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Risk Models of Operative Morbidities in 16,930 Critically Ill Surgical Patients Based on a Japanese Nationwide Database

Zenichiro Saze, MD, PhD, Hiroaki Miyata, PhD, Hiroyuki Konno, MD, PhD, Mitsukazu Gotoh, MD, PhD, Takayuki Anazawa, MD, PhD, Ai Tomotaki, RN, MS, Go Wakabayashi, MD, PhD, and Masaki Mori, MD, PhD

Abstract: The aim of the study was to evaluate preoperative variables predictive of lethal morbidities in critically ill surgical patients at a national level.

There is no report of risk stratification for morbidities associated with mortality in critically ill patients with acute diffuse peritonitis (ADP).

We examined data from 16,930 patients operated during 2011 and 2012 in 1546 different hospitals for ADP identified in the National Clinical Database of Japan. We analyzed morbidities significantly associated with operative mortality. Based on 80% of the population, we calculated independent predictors for these morbidities. The risk factors were validated using the remaining 20%.

The operative mortality was 14.1%. Morbidity of any grade occurred in 40.2% of patients. Morbidities correlated with mortality, including septic shock, progressive renal insufficiency, prolonged ventilation >48 hours, systemic sepsis, central nervous system (CNS) morbidities, acute renal failure and pneumonia, and surgical site infection (SSI), were selected for risk models. A total of 18 to 29 preoperative variables were selected per morbidity and yielded excellent C-indices for each (septic shock: 0.851; progressive renal insufficiency: 0.878; prolonged ventilation >48 h: 0.849; systemic sepsis: 0.839; CNS morbidities: 0.848; acute renal failure: 0.868; pneumonia: 0.830; and SSI: 0.688).

We report the first risk stratification study on lethal morbidities in critically ill patients with ADP using a nationwide surgical database. These risk models will contribute to patient counseling and help predict which patients require more aggressive surgical and novel pharmacological interventions.

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Abbreviations: ADL = activities of daily living, ADP = acute diffuse peritonitis, APACHE II = Acute Physiology and Chronic Health Evaluation II, ASA = American Society of Anesthesiologists, BMI = body mass index, CIs = confidence intervals, CNS = central nervous system, CVA = cerebrovascular accident, JSGS = Japanese Society of Gastroenterological Surgery, NCD = National Clinical Database, ROC = Receiver operating characteristic, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.

INTRODUCTION

Acute diffuse peritonitis (ADP) is defined as the uncontained spread of intraabdominal infection, rapidly proceeding beyond the source of infection into multiple (2–4) quadrants of the intraabdominal cavity.[1] Most patients diagnosed with ADP are critically ill and therefore require emergency surgery, regardless of the source of infection.[2–4] A high incidence of severe postoperative complications such as septic shock, pneumonia, and organ failure has resulted in a high mortality rate of approximately 30%, even in modern case series.[4] Therefore, the identification of postoperative complications associated with mortality and their optimal treatment is necessary to improve outcomes. There have been risk models for mortality in critically ill patients. The Acute Physiology and Chronic Health Evaluation II (APACHE II) score,[5] Sequential Organ Failure Assessment score,[6] and Mannheim Peritonitis Index[7] have all been shown to be quite effective for predicting mortality in critically ill patients. However, there has been no risk model for the morbidity of critically ill patients using a nationwide database.

American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) risk models are powerful predictors of specific morbidities and mortality associated with gastrointestinal surgery.[8–10] However, there has been no nationwide analysis of critically ill surgical patients. In one regional report, Turner et al[11] showed that ACS-NSQIP criteria were associated with high APACHE II scores and poor outcomes in 340 surgical patients (mortality: 20.6%) treated in the intensive care unit of the University of Maryland Medical Center (Baltimore, MD). They found that APACHE II score predictions were consistent with ACS-NSQIP postoperative outcomes. This observation prompted us to hypothesize that ACS-NSQIP preoperative variables could be used to predict both postoperative morbidities and mortalities in ADP patients.

The National Clinical Database (NCD) in Japan, which commenced patient registration in January 2011, is a nationwide project linked to the surgical board certification system.[12,13] Submitting cases to the NCD is a prerequisite for all member institutions of both the Japan Surgical Society and Japanese Society of Gastroenterological Surgery, and only registered cases can be used for board certification. The NCD collaborates with the ACS-NSQIP[10]: they share the common goal of developing a standardized surgery database to achieve an improvement in treatment quality.[14]

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From the Japanese Society of Gastroenterological Surgery (JSGS) (ZS, TA, MM), JSGS Database Committee (HM, HK, MG, GW), and National Clinical Database (HM, AT), Tokyo, Japan.
Correspondence: Mitsukazu Gotoh, Department of Regenerative Surgery, Fukushima Medical University, 1-Hikarigaoka, Fukushima City 960-1295, Japan (e-mail: mgotoh@fmu.ac.jp).
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Previously, we reported that patients with ADP are critically ill, most require emergency surgery, and their 30-day mortality and 90-day in-hospital mortality rates are 9% and 13.9%, respectively.[15] In this study, we used data from 16,930 patients with ADP treated in 2011 and 2012 and registered with the NCD to create risk models for postoperative morbidities associated with mortality.

