantly more patients in Group 2 (CRS 0 to <0.5) have complications than would be expected ($p = 0.001$). No other group had significant differences in observed and expected morbidity.

Table 6 Summary of preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS) for liver resection patients

Score	Group	N	Mean (SD)	p value*
PRS	All patients	243	0.44 (0.20)	
	Mortality			
	Yes	8	0.54 (0.21)	0.150
	No	235	0.44 (0.20)	
	Morbidity			
	Yes	76	0.44 (0.21)	0.866
	No	158	0.44 (0.20)	
SSS	All patients	243	0.37 (0.29)	
	Mortality			
	Yes	8	0.50 (0.38)	0.477
	No	235	0.36 (0.29)	
	Morbidity			
	Yes	76	0.42 (0.36)	0.090
	No	158	0.34 (0.24)	
CRS	All patients	243	0.44 (0.34)	
	Mortality			
	Yes	8	0.67 (0.45)	0.043
	No	235	0.44 (0.34)	
	Morbidity			
	Yes	76	0.50 (0.38)	0.120
	No	158	0.41 (0.31)	

* p values were calculated using the Wilcoxon signed-rank test. Deceased patients were excluded from morbidity analysis. $p < 0.05$ was considered significant

To determine whether the PRS or SSS plays a more important predictive role, we performed a multiple logistic regression analysis with postoperative complications as the dependent variable and PRS, SSS, and their interaction as independent variables. Since the interaction term was not significantly different from zero ($p = 0.321$), we estimated

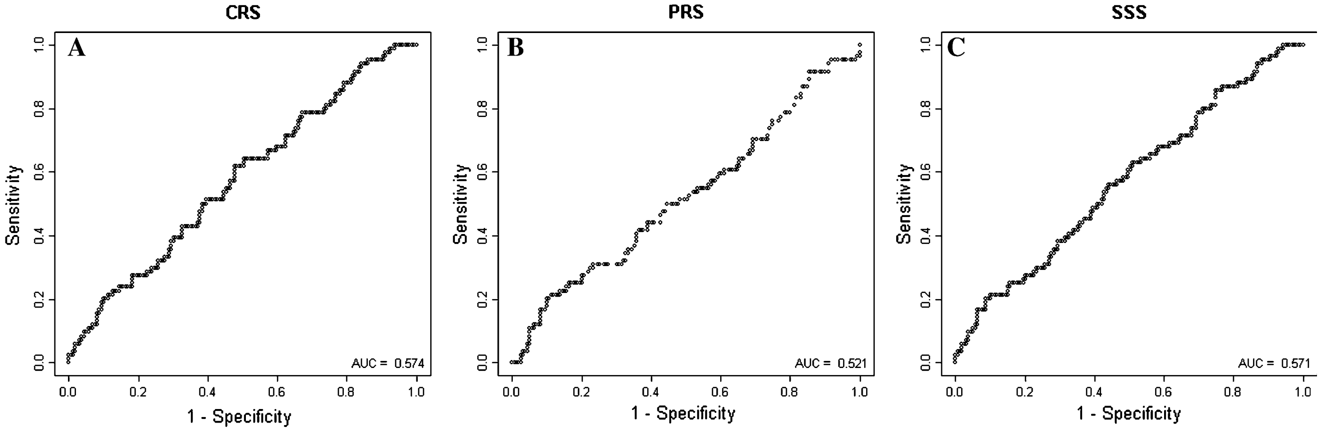
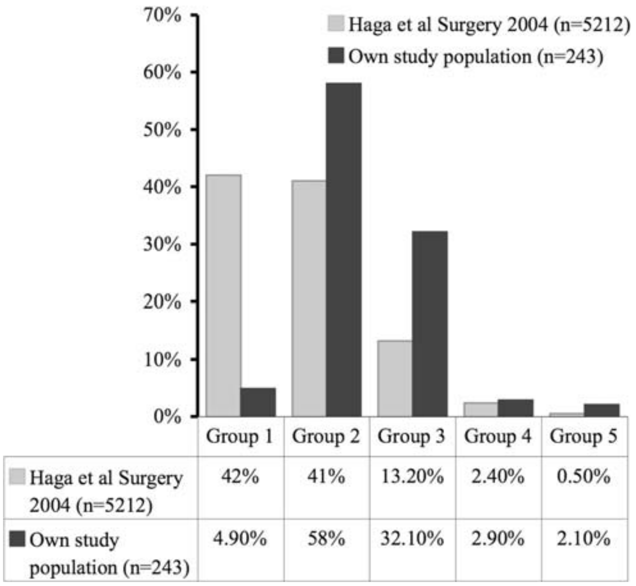


