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Estimation of Physiologic Ability and Surgical Stress (E-PASS) as a New Prediction Scoring System for Postoperative Morbidity and Mortality Following Elective Gastrointestinal Surgery

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Abstract: Overwhelming surgical stress exceeding a patient's reserve capacity causes a disruption of homeostasis, leading to various postoperative complications. This study was undertaken to develop a new scoring system, "E-PASS", standing for the Estimation of Physiologic Ability and Surgical Stress, that predicts the postsurgical risk by quantification of the patient's reserve and surgical stress. E-PASS comprises the preoperative risk score (PRS), the surgical stress score (SSS), and the comprehensive risk score (CRS) that is determined by both scores. These scores were computed by a multiple regression analysis conducted on 292 consecutive patients who underwent elective common gastrointestinal operations at one hospital between 1992 and 1995 (internal group). The usefulness of the scores was evaluated in 989 consecutive patients who underwent the same surgical procedures during the same period at another hospital (external group). The morbidity and mortality rates increased similarly in both groups as the CRS increased. A marked step-up of both rates was observed at a CRS > 1.0, reaching mortality rates of 20% in the internal subjects and 28.5% in the external subjects. These results suggest that the E-PASS scoring system is reproducible, and that it may be useful for surgical decision making. This system requires no special examinations and can be used in every hospital.

Key Words: risk score, surgery, morbidity, mortality

Introduction

Surgical insult induces the production of proinflammatory cytokines, and a characteristic biological response, currently termed "systemic inflammatory response syndrome" (SIRS).[1–3] These biological responses have been considered beneficial by augmenting immune functions and facilitating tissue repair; however, if surgical stress greatly exceeds a patient's reserve capacity, homeostasis cannot be maintained, causing various postoperative complications. Much evidence suggests that surgical insult induces the priming of neutrophils and their accumulation in vital organs. A second attack as a postoperative complication activates the primed neutrophils to attack the vital organs, resulting in the progression of organ dysfunction.[1,4] Therefore, it is important not to exceed the surgical stress able to be tolerated by the patient's physiologic reserve.

Informed consent of the surgical risk is becoming important; however, it is difficult to establish the rates of morbidity and mortality according to the patient's reserve capacity. Although there have been several scoring systems to assess the risk of mortality following special types of surgical procedures, or to assess the risk of developing particular types of complications,[5–12] these scoring systems cannot be applied in the majority of patients, or they do not address the relationship of surgical stress to complications. Some scores have been estimated from limited categories, such as nutritional status or cardiac scales,[5–8] and the generalized scores such as the APACHE II scoring system, widely used for intensive care unit (ICU) patients, only takes physiological scoring into account and ignores the severity of surgical stress.[13] POSSUM (a Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity) was originally developed for the comparison of surgical performance among different hospitals, and is not suitable for surgical decision making.[14] The physiological score of POSSUM comes from limited information; namely, history, vital signs, chest radiograph, and blood tests, since it targets emergency operations as well as elective settings. Thus, no scoring system has been designed to estimate the comprehensive risk in general gastrointestinal operations.

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We hypothesized the fact that morbidity and mortality rates may be correlated with the patient's physiologic risk and surgical stress applied, and that surgical stress may be estimated in general, since tissue destruction, bleeding, and ischemia by basic surgical techniques produce inflammatory cytokines.[1] This study was undertaken to develop a new scoring system that can be applied in a wide variety of elective gastrointestinal operations in order to select the most appropriate surgical procedure for an individual patient, thereby reducing postoperative morbidity and mortality.

