



島根大学学術情報リポジトリ  
S W A N  
Shimane University Web Archives of kNoledge

Title

Accurate prediction of severe postoperative complications after pancreatic surgery: POSSUM vs E-PASS

Author(s)

Hikota Hayashi, Yasunari Kawabata, Takeshi Nishi, Takashi Kishi, Kosuke Nakamura, Shunsuke Kaji, Yusuke Fujii, Yoshitsugu Tajima

Journal

*Journal of hepato-biliary-pancreatic sciences* Volume 28, No. 2, pp.156-164, 2021

Published

15 October 2020

URL

<https://doi.org/10.1002/jhbp.839>

これは出版社版ではありません。引用時は出版社版をご確認のうえご利用ください。

This is the pre-peer reviewed version of the following article:

<https://onlinelibrary.wiley.com/doi/10.1002/jhbp.839>, which has been published in final form at

<https://doi.org/10.1002/jhbp.839>. This article may be used for non-commercial purposes in

accordance with Wiley Terms and Conditions for Use of Self-Archived Versions.

1 **Original article**

2 **Accurate Prediction of Severe Postoperative Complications after Pancreatic Surgery:**

3 **POSSUM vs E-PASS**

4 **Authors:** Hikota Hayashi, Yasunari Kawabata, Takeshi Nishi, Takashi Kishi, Kosuke Nakamura,

5 Shunsuke Kaji, Yusuke Fujii, Yoshitsugu Tajima

6 **Affiliation:** Department of Digestive and General Surgery, Faculty of Medicine, Shimane

7 University

8 **Corresponding Author:** Hikota Hayashi, MD, Department of Digestive and General Surgery,

9 Faculty of Medicine, Shimane University, 89-1, Enya-cho, Izumo, Shimane 693-8501, Japan

10 Tel: +81-853-20-2232, E-mail: hikota@med.shimane-u.ac.jp

11 **Keywords:** POSSUM, E-PASS, pancreatic surgery, postoperative complication, prediction

12 **Manuscript word count:** 3060 words

13 **Tables count:** 3

14 **Figures count:** 3

15

1 **Abstract**

2 **Background/Purpose:** Few reports have evaluated the differences in the predictive accuracy  
3 between the physiological and operative severity score for the enumeration of mortality and  
4 morbidity (POSSUM) and estimation of physiologic ability and surgical stress (E-PASS) in  
5 pancreatic surgery. Thus, we evaluated the accuracy and similarity of POSSUM and E-PASS for  
6 the prediction of severe postoperative complications (PCs) after pancreatic surgery.

7 **Methods:** We enrolled 343 consecutive patients who underwent pancreatic surgery in our  
8 department between April 2006 and September 2017. The difference in predictive values of  
9 POSSUM and E-PASS for the occurrence of PCs  $\geq$  Clavien-Dindo grade IIIa (PCs-CD $\geq$ IIIa)  
10 was nonparametrically compared. The predictive accuracy and similarity of each tool  
11 was examined using the receiver operating characteristic (ROC) curve and linear regression  
12 analyses.

13 **Results:** Forty-five patients developed PCs-CD $\geq$ IIIa. E-PASS had a significantly higher  
14 predictive value for estimating PCs-CD $\geq$ IIIa occurrence ( $P=0.002$ ) than did POSSUM. The area  
15 under the curve value in ROC analysis was significantly higher in E-PASS than in POSSUM  
16 (0.643 vs 0.543,  $P=0.014$ ), with a weak positive correlation in the predictive value between E-  
17 PASS and POSSUM ( $R^2 = 0.333$ ,  $P<0.001$ ).

- 1 **Conclusion:** E-PASS was useful for predicting severe PCs after pancreatic surgery and had a
- 2 higher accuracy than POSSUM.

## 1 **Abbreviations**

- 2 AUC area under the curve
- 3 CD Clavien-Dindo
- 4 CRS comprehensive risk score
- 5 E-PASS estimation of physiologic ability and surgical stress
- 6 O-score operative score
- 7 PC postoperative complication
- 8 POPF postoperative pancreatic fistula
- 9 POSSUM physiological and operative severity score for the enumeration of mortality and
- 10 morbidity
- 11 PRS preoperative risk score
- 12 P-score physiological score
- 13 ROC receiver operating characteristic
- 14 SSS surgical stress score
- 15

## 1 **Introduction**

2       Despite recent advances in the perioperative management of surgical patients and operative  
3 techniques, there is still a high incidence of postoperative complications (PCs) such as  
4 postoperative pancreatic fistula (POPF) after pancreatic surgery which can lead to life-threatening  
5 complications including intra-abdominal infections, severe sepsis, and massive bleeding. The  
6 most commonly used assessment tools for the prediction of PCs after gastrointestinal surgery are  
7 the physiological and operative severity score for the enumeration of mortality and morbidity  
8 (POSSUM) and estimation of physiologic ability and surgical stress (E-PASS) [1, 2]. POSSUM  
9 was developed in the United Kingdom in 1991 for surgical audit [1]. This scoring system is widely  
10 known as the first prevalent tool to predict PCs and has been utilized in various surgical  
11 subspecialties worldwide. On the other hand, E-PASS was developed in Japan in 1999 for the  
12 prediction of PCs in elective gastrointestinal surgeries including laparoscopic surgeries [2]. Both  
13 tools are useful for predicting the occurrence of PCs after pancreatic surgery [3-11]. However,  
14 only a few studies have directly compared the accuracy between POSSUM and E-PASS in  
15 pancreatic surgery [3].

