Table 1. (*Continued*)

	Score 0 (n = 1474)	Score 1(n = 1375)	Score 2 (n = 650)	Score 3 (n = 183)	Score 4 (n = 10)	P value
LAD, n (%)	432 (29.3)	509 (37.0)	275 (42.3)	93 (50.8)	5 (50.0)	<0.001
Procedure						
Urgent PCI, n (%)	332 (22.5)	296 (21.5)	141 (21.7)	38 (20.8)	2 (20.0)	0.961
Emergent PCI, n (%)	90 (6.1)	421 (30.6)	200 (30.8)	53 (29.0)	4 (40.0)	<0.001
Drug Eluting Stent, n (%)	995 (67.5)	920 (66.9)	402 (61.8)	105 (57.4)	6 (60.0)	0.011
Bare Metal Stent, n (%)	365 (24.8)	408 (29.7)	138 (21.2)	34 (18.6)	1 (10.0)	<0.001
IABP support, n (%)	11 (0.7)	21 (1.5)	21 (3.2)	6 (3.3)	1 (10.0)	<0.001
IVUS use, n (%)	596 (40.4)	470 (34.2)	190 (29.2)	56 (30.6)	0 (0.0)	<0.001
RA approach, n (%)	433 (29.4)	280 (20.4)	112 (17.2)	41 (22.4)	1 (10.0)	<0.001
FA approach, n (%)	989 (67.1)	1065 (77.5)	514 (79.1)	139 (76.0)	8 (80.0)	<0.001
Fluoro Time, (min)	59.35±12.75	55.81±13.99	54.78±13.18	54.81±13.09	46.86±13.43	<0.001

Data are expressed as mean ± SD.

ACS, acute coronary syndrome; BMI, body mass index; CABG, coronary artery bypass grafting; CCS, canadian cardiovascular society; FA, femoral approach; GFR. glomerular filtration rate; HF, heart failure; IABP, intra aorta balloon pump; IVUS, intra vascular ultra sound; MI, myocardial infarction; NSTEMI, non-ST-segment elevation myocardial infarction; PCI, percutaneous coronary intervention; RA, radial approach; STEMI, ST-segment elevation myocardial infarction; UA, unstable angina.

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postoperative myocardial infarction, and bleeding with a hemoglobin decrease of more than 3.0 g/dL or transfusion (Fig 2).

The presence of these variables predicted the in-hospital outcome after adjustment for known clinical predictors (Tables 3 and 4; results of the univariate analyses is available in S1 and S2 Tables). Importantly, the in-hospital mortality increased by 1.38 per unit increment in complexity score (odds ratio, OR 1.38; $p < 0.001$). Furthermore, the risk of an in-hospital complication increased by 1.73 per unit increment in complexity score (OR 1.73; $p < 0.001$). Of note, there is a partial overlap in the Type C and CTO lesions, and we performed a secondary analysis excluding CTO from our scoring system (S3 and S4 Tables); however, this did not

Table 2. Periprocedural and In-hospital Complication data.

	Score 0 (n = 1474)	Score 1 (n = 1375)	Score 2 (n = 650)	Score 3 (n = 183)	Score 4 (n = 10)	P value
In hospital mortality, n (%)	11 (0.7)	20 (1.5)	12 (1.8)	2 (1.1)	1 (10.0)	0.02
All complications, n (%)	97 (6.6)	177 (12.9)	118 (18.2)	31 (16.9)	4 (40.0)	<0.001
Cardiogenic shock, n (%)	7 (0.5)	26 (1.9)	19 (2.9)	4 (2.2)	3 (30.0)	<0.001
MI post PCI, n (%)	22 (1.5)	42 (3.1)	25 (3.8)	7 (3.8)	1 (10.0)	0.004
Death/HF/CS, n (%)	25 (1.7)	62 (4.5)	41 (6.3)	13 (7.1)	4 (40.0)	<0.001
Bleeding complications, n (%)	31 (3.1)	117 (11.0)	69 (13.1)	16 (10.3)	2 (28.6)	<0.001
Transfusion, n (%)	24 (1.6)	23 (1.7)	27 (4.2)	7 (3.8)	0 (0)	0.001
Contrast Nephropathy	104 (7.1)	151 (11.0)	98 (15.1)	33 (18.0)	4 (40.0)	<0.001
Introduction of new hemodialysis, n (%)	7 (0.5)	10 (0.7)	5 (0.8)	2 (1.1)	1 (10.0)	0.006
TIMI flow under grade 3, n (%)	30 (2.0)	62 (4.5)	48 (7.4)	13 (7.1)	2 (20.0)	<0.001
Major dissection, n (%)	10 (0.7)	27 (2.0)	16 (2.5)	3 (1.6)	0 (0)	0.012
Coronary perforation, n (%)	7 (0.5)	16 (1.2)	12 (1.8)	3 (1.6)	0 (0)	0.045

CS, Cardiogenic shock; HF, heart failure; MI, myocardial infarction; PCI, percutaneous coronary intervention; TIMI, Thrombolysis In Myocardial Infarction.