Patients and Methods

The study was conducted in accordance with the Helsinki Declaration of 1975. The subjects consisted of two groups of nonselected patients. The current risk scoring system "E-PASS" (Estimation of Physiologic Ability and Surgical Stress) was computed in group A, and the usefulness of the scores was evaluated in an external group B. Group A comprised 292 consecutive patients, who underwent elective common gastrointestinal operations between 1992 and 1995 in the Department of Surgery II, Kumamoto University Medical School, Japan. The operations included transthoracic esophagectomy, transhiatal esophagectomy, conventional pancreatoduodenectomy, pylorus-preserving pancreatoduodenectomy, hepatectomy in the forms of trisegmentectomy, bisegmentectomy, segmentectomy, or wedge resection, total gastrectomy, proximal gastrectomy, distal gastrectomy, colon resections, laparoscopic cholecystectomy, low anterior resection, and Miles' operation. Group B comprised 989 consecutive patients who underwent the same operations during the same period in Kumamoto National Hospital, Japan. The indications for surgery and the selection of surgical procedures for each patient had been independently decided between these hospitals. All patients were analyzed retrospectively for preoperative physiological status, surgical procedures, and postoperative course. Data were collected from all medical and nursing charts. The patients diagnosed as having SIRS preoperatively were excluded from this study. The demographic data of both groups are shown in Table 1. The number of patients undergoing each individual surgical procedure was similar, with the exception of laparoscopic cholecytectomy, which was performed in a much larger proportion of patients in Kumamoto National Hospital where this operation was introduced in our district. All patients received prophylactic antibiotics, in the form of cephalosporins or penicillins, for 5 to 7 days following surgery. Routine laboratory tests for blood and urine were usually done on postoperative days 1, 3, 5, and 7 in both groups. Culture samples were collected from drain fluids, urine, sputum, stool, arterial blood, or catheter tips, when necessary. In both groups, patients who underwent transthoracic radical esophagectomy were routinely given empirical mechanical ventilation as positive end-expiratory pressure or continuous positive airway pressure for a few days. In group A, the peak serum C-reactive protein (CRP) levels and SIRS were usually monitored following surgery. In both groups, patients with severe organ dysfunction who required mechanical support were admitted to ICU until the acute phases had passed. The mechanical support in both hospitals included countershock for ventricular fibrillation, intraaortic balloon pumping for acute heart failure, artificial respiration and nitrogen oxide inhalation for adult respiratory distress syndrome (ARDS), plasma exchange or continuous hemodiafiltration (CHDF) for hepatic failure, and CHDF or hemodialysis for acute renal failure (ARF).

Table 1. Demographic data of the subjects

	Group A (internal subjects)	Group B (external subjects)
No. of patients	292	989
Esophagectomy	24	23
Total gastrectomy	41	29
Partial gastrectomy	68	63
PD	17	15
Hepatectomy	22	12
LC	32	770
Colon resection	53	45
Rectal resection	35	32
Male: female	188:104	433:556
Age	65[46–77.9]*	57[39–73]*
ASA class 1:2:3:4:5	87:174:30:1:0	319:634:36:0:0
Crude morbidity rate	18.8%	8.4%
Crude mortality rate	1.0%	0.91%

PD, pancreatoduodenectomy; LC, laparoscopic cholecstectomy
* A median [10th to 90th percentile range]

Postoperative complications were only included in this analysis when medical or interventional treatment had been carried out. Complications in group A occurred in 55 patients and consisted of pneumonia (n = 14), anastomotic leakage (n = 13), intraabdominal abscess without evident leakage (n = 7), severe atelectasis (n = 5), anastomotic stenosis requiring dilation (n = 5), reflux cholangitis (n = 4), wound infection (n = 4), ARDS (n = 4), hepatic failure (n = 4), severe arrhythmia (n = 3), ileus requiring enteral tube or reoperation (n = 3), ARF (n = 3), severe bronchial asthma (n = 2), urinary tract infection (n = 2), heart failure (n = 2), acute pancreatitis (n = 2), cerebral bleeding (n = 1), femoral thrombosis (n = 1), intrapleural bleeding (n = 1), myocardial infarction (n = 1), osteomyelitis (n = 1), and wound dehiscence

(n = 1). Complications in group B occurred in 83 patients and consisted of wound infection (n = 19), anastomotic leakage (n = 17), pneumonia (n = 13), wound dehiscence (n = 12), ileus requiring enteral tube or reoperation (n = 7), anastomotic stenosis requiring dilation or reoperation (n = 7), ARDS (n = 6), bile leakage (n = 6), hepatic failure (n = 4), intraabdominal abscess without evident leakage (n = 4), pneumothorax (n = 3), severe atelectasis (n = 2), ARF (n = 2), intrapleural bleeding (n = 1), cerebral infarction (n = 1), bronchial asthma (n = 1), acute pancreatitis (n = 1), bilateral recurrent nerve palsy (n = 1), intractable bleeding from duodenal ulcer requiring operation (n = 1), femoral thrombosis (n = 1), and severe paroxysmal atrial tachycardia (n = 1).

