A simplified scoring system for the prediction of pancreatoduodenectomy’s complications

An observational study

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Abstract
To assess the efficiency of several previous scoring systems in the prediction of postoperative complications of pancreatoduodenectomy (PCPD) and to explore a new simplified scoring system for PCPD prediction.

All 183 consecutive patients scheduled for PD from 2010 to 2017 in the Second Affiliated Hospital of Chongqing Medical University were collected retrospectively. The area under the curve (AUC) for the prediction of PCPD was calculated for POSSUM, E-PASS, APACHE-II, and APACHE-III, which were used to test the efficiency of PCPD prediction. The independent risk factors included in the new scoring system were determined by univariate analysis and a logistic regression model. Next, the prediction efficiency was validated.

The results of the univariate analysis showed that such variables as male sex, weight, WBC, serum sodium, arterial pH, postoperative 24 hours urine output, and operation time were influence factors for postoperative complications ($P<0.05$). Arterial pH, serum sodium, postoperative 24 hours urine output, and WBC were independent risk factors of postoperative complications based on the logistic regression analysis ($P<0.05$). The AUC of the novel scoring system for PCPD prediction was 85.4%.

The proposed scoring system might be a more effective tool for predicting PCPD compared with previous multipurpose scoring systems.

Abbreviations: APS = acute physiology score, AUC = area under the curve, CHS = chronic health status, CRS = comprehensive risk score, OR = odds ratio, OS = operative score, PCPD = postoperative complications of pancreatoduodenectomy, PD = pancreatoduodenectomy, PSS = preoperative risk score, PS = physiological score, ROC = receiver operating characteristic, SSS = surgical stress score, TS = total score.

Keywords: complication, pancreatoduodenectomy, prediction, scoring system

1. Introduction
Pancreatoduodenectomy (PD) is a classical operation in the treatment of pancreatic disease. However, the high risk of the procedure and severe postoperative complications have constrained the application of PD in the past several decades.[1,2] The outcomes of patients are assumed to be better when the occurrence of postoperative complications is predicted and interventions are adopted immediately. A scoring system that is applied for evaluation of severity of disease for critical patients in the intensive care unit (ICU) is common. Currently, scoring systems have been determined to have additional uses, such as evaluation of the risk of postoperative complications and death. Doctors have used these types of scoring systems for treatment selection for some diseases to obtain satisfactory outcomes, and these scoring systems have been widely used in departments of orthopedic,[3] thoracic,[4] and vascular surgeries.[5]

Studies on the application of scoring systems in the Department of Hepatobiliary Surgery have been conducted before. However, most of the prior studies adopted multipurpose scoring systems proposed previously that were not specific for PD. Consequently, the application value of these scoring systems is not conclusive.[6]

In addition, although several of these studies explored the postoperative risks of PD, certain disease-specific factors (such as diabetes mellitus, preoperative biliary drainage, and type of pancreatic reconstruction) were not included in the tool for clinical application.[7,8] Moreover, several studies showed that their scoring systems could predict postoperative complications, such as postoperative pancreatic fistula and delayed gastric emptying.[7-9,12] However, the complications included in these studies are too isolated, and the index of previous classic scoring systems was not considered comprehensively. From our perspective, avoiding the omission of some necessary indexes may be difficult if the researchers determined potential risk factors subjectively. One previous study emphasized that most postoperative complications of pancreatoduodenectomy (PCPD)
are special and are associated with the surgical method itself. In this way, previous multipurpose scoring systems may not be applicable in the prediction of postoperative complications of PD,[13] and an improved scoring system is still needed.

This study collected and tested previous multipurpose scoring systems, including POSSUM, E-PASS, APACHE-II, and APACHE-III, among patients who underwent PD in our hospital. In a novel approach, several factors that were strongly associated with PD were added as potential indicators to form our scoring system. Afterwards, a novel simplified and specialized scoring system was proposed to help us predict the risk of postoperative complications objectively and guide doctor-patient communication.