16       Recent advancements in surgical technologies such as the use of energy devices  
17 intraoperatively has led to the simplification of operative procedures and a reduction of  
18 complications such as intraoperative bleeding [12]. In addition, the emergence of new concepts

1 in pancreatic surgery, such as radical antegrade modular pancreatectomy [13] and the  
2 superior mesenteric artery-first approach [14-16], has contributed to the reduction of PC incidence,  
3 minimization of intraoperative blood loss, and improved prognosis [17-19]. These new  
4 developments in pancreatic surgery have evolved since POSSUM and E-PASS were first  
5 introduced.

6 The Clavien-Dindo (CD) classification, established in 2004, is a simple and feasible  
7 severity classification system for PCs characterized by reflecting the magnitude of required  
8 treatment for PCs [20]. POSSUM classifies PCs as positive or negative, and the score is not  
9 always correlated to the degree of therapeutic method for PCs [1]. On the other hand, E-PASS  
10 classifies PCs according to the degree of required therapeutic method for PCs based on its original  
11 definition [2]. This study aimed to compare the accuracy and similarity of POSSUM and E-PASS  
12 for predicting the occurrence of severe PCs in patients who underwent pancreatic surgery.

13

## 14 **Methods**

### 15 **Patients**

1 A total of 343 consecutive patients who underwent pancreatic surgery under general  
2 anesthesia at our institute, from April 2006 to September 2017, were enrolled in this study. The  
3 baseline demographic and clinical characteristics of the patients are shown in Table 1.

#### 4 **Scoring Systems**

5 Pancreatic surgeries included various types of pancreatic resection, such as  
6 pancreaticoduodenectomy (PD), duodenum-preserving pancreatic head resection, distal  
7 pancreatectomy (DP), laparoscopic enucleation, or longitudinal pancreaticojejunostomy. Data on  
8 PCs after pancreatic surgery were retrospectively collected from the patient records and  
9 graded according to the CD classification. Severe PCs were defined as those with CD grade IIIa  
10 or higher (PCs- $CD \geq IIIa$ ) in this study. The POSSUM scoring system includes 12 physiological  
11 and 6 operative factors that are summed to obtain the physiological score (P-score) and operative  
12 score (O-score), respectively [1]. The P-score includes age (yr), cardiac signs, respiratory history,  
13 systolic blood pressure (mmHg), pulse rate (beats/min), the Glasgow coma score, hemoglobin  
14 (g/dL), white cell count (/mm<sup>3</sup>), plasma urea (nmol/L), plasma sodium (mEq/L), plasma  
15 potassium (mEq/L), and the electrocardiogram score. The O-score includes the operation severity  
16 grade, multiple-procedure score, blood loss (mL), peritoneal soiling, malignancy score, and mode  
17 of surgery according to the level of emergency. The morbidity (R') was calculated to predict PCs  
18 according to the following formula:  $\ln [R'/(1-R')] = -5.91 + 0.16 \times (\text{P-score}) + 0.19 \times (\text{O-score})$ .

1 On the other hand, E-PASS consists of a comprehensive risk score (CRS) that is calculated by  
2 combining the preoperative risk score (PRS) consisting of 6 physiological factors and the surgical  
3 stress score (SSS) consisting of 3 operative factors [2]. The PRS was calculated according to the  
4 following formula:  $PRS = -0.0686 + 0.00345 \times X1 + 0.323 \times X2 + 0.205 \times X3 + 0.153 \times X4 +$   
5  $0.148 \times X5 + 0.0666 \times X6$ , where X1 is age (yr); X2 is the absence (0) or presence (1) of severe  
6 heart disease; X3 is the absence (0) or presence (1) of severe pulmonary disease; X4 is the absence  
7 (0) or presence (1) of diabetes mellitus; X5 is the performance status index (0–4); and X6 is the  
8 American Society of Anesthesiologists (ASA) physiological status classification (1–5).

9 The SSS was calculated according to the following formula:  $SSS = -0.342 + 0.0139 \times X1 +$   
10  $0.0392 \times X2 + 0.352 \times X3$ , where X1 is blood loss/body weight (g/kg); X2 is the operative time (h);  
11 and X3 is the extent of skin incision. Finally, the CRS was calculated using the following formula:  
12  $CRS = -0.328 + 0.936 \times (PRS) + 0.976 \times (SSS)$ .