The degree of postoperative complications was arbitrary and determined as follows: grade 0, no complication; grade 1, mild complications, only applied for wound infection and wound dehiscence; grade 2, moderate complications that were potentially life-threatening unless adequate treatment was performed, including pneumonia, anastomotic leakage, and ileus; grade 3, severe organ dysfunction that usually required mechanical support, being equivalent to stage III in our own classification of organ dysfunction, but precise definitions were determined in seven organs;[4] and grade 4, in-hospital death due to complications.

Statistical Analysis

The degree of severity of the postoperative complications was analyzed by multiple regression analysis using 11 preoperative factors and 6 surgical factors, as suggested before.[15] All variables were first screened by a multiple regression analysis to select the variables. In this study, a standardized regression coefficient of more than 0.05 was used as a risk level to determine the variables. The preoperative factors included age, sex, performance status index, American Society of Anesthesiologists physiological status classifications (ASA classes), severe heart disease, severe pulmonary disease, liver cirrhosis, renal failure, cerebral vascular disease, diabetes mellitus, and hypertension. The performance status index was defined as follows.[16] Grade 0, conditions without symptoms that do not restrict social activities. Grade 1, conditions with mild symptoms that restrict muscular labor, but do not restrict walking or mild exertion. Grade 2, conditions that require some physical assistance for daily living, but do not restrict walking or mild exertion; grade 2 patients are not in bed for more than half of the day. Grade 3, conditions that require frequent physical assistance for daily living; grade 3 patients are in bed for more than half of the day. Grade 4, conditions that require constant physical assistance; grade 4 patients are in bed all day long. The ASA classes were defined as previously described,[17] as: class 1, a normally healthy patient; class 2, a patient with mild systemic disease; class 3, a patient with severe systemic disease that is not incapacitating; class 4, a patient with an incapacitating systemic disease that is a constant threat to life; and class 5, a moribund patient who is not expected to survive for 24 h with or without surgery. Severe heart disease was defined as heart failure of New York Heart Association Class III or IV, or severe arrythmia requiring mechanical support. Severe pulmonary disease was defined as any condition involving a %VC (vital capacity) of less than 60% and/or a $FEV_{1.0\%}$ (forced expiratory volume) of less than 50%. Renal failure was defined as conditions requiring hemodialysis or the clearance of creatinine of less than 10 ml/min. The definition of diabetes mellitus was based on the criteria of the World Health Organization. The surgical factors included blood loss/body weight (g/kg), operation time (h), extent of the skin incision, residual cancer following surgery, number of resected organs, and number of anastomoses. The extent of the skin incision was arbitrarily determined as follows: 0, minor incisions for laparoscopic or thoracoscopic surgery including scope-assisted surgery; 1, laparotomy or thoracotomy alone; and 2, both laparotomy and thoracotomy. A dummy coding of 1 or 0 was used for categorical variables, sex (male 1, female 0), and the presence (1) or absence (0) of severe heart disease, severe pulmonary disease, liver cirrhosis, renal failure, cerebral vascular disease, diabetes mellitus, hypertension, and residual cancer following surgery. There were six preoperative factors, namely, age, severe heart disease, severe pulmonary disease, diabetes mellitus, performance status index, and ASA classes, and three surgical factors, namely, blood loss/body weight, operation time, and extent of skin incision, identified as risk factors. Equations for the preoperative risk score (PRS) and surgical stress score (SSS) were computed by a multiple regression analysis using these factors. The PRS and SSS were then reentered into a multiple regression model to obtain a comprehensive risk score (CRS). The PRS in each patient was assessed just before the operation, since preoperative abnormalities were corrected in some patients.

