in redo CABG, and to retrospectively compare isolated redo CABG with or without cardiopulmonary bypass (CPB) using data from the JCVSD through propensity score (PS) matching.

MATERIALS AND METHODS

Study population

The JCVSD was established in 2000 with the goal of evaluating surgical outcomes after cardiovascular procedures in many centres throughout Japan [15, 16]. As of January 2013, JCVSD has recorded clinical information from over 500 hospitals, which comprises almost all hospitals with cardiovascular surgery units in Japan. The data collection form has 255 variables that are almost identical to those in the Society of Thoracic Surgeons (STS) National Database [available at: http://www.sts.org (25 February 2014, date last accessed)]. The definitions of JCVSD variables [available at: http://www.jacvsd.umin.jp (25 February 2014, date last accessed)] are also based on those of The STS National Database (Tables 1 and 2). Through the JCVSD web-based system, each participating hospital enters data and uses a feedback report in real time that includes risk-adjusted outcomes compared with all participating hospitals. Although participation in the JCVSD is voluntary, submissions tend to be thorough, with overall preoperative risk factors used in risk models missing in fewer than 3% of the entries. The accuracy of the submitted data is verified through monthly visits to each hospital by The Site Visit Working Group. The Site Visit Working Group members verify that the number of procedures from the original operative record list in the hospital matches that reported in the JCVSD. These members also examine each clinical chart of procedures and compare it with the JCVSD data.

Table 1: Unadjusted patient characteristics

Variables	Total redo CABG	On-pump redo CABG	Redo OPCAB	P-value
Patients	617	253	364	
Sex (male)	78.8	79.8	78.0	0.62
Age (years), mean (SD)	69.35 ± 9.2	68.87 ± 9.74	69.68 ± 8.81	0.28
Body surface area, mean (SD)	1.64 ± 0.18	1.64 ± 0.18	1.64 ± 0.18	0.54
Smoking	52.4	49.8	54.1	0.33
Body mass index >30 kg/m^2	5.2	5.1	5.2	1.00
Diabetes	46.2	45.5	46.7	0.81
Preoperative creatinine value	1.73 ± 2.29	1.68 ± 2.29	1.76 ± 2.29	0.70
Renal failure	18.5	18.2	18.7	0.92
Dialysis	9.1	9.6	9.4	0.89
Hyperlipidaemia	60.8	59.3	61.8	0.56
Hypertension	77.6	80.2	75.8	0.20
Cerebrovascular disease	11.0	12.6	9.9	0.30
Carotid stenosis	7.9	7.9	8.0	1.00
COPD (moderate and severe)	11.3	10.3	12.1	0.52
Extracardiac disease	20.9	23.7	19.0	0.16
Peripheral	18.0	19.8	16.8	0.34
Myocardial infarction	44.9	46.6	43.7	0.51
Previous coronary artery intervention	45.4	44.7	45.9	0.81
Unstable angina	32.9	38.3	29.1	0.019
Shock	4.9	7.9	2.7	0.0040
Congestive heart failure	14.7	17.0	13.2	0.21
Arrhythmia	11.7	13.8	10.2	0.16
NYHA class III or IV	28.4	31.2	26.4	0.20
Diseased vessels, %				
Left main disease	37.0	42.7	33.0	0.017
1	13.9	9.9	16.8	0.018
2	25.0	20.2	28.3	0.023
Triple-vessel disease	55.3	62.1	50.5	0.0050
LV impairment, %				
Good >EF:60%	34.5	35.2	34.1	0.80
≤EF:60%	65.2	64.0	65.9	0.67
Bad <EF:30%	8.1	9.9	6.9	0.18
Mitral valve insufficiency II–IV	21.1	20.9	21.2	1.00
Tricuspid valve insufficiency II–IV	14.6	17.4	12.6	0.11
Status, %				
Urgent	8.3	9.9	7.1	0.24
Emergency/salvage	8.1	10.7	6.3	0.071
Japan SCORE				
Expected 30 days operative mortality		7.66 ± 0.14	5.51 ± 0.1	0.023
Expected composite 30-day mortality or major morbidity		25.1 ± 0.18	21.9 ± 0.15	0.019

Values are percentage or mean ± SD values.
COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; LV: left ventricular; EF: ejection fraction.

Table 2: Unadjusted outcomes

	Total redo CABG	On-pump redo CABG	Redo OPCAB	P-value
Intraoperative variables				
Operation time (min)	375.21 ± 147.0	427.61 ± 151.23	339.06 ± 132.61	<0.00010
Distal anastomoses mean (SD)	2.12 ± 1.10	2.30 ± 1.04	2.00 ± 1.12	0.0010
Number of distal anastomoses				
1, 2	66.9	60.1	71.7	0.0030
3	21.9	26.9	18.4	0.013
4, 5	10.7	13.0	9.1	0.15
6	0.5	0.0	0.8	0.27
Early outcomes				
30-day mortality	5.2	8.3	3.1	0.0050
Operative mortality	7.0	10.7	4.4	0.0040
Blood transfusion	74.2	88.9	64.0	<0.00010
Initial ventilator time (h)	45.21 ± 147.79	65.49 ± 160.32	31.17 ± 136.92	0.0050
Intensive care unit stay ≥8 days	10.2	15.4	6.6	0.0010
Postoperative morbidity				
Stroke	2.1	2.8	1.6	0.40
Transient	1.8	2.8	1.1	0.14
Continuous coma ≥24 h	1.8	3.2	0.8	0.058
Renal failure requiring dialysis	3.9	5.9	2.5	0.034
Renal failure	9.9	14.6	6.6	0.0010
Deep sternal wound infection	1.3	1.6	1.1	0.72
Prolonged ventilation	10.0	16.6	5.5	<0.00010
Reoperation for bleeding	2.4	3.6	1.6	0.18
Perioperative myocardial infarction	2.8	5.1	1.1	0.0040
Atrial fibrillation	12.3	13.8	11.3	0.38
Heart block	0.3	0.8	0.0	0.17
Gastrointestinal complication	3.1	2.8	3.3	0.82
Pneumonia	3.9	4.0	3.8	1.00
Readmission within 30 days	2.9	4.0	2.2	0.23
Composite 30-day mortality or major morbidity	14.9	22.9	9.3	<0.00010

Values are percentage or mean ± SD values.

Study end points

The study outcomes measured from the JCVSD were as follows: operation time and the number of distal anastomoses as the intraoperative variable, 30-day mortality, operative mortality, initial ventilation time, the number of patients who stayed in the intensive care unit ([ICU] stay) ≥8 days and blood transfusion as early outcomes. The 30-day mortality was defined as death within 30 days of the operation, regardless of the patient's geographic location, even if the patient had been discharged from the hospital. Operative mortality included any patient who died within the index hospitalization, regardless of the length of hospital stay, and including any patient who died after being discharged from hospital up to 30 days from the date of the operation. Hospital-to-hospital transfer was not considered discharge [17].

Major morbidity was defined as any of the five following postoperative in-hospital complications: stroke, reoperation for any reason, need for mechanical ventilation for more than 24 h postoperatively, renal failure with newly required dialysis or deep sternal wound infection [18]. In addition to the above complications, the following complications were defined as postoperative morbidities (Table 2): (i) renal failure (defined as an increase in serum creatinine value to twice preoperative levels or to >2.0 mg/dl, or new requirement for dialysis or haemofiltration); (ii) continuous coma for >24 h; (iii) perioperative myocardial infarction (defined as at least two of the following: continuous angina for >20 min regardless of nitrite treatment or rest, elevation of cardiac enzyme levels [creatine kinase (CK)-MB level >1/20 of the total CK level or twice preoperative levels and/or lactate dehydrogenase isozyme subtype 1 > subtype 2 and/or positive troponin]; new cardiac wall motion abnormalities; Q waves or ST-T elevation on more than 2 serial leads in the electrocardiogram); (iv) atrial fibrillation (new onset); (v) heart block requiring permanent pacemaker; (v) gastrointestinal complications; (vi) pneumonia and (vii) readmission within 30 days of discharge. In this analysis, composite 30-day mortality or major morbidity was considered a postoperative morbidity (Table 2).