Fig. 1 Empirical receiver operating characteristic (ROC) curves to assess the extent to which the comprehensive risk score (CRS), preoperative risk score (PRS), and surgical stress score (SSS) can accurately predict postoperative complications. The area under the curve (AUC) is used as a measure of overall diagnostic accuracy. **a** CRS does not accurately predict morbidity with a low AUC of 0.574. **b** The AUC is very low (0.521), indicating that the PRS is poor in predicting morbidity. **c** The AUC is 0.571, a low value, indicating the poor predictive power of the SSS as far as morbidity is concerned



	Group 1	Group 2	Group 3	Group 4	Group 5
▨ Haga et al Surgery 2004 (n=5212)	42%	41%	13.20%	2.40%	0.50%
■ Own study population (n=243)	4.90%	58%	32.10%	2.90%	2.10%

Fig. 2 The 243 patients from the current study compared to the study population of 5212 patients from Haga et al. [12]. Our study population shows a right-shift with significantly more patients in higher CRS groups ($p < 0.001$), indicating that our population consisted of more high-risk patients. Group 1, CRS <0.0; Group 2, CRS 0.0 to <0.5; Group 3, 0.5 to <1.0; Group 4, 1.0 to <1.5; Group 5, >1.5. Note that <0.0 includes all CRS values below zero, i.e., negative numbers only

a logistic regression model without interaction. In this model, the PRS was not significantly different from zero ($p = 0.578$); however, the SSS was a significant variable ($p = 0.022$). In a third step, we used a model with SSS as the only independent variable and it was still significant ($p = 0.021$). Therefore, in the context of liver surgery, the SSS plays a more important predictive role than the PRS.

Comparing the PRS and SSS of patients with or without complications revealed no overall significant difference ($p = 0.866$ and 0.090, respectively), but group-specific comparisons showed a lack of fit for Groups 1, 2, and 4.

Discussion

This is the first time the E-PASS scoring system has been applied to a specific hepatobiliary surgical patient population. In our institution, the E-PASS system fails to correctly predict patient outcome with respect to morbidity, as demonstrated by the low AUC. If one breaks down the E-PASS scoring system into the two separate contributors, namely, the PRS and the SSS, the predictive strength of either one is poor.

If mortality is looked at by itself, the CRS does seem to correlate with the risk of death ($p = 0.043$). However, these results need to be interpreted with caution because the mortality rate corresponds to only eight patients, resulting in a very small group for analysis. However, we can show that the SSS seems to bear more weight than the PRS. This would imply that surgical stress needs to be kept to a minimum rather than exempting patients from further surgery based solely on their preoperative status or PRS. The authors of an initial E-PASS study also argued that the SSS is potentially better correlated with postoperative complications than the PRS, although this tended to be the case only in younger patients [3].

With a postoperative morbidity rate of 31.3% and an in-hospital mortality rate of 3.3%, our institution lies within the accepted range of complications after hepatic resections [13–15]. However, the risk of postoperative morbidity was

Table 7 Group-specific comparisons of expected and observed morbidity by comprehensive risk score (CRS)

CRS group	Number of patients	Expected morbidity[a] (%)	Expected morbidity (*n*)	Effective morbidity (*n*)	*p**
1 (<0)	12	4.5	1	1	0.425
2 (0 to <0.5)	138	20.4	28	44	0.001
3 (0.5 to <1.0)	75	40.2	30	27	0.482
4 (1.0 to <1.5)	6	66.7	4	2	0.100
5 (≥1.5)	4	64.0	3	2	0.623

n = rounded patient numbers

[a] The expected morbidity was calculated by multiplying the effective patient number per CRS group by the expected percentage of morbidity previously defined

* *p* values were calculated using a two-sided exact binomial test. Deceased patients were excluded from morbidity analysis [12]. $p < 0.05$ was taken as significant

underestimated with the E-PASS scoring system, particularly for the CRS subgroup analysis. The 44 patients (31.9%) with a CRS of zero to less than 0.5 had more complications than would have been expected based on the predicted rate (i.e., 28 patients, 20.4%).