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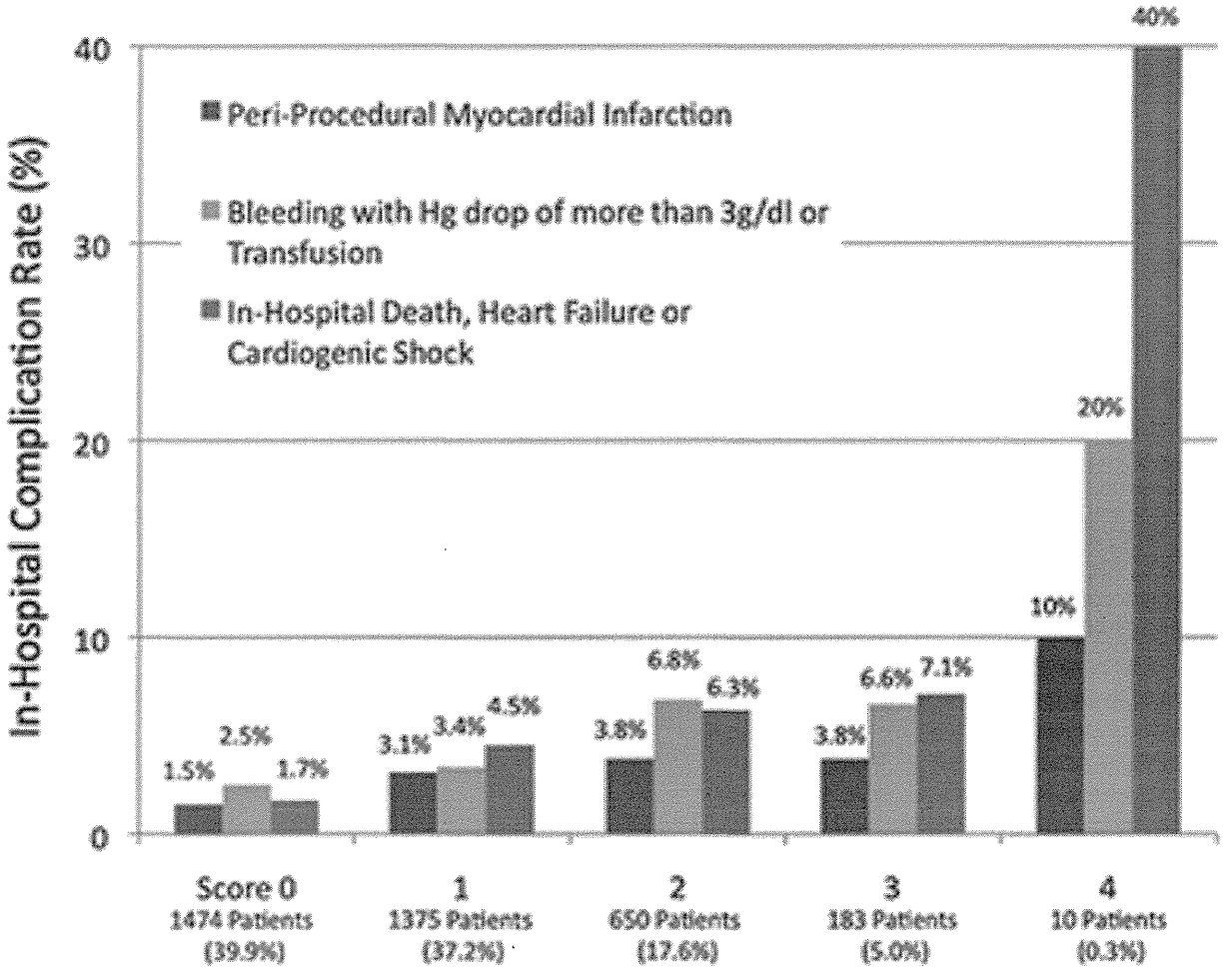

Fig 2. The rates of in-hospital complications.

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alter our main results and complexity score remained an independent predictor for in-hospital death (OR 1.48; $p<0.001$) and complication (OR 1.90; $p<0.001$).

Discussion

We developed a simple PCI scoring system, based on angiographic lesion complexity, for predicting the risk of in-hospital mortality and complications. We tested the system against data from 3692 patients enrolled in a multicenter Japanese registry between 2008 and 2011. This complexity scoring system correlated well with in-hospital mortality and complication rates: patients with higher scores exhibited higher event rates compared with lower score groups, while the mortality and complication rate increased by 1.38 and 1.74, respectively, per unit rise in complexity score. The results of this study suggest that quantification of these angiographic characteristics could be of assistance in in-hospital risk stratification and that patients with a high complexity score warrant special attention.

During the last decade, there has been remarkable development in novel devices for PCI, such as first or second generation DES, along with their delivery systems. Hence, the

Table 3. Multivariable predictors for in-hospital mortality.

	Odds Ratio	Lower 95% CI	Upper 95% CI	P value
Complexity Score (increment by unit)	1.38	1.02	1.88	0.039
Female	1.11	0.56	2.2	0.771
Age over 70 yrs	6.73	2.8	16.19	<0.001
CKD	4.87	2.23	10.6	<0.001
DM	0.72	0.38	1.38	0.322
COPD	2.62	0.82	8.36	0.105
Cerebrovascular Disease	1.39	0.61	3.19	0.435
HF (NYHA4)	2.3	1.07	4.93	0.032
Prior PCI	0.44	0.2	0.94	0.034
Prior CABG	3.63	1.55	8.47	0.003
Prior HF	2.3	1.07	4.93	0.032

CABG, coronary artery bypass grafting; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

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contemporary management of coronary artery diseases has become increasingly dependent on PCI, rather than CABG. However, successful PCI of difficult lesions requires advanced techniques, and the learning curve increases steeply along with the need for greater skill and experience on the part of the operator. Therefore, accurate risk assessment is an essential part of the evaluation in patients undergoing complex PCI. In the present study, each variable showed a tendency to predict in-hospital events (S1 and S2 Tables). When each variable was assigned as a factor to construct a single 'scoring system', each unit increment of the score was cumulatively associated with risk for in-hospital events. Our basis for the selection of each of the 5 angiographic variables was primarily clinical. Chosen variables had to be readily available and clinically relevant when performing complex PCI. These variables are thought to directly reflect the complexity of angiographic lesions seen in practice, and are frequently discussed at the bedside and/or catheterization lab when performing the procedure. This in contrast to previously established "complexity" scores (e.g., the SYNTAX score) that aimed to predict the long-term

Table 4. Multivariable predictors of any complications.

