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ORIGINAL ARTICLE

Predicting surgical outcomes of acute diffuse peritonitis: Updated risk models based on real-world clinical data

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Abstract

Aim: The existing predictive risk models for the surgical outcome of acute diffused peritonitis (ADP) need renovation by adding relevant variables such as ADP's definition or causative etiology to pursue outstanding data collection reflecting the real world. We aimed to revise the risk models predicting mortality and morbidities of ADP using the latest Japanese Nationwide Clinical Database (NCD) variable set.

Methods: Clinical dataset of ADP patients who underwent surgery, and registered in the NCD between 2016 and 2019, were used to develop a risk model for surgical outcomes. The primary outcome was perioperative mortality.

Results: After data cleanup, 45 379 surgical cases for ADP were derived for analysis. The perioperative and 30-day mortality were 10.6% and 7.2%, respectively. The prediction models have been created for the mortality and 10 morbidities associated with the mortality. The top five relevant predictors for perioperative mortality were age >80, advanced cancer with multiple metastases, platelet count of <50 000/mL, serum albumin of <2.0 g/dL, and unknown ADP site. The C-indices of perioperative and 30-day mortality were 0.859 and 0.857, respectively. The predicted value calculated with the risk models for mortality was highly fitted with the actual probability from the lower to the higher risk groups.

Conclusions: Risk models for postoperative mortality and morbidities with good predictive performance and reliability were revised and validated using the recent real-world clinical dataset. These models help to predict ADP surgical outcomes accurately and are available for clinical settings.

KEYWORDS
acute diffuse peritonitis, national clinical database, prediction, risk model

1 | INTRODUCTION

Globally, acute diffused peritonitis (ADP) is a typical medical and surgical emergency that remains a disease with high mortality despite improvements in surgical and intensive care management.[1–3] It is essential to promptly diagnose ADP and appropriate treatments because potentially fatal infectious complications such as septic shock and disseminated intravascular coagulation (DIC) would deteriorate if adequate intervention is delayed. The treatment for ADP involves a comprehensive approach that includes medical and surgical interventions. Prompt and aggressive management is crucial to prevent complications and improve outcomes. Surgical intervention is the mainstay therapy for addressing the underlying cause of ADP and drainage of intra-abdominal infectious fluid[4]; however, the postoperative mortality rates of ADP were reported to be between 8.4% and 34% from isolated studies.[5–8] Indeed, preoperative conditions of ADP patients can be associated with high mortality and severe complications.[9,10] Given that emergency surgery, which could be invasive for clinically ill patients, must be considered for ADP, precious prediction of surgical outcomes is extremely important for decision support between medical providers and the patients or their families.

Knowledge about risk factors for mortality of ADP has been accumulated as several scoring systems for evaluating the severity of ADP were reported, such as APACHE-2, P-POSSUM, or Mannheim peritonitis index.[9–12] Similarly, most scoring systems were developed from a dataset in an author's unit. With the increasing usage of electric health records (EHR) in the medical and healthcare field, it has been recognized that using real-world data from the EHR is significant in developing machine learning-based predictive risk models.[13,14] In Japan, in previous studies, postoperative mortality risk models for eight major gastroenterological surgeries, including ADP, were created using the national clinical database (NCD) and reported separately.[7,15–21] Regarding ADP, a surgical risk model for predicting mortality was initially developed using 8482 surgical cases registered in the NCD in 2011,[7] followed by risk models for predicting operative morbidities using 16 930 cases reported in 2011 and 2012.[22] The developed risk models were implemented as risk calculators on the NCD web system. The probabilities of mortality and morbidities in a patient were calculated and available for any medical provider (http://www.ncd.or.jp).

ADP is a clinical syndrome rather than a definitive diagnosis as the causative etiology varies widely: frequent etiologies were ruptured appendix, ischemic bowel disease, gastrointestinal tract perforation, and so on.[23–25] In addition, the severity of ADP is considered to vary depending on its cause and responsible site. In the initial database between 2011 and 2015, the classification of ADP (primary, secondary, or tertiary peritonitis) and clinical information about the detailed etiology and responsible organ (or site) was not contained in the NCD registry items, which became a limitation of the initially developed risk model. Since 2016, Such information has been added to the NCD items. Under a new NCD project, the current study was conducted to create new NCD risk models for predicting surgical outcomes of ADP using the current and larger database from 2016.

2 | METHODS

2.1 | Data source and patient selection

The NCD is Japan's largest nationwide surgical registry, established in 2010. The NCD project systematically collects and analyzes data and uses them to improve the quality of surgical procedures in Japan.[26] The accuracy of the NCD data was ensured through systematic audits for standard NCD input initiated by the Japanese Society of Gastroenterological Surgery (JSGS) database committee in 2016.[27] In the current study, perioperative data were retrieved from the NCD in patients who underwent surgery for ADP between January 2016 and December 2019. Preoperative and perioperative variables registered in the NCD system were used in the current study.

2.2 | Clinical data registry regarding the definition of ADP

Acute diffused peritonitis can be classified based on various factors, including the underlying etiology or the organs/sites responsible within the abdomen. When classifying ADP, primary peritonitis occurs due to bacterial translocation, hematogenous spread, or iatrogenic contamination of the abdomen without a macroscopic defect in the gastrointestinal tract (e.g., idiopathic). On the other hand, secondary peritonitis arises from direct contamination of the peritoneum by spillage from the gastrointestinal or urogenital tracts or their associated solid organs (e.g., perforation, acute appendicitis, or ruptured suture). Tertiary peritonitis is persistent secondary peritonitis lasting 48 h after an attempted surgical source control.[2,28,29] A clear definition of ADP is crucial for developing a relevant risk model. The NCD registry from 2016 has included variables related to the classification of ADP (primary, secondary, or tertiary peritonitis), detailed etiology, and the responsible organ/site as data items (refer to Table S1).

2.3 | Outcome measures

The primary outcome of this study was perioperative mortality of ADP, which was defined as 30-day postoperative mortality and in-hospital mortality. For the secondary outcomes, 11 postoperative complications strongly associated with perioperative death were selected according to the number of events and their association with mortality. The 11 postoperative complications included 30-day mortality, organ space surgical site infection (SSI), pneumonia, unplanned intubation, mechanical ventilation, acute renal failure,

impaired consciousness, respiratory arrest, sepsis, disseminated intravascular coagulation (DIC), and postoperative transfusion.

2.4 | Statistical analysis

Descriptive statistics were produced for the study subjects' demographic, clinical, and laboratory characteristics. Categorical variables were expressed as numbers and percentages. A risk model was generated for each outcome using a backward stepwise logistic regression with the Akaike information criterion (AIC). According to previous studies and clinical knowledge, candidate covariates for inclusion in the risk models were selected from registry variables relevant to the outcomes. Avoiding quasi-complete separation problems in a logistic regression model, when the number of events (or non-events) for any one of the covariate levels was <5, the levels were merged, or the covariate was excluded from the candidate. If the correlation coefficient between two covariates was >0.9, the covariate considered more important was left in the candidate covariate list to avoid multicollinearity. The performance of the risk model was evaluated using the c-index and a calibration plot. The optimism of the c-index was corrected using Harrell's bias correction method.[30] Confidence intervals for the c-index were calculated using the location-shifted bootstrap method[31] since the sample size was sufficiently large. The number of bootstrap samples was set to 200.

Similarly, bootstrapping was used to correct optimism in the calibration plot.[30] The statistical significance level was set at 0.05; all tests were two-tailed. All statistical analyses were performed using R software version 4.0 and later (R Foundation, Vienna, Austria, https://www.r-project.org/). Backward stepwise variable selection method and calibration plots were performed using the rms R package version 6.2 and later (Frank E Harrell Jr., https://CRAN.R-project.org/package=rms).

3 | RESULTS

3.1 | Patients characteristics and preoperative risk profiles and laboratory data of the study population

Between 2016 and 2019, the NCD registered 3088308 surgical cases in the gastroenterological surgery section. We collected clinical data on 45379 surgical cases for ADP after excluding duplicate patients on the NCD registry ($n=1663$), a patient with categorization mismatch ($n=1$), and patients with missing data ($n=11966$) (Figure 1). The characteristics of the study cohort are summarized in Table 1. Notably, emergency surgery and ambulance transportation accounted for 93.4% and 44.3% of cases, respectively, which is comparable with the previous NCD reports.[7,22] In the classification of ADP, secondary peritonitis was dominant, accounting for 92.7%. Regarding etiology, bowel perforation was a leading cause, accounting for 68.5% of cases. "Upper gastrointestinal tract (stomach, duodenum, or small bowel)" and "large bowel" were the frequent organs causing ADP, accounting for 38.5% and 37.8% of cases, respectively (Table 1).