Statistical analyses

We compared the baseline demographics of patients who underwent off-pump surgery with those of patients who underwent on-pump surgery. The PS matching [19] method was used for adjusting differences in baseline characteristics because the patients were not randomly assigned to receive redo OPCAB.

PS were calculated for each patient to adjust for confounders of group assignment using the following 13 preoperative variables, which include the circumstances under which surgeons generally tend to avoid or prefer to use CPB: age; presence of unstable angina; extracardiac disease; cerebrovascular disease (the presence of stroke or a history of transient ischaemic attack); a history of non-invasive carotid stenosis >75%; diabetes; renal failure; chronic lung disease (mild, moderate or severe); cardiogenic shock; a history of myocardial infarction; ejection fraction <30%; triple-vessel disease and left main disease (variables at the basis of the model are given in Table 3).

We performed a one-to-one matched analysis on the basis of estimated PS of each patient. The log odds of the probability that a patient underwent redo OPCAB was modelled as a function of the confounders, which we identified and included in our data set. C-statistics were calculated for evaluating the goodness of fit. The area under the curve of this PS model was 0.62. The estimated PS were compared between the redo OPCAB and on-pump redo CABG groups, and a 'match' occurred when 1 patient in the redo OPCAB had an estimated score within 0.6 standard deviation (SD) of another patient in the on-pump redo CABG. If two or more patients in the redo OPCAB group met this criterion, we randomly selected 1 patient for matching.

We performed univariate comparisons of patient characteristics and outcome variables between the PS-matched groups of redo OPCAB and on-pump redo CABG, using Fisher's exact tests or Pearson's χ^2 test and t-tests, as appropriate. A P-value of <0.05 was considered statistically significant. All statistical analyses were conducted using PASW version 18.0 (SPSS, Inc.; Chicago, IL, USA).

Table 3: Variables included in the propensity score model

Variables	B Value	P-value
Age	1.013	0.16
Carotid stenosis	0.978	0.94
Renal failure	1.067	0.77
Diabetes (insulin)	1.212	0.45
Cerebrovascular disease	0.853	0.56
COPD (mild, moderate or severe)	1.340	0.29
Extracardiac disease	0.740	0.44
Myocardial infarction	1.005	0.98
Unstable angina	0.807	0.25
Shock	0.401	0.035
Left main disease	0.749	0.36
Triple-vessel disease	0.627	0.0090
<EF:30%	0.720	0.067

COPD: chronic obstructive pulmonary disease; EF: ejection fraction.

RESULTS

We analysed the data of 34 980 patients who underwent isolated CABG and were included in the JCVSD between 2008 and 2011. Of these, 1.8% of patients [n = 617/34980] had undergone redo CABG.

Of these, 253 (41%) underwent an on-pump procedure, whereas the other 364 (69%) underwent an off-pump procedure (Fig. 1). Of note, 7.7% of patients (n = 28/364) who required intraoperative conversion from redo OPCAB to on-pump redo CABG were included in the redo OPCAB group for final analysis.

Unadjusted outcomes

The demographic and preoperative characteristics of patients undergoing redo OPCAB versus on-pump redo CABG before propensity matching are listed in Table 1. The on-pump redo CABG group had a significantly higher preoperative incidence of unstable angina and shock than the redo OPCAB group (38.3 vs 29.1%, P = 0.019; 7.9 vs 2.7%, P = 0.0040). The other preoperative data were similar between the two groups.

As for diseased vessels, the rates of triple-vessel and left main disease were significantly higher in the on-pump redo CABG group than in the redo OPCAB group (62.1 vs 50.5%, P = 0.0050; 42.7 vs 33.0%, P = 0.017). On the other hand, the redo OPCAB

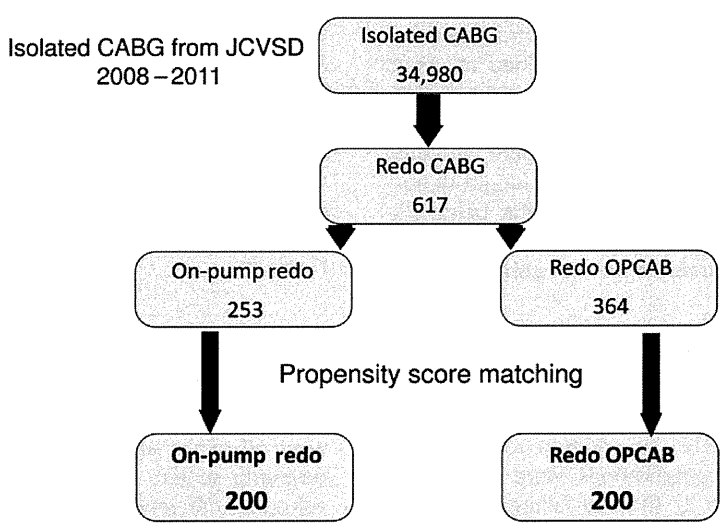

Figure 1: Patient selection. JCVSD: Japan Cardiovascular Surgery Database.

group had a lower number of diseased vessels compared with the on-pump redo CABG group (single-vessel disease: 9.9% in the on-pump redo CABG group versus 16.8% in the redo OPCAB group; double-vessel disease: 20.2% in the on-pump redo CABG group versus 28.3% in the redo OPCAB group). The Japan SCORE, (The Japan SCORE is a risk model based on the JCVSD. Expected mortality and expected composite 30-day mortality or major morbidity are calculated from this risk model.) [15, 16] were significantly higher in the on-pump redo CABG group than in the redo OPCAB group (7.66 ± 0.14% vs 5.51 ± 0.1, $P = 0.023$; 25.1 ± 0.18% vs 21.9 ± 0.15%, $P = 0.019$, respectively).

There were significant differences in intraoperative variables between the two groups (Table 2). The redo OPCAB group underwent a fewer mean number of distal anastomoses compared with the on-pump redo CABG group (2.00 ± 1.12 vs 2.30 ± 1.04, $P = 0.0010$). Operation times were significantly longer in the on-pump redo CABG group than in the redo OPCAB group, at 427.61 ± 151.23 vs 339.06 ± 132.61 min ($P < 0.00010$).

Significant differences between the groups were observed in early outcomes (Table 2). All of the outcomes were significantly worse in the on-pump redo CABG group than in the redo OPCAB group. The 30-day mortality was 8.3% in the on-pump redo CABG group and 3.1% in the redo OPCAB group ($P = 0.0050$).

Postoperative morbidities are given in Table 2. The incidences of renal failure, renal failure requiring dialysis, prolonged ventilation, perioperative myocardial infarction and composite 30-day mortality or major morbidity were higher in the on-pump redo CABG group than in the redo OPCAB group.