METHODS

Patient Selection

The NCD is a nationwide project associated with the board certification system of surgery in Japan into which data from over 1,200,000 surgical cases treated at over 3500 hospitals are entered annually. We have created risk models of mortality for the 8 surgical procedures (esophagectomy, total gastrectomy, distal gastrectomy, right hemicolectomy, low anterior resection, hepatectomy, pancreaticoduodenectomy, and ADP) using NCD data sets, and the respective model was published separately,[15–22] and the results were summarized as a review article.[13] Thus, patient selection, preoperative and perioperative variables, and ethics consideration were quite consistent between the studies. The NCD continuously recruits individuals who approve these data, members of various departments in charge of cases, and data entry officers through a web-based data management system; thus, the traceability of the data is assured.[12] In addition, the project constantly validates the consistency of these data by the inspection of randomly chosen institutions. Current laws, ordinances, and guidelines regarding the confidentiality of data are observed. Patients agree for their data to be included in research projects by using presumed consent with opt-out through the Web page and/or a notice of each hospital.[20] The NCD project was approved on November 2010 by Japan Surgical Society Ethics Committee.

In this study, we focused on ADP in the Gastrointestinal Surgery section of the NCD. In the NCD, we identified 16,930 patients who underwent surgery for ADP in 2011 to 2012. Patients who declined to have their records entered in the NCD were excluded from our analysis. Records with missing data on patient age, sex, or status, 30 days after surgery were also excluded.

Preoperative and Perioperative Variables

The preoperative and perioperative variables used by the NCD are almost identical to those used by the ACS-NSQIP (http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_UserGuide.2012.pdf#search='user+guide+for+the+2012+ACS+NSQIP). All variables, definitions, and inclusion criteria regarding the NCD are accessible to participating institutions on its website (http://www.ncd.or.jp/), which also features an E-learning system to instruct participants in how to input consistent data. The potential independent variables were previously described.[13,15–22] These included patient demographics, preexisting comorbidities, preoperative laboratory values, and perioperative data (Table 1).

Outcome Measures (Mortality and Postoperative Occurrences)

We calculated the 30-day mortality and operative mortality. The former was defined as death within 30 days of surgery, regardless of the patient's geographical location, even if the patient had been discharged from the hospital. The latter was defined as death within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), as well as any death after discharge within 30 days of surgery.

The postoperative morbidities that occurred within 30 days of surgery included relaparotomy within 30 days of surgery; wound-related morbidities (superficial incisional surgical site infection [SSI], deep incisional SSI, organ/space SSI, wound disruption); respiratory morbidities (pneumonia, unplanned intubation, pulmonary embolism, ventilation >48 hours); urinary tract morbidities (progressive renal insufficiency, acute renal failure, urinary tract infection); central nervous system (CNS) morbidities (stroke/cerebrovascular accident [CVA], coma for <24 hours, peripheral nerve injury); cardiac morbidities (cardiac arrest, myocardial infarction); and other occurrences (bleeding 1–4 u or ≥5 u red blood cells, deep-vein thrombosis/thrombophlebitis, septic shock, severe sepsis, systemic inflammatory response syndrome [SIRS]).

Statistical Analysis

We used IBM SPSS Statistics for Windows (Version 20; IBM Corp, Armonk, NY) for data analysis. Univariate analysis of the data was performed using Fisher exact test, the unpaired Student t test, and the Mann–Whitney U test. Correlations between each morbidity and operative mortality and between respective morbidities were analyzed using the Pearson product–moment correlation.

Data were randomly assigned into2 subsets that were split 80/20: the first for model development and the second for validation. The 8 sets of logistic models (septic shock, systemic sepsis, progressive renal insufficiency, acute renal failure, ventilation >48 hours, pneumonia, CNS morbidities, and SSI) were constructed for dataset development using step-wise selection of the predictors with a probability (P) value for inclusion of 0.05. A ''goodness-of-fit'' test was performed to assess how well the model discriminated between patients with or without respective morbidities. Receiver operating characteristic (ROC) curves for respective morbidities were created for the validation dataset. A ROC curve is a plot of a test's true-positive rate (sensitivity) versus its false-positive rate (1−specificity).

