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Risk Assessment of Pancreatic Surgery by Surgical Apgar Score and Body Mass Index

Toru Aoyama[1,2], Yusuke Katayama[1], Masaaki Murakawa[1], Koichiro Yamaoku[1], Amane Kanazawa[1], Akio Higuchi[1], Manabu Shiozawa[1], Makoto Ueno[3], Manabu Morimoto[3], Takaki Yoshikawa[2], Yasushi Rino[2], Munetaka Masuda[2], Soichiro Morinaga[1]

[1]*Department of Gastrointestinal Surgery and* [3]*Department of Hepato-biliary-pancreatic Medicine, Kanagawa Cancer Center, Yokohama, Japan*

[2]*Department of Surgery, Yokohama City University, Yokohama, Japan*

Postoperative morbidity is high after pancreatic surgery. Recently, a simple and easy-to-use surgical complication prediction system, the surgical Apgar score (SAS), calculated using 3 intraoperative parameters (estimated blood loss, lowest mean arterial pressure, and lowest heart rate) has been proposed for general surgery. In this study, we evaluated the predictability of the SAS for severe complications after pancreatic surgery for pancreatic cancer. We investigated 189 patients who underwent pancreatic surgery at Kanagawa Cancer Center between 2005 and 2014. Clinicopathologic data, including the intraoperative parameters, were collected retrospectively. In this study, the patients with postoperative morbidities classified as Clavien-Dindo grade 2 or higher were classified as having severe complications. Univariate and multivariate logistic regression analyses were performed to identify the risk factors for morbidity. Postoperative complications were identified in 73 patients, and the overall morbidity rate was 38.6%. The results of both univariate and multivariate analyses of various factors for overall operative morbidity showed that an SAS of 0 to 4 points and a body mass index ≥25 kg/m^2 were significant independent risk factors for overall morbidity ($P = 0.046$ and $P = 0.013$). The SAS and body mass index were significant risk factors for surgical complications after pancreatic surgery for pancreatic cancer.

Key words: Pancreatic cancer – Risk assessment – SAS – BMI

Corresponding author: Toru Aoyama, Department of Gastrointestinal Surgery, Kanagawa Cancer Center, 2-3-2 Nakao, Asahi-ku, Yokohama 241-8515, Japan.
Tel.: 81 45 520 2222; Fax: +81 45 520 2226; E-mail: aoyamat@kcch.jp

Pancreatic cancer is a major cause of cancer death worldwide, with a 5-year survival rate of less than 5%.[1,2] Complete resection is essential for the cure of pancreatic cancer. However, the morbidity after pancreatic surgery with lymph node dissection has been reported to range from 30% to 65%, and the complications are sometimes fatal.[3–8] Many previous studies have demonstrated that the development of postoperative complications increased the risk of disease recurrence in various types of malignancies.[9–11] Therefore, it is important to predict the occurrence of complications before surgery and to determine the most appropriate perioperative care.

Numerous studies have evaluated perioperative risk factors that may affect the morbidity and mortality associated with pancreatic surgery. Advanced age, male sex, body mass index (BMI), and chronic comorbid conditions have been shown to be independent predictors for postoperative complications following pancreatic surgery.[12,13] For example, Williams *et al*[13] evaluated 262 patients who underwent pancreaticoduodenectomy and categorized them as obese (BMI $\geq$30), overweight (25 $\leq$ BMI $<$ 30), or normal weight (BMI $<$25). They found that the obese patients did have an increased rate of serious complications compared with normal-weight patients (24.2% versus 13.6%). In addition, several scoring models have been reported to be useful for predicting the development of complications. However, the previously reported scoring models, such as the Physiologic and Operative Severity Score for the Enumeration of Mortality (POSSUM), the National Surgical Quality Improvement Program (NSQIP), and the Estimation of Physiologic Ability and Surgical Stress (E-PASS), require complex calculations using numerous perioperative variables that are not available at the bedside.[14–17]

In 2007, Gawande *et al*[18] proposed a simple and easy complication prediction system: the surgical Apgar score (SAS) for general or vascular operations.[18] They found that a simple score based on the estimated blood loss, lowest intraoperative mean arterial pressure (L-MAP), and lowest intraoperative heart rate (L-HR) can be useful in rating the condition of patients after general or vascular operations. However, the significance of the SAS has not been evaluated in patients undergoing pancreatic surgery for pancreatic cancer.