Table 4: Patient characteristics after propensity score matching

Variables	Total redo CABG	On-pump redo CABG	Redo OPCAB	*P*-value
Patients	400	200	200	
Sex (male)	80.5	83.0	78.0	0.26
Age (years), mean (SD)	68.4 ± 9.4	68.7 ± 9.4	68.1 ± 9.3	0.52
Body surface area, mean (SD)	1.65 ± 0.17	1.66 ± 0.2	1.63 ± 0.2	0.19
Smoking	53.3	52.5	54.0	0.84
Body mass index >30 kg/m^2	6.5	6.0	7.0	0.84
Diabetes	46.8	46.5	47.0	1.00
Preoperative creatinine value	1.7 ± 2.24	1.7 ± 2.3	1.7 ± 2.2	0.91
Renal failure	17.8	17.5	18.0	1.00
Dialysis	8.3	8.0	8.5	1.00
Hyperlipidaemia	60.8	61.0	60.5	1.00
Hypertension	76.0	80.0	72.0	0.079
Cerebrovascular disease	12.0	10.5	13.5	0.44
Carotid stenosis	8.5	8.0	9.0	0.86
COPD (moderate and severe)	2.3	2.5	2.0	1.00
Extracardiac disease	21.8	21.0	22.5	0.81
Peripheral	18.8	18.5	19.0	1.00
Myocardial infarction	47.5	47.0	48.0	0.92
Previous coronary artery intervention	46.3	45.0	47.5	0.69
Unstable angina	41.8	40.5	43.0	0.69
Shock	5.5	6.0	5.0	0.83
Congestive heart failure	16.5	16.5	16.5	1.00
Arrhythmia	12.8	13.5	12.0	0.77
NYHA class III or IV	34.5	32.0	37.0	0.34
Diseased vessels, %				
Left main disease	47.5	45.0	50.0	0.37
1	5.8	6.0	5.5	1.00
2	16.3	18.0	14.5	0.42
Triple-vessel disease	74.3	70.0	78.5	0.067
LV impairment, %				
Good >EF:60%	30.8	35.5	26.0	0.051
≤EF:60%	69.0	64.0	74.0	0.040
Bad <EF:30%	9.0	8.0	10.0	0.60
Mitral valve insufficiency II–IV	22.5	20.0	25.0	0.28
Tricuspid valve insufficiency II–IV	15.5	18.0	13.0	0.21
Status, %				
Urgent	10.0	10.0	10.0	1.00
Emergency/salvage	8.5	8.5	8.5	1.00
Japan SCORE				
Expected 30 days operative mortality		6.62 ± 0.12	6.37 ± 0.11	0.85
Expected composite 30-day mortality or major morbidity		24.95 ± 0.17	24.01 ± 0.17	0.58

Values are percentage or mean ± SD values.
COPD: chronic obstructive pulmonary disease; NYHA: New York Heart Association; LV: left ventricular; EF: ejection fraction.

Propensity-matched pairs

We selected 13 preoperative risk factors to eliminate the differences between the two groups (Table 3) and used PS matching with these preoperative risk factors to adjust for differences in baseline characteristics between the two groups. Using one-to-one matching, we selected 200 pairs from each group (Fig. 1).

Table 5: Results after propensity score matching 1

	Total redo CABG	On-pump redo CABG	Redo OPCAB	*P*-value
Intraoperative variables				
Operation time (min)	397.5 ± 148.16	441.3 ± 146.3	353.7 ± 136.9	<0.00010
Distal anastomoses mean (SD)	2.31 ± 1.12	2.41 ± 1.0	2.21 ± 1.2	0.074
Number of distal anastomoses				
1,2	60.0	56.5	63.5	0.18
3	26.3	28.5	24.0	0.36
4,5	13.0	15.0	11.0	0.30
6	0.8	0.0	1.5	0.25
The distribution of grafts				
Left ITA	36.3	36.5	36.0	1.00
Right ITA	32.3	27.5	37.0	0.054
Bilateral ITA	11.5	9.0	14.0	0.16
No ITA use	43.0	45.0	41.0	0.48

Values are percentage or mean ± SD values.
ITA: internal thoracic artery.

Table 6: Results after propensity score matching 2

	Total redo CABG	On-pump redo CABG	Redo OPCAB	*P*-value
Early outcomes				
30-day mortality	5.3	7.0	3.5	0.18
Operative mortality	7.5	9.5	5.5	0.18
Blood transfusion	82.8	94.0	71.5	<0.00010
Initial ventilator time (h)	47.8 ± 146.08	58.9 ± 137.5	36.8 ± 153.7	0.13
Intensive care unit stay ≥8 days	10.8	14.5	7.0	0.023
Cause of all death				0.59
Arrhythmia	1.0	1.0	1.0	
Bleeding	0.3	0.5	0.0	
Infection	0.8	0.5	1.0	
Low output syndrome	4.0	5.0	3.0	
Pulmonary	0.5	0.5	0.5	
Renal	0.3	0.5	0.0	
Others	2.0	3.0	1.0	
Postoperative morbidity				
Stroke	1.5	2.5	0.5	0.22
Transient	1.5	2.0	1.0	0.69
Continuous coma ≥24 h	1.5	2.0	1.0	0.69
Renal failure requiring dialysis	3.8	5.0	2.5	0.29
Renal failure	9.5	12.0	7.0	0.12
Deep sternal wound infection	1.0	1.0	1.0	1.00
Prolonged ventilation	11.0	15.0	7.0	0.016
Reoperation for bleeding	3.5	4.0	3.0	0.79
Perioperative myocardial infarction	3.0	4.5	1.5	0.14
Atrial fibrillation	12.5	14.0	11.0	0.45
Heart block	0.3	0.5	0.0	1.00
Gastrointestinal complication	2.0	2.0	2.0	1.00
Pneumonia	3.3	4.0	2.5	0.58
Readmission within 30 days	3.5	4.5	2.5	0.42
Composite 30-day mortality or major morbidity	16.3	21.5	11.0	0.0060

Values are percentage or mean ± SD values.

There were no significant differences among all preoperative factors, including shock, unstable angina, number of diseased vessels (94.3%: multivessel disease), left ventricular impairment and preoperative status between the two groups. Moreover, there were no significant differences in the Japan SCORE (expected mortality: 6.62 ± 0.12% vs 6.37 ± 0.11%, $P = 0.85$; expected 30-day mortality or composite major morbidity: 24.95 ± 0.17% vs 24.01 ± 0.17%, $P = 0.58$) (Table 4).

As for intraoperative variables (Table 5), there was no significant difference in the mean number of distal anastomoses after matching (2.41 ± 1.00 vs 2.21 ± 1.04, $P = 0.074$). The data of our study show that, in the on-pump redo CABG group, 35.0% of patients were given blood cardioplegia and 10.0% were given the crystalloid cardioplegia solution for myocardial protection. No cardioplegia was provided in 45.5% patients in the on-pump redo CABG group. In almost all patients in whom no cardioplegia was provided, the on-pump beating procedure was performed. Half of the on-pump redo CABG procedures are performed using the beating heart technique in Japan [20]. The JCVSD does not capture whether adequate myocardial protection was provided during CABG, particularly in the setting of patent mammary graft, for example, whether retrograde cardioplegia or systemic hyperkalaemia is used for achieving diastolic arrest and myocardial protection. The distribution of arterial versus vein grafts in the two groups is given in Table 5. There were no significant differences in the distribution of internal thoracic artery graft and the absence of ITA graft use in the two groups. The causes of all deaths in the two groups registered in the JCVSD are given in Table 6.

Operation time was significantly longer in the on-pump redo CABG group than in the redo OPCAB group (441.3 ± 146.3 vs 353.7 ± 136.9 min, $P < 0.00010$) (Table 5).

Regarding early outcomes (Table 6), the patients in the redo OPCAB group had a lower 30-day mortality rate (3.5 vs 7.0%, $P = 0.18$), a lower initial ventilator time (36.8 ± 153.7 vs 58.9 ± 137.5 h, $P = 0.13$), significantly shorter ICU duration (7.0 vs 14.5%, $P = 0.023$) and significantly decreased need for blood transfusions (71.5 vs 94.0%, $P < 0.00010$).

As for postoperative morbidities (Table 6), the redo OPCAB group had a significantly lower rate of prolonged ventilation (>24 h) (7.0 vs 15.0%, $P = 0.016$) and lower rates of composite mortality or major morbidities (11.0 vs 21.5%, $P = 0.0060$) than the on-pump redo CABG group. Although there were no significant differences in other morbidities, the redo OPCAB group had a lower rate in many postoperative morbidities.

DISCUSSION

In the present study, we present the contemporary Japanese results for redo CABG obtained from the JCVSD, which currently contains the clinical data from almost all Japanese institutions performing cardiovascular surgery.