	Odds Ratio	Lower 95% CI	Upper 95% CI	P value
Complexity Score (increment by unit)	1.73	1.45	2.06	<0.001
Female	1.13	0.75	1.71	0.551
Age over 70 yrs	1.69	1.18	2.42	0.004
CKD	1.93	1.05	3.53	0.035
DM	0.87	0.61	1.25	0.457
COPD	1.69	0.73	3.91	0.217
Cerebrovascular Disease	1.21	0.68	2.15	0.515
HF (NYHA4)	3.71	2.17	6.35	<0.001
Prior PCI	0.37	0.24	0.59	<0.001
Prior CABG	2.19	1.19	4.02	0.012
Prior HF	1.83	1.09	3.1	0.023

CABG, coronary artery bypass grafting; CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; NYHA, New York Heart Association; PCI, percutaneous coronary intervention.

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results of PCI compared to CABG [8,10]. This concept is close to that of CHADS2 score for atrial fibrillation.

It is worth emphasizing that the in-hospital complication rate increased approximately two-fold in the score 1 group, threefold in the score 2 and 3 groups, and more than tenfold in the score 4 group, compared to patients with simple lesions (score 0 group). Clearly, the presence of complex lesions must always be taken into account in any attempt to forecast the probability of final procedural success and safety. It may also be possible to assign operators appropriately, according to their level of skill, based on the difficulty of dealing with these complex lesions, or to consider referring the patient for CABG. Complex lesions with a low complexity score can usually be treated successfully, and would be good candidates for training purposes.

Previously published studies have indicated a similar trend in the clinical predictors for in-hospital mortality and complications in PCI patients, based on multivariate logistic regression analysis [3,4,7,13–17]. For example, old age, female sex, current or past heart failure symptoms, renal failure, and peripheral artery disease were included in all of the studies. It is noteworthy that our angiographic complexity score continued to be a significant predictor of in-hospital events, even after adjusting for known clinical predictors. Therefore, lesion complexity should be recognized as an important risk factor, in addition to variables that are related to the patient's background.

In this study, the overall in-hospital mortality rate was 1.2%. This mortality rate is relatively high compared with previous studies, which reflects the high percentage (about 40%) of patients with ACS, cardiogenic shock, or cardiopulmonary arrest. A comparison of the results among patients with stable CAD and those with ACS, shock, or cardiopulmonary arrest will be the subject of further analysis.

Several important limitations of the present analysis should be discussed. The first is sample size. The high score groups contained only small numbers of patients and the full score group had none. Additional validation in the high score groups with larger samples might be needed. A second limitation is that we did not analyze the potential relationship between hospital or operator procedure volume and in-hospital complications. In particular, there may be a relationship between an institution's or operator's procedure experience and volume and the outcomes of PCI for complex lesions. Third, it may not have been possible to distinguish Type C lesions from bifurcation lesions and CTO. However, the number of patients with Type C lesions was small, less than 10%. Fourth, we did have clear discrimination between Type C and heavily calcified lesions. In usual practice, defining universal 'heavy' calcification nor its quantification would be a major challenge. Because our goal was to generate a bedside-friendly tool to assess complexity of PCI that would predict the clinical outcome, we chose to incorporate type C lesion as a variable in the scoring system, which is widely appreciated among interventional cardiologists. Lastly, the odds ratio for each complex lesion in our scoring system was not evaluated separately using multivariate logistic regression analysis. We believe that the risk weights for each type of complex lesion are likely to be slightly different. Further analysis, multiplication of the predicted risk for each risk score by the odds ratio for the in-hospital mortality and complications could lead to an improved risk score for evaluation in future studies.

Conclusions

Accurate risk assessment can aid in the identification of patients who are at high risk of an in-hospital event. The proposed complexity score was cumulatively associated with in-hospital mortality and complication rate and could be used for event prediction in PCI patients. PCI operators should take special care in order to perform PCI successfully in these complex lesions.

Supporting Information

S1 Table. Univariable predictors for in-hospital mortality.
(DOCX)

S2 Table. Univariable predictors of any complications.
(DOCX)

S3 Table. Multivariable predictors of in-hospital mortality without CTO lesion.
(DOCX)

S4 Table. Multivariable predictors of any complications without CTO lesion.
(DOCX)

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Author Contributions

Conceived and designed the experiments: AE SK HM. Performed the experiments: SK HM. Analyzed the data: AE SK HM. Contributed reagents/materials/analysis tools: AE SK HM AK S. Noma MS TK SI S. Nakagawa ST YN. Wrote the paper: AE SK KF.

References

1. Wilensky RL, Selzer F, Johnston J, Laskey WK, Klugherz BD, Block P, et al. Relation of percutaneous coronary intervention of complex lesions to clinical outcomes (from the NHLBI Dynamic Registry). Am J Cardiol 2002; 90:216–21. PMID: 12127606
2. Harrell L, Schunkert H, Palacios IF. Risk predictors in patients scheduled for percutaneous coronary revascularization. Catheter Cardiovasc Interv 1999; 48:253–60. PMID: 10525222
3. Moscucci M, Kline-Rogers E, Share D, O'Donnell M, Maxwell-Eward A, Meengs W. L, et al. Simple bedside additive tool for prediction of in-hospital mortality after percutaneous coronary interventions. Circulation 2001; 104:263–8. PMID: 11457742
4. Resnic FS, Ohno-Machado L, Selwyn A, Simon DI, Popma JJ. Simplified risk score models accurately predict the risk of major in-hospital complications following percutaneous coronary intervention. Am J Cardiol 2001; 88:5–9. PMID: 11423050