The aim of the present study was to determine whether the SAS could be useful for predicting the development of any complication of grade 2 or higher, as defined by the Clavien-Dindo classification,[19] in patients undergoing curative resection for pancreatic cancer.

Patients and Methods

Patients

The patients were selected from the medical records of 216 consecutive patients who underwent pancreatic surgery for pancreatic cancer at Kanagawa Cancer Center from 2005 to 2014, according to the following criteria: (1) those with a pathologically common type of pancreatic cancer according to the International Union Against Cancer (UICC) TNM 6th edition[20]; (2) those who had undergone a gross complete (R0 or R1) resection of the pancreatic cancer as initial treatment. The resected specimens were examined histopathologically and were staged according to the UICC TNM 6th edition. Patients with other pancreatic and periampullary neoplasms, such as intraductal papillary mucinous neoplasm, cystadenocarcinoma, and endocrine tumor, were excluded.

Surgical procedure

All pancreatic surgeries were performed in accordance with standardized procedures described elsewhere.[6,21–23] Briefly, in cases of distal pancreatectomy, dissection of lymph node was performed in the region of the celiac trunk and the superior mesenteric artery and vein, as well as behind the pancreas along the left side of the renal vein and the left adrenal gland. In each case, intraperitoneal drains were placed close to the pancreatic anastomosis and stump. In cases of pancreaticoduodenectomy (PD), we performed subtotal stomach-preserving pancreaticoduodenectomy (SSPPD) as the standard procedure. Lymph node dissection along the hepatoduodenal ligament, common hepatic artery, vena cava, superior mesenteric vein, and the right side of the superior mesenteric artery was a standard part of the procedure. Multiple intraperitoneal drains were placed: the first was posterior to the hepaticojejunostomy, and the second was on the anterior surface of the pancreaticojejunostomy or the closed pancreas remnant.

Perioperative care

In principle, the patients received the same perioperative care. In brief, the patients were allowed to eat until midnight on the day before the surgery and were required to drink the contents of two 500-mL plastic bottles containing oral rehydration solution until 3 hours before surgery. The nasogastric tube was removed on postoperative day 1 (POD 1) after

Table 1 Evaluation of the original surgical Apgar score

	0 Points	1 Point	2 Points	3 Points	4 Points
Estimated blood loss, mL	>1000	>600, ≤1000	>100, ≤600	≥100	—
Lowest mean arterial pressure, mmHg	<40	≥40, <55	≥55, <70	≥70	—
Lowest heart rate	>85	>75, ≤85	>65, ≤75	>55, ≤65	≤55

—, not applicable.

surgery. Oral intake was initiated on POD 2, beginning with water and an oral nutritional supplement. The patients began to eat solid food on POD 5, starting with rice gruel and soft food on POD 3 and advancing in 3 steps to regular food intake on POD 10. The patients were discharged when they had achieved adequate pain relief and soft food intake, had returned to their preoperative mobility level, and exhibited normal laboratory data.

Definition of surgical complications

Complications of grades 2 to 5 according to the Clavien-Dindo classification that occurred during hospitalization and/or within 30 days after surgery were retrospectively determined from the patient's record.[19] Grade 1 complications were not evaluated, in order to exclude the possibility of a description bias in the patient's records. The patients were classified into those with complications and those without complications.

Evaluations and statistical analyses

The parameters evaluated in this study included the intraoperative L-HR, L-MAP, and estimated blood loss. The SAS was calculated using these 3 parameters (Table 1).[18]

Univariate and multivariate logistic regression analyses were performed to identify the risk factors for morbidity. Comparisons between the two groups were analyzed by the χ^2 test. In the multivariate analysis, we fitted linear regression models. To select a model, we used backward elimination. All statistical tests were two-sided, and significance was set at $P < 0.05$. The SPSS software package (v11.0 J Win, SPSS, Chicago, Illinois) was used for all statistical analyses.