3.2 | Occurrence of mortality and morbidity in patients with ADP

The incidence of perioperative mortality and the 30-day postoperative mortality, and the 10 morbidities are summarized in Table 2. Perioperative mortality and the 30-day mortality rates for the 45379 surgical cases were 10.6% and 7.2%, respectively. The association between morbidities of ADP and perioperative mortality or the 30-day mortality is shown in Table 2. The 10 mortalities with a high number of events relatively strongly associated with perioperative mortality were selected as secondary outcomes: organ space SSI, pneumonia, unplanned intubation, respiratory failure, acute renal failure, impaired consciousness, cardio-respiratory arrest, sepsis, and DIC. The "reoperation" was excluded from the secondary outcomes because the mortality rate was not so high as that of "unplanned intubation" or "cardio-respiratory arrest".

3.3 | Risk models for predicting postoperative outcomes and their predictive performance

A risk model was created for each surgical outcome based on multivariate logistic analysis (Table 3 and Table S2). The risk model for perioperative mortality, primary outcome, retained 55 predictors, including variables of etiology and organ or site responsible for ADP (Table 3). The top five relevant predictors for perioperative mortality were selected according to an absolute value of beta coefficient value in the multivariate logistic model. The top five relevant predictors were "age ≥81 (OR = 3.83)", "age;76–80 (OR = 2.82)", "advanced cancer with multiple metastases (OR = 2.43)", "platelet count <50,000/mL (OR = 2.67)", and "serum albumin <2.0 g/dL (OR = 2.60)".

The C-index, which is the area under the ROC curve, and the 95% confidence interval (CI) were calculated with the bootstrap-based optimism correction method to evaluate the discriminative performance of each model.[30] The C-indices of perioperative mortality and 30-day mortality were 0.859 (95% CI: 0.855–0.865) and 0.857 (95% CI: 0.853–0.864), respectively, which were comparable to those of the initially reported model.[7] Regarding postoperative morbidities, the C-indices were >0.80 except for organ space SSI (C-index:0.704), pneumonia (C-index:0.799), and unplanned intubation (C-index: 0.774) (Table 4). To summarize, these findings indicated the good discrimination performance of the risk model developed in the current study.

The calibration plots of the risk model for predicting each outcome are shown in Figure 2. The predicted value of all the surgical outcomes except unplanned intubation, cardio-respiratory arrest, and DIC was highly fitted with the actual probability from the lower to the higher risk groups. The consistency of the calibration plots

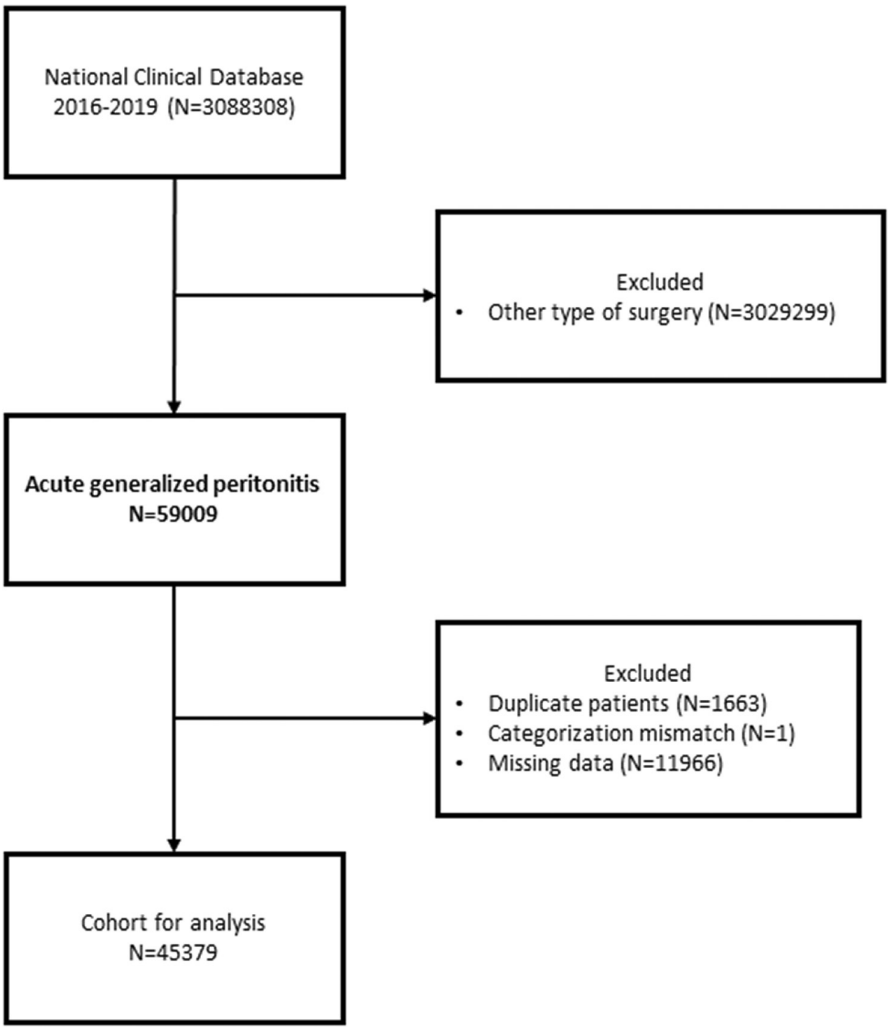

FIGURE 1 Patient flow.

in the three models remained in the low-risk group; however, they overpredicted the incidence in the higher-risk group.

4 | DISCUSSION

In the present study, new risk models for predicting postoperative mortality and morbidities of ADP were revised with newly added variables, causative etiology, and responsible organ or site and validated using the recent NCD dataset. The discrimination performance of the developed risk models of perioperative mortalities and the 30-day mortality was sufficiently high, with 0.857 (95% CI: 0.853–0.864) and 0.859 (95% CI: 0.855–0.865) of the C-index, respectively, which were comparable to those of initial report.[7] The calibration assessment showed all the models except unplanned intubation, cardio-respiratory arrest, and DIC were fitted well from the lower to the higher risk groups, suggesting reliable risk models in clinical use. Therefore, the newly developed risk models were considered valuable and reliable for predicting postoperative outcomes of ADP.

Given the wide variation in causes of ADP, it is crucial to define ADP when developing a risk model precisely. In this study, the latest dataset from the NCD was utilized, providing new relevant variables such as ADP classification, etiology, and causative organ. This addition was aimed at addressing the limitations of the previous study. To our knowledge, this database represents the largest national registry with comprehensive clinical variables for defining the ADP population. Notably, within the entire cohort, 92.7% had secondary peritonitis, which often requires prompt surgical intervention. Therefore, the newly developed risk models exhibit significant strength in predicting surgical outcomes for these patients.

In addition, a novelty of the current study is to reveal the impact of the causative etiology or causative organ of ADP for predicting surgical outcomes. These variables were selected as a predictor of the developed risk models, which was considered to complement the limitation of the previous study. The number of factors comprising the risk models increased; however, most were factors selected in the previous studies.

A recent report of gastroenterological surgery in Japan using the NCD between 2011 and 2019 showed that surgical cases of ADP have been increasing and that the 30- and 90-day mortalities have been steadily decreasing in these years, while the postoperative morbidities classified as Clavien–Dindo grade 3 or higher remained high.[16] Considering the transition, it is meaningful to develop a new

TABLE 1 Profiles and laboratory data of the entire study population and outcome groups.