The correlation between different continuous variables was quantified by Pearson's correlation coefficient (r), the significance of which was determined by Fisher's z-test. The correlation between continuous and ordinal variables was analyzed by Spearman's rank correlation (ϱ), the significance of which was determined by Spearman's rank sum test. The significance of the multiple correlation coefficient (R) was quantified by the analysis of variance (ANOVA). A two-tailed P value of less than 0.05 was considered significant.

Table 2. Equations for Estimation of Physiologic Ability and Surgical Stress (E-PASS) scores: preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS)

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

X_1, age; X_2, presence (1) or absence (0) of severe heart disease; X_3, presence (1) or absence (0) of severe pulmonary disease; X_4, presence (1) or absence (0) of diabetes mellitus; X_5, performance status index (0–4); X_6, American Society of Anesthesiologists physiological status classification (1–5)

Severe heart disease was defined as heart failure of New York Heart Association Class III or IV, or severe arrythmia requiring mechanical support. Severe pulmonary disease was defined as any condition with a% VC of less than 60% and/or a $FEV_{1.0\%}$ of less than 50%. Performance status index was based on the definition by Japanese Society for Cancer Therapy

2. $SSS = -0.342 + 0.0139X_1 + 0.0392X_2 + 0.352X_3$

X_1, blood loss/body weight (g/kg); X_2, operation time (h); X_3, extent of skin incision (0: minor incisions for laparoscopic or thoracoscopic surgery (including scope-assisted surgery); 1: laparotomy or thoracotomy alone; 2: both laparotomy and thoracotomy)

3. $CRS = -0.328 + 0.936\ (PRS) + 0.976\ (SSS)$

VC, vital capacity; FEV, forced expiratory volume

Results

Based on the results of the multiple regression analysis using 11 preoperative factors and six surgical factors, six preoperative and three surgical factors were identified as risk factors. Using these factors, the multiple regression analysis was reperformed to obtain the preoperative risk score (PRS), surgical stress score (SSS), and comprehensive risk score (CRS) determined by the PRS and SSS (Table 2). Multiple correlation coefficients (R) for the PRS, SSS, and CRS, which indicated the goodness of fit, were 0.248 ($P = 0.0057$), 0.456 ($P < 0.0001$), and 0.510 ($P < 0.0001$), respectively. Figure 1 shows a range of SSSs for each surgical procedure. The SSS was higher for major operations, such as radical esophagectomy, hepatectomy, and pancreatoduodenectomy in the internal group A that was used to determine the E-PASS scores, as well as in the external group B. The SSS for laparoscopic cholecystectomy was extremely low in both groups, while that for transhiatal esophagectomy, a less invasive alternative to transthoracic esophagectomy, was about half of that for transthoracic esophagectomy. The SSS for total gastrectomy was about 1.7-fold that for partial gastrectomy, indicating that the SSS seems to represent surgical stress. Furthermore, the SSS and CRS were significantly correlated with postoperative inflammatory parameters, peak serum CRP levels, and the duration of SIRS, whereas PRS had no correlation with these factors (Table 3).

The relationship between the CRS and postoperative complications is shown in Fig. 2. The incidence of postoperative complications gradually increased as the CRS increased in both the internal and external groups. A marked step-up of morbidity rates was observed with a CRS of more than 1.0, reaching 86.7% in the internal group and 78.5% in the external group. The mortality rates associated with a CRS greater than 1.0 reached

