pancreaticoduodenectomy (PD), surgery for acute diffuse peritonitis (ADP), aortic valve replacement (AVR), total arch replacement (TAR), descending thoracic aorta replacement (descending TAR), coronary artery bypass graft (CABG) on-pump, and CABG off-pump. Patients who did not consent to their data being used were excluded from this analysis. Records with missing data for age, sex, or status at postoperative day (POD) 30 were also excluded, as were data related to patients with a BMI of less than 10 or over 50 as these values were obviously erroneous.

### Study outcomes

The three outcomes examined using the NCD were BMI, operation time, and operative mortality. BMI is calculated as weight (in kilograms) divided by the square of height (in meters). Operative mortality included all deaths occurring within the index hospitalization period, regardless of the length of hospital stay (up to 90 days), or after hospital discharge (within 30 days after surgery). We evaluated influences of stratified BMI on operation time and operative mortality.

### Statistical analyses

All statistical analyses were conducted using SPSS (version 20). We performed univariate comparisons of BMI and operation time, using the unpaired Student's *t* test and Chi-square test. A *P* value of 0.05 was considered significant.

## Results

Table 2 summarizes the backgrounds of each procedure. There were 232,199 patients undergoing 1 or more of 8 gastroenterological surgery procedures and 56,219 patients undergoing 1 or more of 5 cardiovascular surgery procedures.

**Table 2** Background parameters

| Operation | Number | Sex (male/female) | Age (mean ± SD) |
|---|---|---|---|
| Eso | 10,825 | 9124/1701 | 66.1 ± 9.3 |
| DG | 63,650 | 42,438/21,212 | 69.1 ± 11.5 |
| TG | 37,817 | 27,877/9940 | 69.0 ± 11.0 |
| RHC | 37,750 | 18,878/18,872 | 71.7 ± 12.1 |
| LAR | 33,217 | 21,436/11781 | 66.2 ± 11.6 |
| Hx | 14,903 | 10,456/4447 | 67.0 ± 11.5 |
| PD | 17,485 | 10,841/6644 | 68.5 ± 10.2 |
| ADP | 16,552 | 10,020/6532 | 64.9 ± 18.6 |
| AVR | 14,827 | 7914/6913 | 72.4 ± 10.7 |
| TAR | 10,594 | 7421/3173 | 69.5 ± 11.6 |
| Descending TAR | 5605 | 4129/1476 | 69.6 ± 12.3 |
| CABG on-pump | 9221 | 7232/1989 | 67.7 ± 9.9 |
| CABG off-pump | 15,972 | 12,547/3425 | 69.1 ± 9.7 |

*Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment except for the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft

### BMI distribution

Figure 1 shows the BMI distribution of all the patients whose data were analyzed. Approximately 60 % of the procedures (61.2–69.9 %) were performed on patients with a normal physique, with a BMI of 18.5–25. Of the remaining patients, 2.6 % were obese, 20.3 % were overweight, and 13.4 % were underweight. There were differences in BMI distributions between patients undergoing gastroenterological and cardiovascular procedures. The largest category of patients undergoing gastroenterological surgery had a BMI of 18.5–22, and the largest category of those undergoing cardiovascular surgery had a BMI of 22–25. The proportion of overweight patients (with a BMI of 25–30) among those undergoing gastroenterological surgery was less than 20 %, whereas the proportion of overweight patients among those undergoing cardiovascular surgery was more than 20 %. The proportion of obese patients did not exceed 3 % in any of the gastroenterological surgery groups, but it exceeded 4 % in all of the cardiovascular surgery groups, being especially low in the Eso (1 %) group and especially high in the on-pump (5 %) and off-pump (4.6 %) CABG groups. The proportion of underweight patients (with a BMI of <18.5) among those undergoing gastroenterological surgery, apart from Hx, was at least 10 %, whereas among those undergoing cardiovascular surgery, apart from AVR, it was no more than 10 %. This rate was high for ADP (23.3 %), Eso (21.1 %), and PD (14.9 %), but low for off-pump (5 %) and on-pump (5.1 %) CABG.

### Operation time by BMI

Figure 2 shows the operation times for all procedures, which became longer as the BMI rose. When a BMI cutoff of 30 was used, the operation time for obese patients was significantly longer than that for those who were not obese, for all procedures except Eso (Table 3). Among the gastroenterological operations, the operation time for obese patients was prolonged for PD (56 ± 8.3 min, mean ± SE), TG (50 ± 4.0 min), and LAR (50 ± 3.9 min), while among the cardiovascular operations, the operation time for obese patients was prolonged for TAR (55 ± 8.4 min) and descending TAR (54 ± 13.8 min). The operation times were originally longer for men than for women, for all of

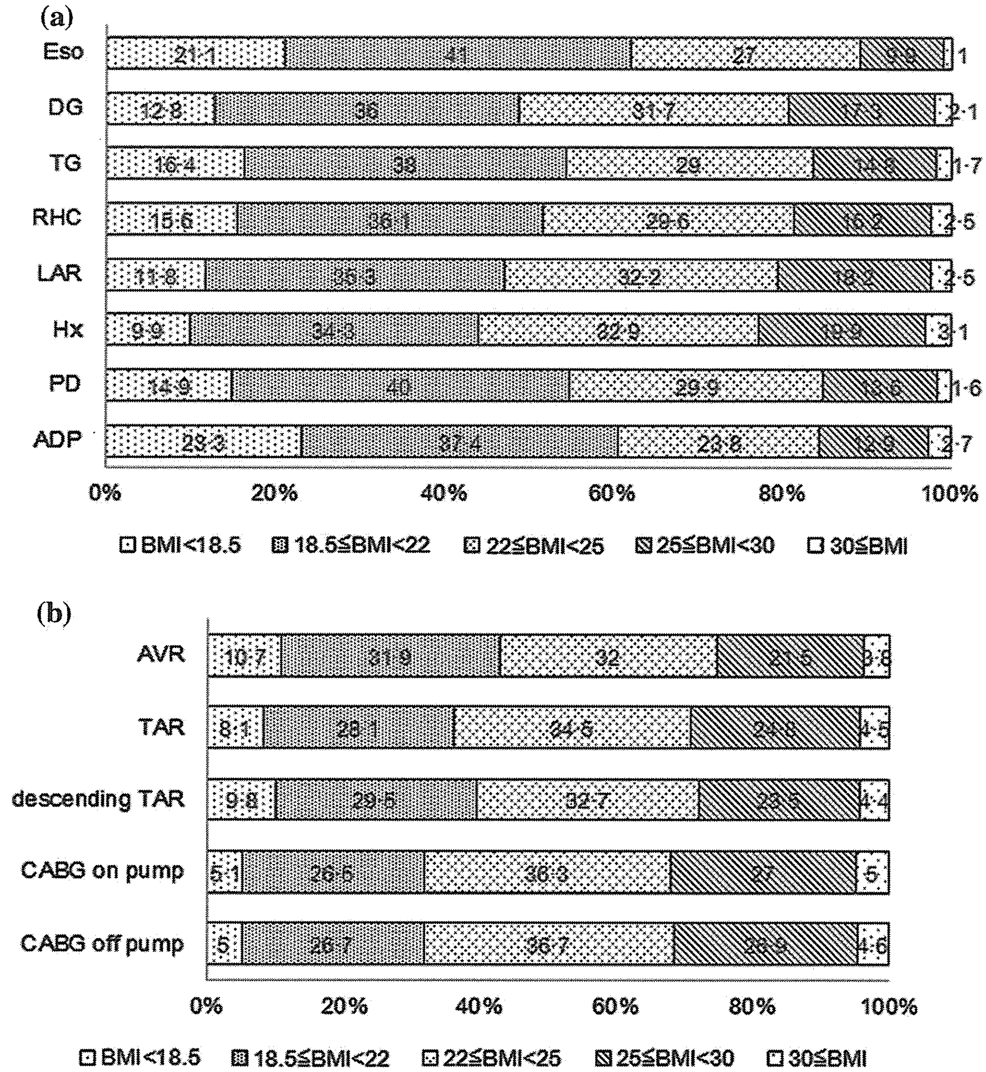



**Fig. 1** **a** Body mass index (BMI) distribution in the gastroenterological surgery procedures (%). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** BMI distribution in the cardiovascular surgery procedures (%). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft

the procedures (Table 4). The operation time was significantly longer for obese men than for men who were not obese, and this result was consistent among all procedures. The differences in the effects of obesity on operation times between men and women varied among the procedures. The prolongation of operation time by at least 60 min because of obesity was greater in men than in women undergoing LAR, TAR, and descending TAR. Among patients undergoing Hx, the impact of obesity on operation time was greater for women than for men.

### Influence of BMI on operative mortality

Figure 3 shows the operative mortality rates. The mortality rate according to BMI had a U-shaped distribution for most procedures, with both underweight and obese patients having higher mortality rates. Overweight patients tended to have the lowest mortality risk among those undergoing cardiovascular surgery, but not among those undergoing gastroenterological surgery. Obesity tended to have a small effect on mortality among patients undergoing Eso or DG. Among patients undergoing PD, those who were underweight had the lowest mortality rate.