Variables	Entire study population	Surgical outcomes											
		Perioperative mortality	30-day mortality	Organ space SSI	Pneumonia	Unplanned intubation	Respiratory failure	Acute renal failure	Impaired consciousness	Cardio-respiratory arrest	Sepsis	DIC	Transfusion
Number of patients (% of the entire population)	*n* = 45 379	*n* = 4809 (10.6)	*n* = 3259 (7.2)	*n* = 3997 (8.8)	*n* = 2869 (6.3)	*n* = 1568 (3.5)	*n* = 5535 (12.2)	*n* = 2317 (5.1)	*n* = 1508 (3.3)	*n* = 743 (1.6)	*n* = 6647 (14.6)	*n* = 2295 (5.1)	*n* = 5490 (12.1)
Demographics		No. (%)											
Age, Under 60 years	12 496	413 (3.3)	263 (2.1)	820 (6.6)	250 (2.0)	172 (1.4)	672 (5.4)	260 (2.1)	180 (1.4)	89 (0.7)	902 (7.2)	250 (2.0)	779 (6.2)
61–65 years	3911	338 (8.6)	206 (5.3)	361 (9.2)	137 (3.5)	104 (2.7)	357 (9.1)	168 (4.3)	75 (1.9)	32 (0.8)	452 (11.6)	146 (3.7)	442 (11.3)
66–70 years	6076	588 (9.7)	360 (5.9)	613 (10.1)	342 (5.6)	208 (3.4)	728 (12.0)	304 (5.0)	177 (2.9)	88 (1.4)	892 (14.7)	287 (4.7)	751 (12.4)
71–75 years	5785	720 (12.4)	476 (8.2)	611 (10.6)	442 (7.6)	246 (4.3)	812 (14.0)	351 (6.1)	215 (3.7)	107 (1.8)	995 (17.2)	353 (6.1)	826 (14.3)
76–80 years	6063	831 (13.7)	573 (9.5)	634 (10.5)	519 (8.6)	305 (5.0)	991 (16.3)	425 (7.0)	253 (4.2)	135 (2.2)	1158 (19.1)	427 (7.0)	924 (15.2)
81 and over years	11 048	1919 (17.4)	1381 (12.5)	958 (8.7)	1179 (10.7)	533 (4.8)	1975 (17.9)	809 (7.3)	608 (5.5)	292 (2.6)	2248 (20.3)	832 (7.5)	1768 (16.0)
Sex, male	27 000	2763 (10.2)	1829 (6.8)	2396 (8.9)	1840 (6.8)	980 (3.6)	3256 (12.1)	1388 (5.1)	827 (3.1)	423 (1.6)	3753 (13.9)	1269 (4.7)	3077 (11.4)
BMI: <26 kg/m^2	39 900	4219 (10.6)	2830 (7.1)	3429 (8.6)	2563 (6.4)	1348 (3.4)	4728 (11.8)	1938 (4.9)	1290 (3.2)	629 (1.6)	5770 (14.5)	2012 (5.0)	4811 (12.1)
≥26, and <30 kg/m^2	4114	435 (10.6)	310 (7.5)	424 (10.3)	228 (5.5)	155 (3.8)	560 (13.6)	267 (6.5)	152 (3.7)	91 (2.2)	630 (15.3)	212 (5.2)	506 (12.3)
≥30 kg/m^2	1365	155 (11.4)	119 (8.7)	144 (10.5)	78 (5.7)	65 (4.8)	247 (18.1)	112 (8.2)	66 (4.8)	23 (1.7)	247 (18.1)	71 (5.2)	173 (12.7)
General													
Ambulance transportation	20 111	2350 (11.7)	1735 (8.6)	1510 (7.5)	1465 (7.3)	736 (3.7)	3043 (15.1)	1291 (6.4)	878 (4.4)	406 (2.0)	3542 (17.6)	1245 (6.2)	2658 (13.2)
Emergent surgery	42 397	4524 (10.7)	3076 (7.3)	3776 (8.9)	2717 (6.4)	1479 (3.5)	5321 (12.6)	2204 (5.2)	1429 (3.4)	718 (1.7)	6370 (15.0)	2208 (5.2)	5196 (12.3)
ADL within 30 days, any assistance	7143	1667 (23.3)	1160 (16.2)	898 (12.6)	1072 (15.0)	467 (6.5)	1752 (24.5)	643 (9.0)	594 (8.3)	257 (3.6)	1885 (26.4)	653 (9.1)	1571 (22.0)
ADL just before surgery, any assistance	11 942	2391 (20.0)	1678 (14.1)	1416 (11.9)	1435 (12.0)	736 (6.2)	2694 (22.6)	1013 (8.5)	837 (7.0)	371 (3.1)	2792 (23.4)	1098 (9.2)	2390 (20.0)
ASA classifications 3, 4 and 5	21 736	3975 (18.3)	2753 (12.7)	2632 (12.1)	2221 (10.2)	1237 (5.7)	4599 (21.2)	1887 (8.7)	1282 (5.9)	628 (2.9)	5147 (23.7)	1868 (8.6)	4239 (19.5)
Smoking habit within 1 year	9491	661 (7.0)	432 (4.6)	755 (8.0)	483 (5.1)	253 (2.7)	869 (9.2)	388 (4.1)	212 (2.2)	113 (1.2)	1071 (11.3)	346 (3.6)	909 (9.6)
Alcohol consumption habitat	10 447	816 (7.8)	534 (5.1)	936 (9.0)	574 (5.5)	337 (3.2)	1092 (10.5)	487 (4.7)	260 (2.5)	140 (1.3)	1271 (12.2)	473 (4.5)	1115 (10.7)
Diabetes	7150	925 (12.9)	626 (8.8)	768 (10.7)	571 (8.0)	307 (4.3)	1105 (15.5)	494 (6.9)	317 (4.4)	146 (2.0)	1282 (17.9)	455 (6.4)	1065 (14.9)
Esophageal varix within 6 months	248	57 (23.0)	44 (17.7)	35 (14.1)	25 (10.1)	14 (5.6)	60 (24.2)	35 (14.1)	20 (8.1)	6 (2.4)	69 (27.8)	17 (6.9)	75 (30.2)
Chronic steroid use	1927	407 (21.1)	282 (14.6)	240 (12.5)	244 (12.7)	126 (6.5)	423 (22.0)	177 (9.2)	114 (5.9)	67 (3.5)	505 (26.2)	179 (9.3)	427 (22.2)
Blood coagulation abnormality without anticoagulant	1695	439 (25.9)	313 (18.5)	296 (17.5)	281 (16.6)	114 (6.7)	531 (31.3)	282 (16.6)	187 (11.0)	73 (4.3)	619 (36.5)	236 (13.9)	478 (28.2)
Blood coagulation abnormality with anticoagulant	2468	465 (18.8)	338 (13.7)	305 (12.4)	305 (12.4)	160 (6.5)	595 (24.1)	267 (10.8)	165 (6.7)	85 (3.4)	638 (25.9)	232 (9.4)	545 (22.1)
Sepsis just before surgery	7063	1851 (26.2)	1370 (19.4)	1261 (17.9)	1105 (15.6)	602 (8.5)	2575 (36.5)	1267 (17.9)	853 (12.1)	352 (5.0)	3440 (48.7)	1099 (15.6)	2024 (28.7)
Cardiovascular factors													
Hypertension within 30 days	16 508	2133 (12.9)	1473 (8.9)	1596 (9.7)	1318 (8.0)	723 (4.4)	2529 (15.3)	1115 (6.8)	681 (4.1)	340 (2.1)	2950 (17.9)	1098 (6.7)	2401 (14.5)

(Continues)

TABLE 1 (Continued)