5. Rihal CS, Grill DE, Bell MR, Berger PB, Garratt KN, Holmes D. R. Jr.. Prediction of death after percutaneous coronary interventional procedures. Am Heart J 2000; 139:1032–8. PMID: 10827384
6. Chowdhary S, Ivanov J, Mackie K, Seidelin PH, Dzavík V. The Toronto score for in-hospital mortality after percutaneous coronary interventions. Am Heart J 2009; 157:156–63. doi: 10.1016/j.ahj.2008.08.026 PMID: 19081413
7. Wu C, Hannan EL, Walford G, Ambrose JA, Holmes DR, King S. B. 3rd, et al. A risk score to predict in-hospital mortality for percutaneous coronary interventions. J Am Coll Cardiol 2006; 47:654–60. PMID: 16458151
8. Sianos G, Morel MA, Kappetein AP, Morice MC, Colombo A, Dawkins K, et al. The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. EuroIntervention 2005; 1:219–27. PMID: 19758907
9. Ong AT, Serruys PW, Mohr FW, Morice MC, Kappetein AP, Holmes D. R. Jr, et al. The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) study: design, rationale, and run-in phase. Am Heart J 2006; 151:1194–204. PMID: 16781219
10. Serruys PW, Onuma Y, Garg S, Sarno G, van den Brand M, Kappetein A. P, et al. Assessment of the SYNTAX score in the Syntax study. EuroIntervention 2009; 5:50–6. PMID: 19577983
11. Roe MT, Messenger JC, Weintraub WS, Cannon CP, Fonarow GC, Dai D, et al. Treatments, trends, and outcomes of acute myocardial infarction and percutaneous coronary intervention. J Am Coll Cardiol 2010; 56:254–63. doi: 10.1016/j.jacc.2010.05.008 PMID: 20633817
12. Smith SC Jr., Feldman TE, Hirshfeld JW Jr., Jacobs AK, Kern MJ, King S. B. 3rd, et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention-Summary Article: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). J Am Coll Cardiol 2006; 47:216–35. PMID: 16386696
13. Hannan EL, Arani DT, Johnson LW, Kemp HG Jr, Lukacik G. Percutaneous transluminal coronary angioplasty in New York State. Risk factors and outcomes. JAMA 1992; 268:3092–7. PMID: 1433740
14. Kimmel SE, Berlin JA, Strom BL, Laskey WK. Development and validation of simplified predictive index for major complications in contemporary percutaneous transluminal coronary angioplasty practice. The Registry Committee of the Society for Cardiac Angiography and Interventions. J Am Coll Cardiol 1995; 26:931–8. PMID: 7560620
15. Ellis SG, Omoigui N, Bittl JA, Lincoff M, Wolfe MW, Howell G, et al. Analysis and comparison of operator-specific outcomes in interventional cardiology. From a multicenter database of 4860 quality-controlled procedures. Circulation 1996; 93:431–9. PMID: 8565159
16. Jollis JG, Peterson ED, DeLong ER, Mark DB, Collins SR, Muhlbaier L. H, et al. The relation between the volume of coronary angioplasty procedures at hospitals treating Medicare beneficiaries and short-term mortality. N Engl J Med 1994; 331:1625–9. PMID: 7969344
17. Hannan EL, Racz M, Ryan TJ, McCallister BD, Johnson LW, Arani D. T, et al. Coronary angioplasty volume-outcome relationships for hospitals and cardiologists. JAMA 1997; 277:892–8. PMID: 9062327

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OBSERVATIONAL STUDY

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

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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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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

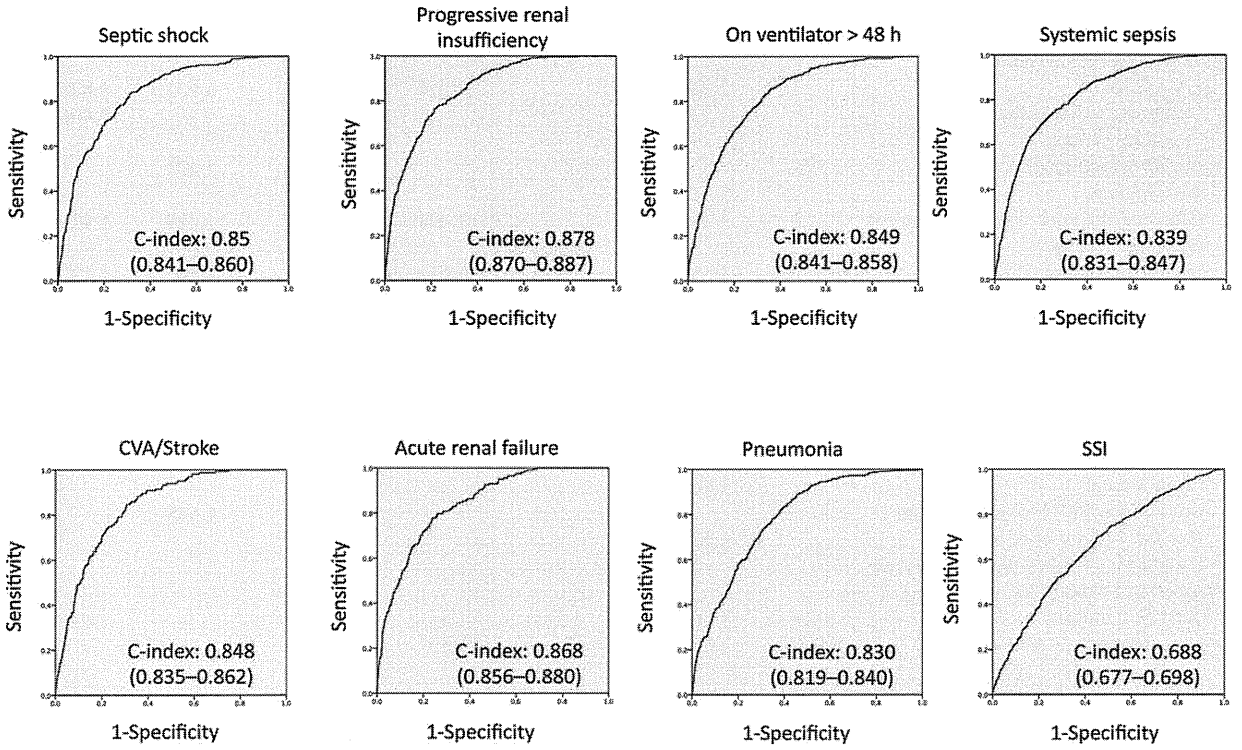

FIGURE 1. Receiver operating characteristic (ROC) curves of each postoperative complication was shown with the C-indices and 95% CIs of each occurrence. ROC = receiver operating characteristic, CIs = confidence intervals.