## Discussion

We conducted a large-scale trans-disciplinary study on the effects of BMI on gastroenterological vs. cardiovascular surgery, using NCD accumulated in Japan. Several previous studies have demonstrated a cause-and-effect relationship between BMI and operative outcomes, including operation time and operative mortality in various fields, including gastroenterological procedures for esophageal

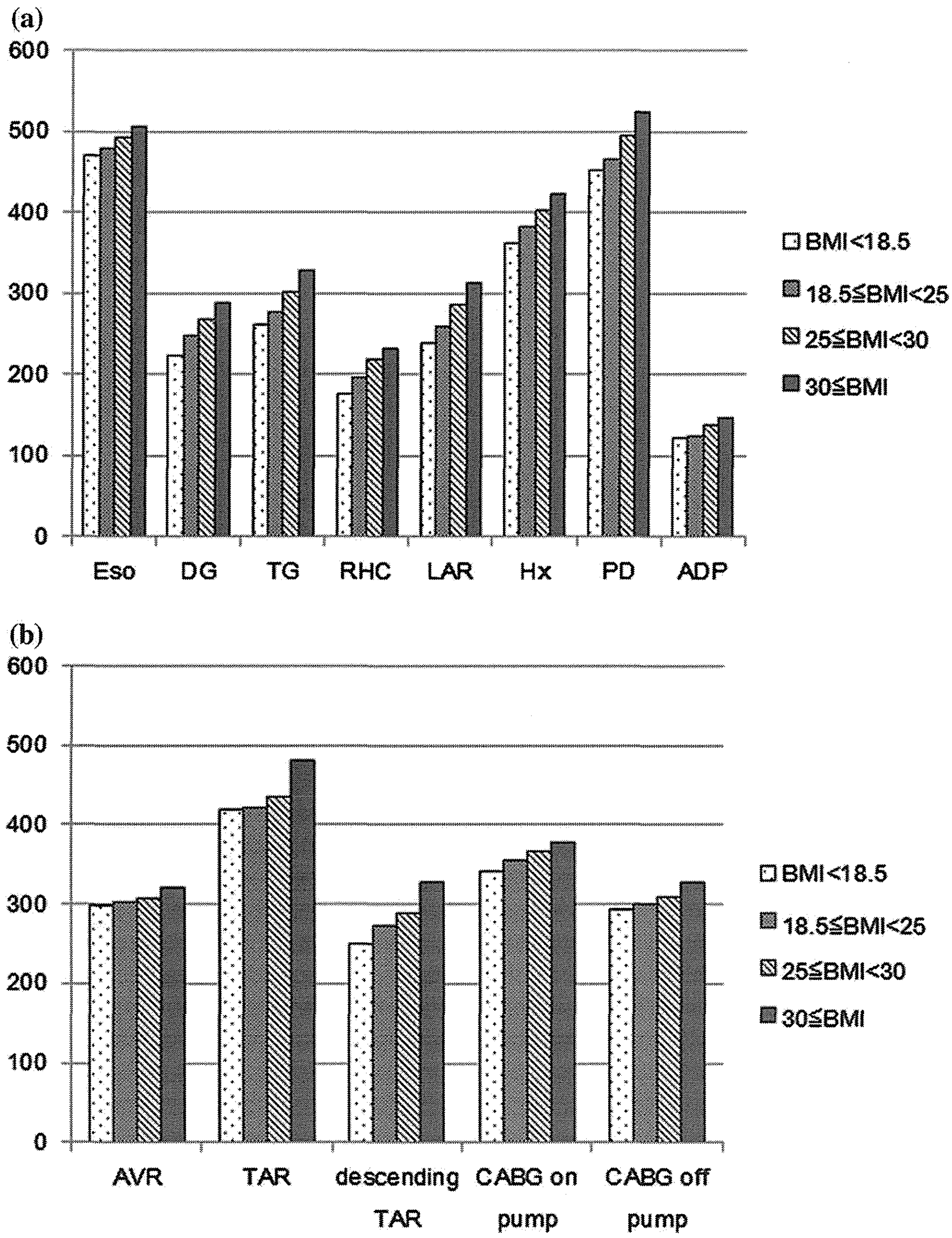



**Fig. 2** **a** Operation times for the gastroenterological surgery procedures (min). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment, apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** Operation times for the cardiovascular surgery procedures (min). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft

cancer [8], gastric cancer [9], colon cancer [10], liver cancer [11], pancreatic cancer [12], and laparoscopic cholecystectomy [13], as well as cardiac procedures, including CABG and valve replacement [14, 15]. However, according to the literature, the influences of BMI on surgery vary among operative procedures and even for the same procedure, so the effects of BMI on operative outcomes remain controversial. To date, two studies involving a large number of cases have been reported. In a study of 30,765 patients undergoing surgery for gastric cancer or colorectal cancer in Japan, Yasanuga et al. found that obese patients had significantly higher rates of postoperative complications and that underweight patients had significantly higher rates of both postoperative complications and operative mortality than those with a normal BMI [19]. In a study of 13,115 patients undergoing CABG, Alam et al. found that obese patients had significantly prolonged total circulatory bypass and aortic clamp times, as well as an increased risk of postoperative respiratory failure, postoperative renal failure, and surgical site infections, but not of operative mortality [14]. The number of patients in the present study was greater than that in either of the previous studies and we also examined data for various procedures in two major fields. We confirmed that BMI has similar effects on nearly all procedures in the fields of gastroenterological and cardiovascular surgery in this nationwide survey.

**Table 3** Operation times (min) according to a body mass index cut-off value of 30

| Operation | Total number | Operation time (min) | | Prolongation (min) | *P* value |
|---|---|---|---|---|---|
| | (BMI < 30:30 ≤ BMI) | BMI < 30 | 30 ≤ BMI | | |
| Eso | 10,825 (10,727:98) | 479 | 505 | 26 | ns |
| DG | 63,650 (62,391:1259) | 248 | 288 | 40 | <0.001 |
| TG | 37,817 (37,215:602) | 279 | 329 | 50 | <0.001 |
| RHC | 37,750 (36,850:900) | 197 | 233 | 36 | <0.001 |
| LAR | 33,217 (32,409:808) | 262 | 312 | 50 | <0.001 |
| Hx | 14,903 (14,459:444) | 384 | 424 | 40 | <0.001 |
| PD | 17,485 (17,229:256) | 468 | 524 | 56 | <0.001 |
| ADP | 16,552 (16,117:435) | 127 | 148 | 21 | <0.001 |
| AVR | 14,827 (14,257:570) | 304 | 321 | 17 | <0.001 |
| TAR | 10,594 (10,114:480) | 426 | 481 | 55 | <0.001 |
| Descending TAR | 5605 (5356:249) | 274 | 328 | 54 | <0.001 |
| CABG on-pump | 9221 (8760:461) | 358 | 379 | 21 | <0.001 |
| CABG off-pump | 15,972 (15,238:734) | 303 | 328 | 25 | <0.001 |

Student's *t* test was used to compare the mean operation time between obese (BMI ≥ 30) and non-obese (BMI < 30) patients. Statistical significance was set at $P < 0.05$

*Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft, *BMI* body mass index

Operation times were longer for patients with a higher BMI. When a BMI cut-off of 30 was used, the operation time was significantly longer for obese patients for all procedures except Eso. The procedure associated with the greatest prolongation of operation time was PD, by 56 min, while AVR was prolonged by at least 17 min. The results of the previous studies were conflicting about the influences of obesity on operation time, but those of the present study allowed us to conclude that obesity prolongs the operation time for nearly all the procedures studied. Interestingly, for all procedures, the operation times were longer for men than for women, and they were significantly longer for men who were obese than men who were not. We also noted differences among procedures in the prolongation of operation time due to obesity between men and women. It is noteworthy that men typically have a body type characterized by visceral fat accumulation, whereas women tend to show subcutaneous fat accumulation. These body type differences may account for the differences in operative times and the prolongation of surgery because of obesity.

The mortality rates according to BMI showed a U-shaped distribution, with both underweight and obese patients having high mortality rates, except when PD was the procedure performed. Prior reports from Western countries showed similar mortality curves. These studies demonstrated the so-called 'obesity paradox' in that obesity exerts an advantageous effect on morbidity and mortality, compared with normal BMI, in surgical patients [20–22]. Davenport et al. [22] reported that patients with mild obesity, defined as a BMI over 30 but under 35, had a lower 30-day mortality rate than patients of normal weight following vascular surgery. The BMI category with the lowest mortality risk is lower in Asians than in Western populations because Asians have a higher percentage of body fat than Westerners at the same BMI [3, 23]. Deurenberg et al. [24] reported the BMI values of East Asians to be lower, by 1.9–3.2 %, than in Western people when the percentage of body fat was the same. The adverse effect of obesity on short-term prognosis in patients undergoing surgery for a malignant disease would be due to not only the high technical difficulty of the necessary surgical procedures in the obese patient, but to BMI-dependent differences in the severity of the cancer. However, the influence of BMI on malignancy remains controversial [25, 26]. Mullen et al. [27] reported that underweight patients had a significantly higher postoperative death rate, with an odds ratio (OR) of 5.24 and a 95 % confidence interval (CI) of 1.7–16.2, after major surgery for gastrointestinal cancer. As in previous studies, the underweight patients in the present series had higher mortality, which we speculate is related to a reduced capacity to tolerate surgery because of their underlying nutritional deficiencies and probable advanced stages of gastroenterological cancer.

This study has the advantages of being nationwide and including a very large number of cases; however, there are limitations because of its retrospective nature and cross-sectional design. Moreover, certain details were not

**Table 4** Operation times (min) according to a body mass index cut-off value of 30 and gender

| Operation | Gender | Total number | Operation time (min) | | Prolongation (min) | *P* value |
|---|---|---|---|---|---|---|
| | | (BMI < 30:30 ≤ BMI) | BMI < 30 | 30 ≤ BMI | | |
| Eso | Male | 9124 (9036:88) | 488 | 521 | 33 | <0.05 |
| | Female | 1701 (1691:10) | 432 | 363 | −69 | ns |
| DG | Male | 42438 (41674:764) | 255 | 303 | 48 | <0.001 |
| | Female | 21212 (20717:495) | 234 | 265 | 31 | <0.001 |
| TG | Male | 27877 (27484:393) | 284 | 338 | 54 | <0.001 |
| | Female | 9940 (9731:209) | 264 | 313 | 49 | <0.001 |
| RHC | Male | 18878 (18505:373) | 206 | 251 | 45 | <0.001 |
| | Female | 18872 (18345:527) | 187 | 221 | 34 | <0.001 |
| LAR | Male | 21,436 (21,013:423) | 269 | 334 | 65 | <0.001 |
| | Female | 11,781 (11,396:385) | 248 | 287 | 39 | <0.001 |
| Hx | Male | 10,456 (10,162:294) | 392 | 428 | 36 | <0.001 |
| | Female | 4447 (4297:150) | 368 | 417 | 49 | <0.001 |
| PD | Male | 10,841 (10,715:126) | 480 | 540 | 60 | <0.001 |
| | Female | 6644 (6514:130) | 448 | 508 | 60 | <0.001 |
| ADP | Male | 10,020 (9790:230) | 127 | 153 | 26 | <0.001 |
| | Female | 6532 (6327:205) | 126 | 142 | 16 | <0.001 |
| AVR | Male | 7914 (7687:227) | 314 | 354 | 40 | <0.001 |
| | Female | 6913 (6570:343) | 292 | 300 | 8 | ns |
| TAR | Male | 7421 (7075:346) | 427 | 494 | 67 | <0.001 |
| | Female | 3173 (3039:134) | 422 | 450 | 28 | <0.05 |
| Descending TAR | Male | 4129 (3945:184) | 275 | 343 | 68 | <0.001 |
| | Female | 1476 (1411:65) | 269 | 286 | 17 | ns |
| CABG on-pump | Male | 7232 (6885:347) | 360 | 380 | 20 | <0.001 |
| | Female | 1989 (1875:114) | 351 | 375 | 24 | <0.05 |
| CABG off-pump | Male | 12,547 (12,020:527) | 305 | 334 | 29 | <0.001 |
| | Female | 3425 (3218:207) | 293 | 312 | 19 | <0.01 |