Variables	Entire study population	Surgical outcomes											
		Perioperative mortality	30-day mortality	Organ space SSI	Pneumonia	Unplanned intubation	Respiratory failure	Acute renal failure	Impaired consciousness	Cardio-respiratory arrest	Sepsis	DIC	Transfusion
Congestive heart failure within 30 days	801	270 (33.7)	198 (24.7)	121 (15.1)	161 (20.1)	86 (10.7)	299 (37.3)	156 (19.5)	117 (14.6)	60 (7.5)	289 (36.1)	111 (13.9)	245 (30.6)
Myocardial infarction within 6 months	219	69 (31.5)	49 (22.4)	28 (12.8)	32 (14.6)	25 (11.4)	63 (28.8)	28 (128)	21 (9.6)	19 (8.7)	73 (33.3)	18 (8.2)	56 (25.6)
Angina pectoris within 30 days	527	98 (18.6)	74 (14.0)	44 (8.3)	60 (11.4)	38 (7.2)	104 (19.7)	47 (8.9)	28 (5.3)	26 (4.9)	125 (23.7)	39 (7.4)	97 (18.4)
Previous PCI	1139	225 (19.8)	158 (13.9)	127 (11.2)	129 (11.3)	80 (7.0)	248 (21.8)	99 (8.7)	62 (5.4)	43 (3.8)	279 (24.5)	105 (9.2)	232 (20.4)
Previous cardiac surgery	742	154 (20.8)	105 (14.2)	98 (13.2)	79 (10.6)	55 (7.4)	207 (27.9)	83 (11.2)	47 (6.3)	28 (3.8)	187 (25.2)	86 (11.6)	175 (23.6)
Previous PVD with a symptom	196	75 (38.3)	49 (25.0)	44 (22.4)	32 (16.3)	25 (12.8)	77 (39.3)	31 (15.8)	26 (13.3)	16 (8.2)	68 (34.7)	29 (14.8)	53 (27.0)
Previous PVD surgery	301	88 (29.2)	57 (18.9)	46 (15.3)	45 (15.0)	24 (8.0)	87 (28.9)	33 (11.0)	29 (9.6)	16 (5.3)	91 (30.2)	42 (14.0)	79 (26.2)
Respiratory factors													
Ventilator dependent within 48 h	1161	477 (41.1)	345 (29.7)	246 (21.2)	255 (22.0)	145 (12.5)	726 (62.5)	251 (21.6)	244 (21.0)	101 (8.7)	532 (45.8)	196 (16.9)	476 (41.0)
COPD	1390	276 (19.9)	185 (13.3)	190 (13.7)	252 (18.1)	118 (8.5)	341 (24.5)	145 (10.4)	87 (6.3)	47 (3.4)	352 (25.3)	126 (9.1)	271 (19.5)
Current pneumonia	1026	331 (32.3)	233 (22.7)	178 (17.3)	455 (44.3)	128 (12.5)	456 (44.4)	172 (16.8)	127 (12.4)	49 (4.8)	393 (38.3)	150 (14.6)	323 (31.5)
Respiratory distress within 30 days	2100	706 (33.6)	494 (23.5)	386 (18.4)	467 (22.2)	225 (10.7)	856 (40.8)	361 (17.2)	290 (13.8)	127 (6.0)	783 (37.3)	277 (13.2)	650 (31.0)
Renal factors													
Acute renal failure within 24 h	1384	495 (35.8)	366 (26.4)	291 (21.0)	270 (19.5)	129 (9.3)	644 (46.5)	623 (45.0)	265 (19.1)	103 (7.4)	723 (52.2)	261 (18.9)	476 (34.4)
Dialysis within 14 days	1632	540 (33.1)	379 (23.2)	258 (15.8)	192 (11.8)	119 (7.3)	453 (27.8)	127 (7.8)	175 (10.7)	84 (5.1)	501 (30.7)	197 (12.1)	474 (29.0)
Cerebral nerve factors													
Previous cerebrovascular disease	2469	382 (15.5)	258 (10.4)	277 (11.2)	321 (13.0)	145 (5.9)	529 (21.4)	219 (8.9)	164 (6.6)	60 (2.4)	568 (23.0)	218 (8.8)	475 (19.2)
Oncological factors													
Cancer chemotherapy within 30 days	1845	410 (22.2)	227 (12.3)	241 (13.1)	134 (7.3)	69 (3.7)	233 (12.6)	108 (5.9)	65 (3.5)	24 (1.3)	356 (19.3)	138 (7.5)	358 (19.4)
Cancer chemotherapy within 90 days	2487	531 (21.4)	281 (11.3)	347 (14.0)	171 (6.9)	84 (3.4)	287 (11.5)	125 (5.0)	72 (2.9)	27 (1.1)	449 (18.1)	154 (6.2)	462 (18.6)
Cancer radiotherapy within 90 days	275	62 (22.5)	36 (13.1)	35 (12.7)	25 (9.1)	5 (1.8)	38 (13.8)	15 (5.5)	6 (2.2)	2 (0.7)	42 (15.3)	19 (6.9)	39 (14.2)
Cancer immunotherapy within 90 days	146	23 (15.8)	19 (13.0)	12 (8.2)	12 (8.2)	8 (5.5)	23 (15.8)	7 (4.8)	7 (4.8)	6 (4.1)	30 (20.5)	13 (8.9)	30 (20.5)
Advanced cancer with multiple metastases	1721	557 (32.4)	323 (18.8)	240 (13.9)	151 (8.8)	72 (4.2)	270 (15.7)	144 (8.4)	103 (6.0)	35 (2.0)	433 (25.2)	131 (7.6)	383 (22.3)
Benign tumor	472	27 (5.7)	20 (4.2)	12 (2.5)	17 (3.6)	7 (1.5)	33 (7.0)	12 (2.5)	8 (1.7)	2 (0.4)	36 (7.6)	8 (1.7)	31 (6.6)
Malignant tumor	5029	973 (19.3)	625 (12.4)	509 (10.1)	376 (7.5)	181 (3.6)	776 (15.4)	355 (7.1)	236 (4.7)	104 (2.1)	1114 (22.2)	385 (7.7)	901 (17.9)
Hematological factors													
Preoperative transfusion within 72 h	1412	432 (30.6)	301 (21.3)	294 (20.8)	217 (15.4)	131 (9.3)	523 (37.0)	222 (15.7)	187 (13.2)	85 (6.0)	491 (34.8)	167 (11.8)	615 (43.6)
Other factors													
Open wound	610	133 (21.8)	77 (12.6)	145 (23.8)	79 (13.0)	46 (7.5)	162 (26.6)	52 (8.5)	57 (9.3)	15 (2.5)	144 (23.6)	50 (8.2)	165 (27.0)

TABLE 1 (Continued)