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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REFERENCES

1. Seiler CA, Brugger L, Forssmann U, et al. Conservative surgical treatment of diffuse peritonitis. *Surgery.* 2000;127:178–184.
2. Ordonez CA, Puyana JC. Management of peritonitis in the critically ill patient. *Surg Clin North Am.* 2006;86:1323–1349.
3. Blot S, De Waele JJ. Critical issues in the clinical management of complicated intra-abdominal infections. *Drugs.* 2005;65:1611–1620.
4. Pieracci FM, Barie PS. Management of severe sepsis of abdominal origin. *Scand J Surg.* 2007;96:184–196.
5. Knaus WA, Draper EA, Wagner DP, et al. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13:818–829.
6. Vincent JL, Moreno R, Takala J, et al. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. On behalf of the Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. *Intensive Care Med.* 1996;22:707–710.
7. Linder MM, Wacha H, Feldmann U, et al. The Mannheim peritonitis index. An instrument for the intraoperative prognosis of peritonitis. *Chirurg.* 1987;58:84–92.
8. Huffman KM, Cohen ME, Ko CY, et al. A Comprehensive Evaluation of Statistical Reliability in ACS NSQIP Profiling Models. *Ann Surg.* 2014.
9. Raval MV, Cohen ME, Ingraham AM, et al. Improving American College of Surgeons National Surgical Quality Improvement Program risk adjustment: incorporation of a novel procedure risk score. *J Am Coll Surg.* 2010;211:715–723.
10. Hall BL, Hamilton BH, Richards K, et al. Does surgical quality improve in the American College of Surgeons National Surgical Quality Improvement Program: an evaluation of all participating hospitals. *Ann Surg.* 2009;250:363–376.
11. Turner PL, Ilano AG, Zhu Y, et al. ACS-NSQIP criteria are associated with APACHE severity and outcomes in critically ill surgical patients. *J Am Coll Surg.* 2011;212:287–294.
12. Miyata H, Gotoh M, Hashimoto H, et al. Challenges and prospects of a clinical database linked to the board certification system. *Sur Today.* 2014;44:1991–1999.
13. Gotoh M, Miyata H, Hashimoto H, et al. National Clinical Database feedback implementation for quality improvement of cancer treatment in Japan: from good to great through transparency. *Surg Today.* 2015.
14. Viehl CT, Kraus R, Zurcher M, et al. The Acute Physiology and Chronic Health Evaluation II score is helpful in predicting the need of relaparotomies in patients with secondary peritonitis of colorectal origin. *Swiss Med Wkly.* 2012;142:w13640.
15. Nakagoe T, Miyata H, Gotoh M, et al. Surgical risk model for acute diffuse peritonitis based on a Japanese nationwide database: an initial report on the surgical and 30-day mortality. *Surg Today.* 2014.
16. Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a Japanese nationwide web-based database. *Ann Surg.* 2014;260:259–266.
17. Watanabe M, Miyata H, Gotoh M, et al. Total gastrectomy risk model: data from 20,011 Japanese patients in a nationwide internet-based database. *Ann Surg.* 2014;260:1034–1039.
18. Kurita N, Miyata H, Gotoh M, et al. Risk model for distal gastrectomy when treating gastric cancer on the basis of data from 33,917 Japanese patients collected using a nationwide web-based data entry system. *Ann Surg.* 2015.
19. Kobayashi H, Miyata H, Gotoh M, et al. Risk model for right hemicolectomy based on 19,070 Japanese patients in the National Clinical Database. *J Gastroenterol.* 2014;49:1047–1055.
20. Matsubara N, Miyata H, Gotoh M, et al. Mortality after common rectal surgery in Japan: a study on low anterior resection from a newly established nationwide large-scale clinical database. *Dis Colon Rectum.* 2014;57:1075–1081.
21. Kenjo A, Miyata H, Gotoh M, et al. Risk stratification of 7,732 hepatectomy cases in 2011 from the National Clinical Database for Japan. *J Am Coll Surg.* 2014;218:412–422.
22. Kimura W, Miyata H, Gotoh M, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. *Ann Surg.* 2014;259:773–780.
23. Artigas A, Niederman MS, Torres A, et al. What is next in sepsis: current trials in sepsis. *Expert Rev Anti Infect Ther.* 2012;10:859–862.
24. Hutchins NA, Unsinger J, Hotchkiss RS, et al. The new normal: immunomodulatory agents against sepsis immune suppression. *Trends Mol Med.* 2014;20:224–233.
25. Vacanti CJ, VanHouten RJ, Hill RC. A statistical analysis of the relationship of physical status to postoperative mortality in 68,388 cases. *Anesth Analg.* 1970;49:564–566.
26. Prause G, Ratzenhofer-Comenda B, Pierer G, et al. Can ASA grade or Goldman's cardiac risk index predict peri-operative mortality? A study of 16,227 patients. *Anaesthesia.* 1997;52:203–206.
27. Jones DR, Copeland GP, de Cossart L. Comparison of POSSUM with APACHE II for prediction of outcome from a surgical high-dependency unit. *Br J Surg.* 1992;79:1293–1296.
28. Cerra FB, Negro F, Abrams J. APACHE II score does not predict multiple organ failure or mortality in postoperative surgical patients. *Arch Surg.* 1990;125:519–522.
29. Copeland GP, Jones D, Walters M. POSSUM: a scoring system for surgical audit. *Br J Surg.* 1991;78:355–360.
30. Whiteley MS, Prytherch DR, Higgins B, et al. An evaluation of the POSSUM surgical scoring system. *Br J Surg.* 1996;83:812–815.
31. Prytherch DR, Whiteley MS, Higgins B, et al. POSSUM and Portsmouth POSSUM for predicting mortality. Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity. *Br J Surg.* 1998;85:1217–1220.