RESULTS

Preoperative Risk Profiles and Laboratory Data of the Study Population

The demographic data and risk profile of 16,930 patients with ADP are shown in Table 1. The patient population had a mean age of 64.9 ± 18.6 years (range: 0–106 years), and 60.5% ($n = 10,248$) were male. In this population, 37.7% arrived at hospital by ambulance, and 92.9% required emergency surgery. Their original disease and associated operative mortalities were acute peritonitis (15.1%), appendicitis (1%), gastroduodenal ulcer/perforation (9.5%), intestinal perforation (18.4%), intestinal obstruction (18.9%), cholecystitis/cholangitis (13.3%), and vascular insufficiency (31.2%). These proportions and mortalities are consistent with findings from 2011.[15]

An abbreviated risk profile for the study population is also shown in Table 1. In brief, 58.4% of the patient population had an American Society of Anesthesiologists (ASA) classification of III–V, partial/total dependency for activities of daily living (ADL) was 41.2%, 0.5% of patients had body mass index (BMI) of >30 kg/m^2, and 5.1% of patients had a weight loss of >10%. With regard to preexisting comorbidities, failure of various organs occurred in a percentage of patients, including ventilator

TABLE 1. Preoperative Risk Profiles and Laboratory Data of the Study Population

Characteristics	Cases With Characteristics	% of Entire Population	No. of Death	Operative Mortality	Fisher
Demographics					
Age					
Under 60	5217	30.8%	236	4.5%	<0.001
61–65	1890	11.2%	185	9.8%	
66–70	1677	9.9%	236	14.1%	
71–75	1978	11.7%	349	17.6%	
76–80	2248	13.3%	435	19.4%	
80 and over	3920	23.2%	944	24.1%	
Males	10248	60.5%	1389	13.6%	0.014
Ambulance transportation	6375	37.7%	972	15.2%	<0.001
Emergency case	15731	92.9%	2231	14.2%	0.213
Preoperative risk assessment					
General					
ADL immediately before surgery					
Totally dependent	2278	13.5%	758	33.3%	<0.001
Partially dependent	4690	27.7%	1326	28.3%	<0.001
ASA classification					
Class 4 and 5	2431	14.4%	990	40.7%	<0.001
Class 3	7448	44.0%	1919	25.8%	<0.001
Body mass index $\geq 30\,kg/m^2$	452	0.5%	78	17.3%	0.052
Body mass index $\geq 26\,kg/m^2$	1873	1.5%	249	13.3%	0.307
Alcohol drinking (at times/occasional)	7106	42.0%	784	11.0%	<0.001
Brinkmann index ≥ 600	2605	2.1%	358	13.7%	0.602
Brinkmann index ≥ 400	3551	2.7%	456	12.8%	0.017
>10% loss body weight in last 6 months	861	5.1%	295	34.3%	<0.001
Respiratory					
Ventilator dependent	646	3.8%	283	43.8%	<0.001
Current pneumonia	637	3.8%	278	43.6%	<0.001
History of severe COPD	563	3.3%	150	26.6%	<0.001
Respiratory failure	1391	8.2%	545	39.2%	<0.001
Cardiovascular					
Congestive heart failure	447	2.6%	195	43.6%	<0.001
Hypertension requiring medication	5046	29.8%	901	17.9%	<0.001
Hypertension without treatment	521	3.1%	89	17.1%	0.052
Renal					
Acute renal failure	742	4.4%	321	43.3%	<0.001
Cerebral nervous system					
CVA/Stroke with neurological deficit	482	2.8%	111	23.0%	<0.001
Cerebrovascular disease within 14 days	142	0.8%	32	22.5%	0.006
Cerebrovascular disease	812	4.8%	202	24.9%	<0.001
Hematological					
Bleeding disorder without treatment	1086	6.4%	373	34.3%	<0.001
Bleeding disorder	1828	10.8%	592	32.4%	<0.001
Preop Transfusion of ≥ 1 unit of RBCs	3487	20.6%	1028	29.5%	<0.001
Any blood transfused in the emergency room	702	4.1%	287	40.9%	<0.001
Infectious disorder					
Systemic sepsis	5233	30.9%	1266	24.2%	<0.001
Other					
Epidural anesthesia	3482	20.6%	224	0.064	<0.001
Open wound	450	2.7%	128	28.4%	<0.001
Steroid use for chronic condition	677	4.0%	197	29.1%	<0.001
Ascites without control	3742	22.1%	811	21.7%	<0.001
Esophageal varices without control	89	0.5%	29	32.6%	<0.001
Disease					
Acute peritonitis	8613	50.9%	1300	15.1%	<0.001
Appendicitis	2470	14.6%	24	1.0%	<0.001
Gastroduodenal ulcer/perforation	1742	10.3%	166	9.5%	<0.001
Intestinal perforation	2504	14.8%	461	18.4%	<0.001