Off-pump coronary artery grafting

OPCAB emerged in the mid-1980s and has since become increasingly popular worldwide. In Japan, OPCAB has become the standard management strategy for surgical coronary revascularization. The ratio of OPCAB in CABG has been increasing, especially since the year 2000; the annual rate of performing OPCAB is >60% [20, 21]. Several studies, including those conducted in Japan, have reported the effects of OPCAB and have compared OPCAB with conventional CABG [1–3], especially in patients with high comorbidity [4, 5].

Redo coronary artery bypass grafting

As described in several previous reports, the prevalence of redo CABG has recently reached a plateau [22, 23]. The Japanese Association for Thoracic Surgery (JATS) has been maintaining a registry of cardiovascular procedures in Japan since 1986; the number of isolated redo CABG in Japan has been basically decreasing, and its prevalence reached a plateau over a 10-year period. The latest version of the JATS Annual Report in 2011 showed that 223 patients underwent redo isolated CABG, and the prevalence of reoperation cases was 1.56% of total isolated CABG cases (14 256 patients) in 2011 [20]. This trend is apparently caused by improved medication for post-CABG patients, more frequent use of the internal mammary artery, more complete revascularization, older patient age at the time of primary surgery and increased use of percutaneous coronary intervention (PCI) for recurrent coronary disease after CABG in patients. Compared with Western countries, in Japan, PCI is used for patients with more severe coronary artery disease, and indications for PCI have expanded to include more indications than those included in its early stages.

Redo CABG can be performed safely in certain patients because of growing surgical experience, new technical strategies and better management of patient comorbidities. However, even in recent reports, the morbidity and mortality of such procedures remain higher (in the range of 4.2–6.8%) than those of primary procedures [20, 22–24].

Our data showed that the 30-day mortality in the redo CABG was significantly higher than in the primary CABG group (5.63 vs 1.46%, $P < 0.00010$). We hypothesize that the different characteristics inherent in the redo CABG patients may explain the higher mortality or morbidity rate in this group of patients compared with the primary CABG group. Redo patients are generally older, with a lower ejection fraction, and have multiple risk factors. In addition, their general physical condition is usually worse. Additionally, redo CABG tends to be more technically demanding, e.g. successful re-entry into the chest, management of patent bypass grafts or diseased patent grafts with adhesions, ischaemia caused by embolization of atheromatous debris from venous conduits, location of suitable conduits, aortic atherosclerotic disease that may prevent cross-clamping or aortic cannulation and/or inadequate myocardial protection caused by difficulties in delivering cardioplegia in the face of native and conduit stenoses [23]. The last two factors are directly associated with disadvantages of the on-pump procedure.

Concordantly, many reports have mentioned the benefits of OPCAB, especially in patients with several comorbidities, such as those undergoing redo CABG [4, 5]. Several recent reports of off-pump redo CABG have stated the advantage of morbidity and mortality [6–11]. Conversely, some reports have stated that these benefits may be limited to a selected group of patients because of the higher rate of incomplete revascularization in off-pump CABG. However, the mean number of distal anastomoses in these reports was 2 (Czerny *et al.* [12]: 1.3 ± 0.5; Tugtekin *et al.* [13]: 1.6 ± 0.60 and Kara *et al.* [14]: 1.15 ± 0.41). The present study data indicated that single-vessel disease had a frequency of only 13.9% (Table 1), which was reduced to only 5.8% after matching data were included. Most data (94.2%) were for multivessel disease (Table 4), and the mean number of distal anastomoses was no less than 2 in the redo OPCAB group (Tables 2 and 5). These reports were from many countries that have various circumstances concerning the management of CABG procedures (OPCAB is used only in 30% of cases in Western countries and in other Asian countries). Further, most of these results were reported single-institution studies [6, 7, 10–12, 14]. Therefore, these data might not clarify the specific benefits of off-pump surgery in redo CABG.

The present study was a comparative clinical study utilizing a large nationwide database (JCVSD) to achieve a higher evidence level and to obtain up-to-date clinical outcomes. To the best of our knowledge, thus far, similar comparative clinical studies aiming to clarify the superiority of each variable of the off-pump technique in redo CABG have not been conducted. In addition, Japan is the only country in which >60% of isolated CABGs are performed without a CPB, and our results may be very informative.

Data from the JCVSD in redo CABG

The present retrospective comparison before matching data is presented in Tables 1 and 2.

These data suggest that surgeons in Japan tend to perform off-pump procedures for patients requiring fewer grafts in stable condition and perform on-pump procedures for patients requiring a greater number of grafts in unstable conditions for redo CABG. Thus, longer operative times are observed in the on-pump redo CABG group than in the redo OPCAB group (427.61 ± 151.23 vs 339.06 ± 132.61 min, $P < 0.00010$). Early outcomes and most morbidities in the on-pump redo CABG group were worse than in the redo OPCAB. Thus, off-pump surgery seems to offer certain advantages in cases of redo CABG surgery. However, the indications for off-pump or on-pump reoperations are based on individual surgeon and institutional preferences. In addition, the two groups had unequal patient characteristics and significantly different severities in patient preoperative backgrounds, according to the Japan SCORE. Based on the unadjusted results, we selected 13 preoperative risk factors to eliminate the differences between the two groups; these included the number of diseased vessels, preoperative status and the circumstances under which surgeons in Japan generally tend to avoid or prefer to use CPB (Table 3). After matching the data of these patients with the data of those in the JCVSD, no significant differences were observed in expected mortality and expected 30-day mortality or major composite morbidities between the two groups. Therefore, the severity of patient preoperative backgrounds and the overall picture of the entire patient group profile were adequately adjusted between the two groups (Table 4).

In addition, there were no significant differences in the distribution of grafts (Table 5). Therefore, these factors, including severity of patient preoperative backgrounds, did not influence the results of our study when comparing the two groups after matching. In the present retrospective comparison, the results after propensity matching data from the JCVSD demonstrated that redo OPCAB was safe and effective when each variable was considered.

The most important result of the adjusted portion of the study was the absence of significant differences in the mean number of distal anastomoses after matching. In addition, there were no significant differences in the distribution of grafts. Nevertheless, the mean operation time was significantly shorter in the redo OPCAB group than in the on-pump redo CABG group (353.7 vs 441.3 min, $P < 0.00010$) (Table 5). These results suggests that redo OPCAB reduced the operation time in the equivalent number of distal anastomoses performed by the on-pump procedure, even for over 90% of multivessel disease cases (Table 4). We considered that the operation time increased in the on-pump redo CABG group because of the difficulty in achieving haemostasis during adhesion dissection in patients who developed coagulation abnormalities, a potential side-effect of CPB [25]. This may have led to higher intraoperative and postoperative blood loss and need for blood transfusions. Moreover, patients who developed pulmonary dysfunction secondary to CPB may have also presented longer operation times, contributing to worsening of respiratory insufficiency, prolonged mechanical ventilation and ICU stay (Table 6). These increased operation times emphasize several adverse occurrences associated with potential side-effects of CPB, such as a coagulopathy or pulmonary dysfunction [25], redo CABG procedure such as cardioplegia, arterial cannulation or aortic cross-clamping and the multiple risk factors usually present in redo CABG patients. In other words, by avoiding CPB, the operation time could be decreased, and the complications associated with on-pump redo CABG were reduced. As a result, the incidence of composite mortality or major complication in redo OPCAB was significantly lower than in the on-pump redo CABG. Most morbidities tend to be lower in redo OPCAB (Table 6).

Our findings from the JCVSD indicate that the off-pump surgical technique for redo CABG offers certain advantages, that is, it prevents potential side-effects of CPB and prevents complications of surgical procedures.

Despite these important findings, there were several limitations in the present study regarding data interpretation. It was a retrospective clinical study based on a large-scale database, and it provides weaker clinical evidence than a randomized prospective study and we did not have medium-term or long-term outcomes. In this study, a 30-day mortality rate of 7.00% and an operative mortality rate of 9.5% were observed (Table 6); our observation interval was 30 days, but early risk extends beyond this period. The JCVSD does not have data to account for this.