2. Methods

2.1. Basic characteristics of patients

A total of 183 patients who underwent PD from September, 2010 to September, 2017 in the Second Affiliated Hospital of Chongqing Medical University were collected retrospectively; 150 patients were grouped into the test set (from September, 2010 to September, 2016), and the remaining 33 patients were grouped for the validation dataset (from September, 2016 to September, 2017). The whole study plan was approved by the Ethical Review Committee of the Hospital. All the patients’ disease was diagnosed by contrast computed tomography scan or magnetic resonance imaging. Before surgery, the condition of all patients was controlled to be stable. Commonly, when the conditions of the patients are severe (e.g., severe acute pancreatitis), they would be regulatory given inhibitors of pancreatic secretion intravenously with venous pump. The most common drugs were gabexate mesilate and somatostatin. Once the symptoms are relieved and the imaging result shows a stable focus, these kinds of drugs would be evacuated. If necessary, the patients would have preoperative biliary drainage via percutaneous transhepatic cholangial drainage. All the patients underwent open pancreatoduodenectomy and all the operations were performed by the surgery team in our department. All the pancreatic reconstruction method was pancreatojejunostomy (end to end, binding) and internal drainage was performed for pancreatic and biliary drainage. We conduct pancreatojejunostomy at first and then biliary anastomosis. Blood samples were measured before the operation. Postoperative transfusion was controlled in 300 mL per hour and 10 mg furosemide per day was used via intravenous injection. The general characteristics, laboratory examinations, and treatment methods of the patients were collected and analyzed in detail. In the test set, 96 patients were male, and 54 were female. The patients’ ages ranged from 22 to 83 years. Patients underwent PD because of the following causes: 2 cases for pancreatic cyst, 3 cases for chronic pancreatitis or pancreaticolithiasis, 17 cases for cholangiocarcinoma, 80 cases for pancreatic carcinoma, 5 cases for ampullary carcinoma, and 43 cases for malignant duodenal tumors. For the validation set, 19 patients were male, and 14 were female; their ages ranged from 21 to 76 years.

2.2. Previous scoring systems

In this study, 4 previous multipurpose scoring systems, including POSSUM,[13] E-PASS,[15] APACHE-II,[16] and APACHE-III,[17] were used to predict the postoperative complications of PD. POSSUM contains a physiological score (PS) and an operative score (OS). PS contains 12 variables, and OS contains 6 variables. Each variable has its own range of value and score. Thus, PS, OS, and total score (TS, equal to PS plus OS) can be calculated. E-PASS consists of 6 preoperative risk factors and 3 operative risk factors. Thus, the preoperative risk score (PRS), the surgical stress score (SSS), and the comprehensive risk score (CRS) could be calculated.

At present, the APACHE scoring system has been developed into 3 editions, namely, APACHE-I,[18] APACHE-II,[16] and APACHE-III.[17] APACHE-I contains too many parameters, which might be inconvenient and has resulted in fewer applications. Compared to APACHE-I, APACHE-II has been largely simplified. APACHE-II consists of 3 parts, namely, acute physiology score (APS), chronic health status (CHS), and the ages of patients. APACHE-II has been widely used in clinical settings because of its dependability, convenience, and reasonable design. A high score indicates high mortality and a poor prognosis. Similar to APACHE-II, APACHE-III also consists of APS, CHS, and patients’ age. However, the scores of the old variables were optimized, and APACHE-III also includes several new variables.

2.3. Outcomes

The postoperative complications of PD are regarded as the major outcome. Postoperative complications consist of common complications for most surgeries and special complications for PD. In this study, such complications as pancreatic fistula, biliary fistula, intra-abdominal infection, hemorrhage, upper gastrointestinal hemorrhage, intra-abdominal hemorrhage, acute respiratory distress syndrome (ARDS), abdominal lymphatic fistulas, pulmonary embolism, heart failure, delayed gastric emptying or gastric emptying dysfunction, stoma hemorrhage, anastomotic hemorrhage, liver failure, multiple organ failure syndrome (MODS), sepsis, and fungal enteritis were included.