Student's *t* test was used to compare the mean operation time between obese (BMI ≥ 30) and non-obese (BMI < 30) patients by sex. Statistical significance was set at $P < 0.05$

*Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment apart from the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis, *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft, *BMI* body mass index

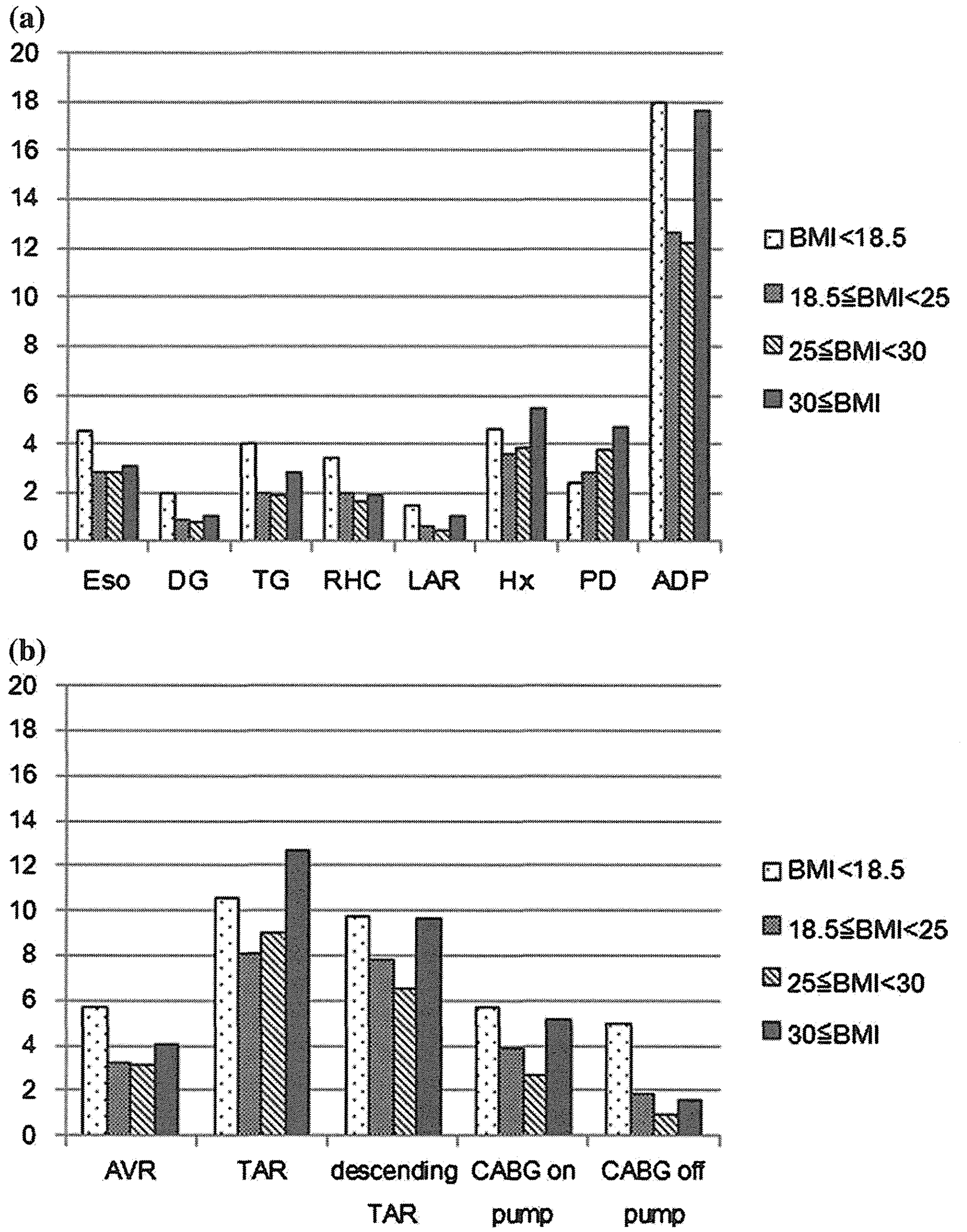
assessed, such as the presence or absence of endoscopic surgery, emergency vs. non-urgent status, and co-existent illnesses, including hypertension and diabetes. Various factors other than BMI can affect operative outcomes, and these factors differ among operative procedures. It is important to analyze precise risks, including all relevant factors, for a broader range of operative procedures in the future. However, we should consider both obesity and very low body weight as the key factors impacting outcomes.

In the present study, a high BMI was shown to influence health economics and inflict excess burden on surgeons, considering the prolonged operation times for all surgical procedures evaluated. Yet, there are no additional fees in relation to obesity, in either Japan or, to our knowledge, any other country. Given the added burden associated with this condition, it is anticipated that the medical economics of providing surgical treatment for obese patients will be reviewed.

## Conclusion

We investigated the effects of BMI on both gastroenterological and cardiovascular surgical procedures based on data from 288,418 patients, obtained from a Japanese nationwide database. The operation time was significantly longer for patients who were obese than for those who were not, for all procedures except Eso. Furthermore, both

**Fig. 3** **a** Operative mortality for the gastroenterological surgery procedures (%). *Eso* esophagectomy, *DG* distal gastrectomy, *TG* total gastrectomy, *RHC* right hemicolectomy, *LAR* low anterior resection, *Hx* hepatectomy performed for >1 segment except for the lateral segment, *PD* pancreaticoduodenectomy, *ADP* surgery for acute diffuse peritonitis. **b** Operative mortality for the cardiovascular surgery procedures (%). *AVR* aortic valve replacement, *TAR* total arch replacement, *CABG* coronary artery bypass graft




obese and underweight patients had high mortality rates. This Japanese nationwide study provides further evidence that obesity and very low bodyweight are both factors with significant adverse effects on operative outcomes.

**Compliance with ethical standards**

**Conflict of interest** None of the authors has any conflicts of interest to disclose.

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ORIGINAL ARTICLE

# Surgical risk model for acute diffuse peritonitis based on a Japanese nationwide database: an initial report on the surgical and 30-day mortality

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**Abstract**

*Purpose* Acute diffuse peritonitis (ADP) is an important surgical complication associated with high morbidity and mortality; however, the risk factors associated with a poor outcome have remained controversial. This study aimed in collecting integrated data using a web-based national database system to build a risk model for mortality after surgery for ADP.

*Methods* We included cases registered in the National Clinical Database in Japan. After data cleanup, 8,482 surgical cases of ADP from 1,285 hospitals treated between January 1 and December 31, 2011 were analyzed.

*Results* The raw 30-day and surgical mortality rates were 9.0 and 14.1 %, respectively. The odds ratios (>2.0) for 30-day mortality were as follows: American Society of Anesthesiologists (ASA) class 3, 2.69; ASA class 4, 4.28; ASA class 5, 8.65; previous percutaneous coronary intervention (PCI), 2.05; previous surgery for peripheral vascular disease (PVD), 2.45 and disseminated cancer, 2.16. The odds ratios (>2.0) for surgical mortality were as follows: ASA class 3, 2.27; ASA class 4, 4.67; ASA class 5, 6.54, and disseminated cancer, 2.09. The C-indices of 30-day and surgical mortality were 0.851 and 0.852, respectively.

*Conclusion* This is the first report of risk stratification after surgery for ADP using a nationwide surgical database. This system could be useful to predict the outcome of surgery for ADP and for evaluations and benchmark performance studies.

**Keywords** Acute diffuse peritonitis · Risk factor · Mortality · Risk model

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## Introduction

Acute diffuse peritonitis (ADP) is an important surgical complication associated with a high incidence of morbidity and mortality [1–4], and is defined as the uncontained rapid spread of an intra-abdominal infection beyond the organ of origin to multiple (2–4) quadrants of the intra-abdominal cavity, regardless of the underlying disease processes, such as a ruptured appendix, ischemic colitis, gastrointestinal (GI) tract perforation, etc. [2–5]. Emergency surgery is defined as a surgery performed on a patient immediately after the diagnosis [6]. Although a definite preoperative diagnosis of a detailed etiology is difficult even using the recently developed imaging modalities [7, 8], the surgical management of ADP involves immediate evacuation of all purulent collections and source control [1–3].

Although the mortality rate from intra-abdominal infections was close to 90 % in the early 1900s, prior to the introduction of the basic principles of surgery, in the modern era, the reduction in mortality to below 20 % has resulted due to the better understanding of the role of damage control, prevention of intra-abdominal compartment syndrome, and improved antibiotic alternatives with newer, broad-spectrum medications [1]. However, most modern case series of secondary peritonitis with severe sepsis or septic shock have reported an average mortality rate of ~30 % [3].