Nonetheless, our data suggest that the off-pump technique for redo CABG reduces operation time for an equivalent number of distal anastomoses performed using the on-pump procedure for multivessel diseases. As a result, the off-pump procedures had significantly lower rates of prolonged ventilation, blood transfusion and shorter duration of ICU stay and lower rates of composite mortality and major morbidities compared with the on-pump procedure.

In conclusion, the off-pump technique reduced operative mortality and reduced the incidence of major complications in redo CABG.

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APPENDIX. CONFERENCE DISCUSSION

Dr E. Wolner *(Vienna, Austria)*: This is a very interesting, very good paper and, for me, an unexpectedly greater difference in the mortality of the off-pump versus the on-pump group, in favour of the OPCAB group. This difference results from a matched group of patients. However, if you look at the unadjusted data in your slide No. 2, you see that you have more hypertension and more cardiovascular disease in the on-pump group. It is not statistically significant, but there are differences. And if you perhaps count all this data together (you have higher New York Heart Association class, you have more heart failure, you have, as you said, more unstable angina and more stroke), my conclusion is that the on-pump group is sicker than the OPCAB group.

So my first question is: Are you sure that your statistical analysis, this propensity score matching, reflects the real data between these two groups? Secondly, for me it is very surprising that in your country you have such a high number, I mean 60% or so, of off-pump versus on-pump coronary surgery. Usually in Germany it's 20%. In the STS database, it is also I believe a little bit more than 20%. What is the explanation that you have for such a high percentage of off-pump surgery in your country?

Dr Dohi: Thank you, a good question about an important point. In fact, before matching data were available, Japanese surgeons performed off-pump procedures for patients requiring fewer grafts and, on other hand, they performed on-pump procedures for patients requiring a greater number of grafts and who were in an unstable condition. Thus, the results are significantly worse in the on-pump group compared to those in the off-pump group. Could you repeat the other question?

Dr Wolner: Percentage of off- versus on-pump as a difference between your country and others.

Dr Dohi: In Japan almost 60% of isolated CABGs are performed as off-pump procedures. Our data indicate that approximately 70% off-pump procedures are performed, and OPCAB has become the standard CABG procedure in Japan. PCI is used for patients with more severe coronary artery disease in Japan compared with Western countries, in some cases in patients with LM lesions, 3-vessel disease or chronic total occlusion. This increased utilization of

ADULT CARDIAC

PCI has led Japanese surgeons to perform less invasive surgical procedures such as OPCAB.

Dr D. Taggart *(Oxford, United Kingdom)*: I think in many Asian countries it's very high. And India is probably even higher, somewhere in the region of 80% to 90%. In Japan the figures I saw were even higher than 60%. So in the Far East and South East Asia, off-pump surgery is the standard.

Could I just ask the audience, on this basis, not for redos but for a first time coronary, which of you five years ago would have been routinely using off-pump surgery in, say, at least 30% or 40% of patients?

(Show of hands.)

Who is still using off-pump surgery in at least 30% to 40% of patients?

(Show of hands.)

It's quite interesting, just looking at this audience indicates that most of the people who five years ago were doing a significant proportion of off-pump surgery are still doing it. In my own practice it was 90% 15 years ago and it's still 90% today. But I think what's happened with recent publications is that people who were a bit less sure about off-pump surgery have now dropped off, because we're seeing the figures for off-pump surgery in the United Kingdom have dropped from around 20% to 14% now in the last year. And I think the recent publications of Coronary and GOPCABE, the big German trial, have had a negative impact on off-pump surgery.

Dr Dohi: Japanese surgeons are familiar with the off-pump procedure. Therefore, even for redo CABG, Japanese surgeons perform the off-pump procedure quite well.

Total Gastrectomy Risk Model

Data From 20,011 Japanese Patients in a Nationwide Internet-Based Database

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Objective: To construct a risk model for total gastrectomy outcomes using a nationwide Internet-based database.

Background: Total gastrectomy is a very common procedure in Japan. This procedure is among the most invasive gastrointestinal procedures and is known to carry substantial surgical risks.

Methods: The National Clinical Database was used to retrieve records on more than 1,200,000 surgical cases from 3500 hospitals in 2011. After data cleanup, 20,011 records from 1623 hospitals were analyzed for procedures performed between January 1, 2011, and December 31, 2011.

Results: The average patient age was 68.9 years; 73.7% were male. The overall morbidity was 26.2%, with a 30-day mortality rate of 0.9%, in-hospital mortality rate of 2.2%, and overall operative mortality rate of 2.3%. The odds ratios for 30-day mortality were as follows: ASA (American Society of Anesthesiologists) grade 4 or 5, 9.4; preoperative dialysis requirement, 3.9; and platelet count less than 50,000 per microliter, 3.1. The odds ratios for operative mortality were as follows: ASA grade 4 or 5, 5.2; disseminated cancer, 3.5; and alkaline phosphatase level of more than 600 IU/L, 3.1. The C-index of 30-day mortality and operative mortality was 0.811 (95% confidence interval [CI], 0.744–0.879) and 0.824 (95% CI, 0.781–0.866), respectively.

Conclusions: We have performed the first reported risk stratification study for total gastrectomy, using a nationwide Internet-based database. The total gastrectomy outcomes in the nationwide population were satisfactory. The risk models that we have created will help improve the quality of surgical practice.

Keywords: National Clinical Database, risk factors of mortality, total gastrectomy, 30-day mortality, risk model

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Gastric cancer is currently the fourth most common malignancy worldwide[1] and is among the most prevalent types of cancer in Eastern Asia, including Japan, Korea, and China.[2] Surgical resection is often the only curative treatment, although some early gastric cancers limited to the mucosa may be treated endoscopically.[3] Total gastrectomy is usually indicated for tumors located in the upper third of the stomach or advanced gastric cancer extending to the cardia.

Total gastrectomy is among the most invasive gastrointestinal procedures and is known to carry substantial surgical risks. Patients with gastric cancer frequently have anemia, malnutrition, or organ dysfunction due to tumor extension.[4] Major complications of total gastrectomy can be fatal; these complications include esophagojejunal anastomotic leakage, duodenal stump leakage, and pancreatic fistula related to suprapancreatic lymphadenectomy.[5] In addition, the proportion of patients with gastric cancer who are elderly is increasing.[6] Although all of these factors may affect mortality, and several additional factors influence the incidence of gastric cancer itself, there are few studies that have used a large patient cohort to describe a risk model of mortality for total gastrectomy.

The National Clinical Database (NCD), which commenced patient registration in January 2011, is a nationwide project that is linked to the surgical board certification system in Japan. In this study, we focused on the NCD division of gastrointestinal surgery that uses patient variables and definitions almost identical to those used by the American College of Surgeons National Surgical Quality Improvement Program.[7] Using this database, we created a risk model of mortality for Japanese patients undergoing total gastrectomy.

METHODS

Data Collection

In 2011, the NCD collected data on more than 1,200,000 surgical cases from 3500 hospitals. In the gastroenterological surgery section, the database registered all surgical cases that fell into this category; in addition, it required detailed input items for the 8 procedures, including total gastrectomy, that were determined to represent the performance of surgery in each specialty. 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. A total of 20,011 patients who underwent total gastrectomy at 1623 institutions between January 1, 2011, and December 31, 2011, were eligible for analysis.

The NCD constructed software for an Internet-based data collection system, and the data managers of participating hospitals were responsible for forwarding their data to the NCD office. The NCD ensures traceability of its data by maintaining continuity in the staff who approve data, the staff of the departments in charge of annual cases, and the data-entry personnel. It also validates data consistency via random inspections by participating institutions. All variables, definitions, and inclusion criteria for the NCD are accessible to participating institutions on its Web site (http://www.ncd.or.jp); the database administrators also provide e-learning systems to teach participants how to input consistent data. The administrators answer all inquiries regarding data entry, answering approximately 80,000 inquiries in 2011, and Frequently Asked Questions are displayed on the Web site.