Variables	Entire study population	Surgical outcomes											
		Perioperative mortality	30-day mortality	Organ space SSI	Pneumonia	Unplanned intubation	Respiratory failure	Acute renal failure	Impaired consciousness	Cardio-respiratory arrest	Sepsis	DIC	Transfusion
Preoperative laboratory values													
WBC <3000/mL	4458	839 (18.8)	590 (13.2)	520 (11.7)	432 (9.7)	272 (6.1)	1031 (23.1)	464 (10.4)	300 (6.7)	127 (2.8)	1260 (28.3)	522 (11.7)	903 (20.3)
Hemoglobin <10 g/dL	9215	1699 (18.4)	1088 (11.8)	1194 (13.0)	867 (9.4)	462 (5.0)	1593 (17.3)	633 (6.9)	444 (4.8)	208 (2.3)	1813 (19.7)	601 (6.5)	2368 (25.7)
Hematocrit <30%	8522	1600 (18.8)	1023 (12.0)	1096 (12.9)	804 (9.4)	445 (5.2)	1517 (17.8)	603 (7.1)	415 (4.9)	192 (2.3)	1671 (19.6)	546 (6.4)	2251 (26.4)
Platelet count: ≥100000, and <150000/mL	4245	738 (17.4)	525 (12.4)	456 (10.7)	377 (8.9)	231 (5.4)	816 (19.2)	344 (8.1)	249 (5.9)	126 (3.0)	914 (21.5)	401 (9.4)	755 (17.8)
≥50000, and <100000/mL	1688	497 (29.4)	350 (20.7)	263 (15.6)	229 (13.6)	137 (8.1)	506 (30.0)	196 (11.6)	160 (9.5)	70 (4.1)	523 (31.0)	229 (13.6)	511 (30.3)
<50000/mL	423	211 (49.9)	160 (37.8)	75 (17.7)	75 (17.7)	46 (10.9)	165 (39.0)	83 (19.6)	59 (13.9)	17 (4.0)	187 (44.2)	86 (20.3)	177 (41.8)
Albumin: ≥2.0, and <3.0 g/dL	14 646	2312 (15.8)	1499 (10.2)	1758 (12.0)	1264 (8.6)	736 (5.0)	2474 (16.9)	1007 (6.9)	688 (4.7)	324 (2.2)	2801 (19.1)	970 (6.6)	2562 (17.5)
<2.0 g/dL	4018	1093 (27.2)	714 (17.8)	724 (18.0)	509 (12.7)	282 (7.0)	1059 (26.4)	425 (10.6)	301 (7.5)	138 (3.4)	1143 (28.4)	398 (9.9)	1138 (28.3)
Total bilirubin: ≥3.0 mg/dL	1435	385 (26.8)	268 (18.7)	216 (15.1)	142 (9.9)	82 (5.7)	359 (25.0)	168 (11.7)	120 (8.4)	38 (2.6)	353 (24.6)	119 (8.3)	329 (22.9)
AST >35 U/L	9092	1726 (19.0)	1240 (13.6)	1082 (11.9)	859 (9.4)	504 (5.5)	1894 (20.8)	866 (9.5)	599 (6.6)	272 (3.0)	1986 (21.8)	755 (8.3)	1711 (18.8)
ALT >35 U/L	6884	1041 (15.1)	748 (10.9)	780 (11.3)	528 (7.7)	316 (4.6)	1167 (17.0)	539 (7.8)	363 (5.3)	170 (2.5)	1224 (17.8)	432 (6.3)	1097 (15.9)
ALP >340 U/L	8157	1440 (17.7)	959 (11.8)	896 (11.0)	619 (7.6)	359 (4.4)	1265 (15.5)	544 (6.7)	370 (4.5)	182 (2.2)	1488 (18.2)	560 (6.9)	1348 (16.5)
BUN >20 mg/dL	20132	3500 (17.4)	2453 (12.2)	2260 (11.2)	1942 (9.6)	1077 (5.3)	3915 (19.4)	1804 (9.0)	1144 (5.7)	548 (2.7)	4450 (22.1)	1642 (8.2)	3706 (18.4)
Serum creatinine ≥2.0 mg/dL	5502	1411 (25.6)	1046 (19.0)	714 (13.0)	610 (11.1)	389 (7.1)	1486 (27.0)	844 (15.3)	472 (8.6)	251 (4.6)	1633 (29.7)	645 (11.7)	1337 (24.3)
Serum sodium <130 mEq/L	2122	391 (18.4)	265 (12.5)	258 (12.2)	183 (8.6)	117 (5.5)	388 (18.3)	177 (8.3)	106 (5.0)	65 (3.1)	440 (20.7)	174 (8.2)	413 (19.5)
Serum sodium ≥147 mEq/L	606	200 (33.0)	154 (25.4)	91 (15.0)	109 (18.0)	74 (12.2)	243 (40.1)	81 (13.4)	62 (10.2)	37 (6.1)	190 (31.4)	82 (13.5)	185 (30.5)
CRP: ≥10, and <20 mg/dL	10007	1186 (11.9)	762 (7.6)	945 (9.4)	694 (6.9)	363 (3.6)	1207 (12.1)	482 (4.8)	334 (3.3)	154 (1.5)	1425 (14.2)	480 (4.8)	1321 (13.2)
≥20 mg/dL	11847	1404 (11.9)	920 (7.8)	1489 (12.6)	886 (7.5)	500 (4.2)	1794 (15.1)	813 (6.9)	462 (3.9)	215 (1.8)	2137 (18.0)	707 (6.0)	1693 (14.3)
APTT ≥30 s	32990	3891 (11.8)	2604 (7.9)	3165 (9.6)	2269 (6.9)	1245 (3.8)	4416 (13.4)	1836 (5.6)	1213 (3.7)	582 (1.8)	5206 (15.8)	1738 (5.3)	4355 (13.2)
INR of PT: >1.1, and <1.67	15597	2207 (14.2)	1451 (9.3)	1719 (11.0)	1267 (8.1)	734 (4.7)	2556 (16.4)	1090 (7.0)	707 (4.5)	314 (2.0)	2892 (18.5)	1033 (6.6)	2521 (16.2)
≥1.67	1762	509 (28.9)	396 (22.5)	243 (13.8)	218 (12.4)	135 (7.7)	573 (32.5)	267 (15.2)	175 (9.9)	98 (5.6)	566 (32.1)	224 (12.7)	512 (29.1)
Classification of ADP													
Primary peritonitis	2566	349 (13.6)	264 (10.3)	151 (5.9)	192 (7.5)	89 (3.5)	353 (13.8)	147 (5.7)	120 (4.7)	66 (2.6)	412 (16.1)	107 (4.2)	342 (13.3)
Secondary peritonitis	42057	4316 (10.3)	2903 (6.9)	3729 (8.9)	2596 (6.2)	1436 (3.4)	5036 (12.0)	2119 (5.0)	1339 (3.2)	657 (1.6)	6071 (14.4)	2132 (5.1)	4997 (11.9)
Tertiary peritonitis	756	144 (19.0)	92 (12.2)	117 (15.5)	81 (10.7)	43 (5.7)	146 (19.3)	51 (6.7)	49 (6.5)	20 (2.6)	164 (21.7)	56 7.4)	151 (20.0)
Etiology of ADP													
Idiopathic	1491	183 (12.3)	135 (9.1)	108 (7.2)	93 (6.2)	59 (4.0)	187 (12.5)	77 (5.2)	62 (4.2)	38 (2.5)	215 (14.4)	63 (4.2)	188 (12.6)
Bowel perforation	31098	3721 (12.0)	2548 (8.2)	2843 (9.1)	2091 (6.7)	1172 (3.8)	4194 (13.5)	1782 (5.7)	1146 (3.7)	572 (1.8)	5190 (16.7)	1829 (5.9)	4124 (13.3)
Bowel ischemia	1154	316 (27.4)	238 (20.6)	141 (12.2)	167 (14.5)	82 (7.1)	361 (31.3)	149 (12.9)	119 (10.3)	53 (4.6)	381 (33.0)	149 (12.9)	284 (24.6)
Bowel obstruction	1494	205 (13.7)	138 (9.2)	117 (7.8)	148 (9.9)	70 (4.7)	244 (16.3)	97 (6.5)	80 (5.4)	31 (2.1)	276 (18.5)	104 (7.0)	235 (15.7)

(Continues)

TABLE 1 (Continued)

Variables	Entire study population	Surgical outcomes											
		Perioperative mortality	30-day mortality	Organ space SSI	Pneumonia	Unplanned intubation	Respiratory failure	Acute renal failure	Impaired consciousness	Cardio-respiratory arrest	Sepsis	DIC	Transfusion
Inflammation of the biliary tract	1032	91 (8.8)	59 (5.7)	77 (7.5)	81 (7.8)	37 (3.6)	114 (11.0)	52 (5.0)	33 (3.2)	17 (1.6)	124 (12.0)	35 (3.4)	130 (12.6)
Pelvic peritonitis due to gynecological disorder	314	15 (4.8)	9 (2.9)	16 (5.1)	15 (4.8)	5 (1.6)	26 (8.3)	12 (3.8)	6 (1.9)	1 (0.3)	37 (11.8)	9 (2.9)	34 (10.8)
Bowel inflammation (appendicitis, diverticulitis, or IBD)	6893	161 (2.3)	111 (1.6)	316 (4.6)	185 (2.7)	72 (1.0)	248 (3.6)	111 (1.6)	50 (0.7)	32 (0.5)	342 (5.0)	115 (1.7)	209 (3.0)
Others	4398	466 (10.6)	270 (6.1)	615 (14.0)	300 (6.8)	179 (4.1)	548 (12.5)	213 (4.8)	155 (3.5)	65 (1.5)	570 (13.0)	190 (4.3)	631 (14.3)
Organ or site responsible for ADP													
Esophagus	184	29 (15.8)	18 (9.8)	43 (23.4)	31 (16.8)	20 (10.9)	42 (22.8)	16 (8.7)	9 (4.9)	6 (3.3)	32 (17.4)	16 (8.7)	34 (18.5)
Appendix	7143	87 (1.2)	61 (0.9)	268 (3.8)	138 (1.9)	54 (0.8)	167 (2.3)	78 (1.1)	30 (0.4)	20 (0.3)	242 (3.4)	64 (0.9)	129 (1.8)
Biliary tract	1160	113 (9.7)	67 (5.8)	107 (9.2)	98 (8.4)	48 (4.1)	136 (11.7)	57 (4.9)	38 (3.3)	19 (1.6)	151 (13.0)	47 (4.1)	168 (14.5)
Unknown	932	153 (16.4)	106 (11.4)	80 (8.6)	68 (7.3)	45 (4.8)	129 (13.8)	58 (6.2)	41 (4.4)	23 (2.5)	157 (16.8)	46 (4.9)	135 (14.5)
Stomach, duodenum, or small bowel	17460	2097 (12.0)	1408 (8.1)	1567 (9.0)	1196 (6.8)	704 (4.0)	2126 (12.2)	892 (5.1)	584 (3.3)	311 (1.8)	2302 (13.2)	735 (4.2)	2306 (13.2)
Large bowel	17140	2294 (13.4)	1603 (9.4)	1810 (10.6)	1277 (7.5)	664 (3.9)	2851 (16.6)	1192 (7.0)	797 (4.6)	371 (2.2)	3682 (21.5)	1371 (8.0)	2590 (15.1)
Others	2096	214 (10.2)	121 (5.8)	228 (10.9)	129 (6.2)	74 (3.5)	275 (13.1)	102 (4.9)	83 (4.0)	26 (1.2)	260 (12.4)	80 (3.8)	296 (14.1)

Abbreviations: ADL, activity of daily living; ADP, acute diffused peritonitis; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; ASA, American Society of Anesthesia; AST, aspartate aminotransferase; BMI, body mass index; BUN, Blood urea nitrogen; COPD, chronic obstructive pulmonary disease; INR, international normalized ratio; PCI, percutaneous coronary intervention; PT, prothrombin time; PVD, peripheral arterial disease; WBC, white blood count.

TABLE 2 Association between morbidities and perioperative mortality or 30-day mortality.