This study was approved by the Institutional Review Board Committee of the Kanagawa Cancer Center.

Results

Patients

We selected 189 patients for this study. The clinicopathologic characteristics of the patients are shown in Table 2. The median age of the study population was 68 years (range, 40–86 years). A total of 107 patients were male and 82 patients were female. A total of 49 patients underwent distal pancreatic surgery, 125 patients underwent pancreaticoduodenectomy, and 15 patients underwent total pancreatic resection. The median length of the operation was 485 minutes (range, 140–1195 minutes). The median blood loss was 1095 mL (range, 60–10,175 mL).

Surgical morbidity and mortality

Postoperative complications were found in 73 of 189 patients (38.6%). Surgical mortality was observed in 3 patients (1.6%) due to a cerebrovascular accident, myocardial infarction, and abdominal abscess. The details of the complications are shown in Table 3. Delayed gastric emptying was the most frequently diagnosed complication, followed by pancreatic fistula, abdominal abscess, surgical site infection, and postoperative bleeding. Grade 2 complications occurred in 73% of the patients, grade 3 in 22%, grade 4 in 2.5%, and grade 5 in 2.5%.

Risk factors for surgical morbidity

The risk factors for surgical morbidity were analyzed by univariate and multivariate analyses using the preoperative and perioperative factors. The results are summarized in Table 4. Among the various factors examined, an SAS of 0 to 4 points ($P = 0.046$) and a BMI ≥ 25 kg/m^2 ($P = 0.013$) were identified as significant independent risk factors for overall morbidity. When comparing the details of the complications after pancreatic surgery between the SAS 0- to 4-point group and the 5- to 10-point group, the occurrence of an abdominal abscess was significantly different between the two groups ($P = 0.034$). The incidence of abdominal abscess was 13.6% (9 of 66) in the SAS 0- to 4-point group and 4.9% (6 of 123) in the SAS 5- to 10-point group. The rate of delayed gastric emptying tended to be higher in patients with an SAS of 0 to 4 points compared with patients with an SAS of 5 to 10 points ($P =$

Table 2 Association between patient characteristic and complication severity according to the Clavien-Dindo classification

Factors	No. (%) of patients with complications Grade 1 or lower	Grade 2 or higher	*P* value
Preoperative factors			
Sex			0.421
Male	63 (58.9)	44 (41.1)	
Female	53 (64.6)	29 (35.4)	
Age			0.468
<75 y	97 (62.6)	58 (37.4)	
≥75 y	19 (55.9)	15 (44.1)	
Body mass index			0.016
<25	104 (65)	56 (35)	
≥25	12 (41.4)	17 (58.6)	
ASA score			0.300
0–1	97 (59.9)	65 (40.1)	
2–3	19 (70.4)	8 (29.6)	
Preoperative albumin			0.909
<3.5 g/dL	9 (60)	6 (40)	
≥3.5 g/dL	107 (61.5)	67 (38.5)	
Clinical stage			0.563
≤IIA	32 (58.2)	23 (41.8)	
≥IIB	84 (62.7)	50 (37.3)	
Perioperative factors			
Operations			0.043
DP	36 (73.5)	13 (26.5)	
PD or TP	80 (57.1)	60 (42.9)	
Operation time			0.060
<480 min	64 (68.1)	30 (31.9)	
≥480 min	52 (54.7)	43 (45.3)	
SAS			0.019
0–4	33 (50)	33 (50)	
5–10	83 (67.5)	40 (32.5)	

ASA, American Society of Anesthesiologists; DP, distal pancreatomy; TP, total pancreatomy.

0.076). The incidence of delayed gastric emptying was 16.7% (11 of 66) in the SAS 0- to 4-point group and 8.1% (10 of 123) in the SAS 5- to 10-point group. On the other hand, when comparing the details of the complications after pancreatic surgery between the BMI ≥25 kg/m^2 group and BMI <25 kg/m^2 group, the pancreatic fistula rate was significantly different between the two groups ($P < 0.001$). The incidence of pancreatic fistula was 34.5% (10 of 29) in the BMI ≥25 kg/m^2 group and 4.4% (7 of 160) in the BMI <25 kg/m^2 group.