32. Barie PS, Hydo LJ, Shou J, et al. Efficacy and safety of drotrecogin alfa (activated) for the therapy of surgical patients with severe sepsis. *Surg Infect.* 2006;7(Suppl 2):S77–S80.

33. Barie PS, Vogel SB, Dellinger EP, et al. A randomized, double-blind clinical trial comparing cefepime plus metronidazole with imipenem-cilastatin in the treatment of complicated intra-abdominal infections. Cefepime Intra-abdominal Infection Study Group. *Arch Surg.* 1997;132:1294–1302.

34. Farthmann EH, Schoffel U. Principles and limitations of operative management of intraabdominal infections. *World J Surg.* 1990;14:210–217.

35. Garcia-Sabrido JL, Tallado JM, Christou NV, et al. Treatment of severe intra-abdominal sepsis and/or necrotic foci by an 'open-abdomen' approach. *Arch Surg.* 1988;123:152–156.

36. Anaya DA, Nathens AB. Risk factors for severe sepsis in secondary peritonitis. *Surg Infect.* 2003;4:355–362.

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ORIGINAL ARTICLE

Propensity-matched analysis of minimally invasive mitral valve repair using a nationwide surgical database

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Abstract
Purpose The aim of this study was to compare the cases of minimally invasive mitral valve surgery (MICS-mitral) performed using right mini-thoracotomy (RT) with those performed using median sternotomy (MS).
Methods Between 2008 and 2012, 6137 patients underwent isolated mitral valve repair at 210 institutions and were registered in the Japan Adult Cardiovascular Surgery Database. We compared 756 who underwent MICS-mitral via RT to 5381 MS patients and performed a one-to-one matched analysis based on the estimated propensity score.
Results The in-hospital mortality was similar between both groups (RT vs. MS: 0.5 vs. 1.1 %). Although the incidence of postoperative stroke, renal failure, and prolonged ventilation was similar, the number of patients with mediastinitis was greater in the MS group (RT vs. MS: 0 vs. 0.7 %, $p < 0.01$). Reexploration for bleeding was more frequent in the RT group (RT vs. MS: 2.9 vs. 1.4 %, $p < 0.01$). Mortality and morbidity occurred at a higher rate in low-volume institutions. The propensity analysis showed that the operation-related times were significantly longer in the RT group, while the length of hospital stay was shorter. In a propensity analysis of patients <60 years of age, there was no in-hospital mortality.
Conclusions MICS-mitral via RT was successful without compromising the clinical outcomes. Although the operation time and postoperative bleeding should be improved, an RT approach is safe in appropriately selected patients, especially those <60 years of age or treated in a high-volume center.

Keywords Mitral valve · Surgery · Valvular diseases

Introduction

There is growing interest worldwide in minimally invasive cardiac surgery (MICS), with minimally invasive mitral valve surgery (MICS-mitral) via right mini-thoracotomy (RT), which had increased in use over the past 20 years [1–7]. Some reports from Western countries have noted that 70–80 % of patients with mitral valve disease underwent MICS-mitral [8, 9]. In addition, a high prevalence (>40 %) of minimally invasive mitral valve surgery has been reported in Germany [10]. However, most reports come from high-volume centers that have extensive experience in minimally invasive techniques and some surgeons may be reluctant to utilize this technique due to the possibility of increased postoperative complications and concerns about the operative outcomes.

Recently, paradigms for the management of mitral valve regurgitation (MR) have shifted to identify benefits earlier in the disease course, before the development of an adverse effect from long-standing MR on the left ventricular function [11–14]. As a result, there is a growing advocacy for the referral of asymptomatic patients for surgery, indicating the need for a high level of safety for mitral valve repair,

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as a nationwide report from Japan showed that the in-hospital mortality related to that procedure was approximately 1 % [15]. MICS-mitral should not compromise the clinical outcome. Although there are several theoretical advantages of this less invasive approach for mitral valve surgery, no randomized comparison studies have been previously conducted. It is important to consider the effect of treatment allocation bias between MICS-mitral and a conventional sternotomy approach. High risk patients are often selected as a sternotomy group, thus it is very important to adjust this selection bias to appropriately evaluate the results of MICS-mitral. A propensity score analysis helps to control for such bias, although it requires a large study population. To date, there have been few reports of such studies [16–18]. To clarify the safety of MICS-mitral, it is essential to remove selection bias as much as possible and evaluate the results using a large cohort, such as in a multicenter database.

In the present study, we evaluated cases of mitral valve repair through RT or median sternotomy (MS) in Japan by utilizing the nationwide Japan Adult Cardiovascular Surgery Database (JACVSD) to examine the safety and efficacy of this approach, as well as the clinical outcomes. We also conducted an age-related propensity score matching analysis and assessed the effect of hospital volume on the clinical outcomes of MICS-mitral.

Patients and methods

Japan Adult Cardiovascular Surgery Database

Data compiled between January 2008 and December 2012 from 210 cardiac surgery units located throughout Japan were obtained. The method used and data contents have been described in a previous study [19]. The data registration project was approved by the institutional review board of each participating hospital. Informed consent was also obtained from all patients in each participating hospital. A high level of data collection was successfully achieved for 255 variables with missing data representing <2 % of all assembled information. The JACVSD variables and their definitions (available online at http://jacvsd.umin.jp) were identical for the most part to those in the Society of Thoracic Surgeons (STS) National Adult Cardiac Database (available online at http://sts.org), with some slight modifications.