2.4. Statistical analysis

In this study, SPSS 23.0 software was used for data analysis. Continuous variables were displayed with mean ± standard deviation. Previous multipurpose scoring systems were used to score each participant, and then the receiver operating characteristic (ROC) curve was plotted and the area under the curve (AUC) was calculated to evaluate whether the previous scoring systems could efficiently predict the postoperative complications of PD. Some indicators that were associated with PD and the indicators that existed in the multipurpose scoring systems were combined. Univariate analysis was conducted to identify some potential risk factors of complications. Next, a logistic regression model was built to determine independent risk factors influencing the incidence of postoperative complications. Finally, these independent risk factors were assigned with corresponding scores according to the odds ratio (OR) values and a new TS was calculated for each patient. Next, the ROC curve was graphed again and the efficiency of the new scoring system in the prediction of postoperative complications was evaluated. The significant difference is considered to be of significance when P < .05.

3. Results

3.1. Basic features of the patients

Table 1 shows the demographic features of all patients in the test set. In the test set, 98 patients were more than 50 years old (65.3%). Three patients (2%) had a history of serious lung
3.2. Evaluation of previous scoring systems

3.2.1. Evaluation with POSSUM. Each patient in the test set was scored according to the indicator and corresponding value in POSSUM. Next, the PS, OS, and TS were calculated. Moreover, the risk coefficient of POSSUM was determined with PS and OS scores using the reported formula of the POSSUM system. After that step, ROC curves for the PS, OS, and TS, and the reported formula were calculated (Fig. 1A). The AUC of the PS, OS, and TS, and risk coefficient for prediction of the PCPD were 44.1%, 52.6%, 47.6%, and 48.2%, respectively.

3.2.2. Evaluation with E-PASS. Each patient in the test set was scored according to the indicator and corresponding value of E-PASS. Then, PRS, SSS, and CRS were calculated. The ROC curve was graphed for the prediction of postoperative complications of PD in terms of PRS, SSS, and CRS. The AUC of PRS, SSS, and CRS were 47.9%, 42.1%, and 43.6%, respectively (Fig. 1B).

3.2.3. Evaluation with APACHE-II and APACHE-III. Each patient in the test set was scored according to the indicators and corresponding values in APACHE-II and APACHE-III. Next, the ROC curve was graphed for the prediction of postoperative complications of PD using the TS of these 2 scoring systems. The AUC of APACHE-II and APACHE-III were 33.3% (Fig. 1C) and 45.7% (Fig. 1D), respectively.

3.3. Risk factors of PCPD

All of the indicators in POSSUM, E-PASS, APACHE-II, and APACHE-III were extracted and later combined. A number of indicators, such as age, sex, body mass index, drinking history, smoking history, history of operation in the upper abdomen, hypertension history, history of coronary heart disease, HBV infection history, HCV infection history, hepatocirrhosis history, diabetes mellitus, American Society of Anesthesiologists grade, focal property, position of carcinoma, preoperative infection of the biliary tract, preoperative alkaline phosphatase, preoperative highest serum bilirubin, preoperative albumin, preoperative hemoglobin, intra-operative bleeding, intra-operative blood transfusion, operative time, the method of pancreaticojunostomy, use of a stent tube in the pancreatic duct, drainage method of the pancreatic duct, texture of the pancreas, diameter of the pancreatic duct, use of somatostatin, preoperative and postoperative nutrient support, relieving jaundice before surgery, and histological differentiation of carcinoma, which are considered to be closely related to PD and clinical practice, were supplemented. Next, the continuous variables were transferred into binary variables based on the best cut-off value that was determined by the ROC curve for postoperative complications. With the clinical data in the test dataset, univariate analysis was conducted. The results of the univariate analysis showed that male sex [OR: 0.347, 95% confidence interval (CI): 0.156–0.771; P = .009], weight (OR: 2.875, 95% CI: 1.096–7.542; P = .032), WBC (OR: 2.473, 95% CI: 1.202–5.089; P = .014), BUN (OR: 2.460, 95% CI: 1.148–5.089; P = .021), serum sodium (OR: 3.385, 95% CI: 1.103–10.350; P = .033), mean arterial pressure (OR: 2.649, 95% CI: 1.056–6.915; P = .037), arterial pH (OR: 4.537, 95% CI: 2.008–10.256; P < .001), serum creatinine (OR: 4.626, 95% CI: 2.082–10.278; P < .001), hematocrit (OR: 3.088, 95% CI: 1.299–7.343; P = .011), total bilirubin (OR: 10.000, 95% CI: 2.035–49.150; P = .005), arterial partial pressure of carbon...
dioxide (OR: 2.479, 95% CI: 1.139–5.398; \(P = .022\)), postoperative 24 hours urine output (OR: 8.167, 95% CI: 2.436–27.379; \(P = .001\)), operation time (OR: 4.900, 95% CI: 1.396–17.194; \(P = .013\)), and frequency of operation during the prior 30 days (OR: 4.900, 95% CI: 1.396–17.194; \(P = .013\)) were influence factors for postoperative complications. The results of the logistic regression analysis showed that arterial pH (OR: 1.286E+12, 95% CI: 37016.3–4.470E+19; \(P = .002\)), serum sodium (OR: 1.707, 95% CI: 1.137–2.563; \(P = .010\)), postoperative 24 hours urine output (OR: 1.001, 95% CI: 1.000–1.002; \(P = .020\)), and WBC (OR: 1.573, 1.121–2.207; \(P = .009\)) were independent risk factors of postoperative complications.