			Perioperative mortality ($n = 4809$)				30-day mortality ($n = 3259$)			
	Morbidities	No. of event	No. of death	Mortality rate (%)	OR	95% CI	No. of death	Mortality rate (%)	OR	95% CI
Selected as secondary outcomes	Sepsis	6647	2503	37.7	9.54	8.94–10.18	1895	28.5	10.92	10.13–11.79
	On ventilator (>48 h)	5535	2092	37.8	8.30	7.77–8.88	1490	26.9	7.93	7.35–8.56
	Postoperative transfusion	5490	1730	31.5	5.50	5.14–5.89	1166	21.2	4.87	4.50–5.27
	Acute renal failure	2317	1064	45.9	8.91	8.16–9.74	828	35.7	9.29	8.46–10.21
	DIC	2295	1061	46.2	9.02	8.26–9.86	787	34.3	8.57	7.79–9.43
	Impaired consciousness (>24 h)	1508	1021	67.7	22.18	19.81–24.84	846	56.1	21.96	19.68–24.50
	Pneumonia	2869	980	34.2	5.24	4.82–5.70	601	20.9	3.97	3.60–4.38
	Organ space SSI	3997	856	21.4	2.58	2.38–2.80	451	11.3	1.75	1.57–1.94
	Unplanned intubation	1568	694	44.3	7.66	6.90–8.51	467	29.8	6.23	5.56–6.99
	Cardio-respiratory arrest	743	626	84.3	51.74	42.37–63.20	573	77.1	52.64	44.17–62.74
Not selected	Reoperation	3395	725	21.4	2.52	2.31–2.75	348	10.3	1.53	1.36–1.72
	Wound disruption	2213	572	25.8	3.20	2.90–3.54	301	13.6	2.14	1.88–2.43
	Intraabdominal abscess	3112	544	17.5	1.89	1.71–2.08	247	7.9	1.12	0.98–1.29
	Failure of the sutures	1811	458	25.3	3.05	2.73–3.41	248	13.7	2.14	1.86–2.46
	Pulmonary atelectasis	1691	427	25.3	3.03	2.70–3.40	246	14.5	2.3	2.00–2.64
	Heart failure	695	316	45.5	7.46	6.40–8.69	230	33.1	6.8	5.78–8.00

Abbreviations: CI, confidence interval; DIC, disseminated intra-vascular coagulation; OR, odds ratio; SSI, surgical site infection.

TABLE 3 Risk models for predicting mortality of acute diffused peritonitis.

	30-day mortality				Perioperative mortality			
Variables	B. Coefficient	*p* value	OR	95% CI	B. Coefficient	*p* value	OR	95% CI
Age <60 years	Reference	–	–	–	Reference	–	–	–
61–65 years	0.51	<0.001	1.67	1.36–2.05	0.6	<0.001	1.82	1.53–2.15
66–70 years	0.53	<0.001	1.71	1.42–2.04	0.64	<0.001	1.9	1.64–2.21
71–75 years	0.83	<0.001	2.3	1.93–2.73	0.86	<0.001	2.37	2.05–2.74
76–80 years	1.02	<0.001	2.77	2.34–3.28	1.04	<0.001	2.82	2.45–3.25
81 and over the years	1.31	<0.001	3.71	3.17–4.35	1.34	<0.001	3.83	3.35–4.38
BMI: <26 kg/m^2	Reference	–	–	–	Reference	–	–	–
≤26, and <30 kg/m^2	0.17	0.016	1.19	1.03–1.37	0.15	0.018	1.16	1.03–1.32
≥30 kg/m^2	0.42	<0.001	1.53	1.22–1.92	0.33	0.002	1.39	1.13–1.71
Brickman index: 0	Reference	–	–	–				
1–199	−0.29	0.029	0.75	0.58–0.97				
200–399	−0.01	0.923	0.99	0.82–1.20				
400 and over	0.06	0.268	1.06	0.96–1.17				
Sex: Female					Reference	–	–	–
Male					0.11	0.004	1.12	1.04–1.20
Diabetes: No					Reference	–	–	–
Yes					−0.09	0.062	0.92	0.84–1.00
Alcohol consumption habitat: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.17	0.003	0.84	0.75–0.94	−0.18	<0.001	0.83	0.76–0.92
Respiratory distress within 30 days: No	Reference	–	–	–	Reference	–	–	–
Yes	0.25	<0.001	1.28	1.11–1.47	0.31	<0.001	1.36	1.20–1.55
ADL within 30 days, no assistance	Reference	–	–	–	Reference	–	–	–
Any assistance	0.17	0.008	1.18	1.05–1.34	0.22	<0.001	1.25	1.12–1.40
ADL just before surgery, no assistance	Reference	–	–	–	Reference	–	–	–
Any assistance	0.27	<0.001	1.31	1.17–1.47	0.22	<0.001	1.25	1.13–1.38
Esophageal varix within 6 months: No	Reference	–	–	–				
Yes	0.37	0.053	1.44	0.99–2.09				
Hypertension within 30 days: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.08	0.064	0.92	0.85–1.00	−0.07	0.059	0.93	0.87–1.00
Previous cerebrovascular disease: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.22	0.005	0.81	0.69–0.94	−0.16	0.022	0.85	0.75–0.98
Chronic steroid use: No	Reference	–	–	–	Reference	–	–	–
Yes	0.27	<0.001	1.3	1.12–1.52	0.31	<0.001	1.36	1.19–1.56
Blood coagulation abnormality: No					Reference	–	–	–
Yes (without anticoagulant)					0.12	0.11	1.12	0.97–1.29
Yes (with anticoagulant)					−0.07	0.269	0.93	0.81–1.06
Sepsis just before surgery: No	Reference	–	–	–	Reference	–	–	–
Yes	0.56	<0.001	1.76	1.61–1.92	0.47	<0.001	1.6	1.47–1.73
ASA classification: 1 and 2	Reference	–	–	–	Reference	–	–	–
3, 4 and 5	0.76	<0.001	2.14	1.92–2.38	0.7	<0.001	2.02	1.85–2.20
Ambulance transportation: No	Reference	–	–	–				

TABLE 3 (Continued)

Variables	30-day mortality				Perioperative mortality			
	B. Coefficient	*p* value	OR	95% CI	B. Coefficient	*p* value	OR	95% CI
Yes	0.11	0.01	1.11	1.03–1.21				
Emergent surgery: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.13	0.14	0.88	0.74–1.04	−0.14	0.055	0.87	0.75–1.00
Cancer chemotherapy within 90 days: No	Reference	–	–	–	Reference	–	–	–
Yes	0.24	0.004	1.27	1.08–1.50	0.54	<0.001	1.72	1.51–1.96
Cancer immunotherapy within 90 days: No	Reference	–	–	–				
Yes	0.42	0.128	1.52	0.89–2.60				
Ventilator dependent within 48 h: No	Reference	–	–	–	Reference	–	–	–
Yes	0.45	<0.001	1.57	1.33–1.85	0.54	<0.001	1.72	1.47–2.00
COPD: No					Reference	–	–	–
Yes					0.14	0.086	1.15	0.98–1.36
Current pneumonia: No	Reference	–	–	–	Reference	–	–	–
Yes	0.15	0.108	1.16	0.97–1.39	0.16	0.052	1.18	1.00–1.39
Congestive heart failure within 30 days: No	Reference	–	–	–	Reference	–	–	–
Yes	0.29	0.003	1.34	1.10–1.63	0.31	<0.001	1.37	1.14–1.64
Myocardial infarction within 6 months: No	Reference	–	–	–	Reference	–	–	–
Yes	0.46	0.015	1.58	1.09–2.29	0.49	0.005	1.64	1.16–2.31
Previous cardiac surgery: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.27	0.032	0.76	0.60–0.98	−0.23	0.042	0.8	0.64–0.99
Previous PVD with symptoms: No					Reference	–	–	–
Yes					0.53	0.003	1.69	1.19–2.41
Acute renal failure within 24 h: No	Reference	–	–	–	Reference	–	–	–
Yes	0.13	0.093	1.14	0.98–1.33	0.19	0.01	1.21	1.05–1.40
Dialysis within 14 days: No	Reference	–	–	–	Reference	–	–	–
Yes	0.25	0.002	1.28	1.09–1.50	0.41	<0.001	1.51	1.31–1.75
Advanced cancer with multiple metastases: No	Reference	–	–	–	Reference	–	–	–
Yes	0.66	<0.001	1.93	1.64–2.27	0.89	<0.001	2.43	2.12–2.79
No neoplastic disease	Reference	–	–	–	Reference	–	–	–
Benign tumor	−0.08	0.739	0.92	0.56–1.51	−0.17	0.435	0.84	0.55–1.30
Malignant tumor	0.54	<0.001	1.72	1.53–1.92	0.56	<0.001	1.74	1.58–1.92
WBC: ≥3000/mL	Reference	–	–	–	Reference	–	–	–
<3000/mL	0.29	<0.001	1.34	1.20–1.49	0.33	<0.001	1.39	1.26–1.53
Hemoglobin: ≥10 g/dL					Reference	–	–	–
<10 g/dL					0.12	0.113	1.13	0.97–1.30
Hematocrit: ≥30%	Reference	–	–	–	Reference	–	–	–
<30%	−0.11	0.028	0.9	0.82–0.99	−0.14	0.063	0.87	0.75–1.01
Plate count: ≥150000/mL	Reference	–	–	–	Reference	–	–	–
≤100000, and <150000/mL	0.29	<0.001	1.33	1.19–1.49	0.26	<0.001	1.29	1.17–1.43
≤50000, and <100000/mL	0.44	<0.001	1.56	1.34–1.81	0.47	<0.001	1.59	1.40–1.82
<50000/mL	0.98	<0.001	2.67	2.10–3.40	0.98	<0.001	2.67	2.11–3.37