From the *The Japanese Society of Gastroenterological Surgery, Working Group Database Committee; †The Japanese Society of Gastroenterological Surgery, Database Committee; ‡National Clinical Database; and §The Japanese Society of Gastroenterological Surgery, Tokyo, Japan.

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Endpoint

The primary outcome measure of this study was 30-day mortality and overall operative mortality. The calculation of operative mortality included all patients who died during the index hospitalization, including hospital stays up to 90 days, and any patient who died after hospital discharge within 30 days of the operation date.

Statistical Analysis

Data were randomly assigned to 2 subsets, with 80% allocated for model development and 20% for validation testing. The development data set comprised 16,036 records, and the validation data set comprised 3975 records. The 2 sets of logistic models, 30-day mortality and operative mortality, were constructed for the development data set using a stepwise selection of predictors, with the P value for inclusion set at 0.05. A goodness-of-fit test was performed to assess how well the model could discriminate between survivors and deceased patients. Model calibration, the degree to which the observed outcomes were similar to the predicted outcomes, was examined by comparing the observed with the predicted average within each of the 10 equal-sized subgroups, arranged in increasing order of patient risk.

RESULTS

Study Population Risk Profile

The total gastrectomy patient population represented in the NCD had an average age of 68.9 years; 73.7% of the population was male. The mean body mass index of the study population was 22.4 kg/m^2. Only 2.0% required emergency surgery. Furthermore, 4.6% of the patients needed assistance in activities of daily life. Weight loss of more than 10% was observed in 8.7% of patients. American Society of Anesthesiologists (ASA) scores of grade 3 and grade 4/5 were seen in 8.9% and 0.6% of patients, respectively. Preoperative comorbidities included diabetes mellitus in 8.9% of patients, preoperative respiratory distress in 2.4% of patients, disseminated cancer in 3.7% of patients, and ascites in 2.0% of patients. An abbreviated demographic and risk profile of the study population is shown in Table 1.

Morbidity

The overall morbidity in the total gastrectomy NCD population was 26.2%; grade II or higher complications, as defined by the Clavien-Dindo Classification of Surgical Complications system,[8] were observed in 18.3% of patients. Surgical complications included surgical site infection in 8.4% of patients, anastomotic leakage in 4.4% of patients, and pancreatic fistula (grades B, C) in 2.6% of patients. Nonsurgical complications included pneumonia in 3.6% of patients, renal failure in 1.3% of patients, central nervous system events in 0.7% of patients, and cardiac events in 0.6% of patients. The postoperative morbidities are presented in Table 2.

TABLE 1. Key Descriptive Data

Variables	N = 20,011
Age, mean, yr	68.9
Males, %	73.7
Body mass index, mean, kg/m^2	22.4
Status (emergent), %	2.0
ADL (any assistance), %	4.6
Weight loss, >10%, %	8.7
ASA score, %	
Grade 3	8.9
Grade 4 or 5	0.6
Diabetes, %	15.7
Previous cardiac surgery, %	1.1
Preoperative respiratory distress, %	2.4
Preoperative dialysis, %	0.5
Cerebrovascular accident, %	2.2
Disseminated cancer, %	3.7
Ascites, %	2.0

ADL indicates activities of daily life.

Outcomes

Total gastrectomy outcomes are presented in Table 3. The 30-day mortality was 0.9%, the in-hospital mortality was 2.2%, and the overall operative mortality was 2.3%.

Model Results

Risk models for 30-day mortality and operative mortality were developed; the final logistic models with the odds ratios and 95% confidence intervals are presented in Tables 4 and 5. The ASA score (grade 4 or 5) was the most significant factor in both models. In addition, there were 11 variables that appeared in both models: a preoperative dialysis requirement; a total bilirubin level of more than 2 mg/dL; the presence of disseminated cancer; an alkaline phosphatase level of more than 600 IU/L; an aspartate aminotransferase level of more than 35 IU/L; a prothrombin time–international normalized ratio of more than 1.25; any assistance needed for preoperative activities of daily living; the presence of ascites; a serum albumin level of less than 3.5 g/dL; and the patient's age category (see Tables 4 and 5 for the definition of age category).

Model Performance

To assess the performance of the models, both the C-index and the model calibration across risk groups were evaluated. The receiver operating characteristic curves of both models are shown in Figure 1. The C-index, a measure of model discrimination represented by the area under the receiver operating characteristic curve, was 0.811 for 30-day mortality (95% confidence interval, 0.744–0.879) (Fig. 1A) and 0.824 for overall operative mortality (95% confidence interval, 0.781–0.866) (Fig. 1B). Figure 2 demonstrates the calibration of the models or how well the rates for the predicted event matched those of observed event among patient risk subgroups. (Figure 2A, 30-day mortality risk model; and Figure 2B, operative mortality risk model)

DISCUSSION

Although mortality due to gastric cancer has been steadily decreasing in recent years,[9] the incidence of this cancer in Japan is still the highest of all solid tumors,[10] probably due to the high incidence of *Helicobacter pylori* infection in the Japanese population.[11] Gastric cancer is one of the most commonly encountered diseases in Japanese surgical units; Japanese surgeons are therefore very familiar with gastric cancer surgery, which explains why our study cases were collected from such a large number of institutes.

Although numerous studies have reported the morbidity and mortality rates for gastrectomy in general, few have described these rates for total gastrectomy alone. Moreover, it is still unknown whether total gastrectomy should be considered a more invasive procedure than distal gastrectomy. A randomized controlled trial comparing D1 subtotal gastrectomy with D3 total gastrectomy for cancers located in the gastric antrum revealed that significantly more abdominal abscesses are observed in patients undergoing total gastrectomy; this is attributed to the extended lymphadenectomy involved in the latter procedure.[12] In contrast, an Italian study demonstrated that postoperative morbidity rates are comparable between subtotal gastrectomy and total gastrectomy,[13] although postoperative quality of life is significantly better after subtotal gastrectomy.[14] Both studies

TABLE 2. Morbidities in the NCD Total Gastrectomy Population

Complications	Test Set (n = 16,036)	Validation Set (n = 3975)	Overall Incidence (N = 20,011)
Overall complications	4216 (26.3)	1033 (26.0)	5249 (26.2)
Grade II or higher*	2965 (18.5)	708 (17.8)	3668 (18.3)
Surgical complications			
Surgical site infection	1355 (8.4)	331 (8.3)	1686 (8.4)
Superficial incisional	503 (3.1)	128 (3.2)	631 (3.2)
Deep incisional	244 (1.5)	66 (1.7)	310 (1.5)
Organ space	1024 (6.4)	251 (6.3)	1275 (6.4)
Anastomotic leak	711 (4.4)	170 (4.3)	881 (4.4)
Pancreatic fistula (grade B, C)	419 (2.6)	110 (2.8)	529 (2.6)
Bile leak	81 (0.5)	15 (0.4)	96 (0.5)
Wound dehiscence	161 (1.0)	37 (0.9)	198 (1.0)
Nonsurgical complications			
Pneumonia	589 (3.7)	137 (3.4)	726 (3.6)
Unplanned intubation	282 (1.8)	57 (1.4)	339 (1.7)
Prolonged ventilation >48 h	308 (1.9)	70 (1.8)	378 (1.9)
Pulmonary embolism	25 (0.2)	3 (0.1)	28 (0.1)
Renal failure	213 (1.3)	46 (1.2)	259 (1.3)
CNS events	121 (0.8)	28 (0.7)	149 (0.7)
Cardiac events	90 (0.6)	23 (0.6)	113 (0.6)
Sepsis	138 (0.9)	24 (0.6)	162 (0.8)

The values given are number (percentage).
*Clavien-Dindo classification.
CNS indicates central nervous system.