Characteristics	Cases With Characteristics	% of Entire Population	No. of Death	Operative Mortality	Fisher
Intestinal obstruction	855	5.1%	162	18.9%	<0.001
Cholecystitis/cholangitis	451	2.7%	60	13.3%	0.676
Vascular insufficiency	253	1.5%	79	31.2%	<0.001
Oncological					
Other than cancer surgery	15202	89.8%	1899	12.5%	<0.001
Preoperative laboratory value					
WBC < 3500/mL	2717	3.3%	567	20.9%	<0.001
Hematocrit over 48% (male), 42% (female)	1056	0.7%	122	11.6%	0.015
Plate count < 150,000/mL	2798	4.7%	799	28.6%	<0.001
Plate count < 50,000/mL	199	0.6%	105	52.8%	<0.001
Serum albumin < 3.5 g/dL	8839	11.0%	1864	21.1%	<0.001
Serum albumin < 2.5 g/dL	3334	5.8%	977	29.3%	<0.001
Serum albumin < 2.0 g/dL	1293	2.8%	471	36.4%	<0.001
SGOT ≥ 40 U/L	3225	4.8%	819	25.4%	<0.001
SGOT ≥ 35 U/L	3848	5.5%	933	24.2%	<0.001
Bilirubin < 0.2 mg/dL	40	0.0%	8	20.0%	0.259
Serum creatinine ≥ 3.0 mg/dL	1104	2.2%	374	33.9%	<0.001
Serum creatinine ≥ 2.0 mg/dL	1980	3.7%	634	32.0%	<0.001
Serum creatinine ≥ 1.2 mg/dL	4378	6.9%	1176	26.9%	<0.001
BUN ≥ 60 mg/dL	905	2.0%	337	37.2%	<0.001
BUN ≥ 25 mg/dL	5458	8.5%	1435	26.3%	<0.001
BUN ≥ 20 mg/dL	7398	10.2%	1728	23.4%	<0.001
Serum sodium < 130 mEq/L	924	1.4%	236	25.5%	<0.001
Serum sodium ≥ 146 mEq/L	316	0.7%	120	38.0%	<0.001
Alkaline phosphatase < 110 mEq/L	372	0.4%	63	16.9%	0.111
CRP > 10 mg/dL	7934	7.3%	1240	15.6%	<0.001
INR of PT values ≥ 1.67	796	1.5%	248	31.2%	<0.001
PT < 10 s	1886	2.4%	398	21.1%	<0.001
PTT < 30 s	4330	2.5%	429	9.9%	<0.001

ADL = activities of daily living; ASA classification = American Society of Anesthesiologists Physical Status Classification; AST = aspartate amino transferase; BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CVA = cerebrovascular accident; WBC = white blood cell.

dependence (3.8%), congestive heart failure (2.6%), and acute renal failure (4.4%). Signs of systemic sepsis were evident in 30.9% of patients. Blood transfusion was required in 4.1% of patients. An ASA classification of >IV and V and organ failure were associated with an operative mortality rate of >40%.

Postoperative Occurrences in Patients with ADP

The 30-day mortality and operative mortality rates after surgery for ADP were 8.8% (1482) and 14.1% (2385), respectively. The incidences of various morbidities and percentage of consequent patient deaths are shown in Table 2. The postoperative morbidities that led to a high percentage of deaths (>40%) included transfusion (1–4 U: 43.5%; >5 U: 52.2%), prolonged ventilation (45.6%), unplanned intubation (51.4%), pneumonia (43%), cardiac and CNS morbidities (90.3% and 64.8%, respectively), acute renal failure (57.1%), progressive renal insufficiency (55.6%), any systemic sepsis (41%), and septic shock (55.8%). These morbidities occurred at a relatively high incidence (4.8%–15%) excepting cardiac morbidities (2.5%). SSI of any type, including organ space, deep incisional, and superficial incisional, occurred in 23.2% of patients and led to an operative mortality rate of 20.8%.

Correlation Between Postoperative Morbidities and Operative Mortality

Correlation between 30-day operative mortality rates and postoperative morbidities were analyzed using the Pearson product–moment correlation. The morbidities highly correlated with mortality (top 7) as well as SSI as the most representative complication of ADP were selected and are compared in Table 3. A better correlation with postoperative morbidities was found when operative rather than 30-day mortality was used. Among the postoperative morbidities, septic shock, progressive renal insufficiency, and ventilation >48 hours were highly correlated with each other ($r > 0.5$). In contrast, SSI was only moderately correlated with systemic sepsis, and weakly correlated with ventilation >48 hours.