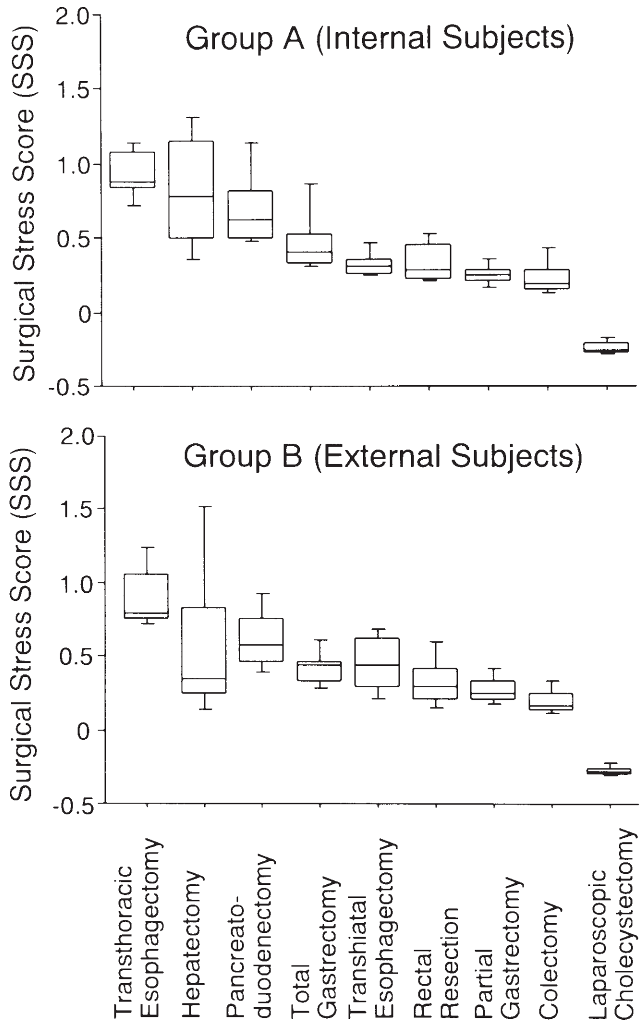

Fig. 1. Surgical stress score (*SSS*) of each surgical procedure. The SSS for each individual surgical procedure is shown in the internal group A where the equation for SSS was determined, as well as in the external group B. A *horizontal bar* within a *box*, a *box*, and *outer bars* represent a median, the 25th to 75th percentile range, and the 10th to 90th percentile range, repectively

Table 3. Correlations between the E-PASS scores and postoperative inflammatory parameters

	Peak serum CRP (mg/dl)	Duration of SIRS (days)
PRS	0.066 (n = 171)	0.026 (n = 236)
SSS	0.496* (n = 171)	0.410* (n = 236)
CRS	0.469* (n = 171)	0.371* (n = 236)

CRP, C-reactive protein; SIRS, systemic inflammatory response syndrome
Data are expressed as Pearson's correlation coefficients (r). These values were analyzed in the group A patients who had no evident postoperative complications
* $P < 0.001$ as determined by Fisher's z-test