TABLE 3. Outcome Rates in the NCD Total Gastrectomy Population

Outcomes	Test Set (n = 16,036)	Validation Set (n = 3975)	Overall Incidence (N = 20,011)
30-d mortality	153 (1.0)	34 (0.9)	187 (0.9)
In-hospital mortality	358 (2.2)	89 (2.2)	447 (2.2)
Operative mortality	367 (2.3)	90 (2.3)	457 (2.3)
Reoperation within 30 d	542 (3.4)	122 (3.1)	664 (3.3)
Readmission within 30 d	311 (1.9)	86 (2.2)	397 (2.0)

The values given are number (percentage).

TABLE 4. Risk Model of 30-Day Mortality

Variables	Status	Hazard Ratio	95% Confidence Interval
ASA score	Grade 4 or 5	9.383	4.85–18.152
Preoperative dialysis	Present	3.906	1.546–9.867
Platelet count	<50,000/μL	3.064	1.256–7.473
Total bilirubin	>2.0 mg/dL	2.919	1.189–7.17
Disseminated cancer	Present	2.641	1.603–4.35
Alkaline phosphatase	>600 IU/L	2.457	1.153–5.232
Previous cardiac surgery	Present	2.346	0.997–5.518
Aspartate aminotransferase	>35 IU/L	2.340	1.549–3.537
Diabetes	Insulin use	2.182	1.116–4.266
PT-INR	>1.25	2.182	1.318–3.613
Preoperative ADL	Any assistance	2.086	1.329–3.272
Ascites	Present	2.018	1.11–3.669
Preoperative transfusion	Present	1.936	1.208–3.102
Blood urea nitrogen	>25 mg/dL	1.886	1.201–2.961
Albumin	<3.5 g/dL	1.714	1.167–2.517
Alkaline phosphatase	>340	1.682	1.032–2.739
Hemoglobin	Male, <13.5 g/dL; female, <12.5 g/dL	1.659	1.03–2.675
Age category		1.194	1.067–1.337

Age category is defined as follows: category 1, <60 years; category 2, ≤60 to <65 years; category 3, ≤65 to <70 years; category 4, ≤70 to <75 years; category 5, ≤75 years.
ADL indicates activities of daily living; PT-INR, prothrombin time–international normalized ratio.

TABLE 5. Risk Model of Operative Mortality

Variables	Status	Hazard Ratio	95% Confidence Interval
ASA score	Grade 4 or 5	5.248	2.735–10.07
Disseminated cancer	Present	3.458	2.514–4.757
Alkaline phosphatase	>600 IU/L	3.116	1.812–5.356
Total bilirubin	>2.0 mg/dL	2.751	1.355–5.587
Preoperative dialysis	Present	2.583	1.146–5.819
Pancreaticosplenectomy	Present	2.219	1.177–4.185
White blood cell count	>11,000/μL	2.037	1.368–3.033
Preoperative ADL	Any assistance	2.015	1.469–2.764
PT-INR	>1.25	1.880	1.292–2.737
Cerebrovascular accident	Present	1.858	1.136–3.037
ASA score	Grade 3	1.819	1.37–2.417
Ascites	Present	1.752	1.133–2.71
Respiratory distress	Present	1.719	1.139–2.594
Aspartate aminotransferase	>35 IU/L	1.685	1.252–2.266
Status	Emergent	1.656	1.031–2.662
White blood cell count	<3500/μL	1.629	1.172–2.265
Weight loss	>10%	1.584	1.185–2.119
Sodium	<138 mEq/L	1.429	1.104–1.85
Albumin	<3.5 g/dL	1.411	1.045–1.905
Albumin	<3.0 g/dL	1.353	0.974–1.88
Hematocrit	<30%	1.339	1.025–1.75
Age category		1.294	1.199–1.396

Age category is defined as follows: category 1, <60 years; category 2, ≤60 to <65 years; category 3, ≤65 to <70 years; category 4, ≤70 to <75 years; category 5, ≤75 years.

ADL indicates activities of daily living; PT-INR, prothrombin time–international normalized ratio.

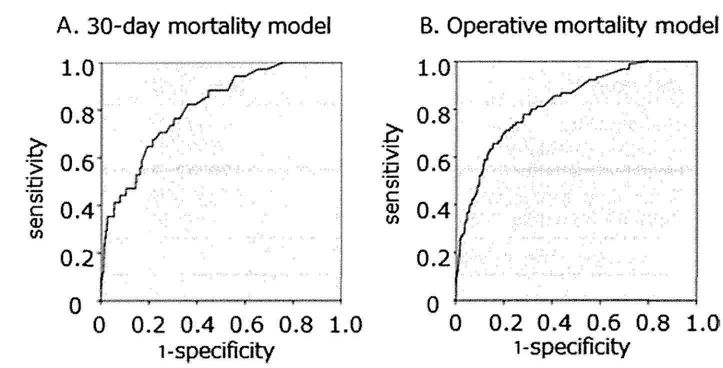

FIGURE 1. Receiver operating characteristic curves of each model. The C-index, a measure of model discrimination represented by the area under the receiver operating characteristic curve, was (A) 0.811 for 30-day mortality (95% CI, 0.744–0.879) and (B) 0.824 for overall operative mortality (95% CI, 0.781–0.866). CI indicates confidence interval.

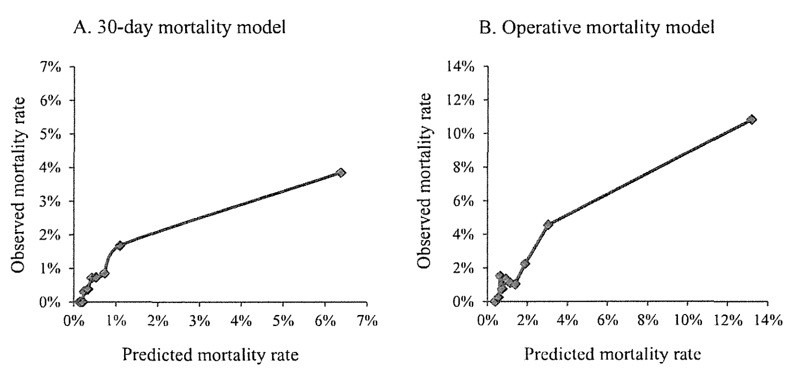

FIGURE 2. The calibration of (A) 30-day mortality model, and (B) operative mortality model.

report that mortality is similar between subtotal gastrectomy and total gastrectomy.[12,13] These results suggest that morbidity experienced after gastrectomy may depend on the extent of lymphadenectomy rather than the extent of gastrectomy. Several randomized controlled trials performed in Western countries have demonstrated that morbidity is significantly higher after D2 or greater lymphadenectomy than after D1 dissection.[15–17]

Although the operative outcomes for gastrectomy have been reported from several high-volume centers,[18] the nationwide outcomes in Japan remain unknown. The advent of the NCD enables the analysis of these nationwide outcomes for several operative procedures, including total gastrectomy. In addition, the database allows researchers to determine interinstitutional differences in the outcomes and factors affecting these differences. Most importantly, development of a risk model using this database is expected to contribute to improved quality control for several procedures.

In this study, we observed an overall morbidity of 26.2% in NCD patients undergoing total gastrectomy. Morbidity in the aforementioned randomized trials ranged from 16.8% to 28% in the D1 groups and 33% to 46% in the D2 or greater groups.[15–17] The 30-day mortality and overall postoperative mortality rates in the NCD total gastrectomy population were 0.9% and 2.3%, respectively. Mortality rates in the other trials ranged from 1.8% to 6.5% in the D1 groups and 3.7% to 13% in the D2 or greater groups. According to a recent report conducted by the Japanese Gastric Cancer Association using a nationwide registry, D2 lymph node dissection is performed in 49.2% of patients and extended D1 dissection is performed in 20.9% of patients whereas D0 or D1 lymphadenectomy is performed in 27.2% of patients.[18] When we consider the fact that such a high percentage of patients undergo D2 lymph node dissection at many institutions, the morbidity and mortality rates for total gastrectomy are satisfactorily low in Japan.