Model Results and Performance

We developed risk models for postoperative morbidities with a relatively high incidence associated with high mortality (Table 4; Supplemental Table, http://links.lww.com/MD/A344, with 95% confidence intervals [CIs]). The postoperative morbidities selected correlated well with operative mortality. Septic shock, systemic sepsis (SIRS, sepsis, or septic shock), progressive renal insufficiency, acute renal failure, ventilation >48 hours, pneumonia, and CNS morbidities were selected, and SSI was also included as the most frequent morbidity.

The logistic models of these morbidities with odds ratios are shown in Table 4. The morbidities with a 95% CI showing statistical significance are shown in the Supplemental Table, http://links.lww.com/MD/A344. To evaluate the performance of the models, the C-index (a measure of model discrimination), which was the area under the ROC curve, was calculated for the

TABLE 2. Postoperative Occurrences After ADP Surgery

Postoperative Outcomes	Cases With the Outcome	% of Entire Population	No. of Death	% Death With the Outcome	% Death Without the Outcome	Fisher
General						
Any complication	6808	40.2	1828	26.9	5.5	<0.001
Bleeding transfusions	2353	13.9	1023	43.5	9.3	<0.001
Bleeding transfusions ≥5 units	1337	7.9	698	52.2	10.8	<0.001
Reoperation within 30 d	1317	7.8	317	24.1	13.2	<0.001
Readmission within 30 d	340	2.0	14	4.1	14.3	<0.001
Respiratory						
On Ventilator >48 h	2592	15.3	1182	45.6	8.4	<0.001
Unplanned intubation	821	4.8	422	51.4	12.2	<0.001
Pneumonia	1693	10.0	728	43.0	10.9	<0.001
Cardiovascular						
Cardiac arrest/myocardial infarction	421	2.5	380	90.3	12.1	<0.001
Pulmonary embolism	55	0.3	16	29.1	14.0	<0.001
Cerebral nervous system						
CVA/Stroke	867	5.1	562	64.8	11.3	<0.001
Renal						
Acute renal failure	960	5.7	548	57.1	11.5	<0.001
Progressive renal insufficiency	1740	10.3	967	55.6	9.3	<0.001
Infectous disorder						
Systemic sepsis	3321	19.6	1361	41.0	7.5	<0.001
Septic shock	1786	10.5	996	55.8	9.2	<0.001
Sepsis	826	4.9	224	27.1	13.4	<0.001
SIRS	709	4.2	141	19.9	13.8	<0.001
SSI	3931	23.2	819	20.8	12.0	<0.001
Organ space SSI	1865	11.0	541	29.0	12.2	<0.001
Deep incisional SSI	1648	9.7	475	28.8	12.5	<0.001
Superficial SSI	3052	18.0	632	20.7	12.6	<0.001
Wound disruption	1179	7.0	403	34.2	12.6	<0.001
Urinary tract infection	440	2.6	124	28.2	13.7	<0.001

CVA = cerebrovascular accident, SIRS = systemic inflammatory response syndrome, SSI = surgical site infection.

validation sets (Figure 1). The C-indices and 95% CIs of each occurrence were 0.851 (0.841–0.860) for septic shock, 0.878 (0.870–0.887) for progressive renal insufficiency, 0.849 (0.841–0.858) for ventilation >48 hours, 0.848 (0.835–0.862) for CNS morbidities, 0.868 (0.856–0.880) for acute renal failure, 0.830 (0.819–0.840) for pneumonia, and 0.851 (0.841–0.860) for systemic sepsis. The C-index of SSI showed a weaker correlation (0.688 [0.677–0.698]) than other morbidities.

A total of 18 to 29 preoperative variables were selected as risk factors of each complication. Age, ASA classification, preoperative ventilation or pneumonia, acute renal failure, blood transfusion, and systemic sepsis, as well as selected preoperative laboratory values suggestive of severe infection and organ failure, were captured in the risk models as predictors of most of the complications.

DISCUSSION

We hypothesized that ACS-NSQIP preoperative variables could be used to predict both postoperative morbidities and mortalities in ADP patients. In total, 93% of 16,930 patients with ADP included in this study required emergency surgery, and the overall operative mortality was 14.1%. This was comparable with the findings of a previous analysis using NCD data from 2011,[15] in which 93.1% of patients with ADP required emergency surgery, and the overall operative mortality was 8.8%. This suggests that there is a consistent population of critically ill surgical patients who require emergency surgery in Japan. By examining the data of a large number of patients with ADP, we were able to identify the postoperative complications associated with mortality and create risk models for each complication. Septic shock, progressive renal insufficiency, ventilation >48 hours and systemic sepsis were moderately correlated ($r > 0.36$) with operative mortality, whereas CNS morbidities, acute renal failure, and pneumonia were weakly ($0.2 < r \leq 0.35$) correlated with operative mortality. For these complications, risk models showed excellent C-indices (>0.830) in the validation dataset. To our knowledge, this is the first report to successfully show and validate using a large-scale dataset that the preoperative variables of the ACS-NSQIP can predict postoperative morbidities in critical ill patients.