### 13 **Statistical Analyses**

14 The difference in predictive values for the occurrence of PCs-CD $\geq$ IIIa between POSSUM  
15 and E-PASS was nonparametrically compared using the Wilcoxon rank sum test (Chi-square  
16 approximation). The predictive accuracy of PCs-CD $\geq$ IIIa in each formula was evaluated using  
17 the area under the curve (AUC) of the receiver operating characteristic (ROC) curve analysis. The

1 difference in AUC values was compared using the DeLong test. The impact of surgical procedures,  
2 such as PD, DP, and total pancreatectomy (TP), on the occurrence of PCs-CD $\geq$ IIIa was analyzed  
3 in the same manner. The predictive accuracy of both formulas for predicting POPF of PCs-  
4 CD $\geq$ IIIa (POPF-CD $\geq$ IIIa) was also analyzed. Predictive similarity was examined using a  
5 coefficient of determination:  $R^2$  in linear regression analysis using the  $F$ -test. In addition, the  
6 cutoff values of POSSUM ( $R'$ ) and E-PASS (CRS) for predicting PCs-CD $\geq$ IIIa were determined  
7 using ROC analysis and evaluated using the two-sided Fischer's exact test and logistic regression  
8 analysis. The correlations between the predictive values of POSSUM ( $R'$ ) and E-PASS (CRS)  
9 and the occurrence of PCs-CD $\geq$ IIIa were estimated using the chi-square test in the contingency  
10 table analysis, where the patients were divided into 4 equal groups based on the upper quartile,  
11 the median, and the lower quartile. All statistical analyses were performed using JMP Pro 14.2.0.  
12 (SAS, Cary, NC, USA). A  $P$ -value less than 0.05 was considered statistically significant.

### 13 **Ethical Considerations**

14 This study was conducted according to the Helsinki Declaration and the domestic Ethical  
15 Guidelines for Medical and Health Research Involving Human Subjects in Japan, and it was  
16 approved by the Shimane University Institutional Committee on Ethics (approval study number:  
17 #3490). The requirement of informed consent was waived due to the retrospective nature of the  
18 study.

## 1 Results

2 Forty-five patients (13.1%) developed PCs-CD $\geq$ IIIa after pancreatic surgery (Table 2). The  
3 remaining 298 (86.9%) patients had grade I PCs (65 patients), grade II PCs (49 patients), or no  
4 PC (184 patients). Among 45 patients with PCs-CD $\geq$ IIIa, POPF (20 patients), bile leakage (7  
5 patients), peritoneal abscess (7 patients), intra-abdominal hemorrhage (2 patients), wound  
6 infection (2 patients), ileal obstruction (2 patients), deep vein thrombosis (1 patient), portal vein  
7 thrombosis (1 patient), pneumonia (1 patient), and other complications (2 patients) were observed.

8 In POSSUM, the predictive values for PCs-CD $\geq$ IIIa and PCs-CD<IIIa after pancreatic  
9 surgery were 0.70 and 0.65, respectively, showing no statistical significance ( $P=0.353$ ), whereas  
10 in E-PASS, the predictive values for PCs-CD $\geq$ IIIa and PCs-CD<IIIa were 0.46 and 0.33,  
11 respectively, demonstrating a statistically significant predictive power ( $P=0.002$ ), as shown in  
12 Table 3. The O-score of POSSUM and the SSS of E-PASS, which represent operative factors,  
13 were significantly higher in patients with PCs-CD $\geq$ IIIa than in those with PCs-CD<IIIa: 19.0 vs  
14 17.0 ( $P=0.001$ ) in POSSUM and 0.64 vs 0.46 ( $P<0.001$ ) in E-PASS, respectively. With regard to  
15 the O-score of POSSUM, the total blood loss score and the presence of malignancy score were  
16 significantly higher in patients with PCs-CD $\geq$ IIIa than in those with PCs-CD<IIIa: 4.00 vs 2.00  
17 ( $P=0.003$ ) and 4.00 vs 2.00 ( $P=0.013$ ), respectively. In terms of the SSS of E-PASS, X1 (blood  
18 loss/body weight) and X2 (operation time) were significantly higher in patients with PCs-CD $\geq$ IIIa

1 than in those with PCs-CD<IIIa: 15.69 vs 8.86 ( $P=0.003$ ) and 9.20 vs 8.08 ( $P<0.001$ ), respectively.  
2 On the other hand, the preoperative physiological condition of the patients, namely the P-score of  
3 POSSUM and the PRS of E-PASS, showed no predictive value for the occurrence of severe PCs  
4 after pancreatic surgery.

5 The results of the AUC-ROC curve analysis are shown in Figure 1. The AUC value of E-  
6 PASS in the ROC analysis was 0.643. It was significantly superior to that of POSSUM (0.543,  
7  $P=0.014$ ). The cutoff values for POSSUM ( $R'$ ) and the E-PASS (CRS) were 0.869 and 0.401,  
8 respectively. When using these cutoff values, both POSSUM ( $P=0.034$ ) and E-PASS ( $P=0.002$ )  
9 predicted the occurrence of PCs-CD  $\geq$ IIIa. However, only the cutoff value of the E-PASS (CRS)  
10 was identified as an independent predictor of PCs-CD  $\geq$ IIIa (hazard ratio, 2.498; 95%  
11 confidential intervals, 1.255-4.972;  $P=0.009$ ) in multivariate analysis. The correlation between  
12 the E-PASS (CRS) and the occurrence of PCs-CD  $\geq$ IIIa is demonstrated in Figure 2. The  
13 occurrence of PCs-CD  $\geq$ IIIa gradually increased as the CRS of E-PASS increased ( $P=0.014$ ).  
14 Alternatively, in POSSUM, there was no correlation between  $R'$  and the occurrence of PCs-  
15 CD  $\geq$ IIIa ( $P = 0.497$ ).