Discussion

This is the first report to evaluate whether the SAS can predict the development of any complication of grade 2 or higher, as defined by the Clavien-Dindo classification, in patients undergoing pancreatic surgery for pancreatic cancer. The present study demonstrated that the SAS was an independent risk factor for surgical complications in the patients who underwent curative pancreatic surgery for pancreatic cancer.

The SAS was first proposed by Gawande *et al*[18] in 2007 and was intended for use immediately after surgery to predict patient outcomes. This surgical score reflects intraoperative hemodynamic stability and is influenced by various factors, such as the quality of surgery and anesthesia, and the patient's condition before and during surgery.[24] Previously, intraoperative hemodynamic changes were considered to be risk factors for surgical complications.[25,26] For example, Reich *et al*[25] reported that intraoperative hemodynamic changes were independently associated with an adverse outcome. In their study, they evaluated 797 patients who underwent noncardiac surgery and they analyzed the risk factors for negative surgical outcomes using intraoperative measurements of heart rate, mean arterial blood pressure, and systolic arterial blood pressure. They reported that intraoperative tachycardia and hypertension were independently associated with a negative surgical outcome after major noncardiac surgery of a long duration.[25] Although the estimated blood loss, L-MAP, and L-HR alone have been shown to be important predictors for complications in the past, the combination of these 3 variables is a unique characteristic of the SAS.[18] We were able to evaluate the intraoperative hemodynamic changes precisely using the 3 variables together, but this would not have been possible with a single variable. We consider that intraoperative hypovolemia and hypoperfusion, reflected by an increased estimated blood loss, increased L-HR, and decreased L-MAP, lead to lower perioperative tissue oxygenation, resulting in surgical complications.[27,28] In addition, a lower L-MAP and higher L-HR might reflect an intraoperative systemic inflammatory response syndrome, which is also associated with an increased postoperative complication rate.[29]

Previously, few reports had shown that a correlation exists between SAS and surgical complications in patients who had undergone PD. In one study, Assifi *et al*[30] reported that the SAS in patients who had undergone PD can serve as a predictor of surgical complications. In their study, they evaluated 553 patients undergoing PD and determined the association between grouped SASs (0–2, 3–4, 5–6, 7–8, and 9–10) and each type of postoperative complication. They demonstrated that the SAS is a significant predictor of perioperative complications for patients undergoing PD. However, there were

Table 3 Details of complications

	Grade 2	Grade 3a/3b	Grade 4a/4b	Grade 5	%
Pancreatic fistula	10	3/3	0/1	0	9.0
Abdominal abscess	4	6/2	0/1	1	7.4
Anastomotic leakage	1	2/0	0/0	0	1.6
Pneumonia	3	0/0	0/0	0	1.6
Postoperative bleeding	2	1/1	0/0	0	2.1
Wound abscess	9	0/0	0/0	0	4.8
Delayed gastric empty	21	0/0	0/0	0	11.1
Anastomotic stenosis	3	0/0	0/0	0	1.6
Portal vein thrombosis	2	0/0	0/0	0	1.1
Atrial fibrillation	1	0/0	0/0	0	0.5
Paralytic ileus	1	0/0	0/0	0	0.5
Delirium	7	0/0	0/0	0	3.7
Cholangitis	4	0/0	0/0	0	2.1
Chylous ascites	2	2/0	0/0	0	2.1
Ascites	6	0/0	0/0	0	3.2
Upper gastrointestinal bleeding	3	0/0	0/0	0	1.6
Cerebrovascular accident	0	0/0	0/0	1	0.5
Myocardial infarction	0	0/0	0/0	1	0.5
Urinary tract infection	1	0/0	0/0	0	0.5
Pleural effusion	1	0/0	0/0	0	0.5
Pulmonary edema	0	0/0	1/0	0	0.5
Septic shock	0	0/0	1/1	0	1.1