The prediction of postoperative complications is essential to the decision-making process before surgery, and useful to identify patients eligible for participation in the evaluation of novel pharmacologic interventions[23,24] or more aggressive surgical interventions. In the past, several scoring systems have been used to predict complications.[25–31] ASA score is a useful predictor for mortality,[25,26] but suffers from its reproducibility because of subjective parameters.[26] APACHE II was developed in a mixed group of medical and surgical patients.[27] It failed to

TABLE 3. Correlation Between Operative Mortality and Respective Postoperative Occurrences

Occurences	thirtyday mortality	operative mortality	Septic shock	Progressive renal insufficiency	On Ventilator > 48 Hours	Any systemic sepsis	CVA/Stroke	Acute renal failure	Pneumonia	SSI
30-day mortality	1	.765	.398	.365	.327	.336	.328	.301	.187	.034
Operative mortality	.765	1	.411	.404	.385	.382	.339	.303	.277	.107
Septic shock	.398	.411	1	.526	.579	.695	.390	.465	.371	.268
Progressive renal insufficiency	.365	.404	.526	1	.554	.536	.411	.724	.390	.283
On Ventilator > 48 h	.327	.385	.579	.554	1	.621	.434	.444	.491	.329
Any systemic sepsis	.336	.382	.695	.536	.621	1	.367	.421	.439	.428
CVA/Stroke	.328	.339	.390	.411	.434	.367	1	.343	.265	.157
Acute renal failure	.301	.303	.465	.724	.444	.421	.343	1	.303	.195
Pneumonia	.187	.277	.371	.390	.491	.439	.265	.303	1	.285
SSI any	.034	.107	.268	.283	.329	.428	.157	.195	.285	1

The column mark indicates the following:

0.3 ≤ r < 0.4 0.4 ≤ r < 0.5 0.5 ≤ r

CVA = cerebrovascular accident, SSI = surgical site infection.

predict the development of multiple organ failure syndrome or mortality with clinical utility in postoperative surgical patients.[28] Physiological and Operative Severity Score for the enUmeration of Mortality and Morbidity has been studied as a possible surgical audit system[29]; however, it seems to overestimate mortality, particularly for the low risk group.[30,31] A reliable model for predicting complications can only be based on the accurately recorded incidences of those complications. A comparison of the outcomes of patients with ADP registered with the NCD in 2011 with those registered in 2012 revealed that mortality and morbidities were highly correlated between these years ($r = 0.9932$; Supplemental Figure, http://links.lww.com/MD/A344). The thorough data retrieval system of the NCD and clinically clear entity of ADP made it possible to create successful risk models for these morbidities.

Severe sepsis/septic shock, defined as the presence of acute organ dysfunction in the context of infection, has a mortality rate of approximately 25% to 35%,[32,33] but which can exceed 70%.[34,35] Anaya and Nathens[36] analyzed risk factors of severe sepsis in 11,202 patients using Washington State administrative hospital discharge data. They identified 11% with severe sepsis, which was present in 424 (62%) of the 686 decedents, and showed that source of infection, extent of peritonitis, increasing age, and preexisting organ dysfunction were independently associated with severe sepsis. Our findings on the mortality of patients with ADP were consistent with their study. The mortality of patients with ADP as a result of appendicitis was low (1%) compared with that associated with other causes such as intestinal/gastroduodenal perforation (18.4%/9.5%), vascular insufficiency (31.2%), and cholecystitis/cholangitis (13.3%). Regarding peritonitis, when it is localized within an abscess, the operative mortality rate of cases registered with the NCD was relatively low (4.6%; 254 deaths/5470 cases) compared with that of patients with ADP (14.1%). This study provides more reliable information on clinical variables and laboratory data compared with the findings of Anaya and Nathens.[36] We were able to select significant variables to predict each complication, and discrimination and calibration using validation tests clearly showed the excellent performance of these models.