(Continues)

TABLE 3 (Continued)

	30-day mortality				Perioperative mortality			
Variables	B. Coefficient	*p* value	OR	95% CI	B. Coefficient	*p* value	OR	95% CI
Albumin: ≥3.0 g/dL	Reference	–	–	–	Reference	–	–	–
≤2.0, <3.0 g/dL	0.38	<0.001	1.47	1.33–1.62	0.58	<0.001	1.78	1.63–1.94
<2.0 g/dL	0.71	<0.001	2.04	1.79–2.33	0.96	<0.001	2.6	2.32–2.92
Total bilirubin: <3.0 mg/dL	Reference	–	–	–	Reference	–	–	–
≥3.0 mg/dL	0.53	<0.001	1.71	1.43–2.03	0.63	<0.001	1.88	1.60–2.20
AST: ≤35 U/L	Reference	–	–	–	Reference	–	–	–
>35 U/L	0.39	<0.001	1.48	1.35–1.62	0.4	<0.001	1.49	1.36–1.64
ALT: =<35 U/L					Reference	–	–	–
>35 U/L					−0.14	0.012	0.87	0.78–0.97
ALP: =<340 U/L	Reference	–	–	–	Reference	–	–	–
>340 U/L	0.36	<0.001	1.43	1.30–1.57	0.39	<0.001	1.48	1.37–1.61
BUN: =<20 mg/dL	Reference	–	–	–	Reference	–	–	–
> 20 mg/dL	0.46	<0.001	1.59	1.44–1.75	0.44	<0.001	1.56	1.43–1.69
Serum creatinine: < 2.0 mg/dL	Reference	–	–	–	Reference	–	–	–
≥2.0 mg/dL	0.67	<0.001	1.96	1.76–2.18	0.57	<0.001	1.77	1.61–1.96
Serum sodium: <130 mEq/L	Reference	–	–	–	Reference	–	–	–
≥130, and < 147 mEq/L	−0.36	<0.001	0.7	0.60–0.81	−0.35	<0.001	0.7	0.61–0.80
≥147 mEq/L	0.09	0.494	1.09	0.85–1.41	0.02	0.859	1.02	0.81–1.29
CRP: <10 mg/dL	Reference	–	–	–	Reference	–	–	–
≥10, and < 20 mg/dL	−0.34	<0.001	0.71	0.64–0.79	−0.28	<0.001	0.76	0.69–0.83
≥20 mg/dL	−0.56	<0.001	0.57	0.51–0.63	−0.51	<0.001	0.6	0.55–0.66
INR of PT: ≤1.1	Reference	–	–	–	Reference	–	–	–
1.1<, <1.67	0.15	0.001	1.16	1.06–1.27	0.19	<0.001	1.21	1.12–1.30
≥1.67	0.64	<0.001	1.89	1.63–2.19	0.57	<0.001	1.77	1.54–2.03
Etiology of ADP								
Idiopathic: No	Reference	–	–	–	Reference	–	–	–
Yes	0.32	0.009	1.37	1.08–1.75	0.26	0.027	1.3	1.03–1.65
Bowel perforation: No	Reference	–	–	–	Reference	–	–	–
Yes	0.3	<0.001	1.34	1.19–1.52	0.36	<0.001	1.44	1.23–1.69
Bowel ischemia: No	Reference	–	–	–	Reference	–	–	–
Yes	0.47	<0.001	1.6	1.32–1.95	0.53	<0.001	1.69	1.39–2.06
Bowel obstruction: No					Reference	–	–	–
Yes					0.19	0.048	1.21	1.00–1.47
Inflammation of the biliary tract: No					Reference	–	–	–
Yes					−0.3	0.099	0.74	0.52–1.06
Appendicitis, diverticulitis, or IBD: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.24	0.046	0.79	0.62–1.00	−0.21	0.06	0.81	0.66–1.01
Others: No					Reference	–	–	–
Yes					0.14	0.145	1.15	0.95–1.38
Organ or site responsible for ADP								
Esophagus: No	Reference	–	–	–	Reference	–	–	–
Yes	0.45	0.117	1.56	0.89–2.73	0.61	0.014	1.84	1.13–2.98

TABLE 3 (Continued)

Variables	30-day mortality				Perioperative mortality			
	B. Coefficient	*p* value	OR	95% CI	B. Coefficient	*p* value	OR	95% CI
Appendix: No	Reference	–	–	–	Reference	–	–	–
Yes	−0.55	0.001	0.58	0.41–0.80	−0.56	<0.001	0.57	0.42–0.78
Biliary tract: No					Reference	–	–	–
Yes					0.44	0.017	1.55	1.08–2.22
Others: No	Reference	–	–	–	Reference	–	–	–
Yes	0.19	0.159	1.21	0.93–1.58	0.42	0.002	1.52	1.17–1.99
Unknown: No	Reference	–	–	–	Reference	–	–	–
Yes	0.65	<0.001	1.92	1.39–2.63	0.75	<0.001	2.11	1.55–2.88
Stomach, duodenum, or small bowel: No	Reference	–	–	–	Reference	–	–	–
Yes	0.57	<0.001	1.77	1.45–2.15	0.64	<0.001	1.89	1.52–2.36
Large bowel: No	Reference	–	–	–	Reference	–	–	–
Yes	0.64	<0.001	1.89	1.55–2.31	0.67	<0.001	1.96	1.58–2.44
(Intercept)	−5.61	<0.001	0.00	0.00–0.01	−5.40	<0.001	0.00	0.00–0.01

Abbreviations: ADP, acute diffused peritonitis; CI, confidence interval; DIC, disseminated intra-vascular coagulation; OR; odds ratio; SSI, surgical site infection.

TABLE 4 C-index of the logistic regression models for predicting the outcome.

Outcomes	C-index	95% CI
Mortality within 30 days	0.857	0.853–0.864
Perioperative mortality	0.859	0.855–0.865
Organ space SSI	0.704	0.700–0.717
Pneumonia	0.799	0.794–0.810
Unplanned intubation	0.774	0.768–0.790
On ventilator (>48 h)	0.849	0.845–0.854
Acute renal failure	0.858	0.852–0.867
Impaired consciousness (>24 h)	0.856	0.849–0.867
Cardio-respiratory arrest	0.817	0.810–0.834
Postoperative transfusion	0.81	0.806–0.817
Sepsis	0.837	0.832–0.842
DIC	0.823	0.819–0.834

Abbreviations: CI, confidential interval; DIC, disseminated intravascular coagulation; SSI, surgical site infection.

risk model based on the current database for accurate prediction in future use. In this study, the incidence rate of the 30- and perioperative mortality were lower than those of the initial reports (7.2% vs. 8.9%, and 10.6% vs. 13.9%, respectively).[7,22] Possible reasons for this may be (1) improvement of perioperative management for ADP patients and (2) a contribution of the NCD risk calculator developed with the initial study, which may lead to excluding the most seriously ill patients of ADP for surgery.

When comparing the discrimination performance of the newly developed risk models with the initial risk models, the c-indices of the new mortality models were compared with those of previous models (Table S3). Regarding the 10 morbidities, the eight morbidities, except "pneumonia" and "acute renal failure," were newly selected as secondary outcomes in this study. The c-index of the two common outcomes was slightly lower than those of the previous study.[22] However, it is considered that this result can not conclude which is superior to the other because their discrimination performance was not compared directly using the same dataset. In addition, the background difference in mortality between the initial and the present dataset mentioned above may need to be considered.