Table 4 Univariate and multivariate analyses of risk factors for complications

		Univariate analysis			Multivariate analysis		
Factors	No. of patients	OR	95% CI	*P* value	OR	95% CI	*P* value
Sex				0.421			
Female	82	1.000					
Male	107	1.276	0.704–2.313				
Age				0.468			
<75 y	155	1.000					
≥75 y	34	1.320	0.623–2.798				
Body mass index				0.019			0.013
<25	160	1.000			1.000		
≥25	29	2.631	1.174–5.897		2.894	1.256–6.670	
ASA score				0.303			
0–1	162	1.000					
2–5	27	1.591	0.657–3.849				
Preoperative albumin				0.909			
≥3.5 g/dL	174	1.000					
<3.5 g/dL	15	1.065	0.363–3.126				
Clinical stage				0.564			
≤IIA	55	1.000					
≥IIB	134	1.207	0.637–2.290				
Operation				0.046			0.081
DP	49	1.000			1.000		
PD or TP	140	2.077	1.014–4.255		1.956	0.921–4.156	
Operation time				0.061			
<480 min	94	1.000					
≥480 min	95	1.764	0.975–3.190				
SAS				0.019			0.046
5–10	123	1.000			1.000		
0–4	66	2.075	1.125–3.828		1.910	1.011–3.612	

ASA, American Society of Anesthesiologists; CI, confidence interval; DP, distal pancreatomy; OR, odds ratio; TP, total pancreatomy.

some differences between the present study and the previous study. First, the surgical procedures were different. The present study included distal pancreatectomy, PD, and total pancreatomy, whereas the previous study included only PD. Our findings suggested that SAS was still a predictor for postoperative complications, regardless of the type of pancreatic surgery. Generally, pancreatic cancer surgery requires a variety of surgical procedures for curative treatment. Second, the patients' backgrounds were different. In the present study, all of the patients who underwent pancreatic surgery for pancreatic cancer and periampullary neoplasms, such as intraductal papillary mucinous neoplasm, cystadenocarcinoma, and endocrine tumor, were excluded, because there are some biologic differences between pancreatic cancer and these other pancreatic diseases. The background of the patients in the previous study was unclear. Considering these factors, our findings might be more relevant for pancreatic cancer treatment.

In the present study, BMI was also an independent risk factor for surgical complications, and it was related to the occurrence of a pancreatic fistula after surgery. Some authors have reported a relationship between BMI and the development of a pancreatic fistula after surgery. For example, Gaujoux *et al*[31] evaluated 100 patients with pancreatic cancer and clarified that a BMI $\geq$25 kg/m^2 was one of the risk factors for a pancreatic fistula after surgery.[31] They showed that a higher BMI was associated with a higher frequency of pancreatic fistula formation. Similar results were presented in other reports. Although we set the cutoff value for the BMI at $\geq$25 kg/m^2, the cutoff value used for the BMI differed among the previous reports.[32,33] The differences in the findings of the study may be explained by the classification of surgical complications, the number of patients, and interinstitutional variability.

Special attention is required when interpreting the current results, because there are several potential limitations associated with this study. First, this study was a retrospective single-center study with a relatively small sample size. Our findings might have been obtained by chance. Second, the definition and classification of morbidity were different from those used in the previous study. These differences might have affected the results. However, the incidence of surgical morbidity was similar to that in the previous reports. For example, the incidence of pancreatic fistula formation in our study was nearly 9.0%, similar to the reported rates in many other large studies.[3,4] Third, the optimal cutoff value for the SAS is unclear. When comparing the surgical complications between the patients with complications and those without complications, there were clear separations between patients with an SAS of 0 to 4 points and those with a higher score according to the original report. However, the cutoff value might depend on the patient's background. Thus, an appropriate cutoff value should be determined in other validation studies in other populations. Considering these limitations, the current results should be validated in other series with a larger number of patients.

In summary, the SAS can predict the development of a complication of grade 2 or higher, as defined by the Clavien-Dindo classification, in patients undergoing curative resection for pancreatic cancer. Careful attention is required for patients with a low SAS when surgeons perform pancreatic surgery for pancreatic cancer.

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