16 Twenty patients developed POPF  $\geq$ CD-IIIa. The predictive value of the E-PASS (CRS) for  
17 POPF  $\geq$ CD-IIIa was 0.50 (0.34-0.63) (median, interquartile range) and it was significantly higher  
18 than that of 0.33 (0.19-0.51) for POPF <CD-IIIa ( $P=0.025$ ). While in POSSUM, there was no

1 difference between R' for POPF $\geq$ CD-IIIa (0.72, 0.44-0.88) and POPF<CD-IIIa (0.66, 0.46-0.82)  
2 ( $P=0.414$ ). The AUC values of the E-PASS (CRS) and POSSUM (R') in ROC analysis were  
3 0.650 and 0.554, respectively. However, the superiority of E-PASS over POSSUM in predictive  
4 accuracy for POPF was not confirmed in the DeLong test ( $P=0.120$ ).

5 The predictive accuracy (AUC) of E-PASS and POSSUM for the occurrence of PCs-  
6 CD $\geq$ IIIa in each surgical procedure for pancreatectomy was as follows: 0.639 vs. 0.518  
7 ( $P=0.049$ ) in PD, 0.662 vs. 0.568 ( $P=0.112$ ) in DP, and 1.000 vs. 1.000 ( $P$ : not computable) in  
8 TP, respectively, and E-PASS had a higher predictive accuracy than POSSUM in PD.

9 An analysis of 315 patients who underwent open surgery, excluding 28 cases of  
10 laparoscopic surgery, showed that the AUC values of E-PASS and POSSUM for predicting PCs-  
11 CD $\geq$ IIIa were 0.654 and 0.563 ( $P=0.046$ ), respectively, indicating the superiority of E-PASS in  
12 accuracy.

13 With respect to predictability, there was a weak positive correlation in the predictive value  
14 between POSSUM and E-PASS:  $R^2 = 0.333$  in the linear regression analysis ( $P<0.001$ ), as is  
15 shown in Figure 3.

## 16 Discussion

1           The development of PCs after pancreatic surgery can lead to serious consequences  
2 including prolonged hospital stays, the delay of subsequent treatments, and impaired prognosis  
3 [21-23]. A precise preoperative risk assessment enables surgeons to formulate appropriate  
4 management strategies for individual patients undergoing pancreatic surgery.

5           In this study, severe PCs, defined as those of CD grade IIIa or higher, occurred in 13.1% of  
6 patients who underwent pancreatic surgery, with an overall morbidity rate of 46.4% including CD  
7 grade I or II. These incidence rates of PCs after pancreatic surgery were comparable to those of  
8 recent studies [21-25]. This study revealed that E-PASS was superior to POSSUM in terms of the  
9 predictive power for the occurrence of PCs-CD $\geq$ IIIa. This result was supported by the fact that  
10 the CRS of E-PASS was an independent predictor of PCs-CD  $\geq$ IIIa in multivariate analysis and  
11 that PCs-CD  $\geq$ IIIa can be predicted using the cutoff value of CRS set at 0.401. Furthermore, the  
12 CRS of E-PASS was proportional to the increase in PCs-CD  $\geq$  IIIa. In other words, E-PASS was  
13 superior to POSSUM in accurately predicting severe PCs after pancreatic surgery. These results  
14 can help surgeons decide which of the two tools, POSSUM or E-PASS, should be chosen to  
15 accurately predict clinically important severe PCs after pancreatic surgery using the most popular  
16 CD classification.

17           In the POSSUM scoring system, all physiological and operative components are translated  
18 into several numbers of limited exponential scores, such as 1, 2, 4 and 8, and morbidity, which is

1 the predictive value, is logically discontinuous and has clear minimum and maximum ranges. On  
2 the other hand, the E-PASS system includes some continuous variables without an upper limit,  
3 such as X1 (blood loss/body weight) and X2 (operation time) in the SSS. In this study, both X1  
4 and X2 were strong predictors of severe PCs. Pancreatic surgery is often associated with a longer  
5 operative time and higher intraoperative blood loss compared to other gastrointestinal surgeries.  
6 This may explain why the E-PASS scoring system might be superior to that of POSSUM in terms  
7 of the power and accuracy for predicting severe PCs after pancreatic surgery. Furthermore, PCs  
8 are originally evaluated as positive or negative in POSSUM, and they are not always correlated  
9 with the degree of therapeutic method for PCs. On the other hand, PCs are assessed according to  
10 the requirement for medication or interventional treatment in E-PASS [2]. This inherent  
11 difference in risk-scoring between POSSUM and E-PASS can lead to differences in the accuracy  
12 for predicting severe PCs after pancreatic surgery, and it might be the reason why the predictive  
13 value both in POSSUM and in E-PASS showed only weak similarity in linear regression analysis  
14 in this study.