3.4. **Efficiency of the new scoring system for PCPD prediction**

The novel scoring system consists of 4 independent risk factors, namely, arterial pH, serum sodium, postoperative 24 hours urine output, and WBC (Table 3). Each indicator was assigned different points based on different ORs. If WBC (\(\geq 8.175 \times 10^9/L\)), serum sodium (\(\geq 137.25 \text{ mmol/L}\)), and postoperative 24-hour urine output (<2325 mL) are observed, then each abnormal indicator would be scored with 1 point. Two points were scored for the patient with abnormal arterial pH < 7.427. If all of these indicators show no abnormal value, then no point would be assigned to those patients. Therefore, the TS for each patient with this new scoring system ranges from 0 to 5.

![Figure 1](image-url) Evaluation of 4 previous scoring systems for PCPD prediction. Note: The prediction value for the postoperative complications of pancreatoduodenectomy was evaluated by POSSUM (Figure 1A), E-PASS (Figure 1B), APACHE-II (Figure 1C), and APACHE-III (Figure 1D), with a ROC curve and AUC. For POSSUM, as shown in Figure 1A, the AUC of PS, OS, TS, and the risk coefficient for the prediction of the postoperative complication of PD were 44.1%, 52.6%, 47.6%, and 48.2%, respectively. For E-PASS, as shown in Figure 1B, the AUC of PRS, SSS, and CRS were 47.9%, 42.1%, and 43.6%, respectively. For APACHE-II and APACHE-III, as shown in Figure 1C and D, the AUCs were 53.3% and 46.7%, respectively. AUC = area under the curve, CRS = comprehensive risk score, PD = pancreatoduodenectomy, PRS = preoperative risk score, OS = operative score, PS = physiological score, ROC = receiver operating characteristic, SSS = surgical stress score, TS = total score.

| Table 3 | Novel scoring system. |
|---------|------------------------|
| **Items** | **Score** |
| Arterial pH | 0 | 1 | 2 |
| \(\geq 7.427\) | / | <7.427 |
| Serum Na+ (mmol/L) | \(\geq 137.25\) | <137.25 | / |
| Postoperative 24 hours urine output (mL) | \(\geq 2325\) | <2325 | / |
| WBC (\(10^9/L\)) | <8.175 | \(\geq 8.175\) | / |

Total score: lower than or equal to 2 scores indicates low incidence rate of complication; higher than 2 scores indicates high incidence rate of complication.
Each patient in the test set was scored with this new scoring system, and a TS was calculated. Next, the ROC curve was graphed for the prediction of postoperative complications using the TS (Fig. 2). From the ROC curve, the best cut-off value was set based on the maximum Youden’s index. When the set cut-off value was 2.5, Youden’s index was at a maximum, and the corresponding specificity and sensitivity were 82.4% and 82.6%, respectively. Furthermore, the AUC was 85.4%, which is larger than any previous multipurpose scoring systems.