Regarding calibration of the risk prediction models, the predicted value of each surgical outcome using the developed risk model was highly consistent with the actual probability except for unplanned intubation, cardio-respiratory arrest, and DIC (Figure 2). In the three models, poor calibration was found in the high-risk group, suggesting that the reliability of the predictions from the models was inferior. A possible cause of this may be unknown preoperative or intraoperative factors not included in explanatory variables for developing the new risk models in this study. Except for the three models, the risk models for predicting surgical outcomes of ADP were reliable enough for clinical use.

In the newly developed risk models, the number of independent predictors increased compared with the previous models, reaching 55 for perioperative mortality. Indeed, the sample size for this study was five times larger ($n = 45\,379$ vs. $n = 8482$). For the perioperative mortality, the top five were "age >81 (OR = 3.83)",

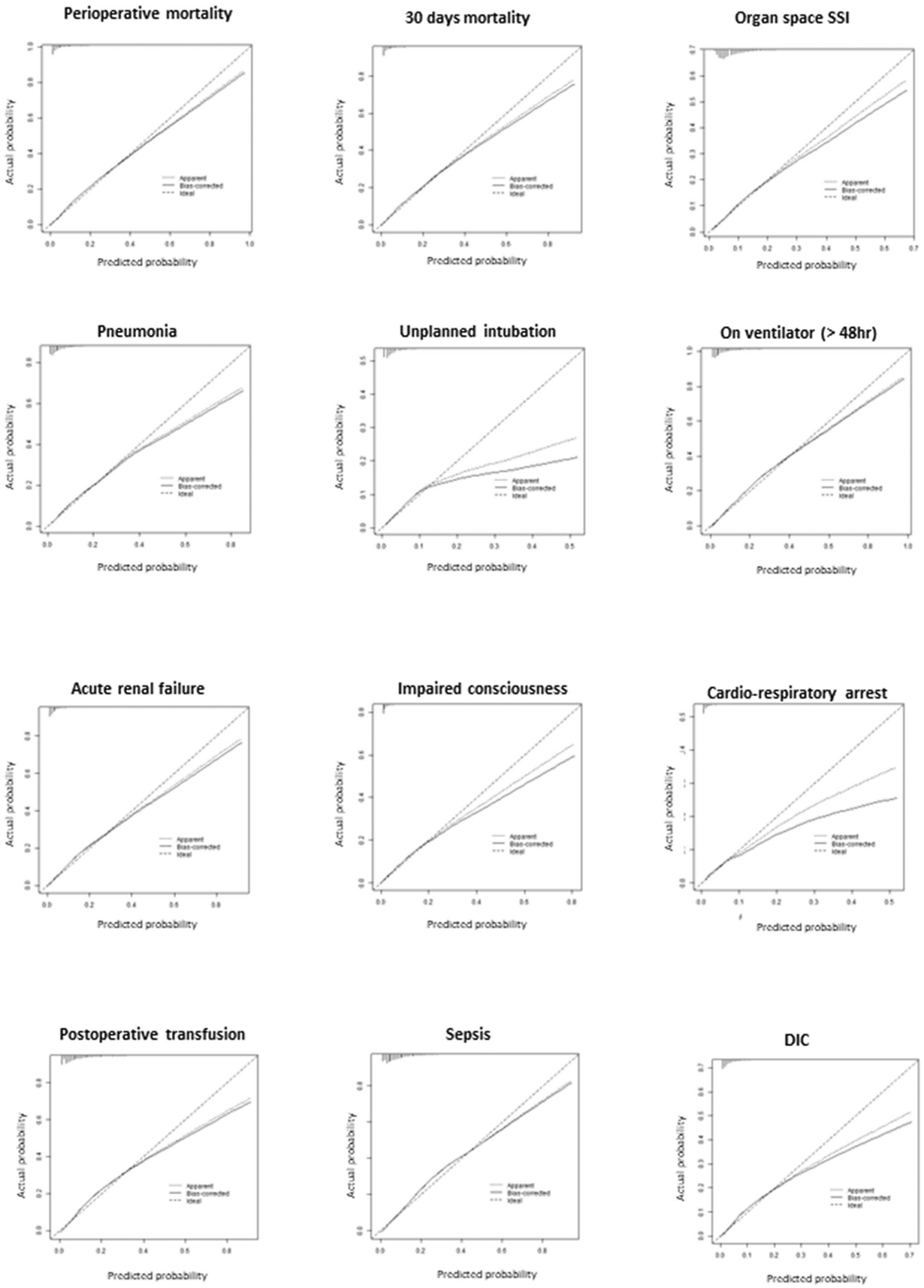

FIGURE 2 Calibration plot of prediction models for mortalities and morbidities of acute diffused peritonitis. Observed event rates (95% CI) were plotted with predicted event rates for each prediction model in the whole dataset ($n = 45\,379$).

"advanced cancer with multiple metastases (OR = 2.43)", "platelet count <50000/mL (OR = 2.67)", "serum albumin <2.0 g/dL (OR = 2.60)", and "unknown site responsible for ADP (OR = 2.11)", among which the three variables were consistent with those of 30-day mortality. This finding suggested that preoperative severity, especially in elderly patients, was highly relevant to mortality after surgery. Naturally, this also applies to the risk models of the 10 morbidities.

ADP is a clinical syndrome rather than a definitive diagnosis, as the causative etiology varies widely from one setting to another, and it seems to be correlated to mortality.[32] For example, it is recognized by clinicians that ADP due to large bowel perforation must be more serious than that of the upper intestinal tract, such as gastric or duodenum.[32,33] To our knowledge, few studies have quantified a relative risk measure of the causative etiology. Therefore, revealing the impact of the causative etiology for predicting outcomes of ADP could be a novel finding of the present study. This study's new risk models selected causative etiology or responsible organ as a covariate. Etiology ("bowel perforation", or "bowel ischemia") and causative site ("esophagus", "unknown", "upper gastrointestinal tract", or "lower gastrointestinal tract") are shown to be relevant to perioperative mortality (Table 3). Regarding the 10 morbidities, the variable of the causative site of ADP was selected in the top five relevant predictors (Table S2). As expected, "esophagus" or "lower gastrointestinal tract" had a greater negative impact on morbidities, whereas "appendix" was less associated with severe complications. "Esophagus" was strongly relevant to the three outcomes associated with respiratory failures, such as "pneumonia", "unplanned intubation," and "on ventilator >48 h". "Lower gastrointestinal tract" was relevant to the incidence of sepsis, DIC, and impaired consciousness. The definitive preoperative diagnosis of a detailed etiology of ADP is challenging; however, recent advances in imaging modalities could evaluate the etiology or causative organ (site) of ADP in most cases.

This study has several limitations. First, the newly developed risk models need to be validated using a truly external dataset, even though internal validation was performed in this study. In addition, validation using a database outside Japan is mandatory for evaluating generalization. Existing literature shows that etiologies of peritonitis vary by geographic location and local environmental factors with genetic predisposition.[21] Second, the present models seem to be complicated regarding many independent variables, which may burden the working time for data input. However, as far as Japanese users, these variables are already registered in the NCD system, so prediction calculated by the models is available automatically at participating hospitals.

5 | CONCLUSION

We constructed and validated the new prediction models of postoperative surgical outcomes of ADP using the recent NCD dataset. Evaluation of predictive power and calibration of these risk models showed they were sufficiently reliable for clinical settings. The developed risk models in this study were updated and revised with the latest real-world data, which can lead to providing realistic predictions. Since treatment decisions for ADP are made under dynamic circumstances, accurate prediction of postoperative complications is useful for shared decision-making processes between patients and/or their families and medical providers.

AUTHOR CONTRIBUTIONS

Study concepts: Kitagawa, Oshikiri, Kakeji, Marubashi, Miyata. Study design: Sato, Marubashi, Oshikiri, Kakeji. Data acquisition: Kitagawa, Oshikiri, Kakeji. Quality control of data and algorithms: Kitagawa, Oshikiri, Kakeji, Marubashi, Miyata, Tachimori. Data analysis and interpretation: Sato, Hirakawa, Tachimori, Marubashi Kakeji. Statistical analysis: Hirakawa, Tachimori, Miyata. Manuscript preparation: Sato, Hirakawa, Marubashi. Manuscript editing: Sato, Marubashi. Manuscript review: Marubashi. All authors approved the final version of this manuscript.

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CONFLICT OF INTEREST STATEMENT

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DATA AVAILABILITY STATEMENT

Research data are not shared. We used (1) data from the National Clinical Database (NCD) registry in Japan.

ETHICS STATEMENTS

Approval of the research protocol: The study protocol was approved by the Japanese Society of Gastroenterological Surgery and the Ethics Committee of Kobe University (approval number 20190128).
Informed Consent: N/A.
Registry and the Registration No. of the study/trial: N/A.
Animal Studies: N/A.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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