15 For predicting PCs, POSSUM and E-PASS require 12 and 6 physiological factors,  
16 respectively [1, 2]. When trying to apply these assessment tools to pancreatic surgery,  
17 physiological factors had minimal impact on the prediction of severe PCs in this study. A possible  
18 reason for this is that the present study included only elective pancreatic surgeries and no

1 emergency surgeries. This may have resulted in an unintended patient selection bias, as elective  
2 surgeries were performed for patients who were in a relatively good physical condition and who  
3 were presumed to be able to tolerate invasive pancreatic surgery. It is possible that this bias might  
4 have rendered both the P-score in POSSUM and the PRS in E-PASS incompetent. In contrast, 2  
5 of the 6 operative scores of POSSUM (“operative blood loss score” and “presence of  
6 malignancy”) and 2 of the 3 factors of the SSS in E-PASS (“blood loss/body weight” and  
7 “operation time”) were strongly correlated with the occurrence of severe PCs in this study. In  
8 both cases, these are factors related to the quality of the surgery. In other words, the operative  
9 factors of both POSSUM and E-PASS had a strong impact on the operative outcomes after  
10 pancreatic surgery compared to the physiological factors included in both of these scoring systems.

11 The utility and reliability of a formula based on a regional clinical database might be  
12 influenced by various factors, including the current locoregional or domestic healthcare  
13 environment and individual hospital factors. Both POSSUM and E-PASS appear to have a  
14 limitation in the precise prediction of PCs after surgery because their formulas were originally  
15 established according to a database at a single hospital or at domestically selected middle or large  
16 centers that might be functionally similar or slightly different to each other [1, 2]. This study also  
17 has other limitations worth noting. First, this study used a retrospective single-institution design  
18 employing a relatively small-sized database. Second, predictive values of both POSSUM and E-

1 PASS assessed using the AUC values in the ROC analysis were not very high, suggesting that  
2 both tools are not very satisfactory. This may be due to the historical fact that both were not  
3 developed specifically for pancreatic surgery. In the present study, preoperative physiological  
4 severity scores had no impact on PCs both in POSSUM and E-PASS. This is inconsistent with  
5 the results of a previous study which demonstrated that preoperative factors such as age, activities  
6 of daily living, body mass index, and the ASA grade were strong risk factors for in-hospital  
7 mortality in an analysis of 8575 patients who underwent PD [26]. Precise preoperative estimation  
8 of PCs including POPF after various surgical procedures for pancreatectomy requires a large  
9 clinical database that includes potential predictive factors not included in POSSUM or E-PASS  
10 [26-30]. The development of a novel scoring system for predicting postoperative complications  
11 after pancreatic surgery based on a multicenter setting or a nationwide study [29, 30] would  
12 contribute to preoperative identification of high-risk patients, adequate patient selection, and  
13 treatment planning in pancreatic surgery. Nevertheless, POSSUM and E-PASS are still widely  
14 available for various surgical units, and they play an important role as convenient and useful  
15 assessment tools for predicting morbidity in patients undergoing pancreatic surgery.  
16 In recent years, there has been a growing concern regarding neoadjuvant chemotherapy for  
17 pancreatic cancer or laparoscopic surgery for various pancreatic disorders. Although a small  
18 number of patients with pancreatic cancer had received neoadjuvant chemotherapy in this study,

1 neoadjuvant chemotherapy as well as laparoscopic pancreatic surgery need to be considered as  
2 potential predictive factors of PCs after pancreatic surgery in future research.

3

#### 4 **Conclusions**

5 This study demonstrated that E-PASS is superior to POSSUM at accurately predicting  
6 severe PCs after pancreatic surgery. However, the accuracy of both tools is not considered as  
7 satisfactory. In order to optimize the safety of pancreatic surgery and improve patient outcomes,  
8 it is important to continue to objectively validate the accuracy of any future PCs prediction  
9 formula that may be generated.