Knowledge regarding the predictive factors and arrival at a consensus scoring system for the risk of mortality after surgery for ADP would be useful. Many hospitals and surgeons have tried to clarify these factors and develop scoring systems in their own units [1, 3, 9–13]. Although nationwide data regarding the quality of emergency surgical care using the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP) have been reported in several studies [14–17], to date, there has been no report of a nationwide study focused on ADP.

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. Submitting cases to the NCD is a prerequisite for all member institutions of both the Japan Surgical Society and the Japanese Society of Gastroenterological Surgery (JSGS), and only registered cases can be used for board certification. The NCD collaborates with the ACS-NSQIP [12], which shares a similar goal of developing a standardized surgery database for quality improvement. The NCD contains >1,200,000 surgical cases collected from >3,500 hospitals in 2011, and risk models of some of the procedures (total gastrectomy, right hemicolectomy, hepatectomy, pancreaticoduodenectomy, hepatectomy, etc.) have been created using these data [18–21]. In this study, a risk model was developed using 8,482 surgical cases of ADP from 1,285 hospitals throughout Japan. This risk model will hopefully contribute to the future improvement in the quality control of surgery for ADP.

## Methods

### Data acquisition

The NCD continuously recruits individuals to approve the inputted data from members of various departments in charge of annual cases, as well as data entry officers, through a web-based data management system to assure the traceability of the data. Furthermore, the project managers consecutively and consistently validate the data by inspection of randomly chosen institutions.

In this study, we focused on ADP cases in the GI surgery section of the NCD that were characterized by variables and definitions that were almost identical to those applied in the ACS-NSQIP [14–17, 22]. In the GI surgery section, all of the surgical cases are registered and require detailed input items for the eight procedures representing the performance of surgery in each specialty (low anterior resection, right hemicolectomy, hepatectomy, total gastrectomy, partial gastrectomy, pancreatoduodenectomy, esophagectomy, and ADP). All variables, definitions and inclusion criteria regarding the NCD are accessible from the website (http://www.ncd.or.jp/) to participate institutions, and are also intended to support an E-learning system in order for participants to input consistent data. The NCD provides answers to all queries regarding data entry (~80,000 inquiries in 2011) and regularly includes the responses to some of the queries as Frequently Asked Questions on the website.

### Patient selection

A total of 8,482 patients who underwent surgery for ADP were identified from the NCD in 2011. Most of the patients who underwent surgery for ADP required emergency surgery within 24 h after admission, because the condition of the patients would otherwise have proven fatal or would have caused severe damage to the patients. This is differentiated from localized intra-abdominal abscess, which allows for a time-rich detailed exploration. Surgery for ADP (i.e., surgical debridement and/or drainage) is a procedure representing the performance of a surgery that has been allowed by the national Japanese insurance system. To reduce the bacterial load, the abdominal cavity is lavaged, with particular attention to areas prone to abscess formation (e.g., the paracolic gutters and subphrenic areas). When surgery is performed to address underlying diseases or resection of a perforated viscus with reanastomosis or the creation of a fistula, supplemental procedures, such as resection of the small intestine, colorectal resection and enterostomy, are also recorded. The NCD allows the inclusion of up to eight ICD-10 codes for the preoperative/postoperative diagnosis of each case. Possible causative diseases necessitating surgery in the NCD include peritonitis, intestinal perforation, appendicitis, gastroduodenal ulcer/perforation, intestinal obstruction and vascular insufficiency, etc.

### Pre- and perioperative variables

The potential independent variables included the patient demographics, pre-existing comorbidities, preoperative laboratory values, and perioperative data. The demographic variables of age, gender, smoking status, and drinking status were considered. Patients were categorized on the basis of whether they were transferred directly by ambulance or not. General factors, such as the preoperative functional status [independent, partially dependent, and totally dependent with regard to a patient's ability to perform activities of daily living (ADL) 30 days and immediately before surgery] and the body mass index (BMI), were also considered. The ASA physical status classification was evaluated. We also considered preexisting comorbidities, including the cardiovascular status (congestive heart failure, coronary diseases, hypertension, previous cardiac surgery, and peripheral vascular disease), respiratory status (dyspnea, ventilator dependence, pneumonia, and chronic obstructive pulmonary disease), renal status (acute renal failure and dialysis), hematological status (bleeding disorders and preoperative blood transfusion), oncological status (disseminated cancer, chemotherapy and radiotherapy), preoperative blood transfusion, chronic steroid use, ascites, sepsis, diabetes, open wound, and pregnancy. The laboratory parameters included in the analysis were the white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate amino transferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A1c, and C-reactive protein (CRP). The length of the surgery, intraoperative blood loss and relaparotomy within 30 days after surgery for ADP were also considered. A total of 4,192 supplemental procedures for source control were also included.

### Endpoints

The outcome measures of this study were the 30-day and surgical mortality rates. 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 patient who died after being discharged, up to 30 days from the date of surgery.

### Statistical analysis

Data were randomly assigned into two subsets that were split 80/20, the first for model development, and the second for validation. The two sets of logistic models (30-day mortality and surgical mortality) were constructed for dataset development using stepwise selection of the predictors with a probability ($P$) value for inclusion of 0.05. A "goodness-of-fit" test was performed to assess how efficiently the model could discriminate between surviving and deceased patients. Model calibration (the degree to which the observed outcomes were similar to the predicted outcomes from the model across patients) was examined by comparing the observed with the predicted average within each of 10 equally sized subgroups arranged in increasing order of patient risk [6, 23].

## Results

### Outcomes

Among the data for the 8,482 patients stored in the NCD for 2011, the 30-day and postoperative mortality rates for ADP were 9.0 and 14.1 %, respectively. The causative diseases leading to the need for surgery are listed in Table 1. The development dataset (test set) included 6,759 records, and the validation dataset (validation set) included 1,723 records (Table 2). The rates of relaparotomy and readmission within 30 days in all records were 8.1 and 1.7 %, respectively, in these datasets.

### Risk profile for the study population

The patient population that underwent surgery for ADP had an average age of 64.7 years (SD 18.6), 59.8 % of whom were males, and 38.7 % of patients were taken to the hospital by ambulance, 93.1 % of whom required emergency surgery. An abbreviated risk profile of the study population is shown in Table 3. The patients with partially/totally dependent and totally dependent evaluations of the ADL within 30 days before surgery comprised 20.7 and 7.7 % of the patients, respectively. Only 0.6 % of the patients had a BMI $\geq$35 kg/m$^2$. Of the included patients, 43.2 %

**Table 1** The causative disease leading to the need for surgery

| Diagnosis | Number | 30-Day mortality | | Surgical mortality | |
|---|---|---|---|---|---|
| | | Number | Percent (%) | Number | Percent (%) |
| Acute peritonitis | 4,378 | 429 | 9.8 | 652 | 14.9 |
| Appendicitis | 1,183 | 4 | 0.3 | 10 | 0.8 |
| Intestinal perforation | 1,576 | 148 | 12.9 | 222 | 19.3 |
| Gastroduodenal ulcer/perforation | 833 | 63 | 7.3 | 64 | 9.7 |
| Intestinal obstruction | 396 | 50 | 12.6 | 80 | 20.2 |
| Cholecystitis/cholangitis | 218 | 18 | 9.0 | 26 | 13.1 |
| Vascular insufficiency | 121 | 21 | 17.4 | 35 | 28.9 |
| All cases | 8,482 | 762 | 9.0 | 1,195 | 14.1 |

The listed diseases were not mutually exclusive

Causative diseases with fewer than 100 cases were not listed

**Table 2** The outcomes of surgery for acute diffuse peritonitis

| Outcomes | Test set ($n = 6,759$) | | Validation set ($n = 1,723$) | | Overall incidence ($n = 8,482$) | |
|---|---|---|---|---|---|---|
| | Number | Percent (%) | Number | Percent (%) | Number | Percent (%) |
| 30-Day mortality | 604 | 8.9 | 158 | 9.2 | 762 | 9.0 |
| In-hospital mortality | 938 | 13.9 | 241 | 14.0 | 1,179 | 13.9 |
| Surgical mortality | 950 | 14.1 | 245 | 14.2 | 1,195 | 14.1 |
| Relaparotomy within 30 days | 546 | 8.1 | 145 | 8.4 | 691 | 8.1 |
| Readmission within 30 days | 107 | 1.6 | 39 | 2.3 | 146 | 1.7 |

were ASA class 3–5. Regarding preexisting comorbidities, 20.5 % of patients had received preoperative blood transfusions, 22.7 % had ascites, 31.8 % had sepsis, and 13.5 % had diabetes.

The types of supplemental surgical procedures ($n = 4,192$) performed for source control are listed in Table 4. The primary surgical procedures were enterostomy (30.4 %), colorectal resection (19.9 %), closure of a perforated stomach/duodenum (13.0 %), appendectomy (12.4 %), resection of the small intestine (8.2 %), the Hartmann procedure (6.5 %), cholecystectomy/cholecystotomy (3.5 %), closure of a perforated small intestine (3.3 %), and surgery for intestinal obstruction (2.5 %).

Model results

Two different risk models were developed, and the final logistic model with odds ratios and 95 % confidence intervals are presented in Table 5. The scoring system for the mortality risk models according to the logistic regression equation was as follows:

Predicted mortality $= e(\beta 0 + \Sigma \beta i\ Xi)/1 + e(\beta 0 + \Sigma \beta i\ Xi)$, where $\beta i$ is the coefficient of the variable $Xi$ in the logistic regression equation provided in Table 5 for the 30-day mortality and surgical mortality. $Xi = 1$ if a categorical risk factor is present and 0 if it is absent. For the age category, $Xi = 1$ if the patient age is <59 years old; 2 if the patient age is between 60 and 64; 3 if 65 and 69; four if 70 and 74; 5 if 75–79 and the $Xi = 6$ if the age was ≥80 years old. Between the two models, there were 16 overlapping variables: the age, ASA class 5, ASA class 4, ASA class 3, disseminated cancer, nontumor-bearing, preoperative transfusion, chronic steroid use, serum albumin <2.0 g/dL, serum total bilirubin ≥3.0 mg/dL, serum AST ≥35 U/L, serum ALP ≥600 U/L, serum urea nitrogen ≥20 or 25 mg/dL, serum Na <130 mEq/L and serum CRP ≥10.0 mg/dL.