It is evident that the risk of postoperative complications or death is not solely determined by the surgeon's technical skills and his or her manual ability, but also by the patient's physiologic status, the underlying disease necessitating the surgical intervention, and perioperative care [16]. It is the combination of these factors that overtly influences the final outcome. The difficulty lies in trying to determine which patient tolerates which degree of surgical intervention. In the future, this could influence the extent of surgery and the selection of less invasive methods, especially for patients with a high expected CRS (>1.0), who may be at a greater risk for developing multiple-organ failure [17]. Although a surgeon's instinct is important, obtaining reproducible measures using a preoperative estimate of the expected CRS, based on the calculated PRS and the estimated range of SSS, will allow surgeons to more accurately inform their patients of the potential risks prior to surgery. This estimated preoperative SSS has to be based on personal experience and the average scores obtained from previous similar interventions.

Haga et al. [3] based their initial findings on a very heterogeneous group of patients, of which only a small number (7.5%) underwent LR. Further studies validating E-PASS either did not include hepatic surgery [4] or, again, included only a small percentage of patients with LR [12]. We base our findings on a subgroup that underwent only hepatic resection, with only very few selected patients undergoing additional visceral resection. These two patient populations were characterized by a significantly different CRS distribution ($p < 0.001$), with more of our patients belonging to the higher CRS groups.

To minimize postoperative complications, many specialized liver centers currently use computerized tomographic (CT) liver volume measurements to help estimate remnant volume and combine these results with the Child-Pugh score to maximize the assessment of preoperative liver function, which itself has been overtly linked to postoperative liver failure and possible death [18, 19]. Other studies looked at a combination of the Child-Pugh score with the indocyanine green retention test and CT volumetry to best predict the short- and long-term outcome after extended LR [20–22]. Although recent findings possibly contradict the long-held belief that postoperative liver failure is the main cause of mortality after major LR, an assessment of preoperative liver function remains the gold standard for patients requiring extensive surgery or for those with varying degrees of cirrhotic liver parenchyma [23]. One might argue that in this setting, the E-PASS model does not take into account the complexity and organ-specific problems unique to hepatic surgery. Because our study population included only a very small percentage (8.6%) of patients with cirrhosis, no statistically significant differences were found when comparing the reliability of E-PASS for patients with normal hepatic function to that for patients with reduced hepatic function.

There have been numerous studies to develop audit tools for a variety of surgical specialities, each one trying to accommodate a specific setting [19, 24–30]. The overall advantage of the E-PASS scoring system would seem to be the relative ease with which data are acquired. No special tests are required and intraoperative data collection is limited to a few straightforward measurements. This is favorable to, for example, the POSSUM or P-POSSUM score, which requires 18 different variables compared with the nine variables needed for the E-PASS score, making its use in daily clinical practice tedious and impractical [31, 32].

Other scoring models, such as the acute physiology and chronic health evaluation (APACHE) II score used mainly for patients in intensive care units, take into account only physiologic factors and completely ignore the severity of intraoperative stress. Furthermore, some of these scores, such as the APACHE II score, date back to the mid-1980s and the data obtained from this era may not be applicable to the current standard of care [33]. Despite the relative ease with which the E-PASS score can be used, such a score is valuable only if it allows for the reliable acquisition of prognostic data.

In conclusion, the E-PASS scoring system has many advantages such as simple evaluation steps involving easily accessible data and the incorporation of preoperative measurements with equally important intraoperative measurements. The system has already been validated for use in general gastrointestinal surgery and has exhibited a correlation with expected and observed morbidity and mortality. However, the E-PASS scoring system, within the setting of hepatic surgery, cannot be used in its current form and requires further evaluation and validation, with possible adaptations of the original parameters to better fit the postoperative predictions specific to liver surgery.

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