It is interesting to note that the risk models for morbidities moderately associated with mortality (septic shock, any systemic sepsis, renal failure, acute renal failure, prolonged ventilation, pneumonia, and CNS morbidities) picked up similar variables as risk factors—age, ADL status, ASA classification, blood transfusions, and systemic sepsis—to those found to be

TABLE 4. Risk Models of Postoperative Occurrences After ADP Surgery

Variable	Septic Shock	Any Systemic Sepsis	Progressive Renal Insufficiency	Acute Renal Failure	On Ventilator > 48 Hours	Pneumonia	CVA/ Stroke	SSI Any
Demographics								
Age 60–75	1.144	1.095	1.105	1.144	1.16	1.214	1.174	1.04
Males		1.153			1.13	1.317		
Preoperative risk assessment								
General								
ADL totally dependent	1.178				1.399		1.426	
ADL partially dependent		1.175	1.23			1.278		
ASA class 4 and class 5	3.635	2.993	3.147	3.474	3.341	2.321	3.433	1.705
ASA class 3	1.77	1.888	1.957	1.922	2.066	1.837	1.691	1.347
Body mass index $\geq 30\,kg/m^2$					1.567			
Body mass index $\geq 26\,kg/m^2$			1.438	1.614	1.224			1.274
Alcohol drinking (at times/ occasional)			1.181	1.256		1.206		1.118
Brinkmann index ≥ 600	1.199				1.217			
Brinkmann index ≥ 400		1.162						
>10% loss body weight in last 6 months								1.561
Respiratory								
Ventilator dependent	1.519	1.404	1.305		2.734		2.035	
Current pneumonia		1.35	1.667	1.704	1.89	4.994	1.599	
History of severe COPD	1.371				1.472	1.403		
Respiratory failure	1.236					1.292		
Cardiovascular								
Congestive heart failure			1.501		1.331			
Hypertension requiring medication		1.119	1.199		1.235			
Hypertension without treatment								
Renal								
Acute renal failure	1.471	1.258	2.975	3.869	1.26	1.504		
Cerebral nervous system								
CVA/Stroke		1.346		1.675	1.376	1.631	1.826	
Cerebrovascular disease within 14 days		1.933					3.406	
Cerebrovascular disease	1.373					1.421		
Hematological								
Bleeding disorder without treatment	1.437	1.494		1.471	1.377	1.289	1.92	
Bleeding disorder			1.361					
Blood transfusions	1.511	1.556	1.514	1.61	1.887	1.546	1.432	1.17
Preoperative transfusion of ≥ 1 unit of RBCs			1.303		1.369			1.355
Infectious disorder								
Systemic Sepsis	2.821	4.086	1.974	2.035	2.092	1.901	1.776	1.824
Oncological								
Other than cancer surgery	0.734		0.803					
Other								
Open wound		1.469						2.186
Steroid use for chronic condition	1.486		1.585		1.586	1.545		1.507
Ascites without control		1.17						
Esophageal varices without control					1.846			
Preoperative laboratory value								
WBC < 3500/mL	1.989	1.462	1.318	1.55	1.553		1.428	1.225
Hematocrit over 48% (male), 42% (female)	1.441	1.334		1.52	1.493			
Plate count < 150,000/mL		1.175	1.192					
Plate count < 50,000/mL	1.741							
Serum albumin < 3.5 g/dL		1.286			1.153			1.162
Serum albumin < 2.5 g/dL	1.267					1.18	1.251	
Serum albumin < 2.0 g/dL		1.287	1.403		1.606	1.255		1.227

Variable	Septic Shock	Any Systemic Sepsis	Progressive Renal Insufficiency	Acute Renal Failure	On Ventilator > 48 Hours	Pneumonia	CVA/ Stroke	SSI Any
SGOT ≥ 40 U/L							1.252	
SGOT ≥ 35 U/L	1.272	1.198	1.4	1.454	1.281			
Bilirubin < 0.2 mg/dL						2.611		
Serum creatinine ≥ 3.0 mg/dL							1.626	
Serum creatinine ≥ 2.0 mg/dL		1.233	1.637					
Serum creatinine ≥ 1.2 mg/dL	1.454		1.721	1.566	1.202		1.31	
BUN ≥ 60 mg/dL				1.388				
BUN ≥ 25 mg/dL			1.362	1.43				
BUN ≥ 20 mg/dL	1.355	1.357	1.344		1.404	1.278	1.415	1.156
Serum sodium < 130 mEq/L		1.233						
Serum sodium ≥ 146 mEq/L		1.482	1.432	1.586	1.68	1.501	1.499	
Alkaline phosphatase < 110 mEq/L								1.487
CRP > 10 mg/dL								1.353
INR of PT values ≥ 1.67	1.44	1.239						
PT < 10 s						1.232		1.157
PTT < 30 s	1.181							1.137

ADL = activities of daily living; ASA = American Society of Anesthesiologists Physical Status; AST = aspartate amino transferase; BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CVA = cerebrovascular accident; WBC = white blood cell.