The important variables (odds ratio >2.0) affecting the 30-day mortality were ASA class 3 (OR, 2.69; 95 % CI, 2.05–3.54), ASA class 4 (OR, 4.28; 95 % CI, 3.11–5.87), ASA class 5 (OR, 8.65; 95 % CI, 6.14–12.18), previous PCI (OR, 2.05; 95 % CI, 1.26–3.31), previous PVD surgery (OR, 2.45; 95 % CI, 1.16–5.17) and disseminated cancer (OR, 2.16; 95 % CI, 1.53–3.05), whereas those affecting the surgical mortality were ASA Class 3 (OR, 2.27; 95 % CI, 1.83–2.82), ASA Class 4 (OR, 4.67; 95 % CI, 3.61–6.05), ASA class 5 (OR, 6.54; 95 % CI, 4.83–8.84) and disseminated cancer (OR, 2.09; 95 % CI, 1.54–2.83).

Model performance

To evaluate the model performance, both a C-index (a measure of model discrimination) with a 95 % CI, which is the area under the receiver operating characteristic curve, and the model calibration across risk groups were evaluated. As a performance parameter of the risk model, the C-indices of the 30-day and surgical mortality were 0.851 (95 % CI, 0.822–0.880) and 0.852 (95 % CI, 0.828–0.875), respectively (Fig. 1). Figure 2 demonstrates the calibration of the models and how well the rates for the predicted events matched those of the observed events among the patient risk subgroups.

## Discussion

Systemic sepsis is a life-threatening condition that may occur as a result of intra-abdominal infections of all types [1, 3]. In complicated intra-abdominal infections, the infection spreads beyond the organ of origin and causes either localized or diffuse peritonitis [2, 10]. Complicated intra-abdominal infections represent an important cause of morbidity, and are frequently associated with a poor prognosis [2, 10]. The mortality is reportedly reduced by 50 % following the introduction of the basic concepts of surgery for intra-abdominal infections by: (1) elimination of the septic foci, (2) removal of necrotic tissue and (3) drainage of purulent material. Advances that have provided a better understanding of the pathophysiology, the role of damage control, the prevention of intra-abdominal

**Table 3** Key risk profiles and outcomes

| | Records for the entire study population (n = 8,482) | | Outcome groups | | | |
|---|---|---|---|---|---|---|
| | | | 30-Day mortality (n = 762) | | Surgical mortality (n = 1,195) | |
| | Number | Percent | Number | Percent | Number | Percent |
| Characteristics | | | | | | |
| Demographics | | | | | | |
| Age, mean (SD), years | 64.7 (18.6) | | 74.8 (13.7) | | 74.5 (13.2) | |
| Males | 5,072 | 59.8 | 416 | 8.2 | 667 | 13.2 |
| Ambulance transportation | 3,283 | 38.7 | 364 | 11.1 | 511 | 15.6 |
| Preoperative risk assessment | | | | | | |
| General | | | | | | |
| ADL within 30 days before surgery | | | | | | |
| Partially/totally dependent | 1,756 | 20.7 | 342 | 19.5 | 535 | 30.5 |
| Totally dependent | 653 | 7.7 | 149 | 22.8 | 231 | 35.4 |
| ADL immediately before surgery | | | | | | |
| Partially/totally dependent | 2,358 | 27.8 | 427 | 18.1 | 654 | 27.7 |
| Totally dependent | 1,162 | 13.7 | 258 | 22.2 | 375 | 32.3 |
| Body mass index ≥35 kg/m$^2$ | 51 | 0.6 | 11 | 20.8 | 14 | 28.3 |
| Weight loss over 10 % | 442 | 5.2 | 77 | 17.4 | 134 | 30.3 |
| ASA class 3, ASA class 4, or ASA class 5 | 3,664 | 43.2 | 641 | 17.5 | 976 | 26.6 |
| Cardiovascular | | | | | | |
| Congestive heart failure | 237 | 2.8 | 71 | 30.0 | 103 | 43.4 |
| Previous myocardial infarction | 51 | 0.6 | 14 | 27.5 | 18 | 35.3 |
| Angina pectoris | 110 | 1.3 | 20 | 18.2 | 26 | 23.6 |
| Hypertension without therapy | 271 | 3.2 | 27 | 10.0 | 45 | 16.7 |
| Previous PCI | 170 | 2 | 37 | 22.0 | 44 | 26.2 |
| Previous cardiac surgery | 119 | 1.4 | 28 | 23.3 | 35 | 29.3 |
| Previous surgery for PVD | 51 | 0.6 | 14 | 28.3 | 24 | 47.2 |
| Pulmonary | | | | | | |
| Dyspnea | 712 | 8.4 | 192 | 27.0 | 267 | 37.4 |
| Ventilator-dependent | 331 | 3.9 | 98 | 29.6 | 147 | 44.3 |
| Pneumonia | 305 | 3.6 | 84 | 27.6 | 125 | 40.9 |
| COPD | 288 | 3.4 | 46 | 15.8 | 71 | 24.6 |
| Renal | | | | | | |
| Acute renal failure | 407 | 4.8 | 127 | 31.1 | 177 | 43.5 |
| Dialysis | 322 | 3.8 | 79 | 24.4 | 118 | 36.7 |
| Oncological | | | | | | |
| Non-tumor-bearing | 7,490 | 88.3 | 618 | 8.3 | 947 | 12.6 |
| Disseminated cancer | 450 | 5.3 | 95 | 21.2 | 161 | 35.8 |
| Chemotherapy | 297 | 3.5 | 49 | 16.6 | 101 | 33.9 |
| Radiotherapy | 51 | 0.6 | 9 | 17.0 | 14 | 27.7 |
| Hematological | | | | | | |
| Bleeding disorder without therapy | 560 | 6.6 | 159 | 28.5 | 214 | 38.2 |
| Preoperative blood transfusion | 1,739 | 20.5 | 351 | 20.2 | 535 | 30.8 |
| Other | | | | | | |
| Previous cerebrovascular disease | 450 | 5.3 | 76 | 17.0 | 119 | 26.4 |
| Chronic steroid use | 365 | 4.3 | 71 | 19.4 | 109 | 29.9 |
| Ascites without therapy | 1,925 | 22.7 | 259 | 13.4 | 412 | 21.4 |
| Sepsis | 2,697 | 31.8 | 453 | 16.8 | 661 | 24.5 |

**Table 3** continued

| | Records for the entire study population ($n = 8{,}482$) | | Outcome groups | | | |
|---|---|---|---|---|---|---|
| | | | 30-Day mortality ($n = 762$) | | Surgical mortality ($n = 1{,}195$) | |
| | Number | Percent | Number | Percent | Number | Percent |
| Diabetes | 1,145 | 13.5 | 152 | 13.3 | 241 | 21.0 |
| Preoperative laboratory value | | | | | | |
| White blood cell count <4,500/μL | 1,993 | 23.5 | 253 | 12.7 | 382 | 19.2 |
| White blood cell count <4,000/μL | 1,789 | 21.1 | 230 | 12.9 | 345 | 19.3 |
| Hemoglobin <13.5 g/dL in males; <12.5 g/dL in females | 4,419 | 52.1 | 541 | 12.3 | 886 | 20.1 |
| Hemoglobin < 10.0 g/dL | 1,734 | 20.4 | 268 | 15.5 | 442 | 25.5 |
| Hematocrit <30 % | 1,671 | 19.7 | 264 | 15.8 | 440 | 26.3 |
| Platelet count <15,000/μL | 1,484 | 17.5 | 297 | 20.0 | 406 | 27.4 |
| Platelet count <12,000/μL | 771 | 9.1 | 192 | 24.9 | 260 | 33.7 |
| Platelet count <8,000/μL | 288 | 3.4 | 104 | 36.1 | 137 | 47.6 |
| Serum albumin <2.0 g/dL | 619 | 7.3 | 141 | 22.8 | 225 | 36.4 |
| Serum albumin <2.5 g/dL | 1,612 | 19 | 291 | 18.1 | 491 | 30.5 |
| Serum albumin <3.0 g/dL | 2,943 | 34.7 | 450 | 15.3 | 746 | 25.3 |
| Serum total bilirubin ≥3.0 mg/dL | 365 | 4.3 | 76 | 20.9 | 113 | 31.0 |
| Serum AST ≥35 U/L | 2,036 | 24 | 331 | 16.2 | 483 | 23.8 |
| Serum ALP ≥340 U/L | 1,442 | 17 | 199 | 13.8 | 317 | 22.0 |
| Serum ALP ≥600 U/L | 407 | 4.8 | 76 | 18.8 | 113 | 27.8 |
| Serum urea nitrogen ≥20 mg/dL | 3,868 | 45.6 | 596 | 15.4 | 898 | 23.2 |
| Serum urea nitrogen ≥25 mg/dL | 2,748 | 32.4 | 503 | 18.3 | 736 | 26.8 |
| Serum creatinine ≥1.2 mg/dL | 2,171 | 25.6 | 401 | 18.5 | 591 | 27.2 |
| Serum creatinine ≥2.0 mg/dL | 984 | 11.6 | 216 | 22.0 | 320 | 32.5 |
| Serum Na <130 mEq/L | 475 | 5.6 | 78 | 16.5 | 135 | 28.3 |
| Serum Na <13 5 mEq/L | 1,976 | 23.3 | 245 | 12.4 | 398 | 20.1 |
| Serum Na ≥145 mEq/L | 314 | 3.7 | 71 | 22.5 | 95 | 30.2 |
| Serum CRP ≥10.0 mg/dL | 3,927 | 46.3 | 369 | 9.4 | 611 | 15.6 |
| Operation | | | | | | |
| Length of operation ≥6 h | 51 | 0.6 | 12 | 24.0 | 16 | 32.0 |
| Intraoperative blood loss ≥2,000 mL | 161 | 1.9 | 40 | 24.5 | 62 | 38.2 |
| Relaparotomy within 30 days | 687 | 8.1 | 81 | 11.7 | 163 | 23.7 |

*SD* standard deviation, *ADL* activities of daily living, *ASA class* American Society of Anesthesiologists Physical Status Classification, *PCI* percutaneous coronary intervention, *PVD* peripheral vascular disease, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *Na* sodium, *CRP* C-reactive protein

compartment syndrome and antibiotic administration have collectively helped to reduce the mortality rate below 20 % [1].