10

#### 11 **Acknowledgments**

12 We would like to thank Editage ([www.editage.com](http://www.editage.com)) for English language editing.

#### 13 **Conflict of Interest**

14 The authors declare no conflict of interest for this article.

## 1   **References**

- 2   1. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.*  
3       1991;78:356–60.
- 4   2. Haga Y, Ikei S, Ogawa M. Estimation of physiologic ability and surgical stress (E-PASS) as  
5       a new prediction scoring system for postoperative morbidity and mortality following elective  
6       gastrointestinal surgery. *Surg Today.* 1999;29:219–25.
- 7   3. Haga Y, Wada Y, Saitoh T, Takeuchi H, Ikejiri K, Ikenaga M. Value of general surgical risk  
8       models for predicting postoperative morbidity and mortality in pancreatic resections for  
9       pancreatobiliary carcinomas. *J Hepatobiliary Pancreat Sci.* 2014;21:599–606.
- 10  4. Rückert F, Kuhn M, Scharm R, Endig H, Kersting S, Klein F, et al. Evaluation of POSSUM  
11       for patients undergoing pancreatoduodenectomy. *J Invest Surg.* 2014;27:338–48.
- 12  5. Hashimoto D, Takamori H, Hirota M, Baba H. Prediction of operative morbidity after  
13       pancreatic resection. *Hepatogastroenterology.* 2013;60:1577–82.
- 14  6. Greenblatt DY, Kelly KJ, Rajamanickam V, Wan Y, Hanson T, Rettammel R, et al.  
15       Preoperative factors predict perioperative morbidity and mortality after  
16       pancreaticoduodenectomy. *Ann Surg Oncol.* 2011;18:2126–35.

- 1 7. Hashimoto D, Takamori H, Sakamoto Y, Ikuta Y, Nakahara O, Furuhashi S, et al. Is an  
2 estimation of physiologic ability and surgical stress able to predict operative morbidity after  
3 pancreaticojejunostomy? *J Hepatobiliary Pancreat Sci.* 2010;17:132–8.
- 4 8. Hashimoto D, Takamori H, Sakamoto Y, Tanaka H, Hirota M, Baba H. Can the physiologic  
5 ability and surgical stress (E-PASS) scoring system predict operative morbidity after distal  
6 pancreatectomy? *Surg Today.* 2010;40:632–7.
- 7 9. Bodea R, Hajjar NA, Bartos A, Zaharie F, Graur F, Iancu C. Evaluation of P-POSSUM risk  
8 scoring system in prediction of morbidity and mortality after pancreaticojejunostomy.  
9 *Chirurgia.* 2018;113:399–404.
- 10 10. Kahn AW, Shah SR, Agarwal AK, Davidson BR. Evaluation of the POSSUM scoring system  
11 for comparative audit in pancreatic surgery. *Dig Surg.* 2003;20:539–45.
- 12 11. Pratt W, Joseph S, Callery MP, Vollmer CM Jr. POSSUM accurately predicts morbidity for  
13 pancreatic resection. *Surgery.* 2008;143:9–19.
- 14 12. Nanashima A, Abo T, Takagi K, Wada H, Arai J, Kunizaki M. Clinical significance of vessel-  
15 sealing device usage for pancreatectomy: a retrospective cohort study.  
16 *Hepatogastroenterology.* 2014;61:1767–74.

- 1 13. Strasberg SM, Drebin JA, Linehan D. Radical antegrade modular pancreatosplenectomy.  
2 Surgery. 2003;133:521–7.
- 3 14. Kawabata Y, Tanaka T, Nishi T, Monma H, Yano S, Tajima Y. Appraisal of a total meso-  
4 pancreatoduodenum excision with pancreaticoduodenectomy for pancreatic head carcinoma.  
5 Eur J Surg Oncol. 2012;38: 574–9.
- 6 15. Kawabata Y, Hayashi H, Takai K, Kidani A, Tajima Y. Superior mesenteric artery-first  
7 approach in radical antegrade modular pancreatosplenectomy for borderline resectable  
8 pancreatic cancer: a technique to obtain negative tangential margins. J Am Coll Surg.  
9 2015;220:e49–54.
- 10 16. Kawai M, Hirano S, Yamaue H. Artery-first approach for pancreaticoduodenectomy. J  
11 Hepatobiliary Pancreat Sci. 2018;25:319–20.
- 12 17. Jiang X, Yu Z, Ma Z, Deng H, Ren W, Shi W, et al. Superior mesenteric artery first approach  
13 can improve the clinical outcomes of pancreaticoduodenectomy: a meta-analysis. Int J Surg.  
14 2020;73:14–24.
- 15 18. Negoï I, Hostiuç S, Runcanu A, Negoï RI, Beuran M. Superior mesenteric artery first  
16 approach versus standard pancreaticoduodenectomy: a systematic review and meta-analysis.  
17 Hepatobiliary Pancreat Dis Int. 2017;16:127–38.

- 1 19. Ironside N, Barreto SG, Loveday B, Shrikhande SV, Windsor JA. Meta-analysis of an artery-  
2 first approach versus standard pancreatoduodenectomy on perioperative outcomes and  
3 survival. *Br J Surg*. 2018;105:628–36.
- 4 20. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal  
5 with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240:205–  
6 13.
- 7 21. Baekelandt BMG, Fagerland MW, Hjermland MJ, Heiberg T, Labori KJ, Buanes TA.  
8 Survival, complications and patient reported outcomes after pancreatic surgery. *HPB*  
9 2019;21:275–82.
- 10 22. Wu W, He J, Cameron JL, Makary M, Soares K, Ahuja N, et al. The impact of postoperative  
11 complications on the administration of adjuvant therapy following pancreaticoduodenectomy  
12 for adenocarcinoma. *Ann Surg Oncol*. 2014;21:2873–81.
- 13 23. Watanabe Y, Nishihara K, Matsumoto S, Okayama T, Abe Y, Nakano T. Effect of  
14 postoperative major complications on prognosis after pancreatectomy for pancreatic cancer:  
15 a retrospective review. *Surg Today*. 2017; 47:555–67.