Study population

For the present study, we selected patients who underwent an isolated mitral valve repair procedure as the study cohort. We excluded those with concomitant operations, such as coronary artery bypass grafting, arrhythmia surgery, and surgery for other valve pathology. Patients who required circulatory arrest or ventricular fibrillation without cross-clamping the aorta and those with a previous cardiac operation history were also excluded. Between 2008 and 2012, 6137 patients underwent isolated mitral valve repair at 210 institutions and were registered in the JACVSD. Of those, we selected 756 who underwent MICS-mitral via RT (56 ± 14 years old, 306 males, 450 females), as the database includes a surgical approach category. These 756 patients were classified as the MICS group, while the other 5381 patients who underwent mitral valve repair via median sternotomy were classified as the MS group.

Study design

The preoperative patient characteristics, cardiac function, and short-term outcomes, including 30-day operative mortality and major morbidity, intensive care unit (ICU) length of stay, and postoperative length of stay in the hospital, were investigated and compared between the two groups. We then selected variables related to the decision for surgical approach (RT vs. MS). We also performed a one-to-one matched analysis based on the estimated propensity scores for patients in the RT and MS groups using these variables, and obtained 750 well-matched patient pairs for the overall cohort. The preoperative patient characteristics and perioperative outcomes were investigated and compared between the 750 well-matched patient pairs.

To clarify the effect of age in relation to MICS-mitral, we also performed a one-to-one matched analysis based on the estimated propensity scores for patients in the RT and MS groups using 425 pairs of patients who were younger than 60 years of age and balanced for the baseline characteristics, and 325 pairs who were 60 years of age and older.

We also determined the effect of patient volume at each institution on the postoperative outcome by examining the distribution of MICS-mitral cases in the most recent year (2012). According to the number of MICS-mitral cases in each institution, we divided 756 MICS-mitral patients into two groups, those treated at institutions that experienced less than 10 cases per year and those that had 10 or more cases per year, and conducted the same analysis.

Statistical analysis

The statistical model was a multiple logistic regression model with variables entered into the model selected using bivariate tests, with Pearson's Chi-square test used for categorical covariates, and an unpaired *t* test or Wilcoxon rank sum test for continuous covariates. We used propensity score matching to adjust for differences in the baseline characteristics because patients were not randomly

assigned to receive either RT or MS. We performed one-to-one matched analyses on the basis of the estimated propensity score of each patient. The log odds for the probability of a patient receiving RT or MS were modeled for potential cofounders. C-statistics were calculated for evaluating the goodness of fit ($c = 0.713$). The estimated propensity scores were compared between the RT and MS groups with a "match" occurring when one patient in the RT group had an estimated score within a standard deviation of 0.6 of another patient in the MS group. We also performed univariate comparisons of the patient characteristics and outcome variables between the propensity score-matched groups of RT and MS patients using Fisher's exact test and t test as appropriate. The SPSS version 20.0J software program (SPSS Japan, Tokyo, Japan) was used for all analyses and a p value < 0.05 was considered to be statistically significant.

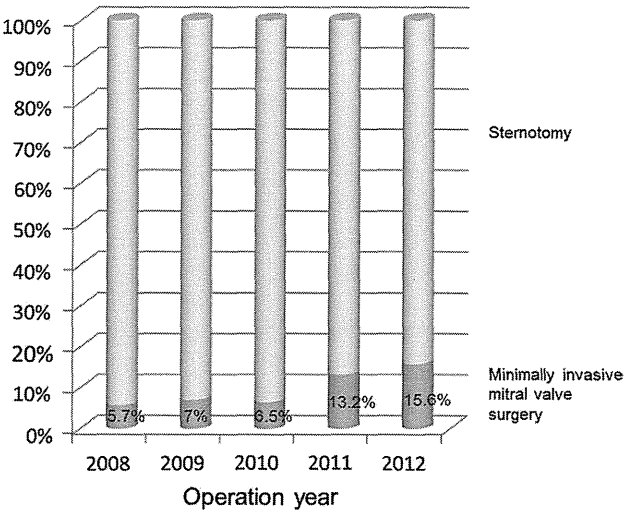

Fig. 1 Ratio of MICS-mitral in patients who underwent isolated mitral valve repair between 2008 and 2012. The ratio within the overall cohort gradually increased over time

Results

Overall cohort

The ratio of RT patients in the overall cohort gradually increased from 2008 to 2012, as shown in Fig. 1. Among patients younger than 60 years of age, the ratio of RT patients was 14.7 %, while that of those between 60 and 65 years of age was 11.9 %, between 66 and 70 years of age was 9.5 %, between 71 and 75 years of age was 8.5 %, and older than 75 years of age was 11.2 %.

Table 1 shows the preoperative patient background information for all 6137 included cases of RT and MS. The groups were homogeneous in terms of sex, BSA, diabetes, hyperlipidemia, and history of cerebrovascular disease, while there were significant differences between the groups regarding age, renal dysfunction, hypertension, current smoker status, and chronic obstructive lung disease. Patients with infective endocarditis, peripheral vascular disease, renal dysfunction, or urgent stage tended not to be selected for RT. In the RT group, the patients were significantly younger and had a normal left ventricular function compared to the MS group.

The operative, cardiopulmonary bypass, and aortic cross-clamp times were significantly longer in the RT group than in the MS group, while the incidence of transfusion was significantly lower in the RT group. The postoperative mortality and morbidity are compared in Table 2. The 30-day and in-hospital mortality rates were quite low in both groups with no significant differences. Significant differences were observed in regard to the incidence of infection; deep sternal wound infection and sepsis were observed at a significantly higher rate in MS patients, while the incidence of other peripheral infections was significantly higher in RT patients. It is interesting to note that significantly fewer RT patients experienced new onset of atrial fibrillation ($p < 0.001$). In the RT group, the incidence of reexploration for bleeding was significantly higher than that in the MS group, while the incidence of cardiac tamponade was significantly higher in the MS group. In contrast, the incidence of other major morbidities such as permanent stroke, perioperative myocardial infarction, renal insufficiency requiring dialysis, gastrointestinal tract complications, and prolonged ventilation did not differ between the two groups.

Propensity score matching

After performing a one-to-one matched analysis based on the estimated propensity score for patients in the RT and MS groups, there were no significant differences in regard to the preoperative patient characteristics except for the incidence of infective endocarditis (Table 1). The operation year and age distribution were also collected using this propensity score analysis.