risk factors of mortality in patients with ADP.[15] Preoperative variables associated with organ dysfunction tended to be included as risk factors in most of the risk models: preoperative ventilation/pneumonia, acute renal failure, bleeding disorders, low white blood cell count, low albumin level, and elevation of blood urea nitrogen.[15] High serum sodium levels, indicative of severe dehydration in patients, were also identified. In contrast, the risk model for SSI, which was poorly associated with mortality ($r = 0.107$), showed a relatively low C-index (0.688) compared with the other risk models. Risk factors such as pulmonary, renal, and cerebral disorders were not included in the risk model. The key part of these risk models is that variables

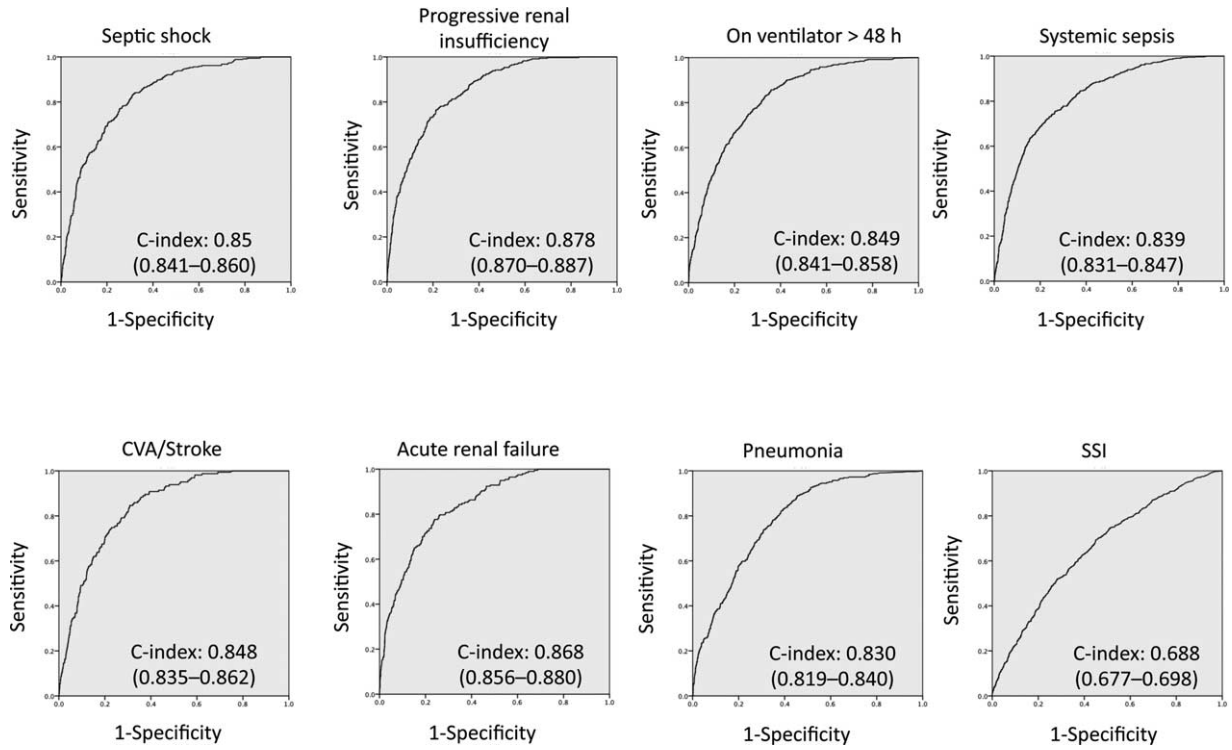

FIGURE 1. Receiver operating characteristic (ROC) curves of each postoperative complication was shown with the C-indices and 95% CIs of each occurrence. ROC = receiver operating characteristic, CIs = confidence intervals.

that were not included as risk factors of mortality were picked up as predictors of morbidities leading to mortality. This will help to improve the postoperative management of patients with ADP.

There are several limitations to this study. First, although these risk models for morbidities effectively predicted their occurrence based on preoperative variables, the source of infection and degree of its control would affect mortality and morbidity. These intraoperative parameters will be evaluated in a future study. Second, in the NCD data-entry system, the final outcome of each morbidity, whether it improved, was unresolved, led to death, and was not recorded. It is not possible to relate each morbidity directly to mortality, although most fatal cases feature multiple organ failure at the end.

ADP is a clinically distinct entity requiring life-saving emergency surgery and intensive care. We created risk models for morbidities in critically ill patients with ADP, using variables recorded by the NCD comparable to those of the ACS-NSQIP, and these models performed well. These models could be formatted to feed information back to the NCD and can be expected to improve the quality of the surgical and postoperative care of patients with ADP.

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