- 1 24. Wegner RE, Verma V, Hasan S, Schiffman S, Thakkar S, Horne ZD, et al. Incidence and risk  
2 factors for post-operative mortality, hospitalization, and readmission rates following  
3 pancreatic cancer resection. *J Gastrointest Oncol.* 2019;10:1080–93.
- 4 25. Baum P, Diers J, Lichthardt S, Kastner C, Schlegel N, Germer CT, et al. Mortality and  
5 complications following visceral surgery. *Dtsch Arztebl Int.* 2019;116:739–46.
- 6 26. Kimura W, Miyata H, Gotoh M, Hirai I, Kenjo A, Kitagawa Y, et al. A  
7 pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race  
8 population (Japanese) using a web-based data entry system: the 30-day and in-hospital  
9 mortality rates for pancreaticoduodenectomy. *Ann Surg.* 2014;259:773–80.
- 10 27. Hashimoto D, Mizuma M, Kumamaru H, Miyata H, Chikamoto A, Igarashi H, et al. Risk  
11 model for severe postoperative complications after total pancreatectomy based on a  
12 nationwide clinical database. *Br J Surg.* 2020;107:734–42.
- 13 28. Ji HB, Zhu WT, Wei Q, Wang XX, Wang HB, Chen QP. Impact of enhanced recovery after  
14 surgery programs on pancreatic surgery: a meta-analysis. *World J Gastroenterol.*  
15 2018;24:1666–78.

- 1 29. Uzunoglu FG, Reeh M, Vettorazzi E, Ruschke T, Hannah P, Nentwich MF, et al. Preoperative  
2 pancreatic resection (PREPARE) score: a prospective multicenter-based morbidity risk score  
3 *Ann Surg.* 2014;260:857–63.
- 4 30. Aoki S, Miyata H, Konno H, Gotoh M, Motoi F, Kumamaru H. Risk factors of serious  
5 postoperative complications after pancreaticoduodenectomy and risk calculators for  
6 predicting postoperative complications: a nationwide study of 17,564 patients in Japan. *J*  
7 *Hepatobiliary Pancreat Sci.* 2017;24:243–51.

8

9

10

11

12

13

14

15

16

1 **Tables**2 **Table 1** Demographic and clinical characteristics of 343 patients who underwent pancreatic surgery

3	Sex (female/male)	190 (55.4%)/153 (44.6%)
	Age*	71 (63-77)
	Operation	
4	Pancreaticoduodenectomy	208 (60.6%)
	Distal pancreatectomy	95 (27.7%)
5	Total pancreatectomy	11 (3.2%)
	Others†	29 (8.5%)
6	<b>Laparoscopic surgery (Yes/ No)</b>	<b>28/ 315</b>
	Malignant/benign	260 (75.8%) / 83 (24.2%)
7	Diseased organ	
	Pancreas	260 (75.8%)
	Biliary tract	77 (22.5%)
8	Duodenum	1 (0.3%)
	Others	5 (1.5%)
9	<b>Neoadjuvant therapy (Yes/ No)</b>	<b>15/ 328</b>

10 Data is shown as the number (%) of patients except age\* shown as the median (interquartile range).

11 † Frey's operation (8 patients), Partington's operation (2 patients), laparoscopic pancreatic enucleation (5 patients), open pancreatic enucleation (2 patients), duodenum-preserving pancreatic head resection (2 patients), partial pancreatectomy (2 patients), ventricular pancreatectomy (1 patient), and re-anastomosis of previous pancreaticojejunostomy (1 patient).

12

13

14

15

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

**Table 2** Severity of PCs after pancreatic surgery based on the CD classification

1	PCs (-)	184 (47.4%)		
2	PCs (+)	159 (53.6%)		
3	Grade I	65	}	PCs-CD < IIIa* 298 (86.9%)
3	Grade II	49		
4	Grade IIIa	30	}	PCs-CD ≥ IIIa † 45 (13.1%)
4	Grade IIIb	10		
4	Grade IVa	1		
4	Grade IVb	1		
5	Grade V	3		