The operative, cardiopulmonary bypass, and aortic cross-clamp times were significantly longer in the RT group than in the MS group, whereas the incidence rate of transfusion was similar (Table 2). Both the 30-day mortality (RT 0.3 %, MS 0 %) and in-hospital mortality (RT 0.5 %, MS 0.3 %) rates were similar between the two groups. The incidence of reexploration for bleeding was significantly higher in RT patients, while there were no significant differences in regard to other postoperative complications between the two groups. Although the length of ICU stay was similar in both groups, the length of postoperative stay until discharge was significantly shorter in the RT group.

Table 1 Baseline characteristics of the study patients (left, overall cohort; right, propensity score matching analysis cohort)

	Overall cohort			Propensity score matching		
	RT group ($n = 756$)	MS group ($n = 5381$)	p value	RT group ($n = 750$)	MS group ($n = 750$)	p value
Age (years)	56 ± 14	59 ± 14	<0.01	56 ± 11	55 ± 14	NS
Gender (male/female)	450/306	3282/2099	NS	450/300	447/303	NS
Body surface area (m^2)	1.64 ± 0.19	1.62 ± 0.20	NS	1.64 ± 0.19	1.63 ± 0.19	NS
History of smoking	269 (36 %)	1942 (36 %)	NS	269 (36 %)	226 (30 %)	<0.05
Diabetes	50 (6.6 %)	470 (8.7 %)	NS	49 (7 %)	55 (7 %)	NS
Renal dysfunction	15 (2.0 %)	211 (3.9 %)	<0.01	15 (2 %)	12 (2 %)	NS
Dialysis	1 (0.1 %)	85 (1.6 %)	<0.01	1 (0.1 %)	1 (0.1 %)	NS
Hyperlipidemia	196 (26 %)	1438 (27 %)	NS	194 (26 %)	193 (26 %)	NS
Hypertension	312 (41 %)	2572 (48 %)	<0.01	311 (42 %)	314 (42 %)	NS
Cerebrovascular disease	18 (2 %)	332 (6 %)	<0.01	18 (2 %)	25 (3 %)	NS
COPD	9 (2 %)	87 (2 %)	NS	86 (2 %)	72 (2 %)	NS
Infective endocarditis	10 (1 %)	397 (7 %)	<0.01	10 (1.3 %)	24 (3 %)	<0.05
PAD	3 (0.4 %)	111 (2 %)	<0.01	3 (0.4 %)	1 (0.1 %)	NS
NYHA function class I/II/III/IV	338/339/82/7	1967/2477/718/215	<0.01	336/336/81/7	332/337/67/14	NS
LV function good/medium/bad	667/86/3	4403/909/65	<0.01	661/86/3	674/74/2	NS
Urgent or emergent	2 (0.3 %)	295 (5 %)	<0.01	2 (0.3 %)	2 (0.3 %)	NS

COPD chronic obstructive heart disease, *LV* left ventricle, *MS* median sternotomy, *NYHA* New York Heart Association, *PAD* peripheral artery disease, *RT* right mini-thoracotomy

Table 2 Postoperative morbidity and mortality rates in both groups (left, overall cohort; right, propensity score matching analysis cohort)

	Overall cohort			Propensity score matching		
	RT group ($n = 756$)	MS group ($n = 5381$)	p value	RT group ($n = 750$)	MS group (750)	p value
Operation time (min)	316 ± 85	272 ± 76	<0.01	317 ± 85	272 ± 72	<0.01
CPB time (min)	190 ± 64	140 ± 49	<0.01	190 ± 64	140 ± 47	<0.01
Cross-clamp time (min)	131 ± 49	100 ± 38	<0.01	132 ± 49	102 ± 36	<0.01
Transfusion	2411 (49 %)	756 (35 %)	<0.01	288 (38 %)	266 (36 %)	NS
30-day mortality	2 (0.3 %)	28 (0.5 %)	NS	2 (0.3 %)	0	NS
In-hospital mortality	4 (0.5 %)	60 (1.1 %)	NS	4 (0.5 %)	2 (0.3 %)	NS
Reoperation for bleeding	22 (2.3 %)	78 (1 %)	<0.01	22 (2.9 %)	9 (1.2 %)	<0.05
Cardiac tamponade	3 (0.4 %)	70 (1 %)	<0.01	3 (0.4 %)	7 (0.9 %)	NS
Stroke	6 (0.8 %)	69 (1 %)	NS	6 (0.8 %)	6 (0.8 %)	NS
Deep sternal infection	0	35 (0.7 %)	<0.05	0	2 (0.3 %)	NS
Other infection	3 (0.4 %)	4 (0.1 %)	<0.05	3 (0.4 %)	4 (0.1 %)	NS
Sepsis	1 (0.1 %)	50 (1 %)	<0.01	1 (0.1 %)	2 (0.3 %)	NS
Prolonged ventilation	20 (3 %)	157 (3 %)	NS	20 (2.7 %)	10 (1.3 %)	NS
Renal failure	8 (1 %)	113 (2 %)	NS	8 (1.1 %)	11 (1.5 %)	NS
New onset of AF	126 (17 %)	1195 (22 %)	<0.01	126 (17 %)	139 (19 %)	NS
PMI	6 (0.8 %)	17 (0.3 %)	NS	6 (0.8 %)	1 (0.1 %)	NS
ICU stay (days)	2.2 ± 4.5	2.9 ± 5.5	<0.01	2.2 ± 4.5	2.4 ± 1.9	NS
Time to discharge (days)	14 ± 11	21 ± 28	<0.01	14 ± 11	17 ± 9	<0.01

AF atrial fibrillation, *CPB* cardiopulmonary bypass, *ICU* intensive care unit, *MS* median sternotomy, *PMI* perioperative myocardial infarction, *RT* right mini-thoracotomy