In this study, the 30-day and surgical mortality rates after surgery for all acute types of primary, secondary and tertiary peritonitis [1–3] were 9.0 and 14.1 %, respectively. Recently, published studies reported that the 30-day mortality rate after surgery for ADP was 8–9 % [24, 25], whereas the surgical mortality rate was 12.8–33.3 % (12.8 % [26], 14 % [5], 19 % [24], 22 % [27], 21.8 % [12], 23.1 % [11] and 33.3 % [28]). For reference, the 30-day mortality rate of the patients in the ACS-NSQIP study of 5,083 patients who underwent emergency colorectal operations was 15.4 % [17]. Thus, although the 30-day mortality rate in this study was similar to that in previous studies, the surgical mortality rates in the previous studies from western countries was higher than that in the current study. We believe that our results were satisfactory for a nationwide outcome of surgery for ADP.

Early prognostic evaluation of complicated intra-abdominal infections is important to assess the severity and prognosis of disease [10]. A number of factors influencing the prognosis of patients with complicated intra-abdominal infections, as well as scoring systems to evaluate these

**Table 4** Supplemental surgical procedures performed for source control and the outcomes

| Surgical | Surgical procedures | | Outcome groups | | | |
|---|---|---|---|---|---|---|
| | | | 30-Day mortality | | Surgical mortality | |
| | Number | Percent | Number | Percent | Number | Percent |
| Gastro-duodenum | | | | | | |
| Closure of perforated stomach and/or duodenum | 545 | 13.0 | 35 | 6.4 | 46 | 8.4 |
| Gastrectomy | 75 | 1.8 | 7 | 9.3 | 8 | 10.7 |
| Postduodenal small intestine | | | | | | |
| Resection of small intestine | 345 | 8.2 | 35 | 10.1 | 67 | 19.4 |
| Closure of perforated intestine | 138 | 3.3 | 10 | 7.2 | 22 | 15.9 |
| Surgery for intestinal obstruction | 106 | 2.5 | 21 | 19.8 | 30 | 28.3 |
| Enterostomy | 1,276 | 30.4 | 185 | 14.5 | 280 | 21.9 |
| Appendix | | | | | | |
| Appendectomy | 519 | 12.4 | 4 | 0.8 | 11 | 2.1 |
| Colon and rectum | | | | | | |
| Right-sided colon resection | 177 | 4.2 | 19 | 10.7 | 32 | 18.1 |
| Left-sided colon resection | 326 | 7.8 | 47 | 14.4 | 68 | 20.9 |
| Anterior resection | 22 | 0.5 | 2 | 9.1 | 2 | 9.1 |
| Hartmann procedure | 273 | 6.5 | 32 | 11.7 | 44 | 16.1 |
| Total colectomy | 19 | 0.5 | 4 | 21.1 | 5 | 26.3 |
| Hepato-biliary-pancreatic | | | | | | |
| Hepatic resection/suturing the liver | 8 | 0.2 | 1 | 12.5 | 2 | 25.0 |
| Cholecystectomy/cholecystostomy | 151 | 3.6 | 12 | 8.1 | 20 | 13.4 |
| Choledocholithotomy/choledochoduodenostomy (-jejunostomy)/choledochostomy | 29 | 0.7 | 7 | 25.0 | 7 | 25.0 |
| Surgery for acute pancreatitis/resection of the pancreas/Drainage of pancreatic duct or cyst, % | 8 | 0.2 | 2 | 22.2 | 4 | 44.4 |
| Others | | | | | | |
| Abdominoperineal resection/total pelvic exenteration | 17 | 0.4 | 4 | 22.2 | 4 | 22.2 |
| Splenectomy | 13 | 0.3 | 3 | 21.4 | 4 | 28.6 |

A total of 4,192 supplemental surgical procedures were included. Surgical procedures performed fewer than eight times were not listed. Some patients underwent more than one surgical procedure

factors, have been reported [3, 10–13, 24]. From our risk model, the important variables identified to affect the 30-day mortality rate were ASA class 3, ASA class 4, ASA class 5, previous percutaneous coronary intervention (PCI), previous surgery for peripheral vascular disease (PVD) and disseminated cancer, whereas those affecting the surgical mortality rate were ASA class 3, ASA class 4, ASA class 5 and disseminated cancer. Although the ASA classification of fitness for surgery was not devised as a risk prediction score, several studies have reported the association between the ASA class and observed postoperative mortality in elderly patients following emergency GI surgery [13, 29]. In univariate and multivariate analyses of the mortality of emergency surgical patients, the ASA class has been consistently shown to be a good predictor of postoperative death, although this is despite its subjective nature and the inter-observer variations in measuring the ASA class [13].

Other significant factors identified by our risk assessment model, including age, ambulance transportation, the ADL, respiratory distress, preoperative pneumonia, bleeding disorders, preoperative blood transfusion and long-term steroid use, were also significant risk factors for the 30-day and/or surgical mortality. Several risk factors (age, dyspnea, previous PCI, disseminated cancer, long-term steroid use, bleeding disorder without therapy and preoperative blood transfusion) have been reported in previous studies [31, 32], although ambulance transportation and the ADL have not been previously reported. The rate of ambulance transport among the elderly is continually increasing along with the rapidly aging population in Japan [33]. In this study, 38.7 % of the 8,482 patients who underwent surgery for ADP were admitted to a hospital by direct ambulance transport. Among the critical components of health care systems, ambulance services play an important

**Table 5** The odds ratios with 95 % confidence intervals for the risk models of surgery for acute diffuse peritonitis

| Variables | 30-Day mortality | | | | Surgical mortality | | | |
|---|---|---|---|---|---|---|---|---|
| | *β* coefficient | OR | 95 % CI | *P* value | *β* coefficient | OR | 95 % CI | *P* value |
| Demographics | | | | | | | | |
| Age category[a] | 0.211 | 1.24 | 1.17–1.31 | <0.001 | 0.234 | 1.26 | 1.20–1.33 | <0.001 |
| Ambulance transport | 0.317 | 1.37 | 1.12–1.68 | 0.002 | | | | |
| Respiratory distress | 0.462 | 1.59 | 1.22–2.06 | <0.001 | | | | |
| ADL, totally dependent immediately before surgery | 0.337 | 1.4 | 1.11–1.77 | 0.005 | | | | |
| ADL, totally dependent within 30 days before surgery | | | | | 0.465 | 1.59 | 1.22–2.07 | 0.001 |
| ADL, partially/totally dependent immediately before surgery, | | | | | 0.303 | 1.35 | 1.12–1.64 | 0.002 |
| Preoperative pneumonia | | | | | 0.342 | 1.41 | 1.01–1.97 | 0.045 |
| ASA class 5 | 2.157 | 8.65 | 6.14–12.18 | <0.001 | 1.877 | 6.54 | 4.83–8.84 | <0.001 |
| ASA class 4 | 1.453 | 4.28 | 3.11–5.87 | <0.001 | 1.542 | 4.67 | 3.61–6.05 | <0.001 |
| ASA class 3 | 0.99 | 2.69 | 2.05–3.54 | <0.001 | 0.822 | 2.27 | 1.83–2.82 | <0.001 |
| Preexisting comorbidity | | | | | | | | |
| Previous PCI | 0.715 | 2.05 | 1.26–3.31 | 0.004 | | | | |
| Previous surgery for PVD | 0.897 | 2.45 | 1.16–5.17 | 0.018 | | | | |
| Disseminated cancer | 0.769 | 2.16 | 1.53–3.05 | <0.001 | 0.735 | 2.09 | 1.54–2.83 | <0.001 |
| Non tumor-bearing | −0.436 | 0.65 | 0.48–0.87 | 0.003 | −0.69 | 0.5 | 0.4–0.64 | <0.001 |
| Bleeding disorder without therapy | 0.499 | 1.65 | 1.24–2.19 | 0.001 | 0.484 | 1.62 | 1.31–2.01 | <0.001 |
| Preoperative blood transfusion | 0.472 | 1.6 | 1.13–2.28 | 0.009 | 0.595 | 1.81 | 1.32–2.49 | <0.001 |
| Chronic steroid use | 0.552 | 1.74 | 1.21–2.50 | 0.003 | 0.651 | 1.92 | 1.39–2.65 | <0.001 |
| Weight loss over 10 % | | | | | 0.331 | 1.39 | 1.02–1.90 | 0.036 |
| Preoperative laboratory value | | | | | | | | |
| White blood cell count <4,500/μL | | | | | 0.404 | 1.5 | 1.25–1.8 | <0.001 |
| White blood cell count <4,000/μL | 0.336 | 1.4 | 1.12–1.75 | 0.003 | | | | |
| Hemoglobin <13.5 g/dL in males; <12.5 g/dL in females | | | | | 0.273 | 1.31 | 1.07–1.62 | 0.01 |
| Hemoglobin <10.0 g/dL | 0.254 | 1.29 | 1.03–1.61 | 0.024 | | | | |
| Hematocrit <30 % | | | | | 0.209 | 1.23 | 1.01–1.51 | 0.044 |
| Platelet count <15,000/μL | 0.413 | 1.51 | 1.19–1.92 | 0.001 | | | | |
| Platelet count <12,000/μL | | | | | 0.356 | 1.43 | 1.13–1.8 | 0.003 |
| Platelet count <8,000/μL | 0.424 | 1.53 | 1.03–2.26 | 0.033 | | | | |
| Serum albumin <2.0 g/dL | 0.51 | 1.67 | 1.25–2.22 | <0.001 | 0.394 | 1.48 | 1.14–1.93 | 0.003 |
| Serum albumin <3.0 g/dL | | | | | 0.316 | 1.37 | 1.13–1.67 | 0.002 |
| Serum total bilirubin ≥3.0 mg/dL | 0.532 | 1.7 | 1.16–2.49 | 0.006 | 0.676 | 1.97 | 1.40–2.76 | <0.001 |
| Serum AST ≥35 U/L | 0.3 | 1.35 | 1.09–1.67 | 0.006 | 0.358 | 1.43 | 1.19–1.72 | <0.001 |
| Serum ALP ≥600 U/L | 0.545 | 1.73 | 1.18–2.51 | 0.005 | 0.474 | 1.61 | 1.15–2.24 | 0.005 |
| Serum urea nitrogen ≥20 mg/dL | 0.569 | 1.77 | 1.28–2.43 | 0.001 | 0.563 | 1.76 | 1.35–2.29 | <0.001 |
| Serum urea nitrogen ≥25 mg/dL | 0.343 | 1.41 | 1.06–1.88 | 0.02 | | | | |
| Serum creatinine ≥2.0 mg/dL | | | | | 0.405 | 1.5 | 1.2–1.89 | <0.001 |
| Serum Na <130 mEq/L | 0.521 | 1.68 | 1.21–2.35 | 0.002 | 0.56 | 1.75 | 1.31–2.33 | <0.001 |
| Serum Na ≥145 mEq/L | 0.526 | 1.69 | 1.16–2.46 | 0.006 | | | | |
| Serum CRP ≥10.0 mg/dL | 0.397 | 1.49 | 1.21–1.83 | <0.001 | 0.423 | 1.53 | 1.27–1.83 | <0.001 |
| Intercept ($\beta 0$) | −5.449 | | | <0.001 | −4.83 | | | <0.001 |