Data is shown as the number (%) of patients

CD: Clavien-Dindo

PCs: postoperative complications

\*PCs-CD<IIIa: no PCs or those of CD grade I or II

† PCs-CD≥IIIa: PCs of CD grade IIIa or higher

1  
2  
3  
3  
4  
4  
5  
  
6  
7  
8  
9  
10  
11  
12  
13  
14  
15

**Table 3.** Accuracy of POSSUM and E-PASS for predicting severe PCs after pancreatic surgery

	PCs*-CD $\geq$ IIIa †	PCs-CD < IIIa ‡	P-value§
	(n=45)	(n=298)	
POSSUM			
Physiological score (P-score) [12-88]	18.00 (14.50-25.50)	20.00 (16.00-25.00)	0.107
Age score (1, 2, 4)	2.00 (2.00-4.00)	4.00 (2.00-4.00)	0.205
Cardiac signs score (1, 2, 4, 8)	2.00 (1.00-4.00)	1.00 (1.00-4.00)	0.635
Respiratory history score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.795
Blood pressure (systolic) score (1, 2, 4, 8)	1.00 (1.00-2.00)	1.00 (1.00-2.00)	0.291
Pulse score (1, 2, 4, 8)	1.00 (1.00-2.00)	1.00 (1.00-1.00)	0.718
Glasgow coma scale score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.000
Hemoglobin score (1, 2, 4, 8)	2.00 (1.00-4.00)	2.00 (1.00-4.00)	0.870
White cell count score (1, 2, 4)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.353
Urea score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.457
Sodium score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.192
Potassium score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.982
Electrocardiogram score (1, 4, 8)	1.00 (1.00-4.00)	1.00 (1.00-1.25)	0.817
Operative score (O-score) [6-48]	19.0 (16.0-23.0)	17.0 (15.0-20.0)	<0.001
Operative severity score (1, 2, 4, 8)	8.00 (8.00-8.00)	8.00 (8.00-8.00)	1.000
Multiple-procedure score (1, 4, 8)	1.00 (1.0-1.00)	1.00 (1.00-1.00)	0.698
Total blood loss score (1, 2, 4, 8)	4.00 (2.00-8.00)	2.00 (2.00-8.00)	0.003
Peritoneal soiling score (1, 2, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.000
Presence of malignancy score (1, 2, 4, 8)	4.00 (2.00-4.00)	2.00 (1.00-4.00)	0.013
Mode of surgery score (1, 4, 8)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	1.000
Morbidity	0.70 (0.44-0.88)	0.65 (0.46-0.82)	0.353
E-PASS			
Preoperative risk score (PRS)	0.25 (0.22-0.39)	0.26 (0.23-0.38)	0.382
X1: age	69.00 (63.00-73.00)	71.50 (63.75-78.00)	0.065
X2: severe heart disease (0, 1)	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.748
X3: severe pulmonary disease (0, 1)	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.647
X4: diabetes mellitus (0, 1)	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.787
X5: performance status index (0-4)	0.00 (0.00-0.00)	0.00 (0.00-0.00)	0.514
X6: ASA physiological status classification (1-5)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.979
Surgical stress score (SSS)	0.64 (0.41-0.87)	0.46 (0.32-0.65)	<0.001
X1: blood loss/body weight (g/kg)	15.69 (5.96-31.31)	8.86 (3.07-18.13)	0.003
X2: operation time (h)	9.20 (7.70-11.95)	8.08 (6.40-9.87)	<0.001
X3: extent of skin incision (0, 1, 2)	1.00 (1.00-1.00)	1.00 (1.00-1.00)	0.849
Comprehensive risk score (CRS)	0.46 (0.29-0.69)	0.33 (0.19-0.49)	0.002

Data is shown as the median (interquartile range)

\* PCs: postoperative complications

† PCs-CD $\geq$ IIIa: PCs of Clavien-Dindo grade IIIa or higher

‡ PCs-CD<IIIa: no PCs or those of Clavien-Dindo classification grade I or II

§ Wilcoxon rank sum test (Chi-square approximation)

1

2

3

4

5

6

7

8

9

10

11

12

13

14

15

1 **Figure Legends**

2 **Figure 1**

3 ROC analysis for the predictive accuracy of PCs-CD $\geq$ IIIa in E-PASS and POSSUM / DeLong test is  
4 used to compare the AUCs. PCs-CD $\geq$ IIIa, postoperative complications of Clavien-Dindo grade IIIa  
5 or higher

6

7 **Figure 2**

8 Correlation between CRS of E-PASS and the occurrence of PCs-CD $\geq$ IIIa. / Patients were categorized  
9 into 4 equal groups, i.e., at a very low, low, high, and very high risk for developing PCs-CD $\geq$ IIIa,  
10 based on the upper quartile, the median, and the lower quartile. PCs-CD $\geq$ IIIa, postoperative  
11 complications of Clavien-Dindo grade IIIa or higher; PCs-CD $<$ IIIa, no postoperative complications  
12 or those of Clavien-Dindo grade I or II; CRS, comprehensive risk score

13

14 **Figure 3**

15 Correlation analysis for the predictive values in POSSUM and E-PASS / The predictive values of PCs  
16 in POSSUM (Y-axis) and E-PASS (X-axis) were shown, in black mark (+) for PCs-CD $\geq$ IIIa, while in

- 1 thin gray mark (-) for PCs-CD<IIIa. Predictive similarity between POSSUM and E-PASS was
- 2 examined using a coefficient of determination ( $R^2$ ). PCs-CD $\geq$ IIIa, postoperative complications of
- 3 Clavien-Dindo grade IIIa or higher; PCs-CD<IIIa, no postoperative complications or those of Clavien-
- 4 Dindo grade I or II; CRS, comprehensive risk score