Figure 2. ROC curve of the novel scoring system. Note: In this figure, the ROC curve was graphed for the prediction of postoperative complications using the total score calculated by the indicators in our proposed scoring system. When setting the cut-off value as 2.5, Youden’s index was maximized, and the corresponding specificity and sensitivity were 82.4% and 82.6%, respectively. The AUC was 85.4%, which was larger than any previous multipurpose scoring systems. AUC = area under curve, ROC = receiver operating characteristic.

Figure 3 shows the scores of the patients and corresponding occurrence of complications in the test set. Although 48 patients had an incidence of postoperative complications, the scores of 14 patients could not be calculated in terms of no postoperative 24 hours urine output or arterial PH value recorded in the electronic medical record system. Patients were divided into 6 groups based on their scores. No significant difference was observed between the group with 1 point and the group with 2 points, based on the chi-square test result ($P = .644$). Meanwhile, no significant difference was observed between the group with 3 points and the group with 4 points ($P = .441$). Therefore, patients were finally divided into 2 groups, namely, the group with score ≤2 points and the group with score >2 points. This classification method was also supported by the best cut-off value determined by the maximum AUC. The rate of postoperative complications was 77.78% in the group with >2 points, whereas it was 13.64% in the group with ≤2 points. The difference in the rate of postoperative complications between these 2 groups was statistically significant ($P < .001$).

3.5. Validation of the new scoring system for PCPD prediction

For validating the reliability of this new scoring system, we collected 33 patients who had undergone PD from September 2016 to September 2017 in our hospital. Among these 33 cases in the validation set, there were 23 patients without complications.
and 10 patients with complications (Supplementary Table S1, http://links.lww.com/MD/C744). We applied this new scoring system to these 33 cases, and we found that the incidence of PCPD for patients having a score > 2 (75.0%) was obviously higher than that in the patients having a score ≤ 2 (16.0%; P < .01), which indicated a good reliability of our newly proposed scoring system.

4. Discussion

After Dr Kausch performed the first resection of periampullary carcinoma with 2 steps in 1909, Wipple developed the procedure into a 1-step resection in 1942. For the operation, Wipple performed the anastomosis in a particular order (i.e., first the bile duct, then the pancreas, stomach, and jejunum), which is the classic surgery that is most frequently used at present. An increasing number of patients with pancreatic head cancer, carcinoma of Vater’s ampulla, carcinoma of the distal common bile duct, duodenal carcinoma, or other malignant carcinomas could benefit from PD. Rapid development of medical technology could improve the long-term survival and quality of life of these patients. PD is difficult to perform because of its complex surgical steps and easy intra-operative bleeding. Moreover, the individual characteristics of different patients, such as age, preoperative amount of skeletal muscle, texture of the pancreas, and renal function, might act as important factors that influence the incidence of postoperative complications and mortality of PD.

Therefore, this might clarify the condition that the operation itself is successful.

Common postoperative complications could be influenced by many different factors. An objective and simplified scoring system, which could be used to predict the occurrence of postoperative complications, is much needed. This study attempted to determine some important factors from the perioperative indicators, from which the risk of postoperative complications could be effectively predicted. In this way, some interventions could be conducted in advance to reduce the occurrence of postoperative complications, even though the classification of surgical complications is complex and varied.

In the test set, a total of 130 patients who underwent PD were evaluated using the previous scoring systems of POSSUM, E-PASS, APACHE-II, and APACHE-III to predict PCPD. POSSUM had low efficiency in PCPD prediction because the AUC of the 3 indicators in the system ranged from 42.1% to 52.6%. One study analyzed 652 patients who underwent PD. In their study, POSSUM performance was evaluated by assessing the “goodness-of-fit” with linear analysis. It was found that POSSUM underestimated the actual morbidity of patients who were at low risk and over-predicted the actual morbidity of patients who were deemed to be at high risk. In their study, they thought that POSSUM failed to accurately predict morbidity and a new equation for POSSUM was still necessary. Rückert et al. found that the POSSUM-predicted average morbidity rate was 58.9%, whereas the observed morbidity rate was 43.4% after analyzing 694 patients who underwent PD. The prediction ability of POSSUM was poor when applied to PD. Khan et al. also presented an opinion that the POSSUM risk scores of the patients with and without complications were similar after analyzing 50 cases. Overall, previous studies support the opinion that the prediction ability of POSSUM for PCPD was poor. In conclusion, further improvement is needed for POSSUM to become a better tool for the prediction of PCPD.