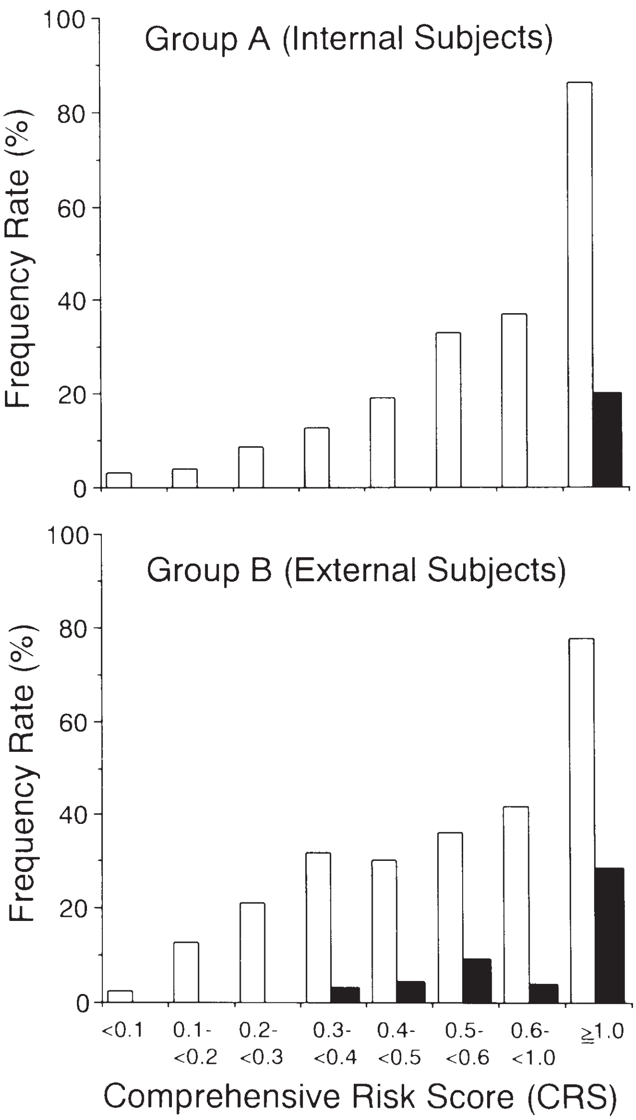

Fig. 2. Relationship between the comprehensive risk score (*CRS*) and postoperative complications. Morbidity and mortality rates were quantified according to the CRS in the internal group A, where the equation for CRS was determined, as well as in the external group B. *Open bars*, morbidity rate; *closed bars*, mortality rate

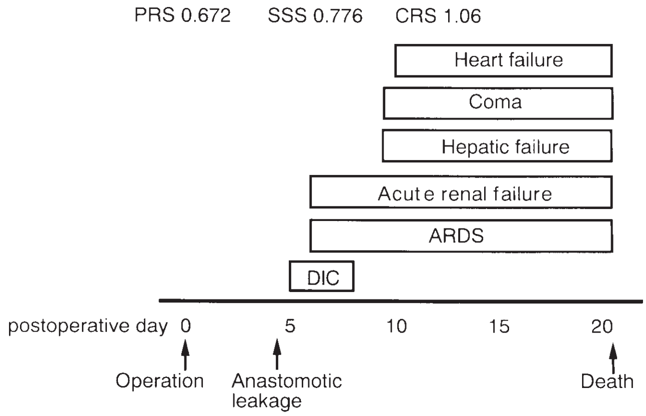

Fig. 3. The clinical course of an in-hospital death. A 71-year-old man with esophageal cancer had no preoperative evidence of severe heart disease, severe pulmonary disease, or diabetes mellitus. His performance status index was 2 and the American Society of Anesthesiologists class was judged as 3 because of his atrial fibrillation, aortic regurgitation, and chronic bronchitis (preoperative risk score 0.672). He underwent a right transthoracic esophagectomy with two-field lymphadenectomy, having an operation time of 7 h 20 min, with a blood loss of 600 g, and a SSS of 0.776. The CRS became 1.06. His postoperative course was disastrous. A leakage of the cervical anastomosis was found on postoperative day 4, followed by progressive multiple organ failure. He died on postoperative day 21. *ARDS*, adult respiratory distress syndrome; *DIC*, disseminated intravascular coagulation

20.0% in the internal group and 28.5% in the external group. The CRS correlated well with the severity of postoperative complications in both the internal and external groups as determined by Spearman's rank correlation test ($\varrho = 0.564$, $n = 292$, $P < 0.0001$ in the internal group A; $\varrho = 0.552$, $n = 989$, $P < 0.0001$ in the external group B).

Figure 3 shows the clinical course of an in-hospital death following radical esophagectomy. A 71-year-old man who had suffered from atrial fibrillation, aortic regurgitation, and chronic bronchitis before his operation had a PRS score of 0.672. He underwent right transthoracic esophagectomy with two-field lymph node dissection (SSS 0.776), subsequent to which the CRS reached 1.06. The surgical stress this patient was subjected to was probably too high for him to maintain homeostasis. Consequently, a second attack of anastomotic leakage induced progressive multiple organ failure and he died on postoperative day 21.