*ADL* activities of daily living, *ASA class* American Society of Anesthesiologists Physical Status Classification, *PCI* percutaneous coronary intervention, *PVD* peripheral vascular disease, *COPD* chronic obstructive pulmonary disease, *AST* aspartate amino transferase, *ALP* alkaline phosphatase, *Na* sodium, *CRP* C-reactive protein, *OR* odds ratio, *CI* confidence interval

[a] Age, years, <59, 60–64, 65–69, 70–74, 75–79, ≥80

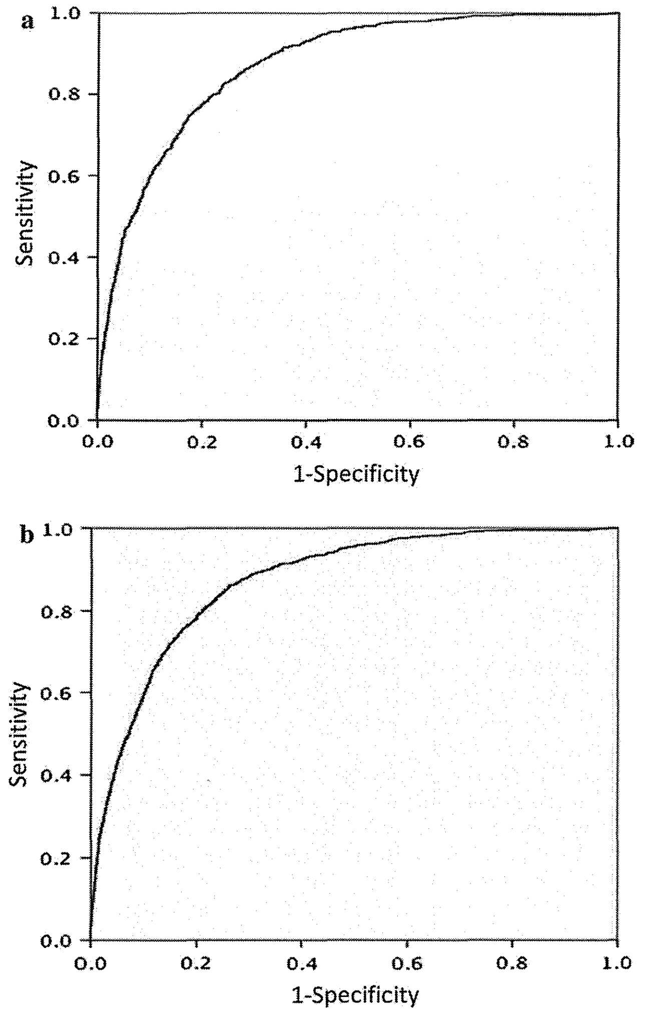


Fig. 1 The receiver operating characteristics (ROC) curves for the 30-day mortality (a) and surgical mortality (b) in the validation set

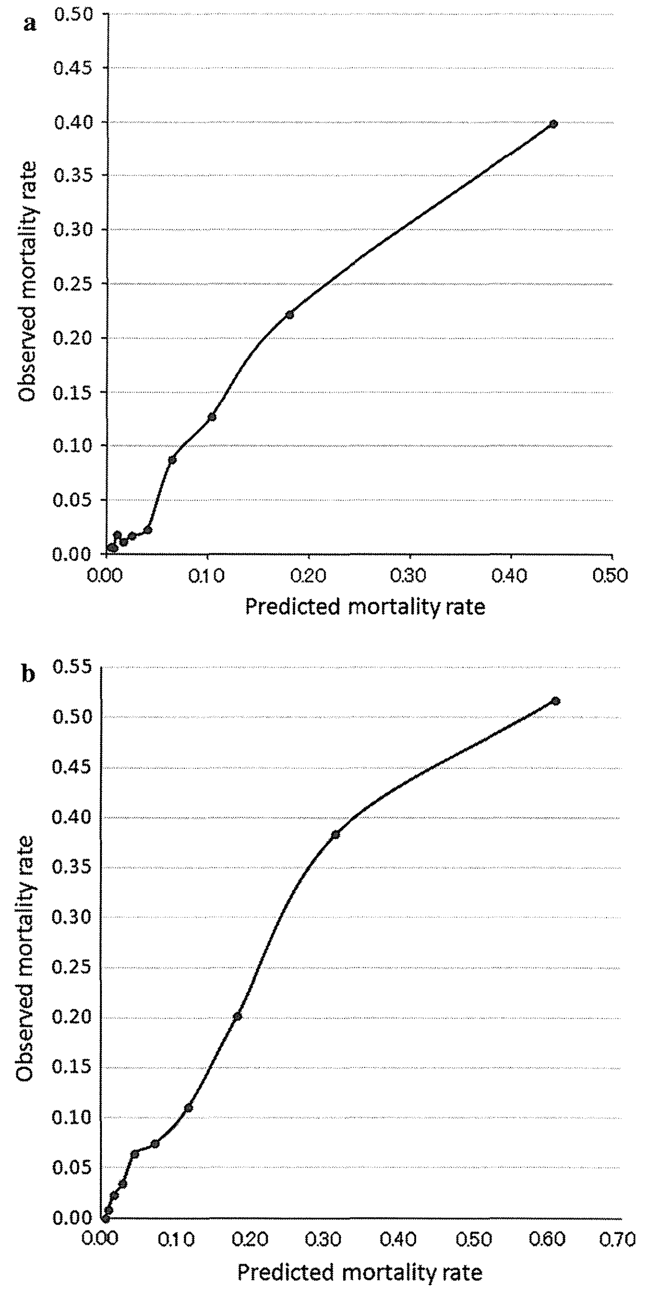


Fig. 2 The model calibration for the 30-day (a) and surgical (b) mortality models

part in the continuum of health care by providing prehospital care and transport in emergency situations [33]. The ADL describes the essential activities that a person needs to perform to be able to live independently. Particularly in the aging individual, the combination of acute and chronic diseases often results in disabilities and limitations in the ADL [34]. Functional limitations are particularly associated with mortality in patients with hip fractures and pulmonary infections, and in acute medical patients [34, 35]. In this risk model, not only the ADL (totally dependent) immediately before surgery, but also the ADL (totally/partially dependent) within 30 days before surgery was a significant risk factor for surgical mortality. These data suggest that assessment of the ADL within 30 days before surgery should be considered for the clinical management of ADP.

From our risk model, 12 laboratory factors (white blood cell count, hemoglobin, hematocrit, platelet count, and the serum levels of albumin, total bilirubin, aspartate amino transferase, alkaline phosphatase, urea nitrogen, creatinine, sodium and CRP) were significant risk factors for the 30-day and surgical mortality. These laboratory data may reflect the degree of physiological derangement due to the intra-abdominal infection and preexisting critical illness, and have been reported in previous studies.

The C-indices of the models for the 30-day and surgical mortality in this study were 0.851 and 0.852, respectively. These data indicate that our models were reliable. Although the usefulness of several scoring systems, such as the Acute Physiology and Chronic Health Evaluation (APACHE) score and the Mannheim Peritonitis Index, have been reported [13], they are not specific for Japanese patients who undergo surgery for ADP. The reliability of existing scores or indices for ADP surgery may be improved by including our risk model. The NCD collects data obtained before admission and during the hospitalization period. On the other hand, the APACHE database is a collection of data obtained only after the patient has been admitted to the intensive care unit [14]. Some NCD preoperative data were predictive of the patient outcomes, which may allow for the earlier identification of potential complications.

This study was associated with several potential limitations. First, except for the ASA class, the other scoring systems to potentially predict the mortality after surgery for ADP, such as the APACHE score and Mannheim Peritonitis Index [13], could not be determined from this database. Second, we could not distinguish between the two different types of intra-abdominal infections (community- and healthcare-acquired), from this database. Third, the risk of mortality differed between ADP due to upper gastrointestinal perforation and that caused by colon perforation, as shown in Table 1. The lack of information regarding the details of the causative diseases in some patients was another limitation of this study. Fourth, the effects of surgical procedures on certain causative disease should be analyzed in a future study.

In conclusion, this report is the first risk stratification study of surgery for ADP to use a nationwide NCD. By analyzing 8,482 patients from 1,285 surgical units throughout Japan, the 30-day and surgical mortality rates were determined to be 9.0 and 14.1 %, respectively. The results of this series are satisfactory regarding the nationwide outcome of surgery for ADP, and this system can be useful in predicting the outcome of surgery for ADP, and may be useful to evaluate and benchmark performance.