In this study, the prediction ability of E-PASS for PD was also poor because the AUC of the 3 indicators in this scoring system ranged from 42.1% to 47.9%. Furthermore, no statistically significant indicator was found in the regression analysis with the indicators of E-PASS, which could also support this point. Therefore, indicators in this system are not suitable for PCPD, and the use of E-PASS in predicting PCPD may be absurd. One study found that the use of E-PASS in predicting PCPD had no significant advantage after analyzing 231 patients who underwent PD. In their opinion, a novel scoring system was desirable for the prediction of PCPD. The AUCs of the ROC curves of APACHE-II and APACHE-III were all less than 50%, also indicating that their prediction ability was poor.

Previous multipurpose scoring systems have poor ability in the prediction of PCPD because of incomplete indicators. Thus, all of the indicators in these 4 scoring systems were gathered together, and other indicators that are closely associated with PD were added to the univariate and the multivariable analyses to search for adequate and important indicators and to form an improved tool for the prediction of PCPD. Finally, arterial pH, serum sodium, postoperative 24 hours urine output, and WBC were found to be independent risk factors for PCPD. That means that they could be significant factors influencing the incidence of postoperative complications.

In reality, many of these factors have been previously proposed to be important factors but have received scant attention. First, arterial PH could to some extent reflect the acid-base balance. When the acid-base balance is disrupted, the patients might not easily recover from strong stimuli, such as the surgical stress. Second, the serum Na+ is an important marker for electrolyte balance. Many electrophysiological activities depend on electrolyte balance. Therefore, when the serum Na+ is abnormal, the whole body condition could be influenced. Furthermore, postoperative 24 hours urine output is also a good marker for reflecting patients’ state, especially for renal and circulatory function. Lastly, the WBC count is an important marker for inflammatory reactions. A higher value might refer to a potential inflammatory reaction. With regard to the significance of these outcomes in clinical practice, their combination in 1 scoring system for complication prediction is reasonable.

The new scoring system was formed by assigning points to each indicator based on the ORs of each indicator. The AUC of the ROC curve for the TS with this new scoring system is 85.4%. Thus, a notable improvement in the prediction of PCPD has been achieved. Furthermore, the rate of postoperative complications in the group with a TS < 2 (13.64%) was significantly lower than the complications in the group with a TS > 2 (77.78%). Therefore, patients who score more than 2 points should receive more attention at the hospital, because their risk of PCPD is high.

For validation of this new scoring system, another 33 patients were included in the validation set for further analysis, proving that the new scoring system has a good predictive ability for PCPD. If the TS can be reduced to less than 3 points using selective strategies and if the parameters of arterial pH, serum sodium, postoperative 24-hour urine output, and WBC are controlled and adjusted, then the occurrence of postoperative complications could be significantly reduced. Moreover, this result strongly supports the importance of preoperative preparation for PD and postoperative care.

Several limitations could be observed in our study. First, the relatively small quantity of cases might provide a low rate of postoperative complications. Second, our proposed scoring system was from a single-center and a retrospective study. Thus,
some limitations on the generalizability of the conclusion in our study to some degree might be present. Multi-center studies with more participants are required to prove the ability of PCPD prediction. Third, when we first thought about how to define the postoperative complications of PD, we took the ISGPS consensus definitions into consideration. As we found, postoperative pancreatic fistula, postpancreaticectomy hemorrhage, and delayed gastric emptying were included in the ISGPS consensus definition. According to our collection of the cases, it seems that complications of ISGPS consensus definition do not completely include the common complications found in our study. A more systematic unique classification of PCPD, not a general complication system, still needs to be designed. In that case, the scoring system could be more objective.

In conclusion, our novel simplified scoring system has strong prediction ability for PCPD and deserves widespread clinical application compared with previous multipurpose scoring systems.

**Author contributions**

YBW proposed this study. LC and DWS collected and interpreted the data. FZ, YHZ, JYS, and YBW analyzed the data. LC and YBW drafted the work. JYS, YHZ and FZ modified the first draft.

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