Discussion

Several methods have been applied to generate the equation for risk estimation. Some researchers have performed an univariate analysis, such as Student's t-

test or the chi-squared test to determine the risk factors, after which a multiple regression analysis or multiple logistic regression analysis was applied for the generation of the equation.[6,7,11] However, this method cannot account for the influence of other factors on the selection of risk factors. In the present subjects, this method did not give the marked step-up of morbidity and mortality rates, as did the CRS. While the stepwise multiple regression analysis is a suitable method to select risk factors and calculate the equations,[5,9] when we performed this method, the SSS was in the same equation as the current SSS. However, a PRS selected only three independent variables, namely, liver cirrhosis, performance status index, and ASA classes, and was an impractical interval variable. Conversely, the scores of the current E-PASS gave higher goodness of fit than those obtained by other methods, and seems to be the best scoring system. The multiple correlation coefficient, which shows a goodness of fit, for the current CRS (R = 510) is close to that of the equation obtained from all the preoperative and surgical variables ($R = 0.523$). The current PRS comes from the comprehensive categories of age, performance status index, ASA class, severe heart disease, severe pulmonary disease, and diabetes mellitus. In patients with severe diseases other than of the heart or lung, the risk will be reflected by the ASA class. The SSS is quite simple, consisting of blood loss/body weight, operation time, and the extent of skin incision. These scores do not require special examinations, and can be determined in every hospital.

Postoperative complications may result depending on three major factors, namely, the quality of the surgical team, the patient's physiological status, and the degree of surgical stress. The quality of the surgical team includes the skill of the surgeons, the quality of postoperative care, the number of staff in attendance, equipment, and the availability of an ICU. Where the quality of a surgical team in one hospital has remained stable for a certain period, the morbidity and mortality rates for individual patients can be estimated by quantification of the patient's physiological status and the surgical stress applied. Using the E-PASS scoring system, a surgeon can clarify the relationship of CRS and the morbidity and mortality rates for a certain period in his hospital as shown in Fig. 2, and calculate a range of SSSs for each surgical procedure from the previous operation records as shown in Fig. 1. The predictive risk for each surgical procedure on an individual patient can then be determined preoperatively. If the risk is too high for a patient, a less invasive procedure can be selected. For example, a 73-year-old man with lower esophageal cancer suffered a severe hemorrhage from the tumor. As a computed tomagraphy scan revealed no evidence of tumor invasion to the heart or large vessels, an operation was performed 5 days after the bleeding. The patient did not have severe heart disease, severe pulmonary disease, or diabetes mellitus. His performance status index was 3, he was classified as ASA class 3, and his PRS was 0.820 at that time. In the hospital, a 10th to 90th percentile range of SSS for transhiatal esophagectomy and esophagectomy via right thoracotomy and laparotomy was [0.253–0.417] and [0.802–1.15], respectively. If he underwent a transhiatal esophagectomy, his CRS was predicted to range from 0.686 to 0.847, and the morbidity and mortality rates were estimated at 37.5% and 0%, respectively. On the other hand, if he underwent a transthoracic esophagectomy, his CRS would vary from 1.22 to 1.56, and the estimated morbidity and mortality rates would be 86.7% and 20.0%, respectively. Thus, the E-PASS scoring system may be useful for the selection of surgical procedures.

In the current subjects, the SSS correlated better with the degree of postoperative complications than did the PRS, the multiple correlation coefficients for PRS, SSS, and CRS, being 0.248, 0.456, and 0.510, respectively. It is conceivable that postoperative complications depend mainly on the SSS, and that the PRS and CRS will not necessarily be calculated; however, this is not true when the subjects were limited to the aged population. Since the preoperative risk is usually high in these patients, limited operations are always performed. In the 67 gastric cancer patients aged over 80 years who underwent elective gastrectomy, the severity of postoperative complications correlated significantly with the PRS and CRS, but not with the SSS (unpublished data). Therefore, the risk of the operation should be analyzed by both preoperative risk factors and the surgical stress.

In conclusion, the E-PASS scoring system was generated based on the quantification of preoperative risk and surgical stress. Prior to surgery, the individual PRS and estimated range of the SSS can predict the morbidity and mortality rates of various surgical procedures. Surgeons can then inform the patient and the referring physicians of the predictive risk. Immediately after the operation, the individual SSS and CRS can be computed to predict the risk in postoperative care. A CRS of 1.0 may be taken as a critical threshold at which homeostasis is maintained in surgical patients.

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