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**Conflict of interest** The authors report no conflicting financial interests.

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# Off-pump versus on-pump coronary artery bypass grafting in patients with left ventricular dysfunction

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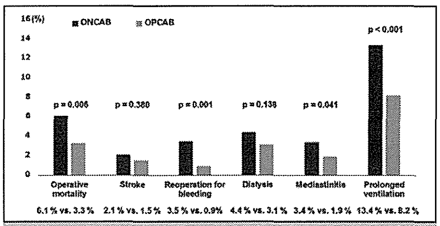
## ABSTRACT

**Objective:** Using data from the Japan Adult Cardiovascular Surgery Database, we evaluated the prognostic influence of off-pump technique in patients with low ejection fraction who underwent coronary artery bypass grafting.

**Methods:** We analyzed 2187 patients with an ejection fraction <0.30 who underwent primary, nonemergency, isolated coronary artery bypass grafting between 2008 and 2012, as reported in the Japan Adult Cardiovascular Surgery Database. Patients were divided into on-pump (n = 1134; 51.1%) and off-pump (n = 1053; 48.9%) coronary artery bypass grafting groups. Propensity-score matching for 20 preoperative variables was performed, and early mortality and morbidity were compared between matched groups.

**Results:** Propensity-score matching created 918 pairs. Of the 918 patients in the off-pump group, conversion to an on-pump procedure occurred in 56 (6.1%). Compared with on-pump, off-pump technique was associated with significantly lower incidences of 30-day death (1.7% vs 3.7%; $P = .01$), operative death (3.3% vs 6.1%; $P = .006$), mediastinitis (1.9% vs 3.4%; $P = .041$), reoperation for bleeding (0.9% vs 3.5%; $P < .001$), and prolonged ventilation (8.2% vs 13.4%; $P < .001$). Comparison of patients undergoing off-pump versus on-pump procedures demonstrated no significant differences in the incidence of stroke (1.5% vs 2.1%; $P = .38$), renal failure (6.1% vs 7.4%; $P = .26$), and postoperative dialysis (3.1% vs 4.4%; $P = .14$). Institutional volume-adjusted analysis confirmed most of these results.

**Conclusions:** Off-pump coronary artery bypass grafting is associated with significantly reduced early mortality and morbidity in patients with an ejection fraction <0.30. (J Thorac Cardiovasc Surg 2015;■:1-7)




Postoperative outcomes of off-pump versus on-pump coronary artery bypass grafting in propensity-matched pairs.

**Central Message**

Off-pump technique may improve operative outcomes in patients with low ejection fraction undergoing coronary artery bypass grafting.

**Perspective**

The clinical benefit of off-pump technique in patients with low ejection fraction is still unclear. In this large, retrospective study with risk adjustment, off-pump coronary artery bypass grafting was associated with significantly reduced early mortality and morbidity in patients with low ejection fraction. These findings will help to establish the best operative strategy in this high-risk population.

ACD

Although the clinical benefits of off-pump coronary artery bypass (OPCAB) have not been demonstrated in large randomized trials,[1,2] multiple observational studies have shown the mortality and/or morbidity benefit of OPCAB versus on-pump coronary artery bypass (ONCAB), especially in high-risk subgroups.[3-6] In addition to other representative risk factors, including advanced age, diabetes, and renal dysfunction, left ventricular dysfunction has been shown to be a predictor of early mortality after coronary artery bypass grafting (CABG).[7]

Recent large randomized trials—the Randomized On/Off Bypass (ROOBY) trial and the CABG Off or On Pump Revascularization Study (CORONARY)—included only a small number of patients with low ejection fraction (EF).[1,2] Hence, these randomized trials could not evaluate the prognostic benefit of OPCAB in patients with low EF. Moreover, most retrospective studies from single centers also have significant limitations such as a relatively low sample size and a strong bias in treatment choice. Considering this situation, a risk-adjusted retrospective study of a large database, such as the Society of Thoracic Surgeons (STS) national database, plays an important role in establishing the best strategy for patients with low EF undergoing CABG.[8]

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**Abbreviations and Acronyms**

| | |
|---|---|
| CABG | = coronary artery bypass grafting |
| CORONOARY | = CABG Off or On Pump Revascularization Study |
| EF | = ejection fraction |
| ICU | = intensive care unit |
| JACVSD | = Japan Adult Cardiovascular Surgery Database |
| MACE | = major adverse cardiovascular events |
| NCD | = National Clinical Database |
| ONCAB | = on-pump coronary artery bypass |
| OPCAB | = off-pump coronary artery bypass |
| ROOBY | = Randomized On/Off Bypass trial |
| STS | = Society of Thoracic Surgeons |

The purpose of this study was to evaluate the prognostic influence of OPCAB in patients with an EF <0.30 using a large sample from the Japan Adult Cardiovascular Surgery Database (JACVSD).

## PATIENTS AND METHODS

The institutional review board of our institution approved this study. Informed consent was obtained from each patient to allow his or her data to be entered into the database.

### The JACVSD

JACVSD, which was created to enable evaluation of surgical outcomes after cardiovascular procedures in hospitals throughout Japan, currently captures clinical information from most Japanese hospitals.

The 255 variables in the data collection form are nearly identical to those of the STS national database. The content of the JACVSD (http://www.jacvsd.umin.jp) and STS databases (http://sts.org) can be viewed online. The JACVSD has developed software for web-based data collection that allows data managers at participating hospitals to submit data electronically to the central office. Participation in JACVSD is voluntary, but there is a high degree of completeness of the data. In addition, the accuracy of submitted data is maintained by regular data auditing in which monthly visits are made to participating hospitals to check the reported data against clinical records. Data validity is further confirmed by independent comparison of specific hospitals' volume of cardiac surgeries entered in JACVSD with that reported in the annual survey of the Japanese Association for Thoracic Surgery. Further, in 2010 and later, the JACVSD served as a part of the National Clinical Database (NCD) in Japan, which includes clinician-initiated databases reflecting all surgical. The NCD covers 95% of total surgical procedures.

### Study Population

We examined the data for patients included in the JACVSD from January 1, 2008, to December 31, 2012. Records with missing age (or out of range), sex, or 30-day status (see Study End Points for an explanation) were excluded. With the exception of body surface area, and preoperative creatinine value, all missing or out-of-range values were imputed using the variable-specific median value. After this data cleaning, patients with an EF <0.30 who underwent isolated CABG were included. In the JACVSD, echocardiography, left ventriculography, radionucleotide scan, physician estimation, and other methods (including magnetic resonance imaging) were permitted for the evaluation of EF. The distribution of determination was equivalent between the 2 groups ($P = .089$) and for most of patients was evaluated by echocardiography (62.6%) and left ventriculography gram (21.5%). Missing evaluation method occurred in 14.3% of all patients, and radionucleotide scan (1.0%), physician estimation (0.4%), and other methods (0.1%) were used in only a small portion of patients. Exclusion criteria were emergency or salvage status and redo surgery. Thus, 2187 consecutive patients were included in the analysis. Because intention-to-treat principle was applied to all statistical analyses, patients were divided into those intended for ONCAB (n = 1134; 51.1%) and OPCAB (n = 1053; 48.9%) procedure. Patients intended for OPCAB were included in the OPCAB group even if they were converted intraoperatively to ONCAB.

### Study End Points

The study end points were 30-day mortality, operative mortality, and postoperative morbidity. Thirty-day mortality was defined as death within 30 days after surgery. Operative mortality was defined as death occurring within 30 days after surgery and death during the index hospitalization. Major adverse cardiovascular events (MACEs) were defined as a combined end point that included operative mortality, perioperative myocardial infarction, and stroke. Renal failure was defined as an increase in serum creatinine concentration to twice preoperative levels or to >2.0 mg/dL, or new requirement for dialysis or hemofiltration. Perioperative myocardial infarction was defined as at least 2 of the following: continuous angina for >20 minutes regardless of nitrite treatment or rest, elevation of cardiac enzyme levels (creatine kinase-myocardial band) >1/20 of the total creatine kinase level or double the preoperative level and/or lactate dehydrogenase isozyme subtype 1 > subtype 2 and/or positive troponin-I and/or troponin-T), new cardiac wall-motion abnormalities, and Q waves or ST-segment elevation/T-wave changes in >2 serial 12-lead electrocardiograms.

### Propensity Matching and Statistical Analysis

Propensity-score matching was used to adjust differences in baseline characteristics because patients were not randomly assigned to receive ONCAB or OPCAB. Each patient's estimated propensity score, which is the likelihood of the patient being intended to undergo OPCAB, was calculated using a multivariate logistic model that included 20 preoperative variables: age, presence of unstable angina, extracardiac vascular disease, cerebrovascular disease (ie, presence of stroke or a history of transient ischemic attack), hypertension, hyperlipidemia, diabetes, preoperative hemodialysis, chronic lung disease (mild, moderate, or severe), arrhythmia, aortic stenosis greater than grade 1, aortic regurgitation greater than grade 2, mitral regurgitation greater than grade 2, tricuspid regurgitation greater than grade 2, cardiogenic shock, history of myocardial infarction, congestive heart failure, New York Heart Association functional class III or IV, triple-vessel disease, and left main disease. The Hosmer-Lemeshow test result was not significant ($P = .292$) and the c-statistic for this propensity model was 0.599 (0.576-0.623; 95% confidence interval). We then performed a 1-to-1 matched analysis on the basis of the estimated propensity score of each patient. The propensity scores were compared between ONCAB and OPCAB patients, with a match occurring when 1 patient in the ONCAB group had an estimated score within 0.6 standard deviations of a patient in the OPCAB group. If 2 or more patients in the ONCAB group met this criterion, we randomly selected 1 patient for matching. We also performed univariate comparisons of patient characteristics and outcome variables between the propensity-score-matched groups of ONCAB and OPCAB patients using Fisher exact test and Student *t* test as appropriate. In addition, an institutional-volume adjusted analysis was performed by using a mixed-effects logistic regression model. In this model, the annual isolated CABG case volumes of hospitals were included as a covariate.