According to our risk models, the most important variable affecting both 30-day and overall operative mortality rates is the ASA score. The ASA classification is among the most commonly used scoring systems, although it is subjective and prone to interobserver variability.[19] The ASA grade has the advantages of simplicity and of universal use[20] and is known to be an effective risk indicator when used either alone[21] or in combination with other parameters.[22,23] Other factors affecting mortality can be divided into 2 groups, with the first group including factors related to patients' general condition such as the need for preoperative dialysis and laboratory test abnormalities and the second group including variables related to tumor extension such as the presence of disseminated cancer and ascites. It is reasonable to presume that a poor preoperative general condition correlates with postoperative mortality. As an example of the impact of the second group of variables, peritoneal dissemination is a progression pattern distinctive for gastric cancer; curative resection is usually impossible in this situation, and palliative resection is often performed for symptom relief. High morbidity and mortality rates have been reported for noncurative gastric cancer surgery.[24]

In our risk model, body mass index was not a significant factor affecting the mortality. Overweight is a well-known risk of postoperative complications after gastrectomy. Tsujinaka et al[25] investigated influence of overweight on surgical complications after gastrectomy using data from Japan Clinical Oncology Group study 9501, which explored survival benefit of para-aortic D3 dissection over standard D2 dissection. They revealed that being overweight increased the risk for surgical complications in patients who underwent D2 dissection.[25] Kulig et al[26] conducted a multicenter study to evaluate the effects of overweight on surgical outcomes in a Western patient population and demonstrated that higher body mass index was associated with a higher rate of cardiopulmonary complications and intra-abdominal abscess. Despite the increase in postoperative complications in overweight patients, obesity did not affect the mortality in both studies, as observed in this study.

Preoperative treatment may also affect the occurrence of mortality after total gastrectomy. In the European countries, perioperative chemotherapy is the standard treatment approach for patients with resectable gastroesophagel cancer.[27] In contrast, postoperative chemotherapy using S-1 is the standard therapy for patients with stage II/III gastric cancer in Japan.[28] Only 4.3% and 0.1% of the NCD total gastrectomy population underwent neoadjuvant chemotherapy and radiotherapy, respectively, and therefore neoadjuvant therapy was not a significant factor affecting the mortality.

The C-indices of the models for 30-day mortality and operative mortality indicate that our models are reliable. Although the usefulness of several scoring systems, such as the Physiological and Operative Severity Score for the enUmeration of Mortality and morbidity (POSSUM)[29] and the Estimation of Physiologic Ability and Surgical Stress (E-PASS),[30,31] in predicting the risks associated with gastrectomy has been reported, these systems are not specific to Japanese patients undergoing total gastrectomy. Using our risk model results, we may be able to create a novel scoring system suitable for total gastrectomy in Japanese patients.

It is unclear whether all total gastrectomy cases all over Japan are really enrolled in the NCD. Basically, the data manager in each participating hospital is responsible for the data enrollment. However, as the NCD is linked to the surgical board certification system, we assume that almost all cases are enrolled in this system. Indeed, the number of cases in this study is almost 5 times higher than that of the nationwide registry maintained by the Japan Gastric Cancer Association.[18]

CONCLUSIONS

We have reported the first risk stratification study on total gastrectomy in Japan by using a nationwide Internet-based database. The nationwide mortality rates after total gastrectomy are quite satisfactory. We have developed risk models for total gastrectomy that will contribute to improving the quality of this procedure.

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REVIEW ARTICLE

Cancer registries in Japan: National Clinical Database and site-specific cancer registries

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Abstract The cancer registry is an essential part of any rational program of evidence-based cancer control. The cancer control program is required to strategize in a systematic and impartial manner and efficiently utilize limited resources. In Japan, the National Clinical Database (NCD) was launched in 2010. It is a nationwide prospective registry linked to various types of board certification systems regarding surgery. The NCD is a nationally validated database using web-based data collection software; it is risk adjusted and outcome based to improve the quality of surgical care. The NCD generalizes site-specific cancer registries by taking advantage of their excellent organizing ability. Some site-specific cancer registries, including pancreatic, breast, and liver cancer registries have already been combined with the NCD. Cooperation between the NCD and site-specific cancer registries can establish a valuable platform to develop a cancer care plan in Japan. Furthermore, the prognosis information of cancer patients arranged using population-based and hospital-based cancer registries can help in efficient data accumulation on the NCD. International collaboration between Japan and the USA has recently started and is expected to provide global benchmarking and to allow a valuable comparison of cancer treatment practices between countries using nationwide cancer registries in the future. Clinical research and evidence-based policy recommendation based on accurate data from the nationwide database may positively impact the public.

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Keywords Cancer registry · Nationwide database · Risk factor · Risk model

Introduction

The cancer registry is an essential part of any rational program of evidence-based cancer control [1, 2]. This information can be used to monitor cancer patterns in certain regions and to formulate an effective cancer control plan [2]. In Japan, the government started promoting and supporting a cancer control plan based on the Cancer Control Act of 2006. Cancer registries in Japan are classified into three types—population-based, hospital-based, and site-specific cancer registries. Each registry plays an important role in the epidemiology, evaluation of patient care quality, and in providing clinically detailed information (Table 1); however, all three types have problems with poor standardization or incomplete follow-up [2].

The cancer control program is required to strategize in a systematic and impartial manner and efficiently utilize limited resources. The National Clinical Database (NCD) in Japan, which was launched in 2010 and commenced patient registration in January 2011, is a nationwide prospective registry linked to the surgical board certification system. The NCD systematically collects accurate data to develop a standardized surgery database for quality improvement and healthcare quality evaluation, considering the structure, process, and outcome [3]. Moreover, submitting cases to the NCD is a prerequisite for all member institutions of the surgical society, and only registered cases can be used for board certification. The NCD contains >1,200,000 surgical

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Table 1 Types of cancer registries in Japan

	Organization	Primary purpose	End point	
				Epidemiological
Population-based cancer registries	Prefecture	Cancer surveillance at population level	Morbidity rate Survival rate	↑
Hospital-based cancer registries	Hospital	Evaluation of cancer care quality	Survival rate	↕
Site-specific cancer registries	Academic society	Collecting in-depth information	Survival rate	↓
				Clinical

cases collected in 2011, and approximately 4,000 institutions were participating at the end of 2013. Detailed information on cancer, such as gastrointestinal, liver, pancreas, thyroid, and breast cancer is also collected in the NCD. The NCD generalizes site-specific cancer registries by taking advantage of their excellent organizing ability [4]. Some site-specific cancer registries, including pancreatic, breast, and liver cancer registries have already been combined with the NCD. Furthermore, it has also been promoted to cooperate with non-surgical fields.

Here, we summarize the current status of the NCD and site-specific cancer registries in conjunction with future perspectives for developing a cancer registration system.

Current status of the NCD

There was no nationwide clinical database for gastroenterological surgery for cancer treatment in Japan before 2006. The Japanese Society of Gastroenterological Surgery organized preliminary nationwide surveys in gastroenterological surgery in 2006 and 2007. These surveys, without using risk-adjustment techniques, indicated that hospital volume may influence the mortality rate after major gastroenterological surgery [5]. However, it was considered that upgraded analysis using risk-adjustment techniques should have been conducted to reveal the specific contribution of the variables. The NCD was established in 2010 as a general incorporated association in partnership with several clinical societies. The activities of the NCD primarily focus on providing the highest quality healthcare possible to patients and to the general public with the clinical setting serving as the driving force behind improvements [3, 4]. The NCD was developed in collaboration with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP). The ACS-NSQIP is the first nationally validated database using web-based data collection software. It is risk adjusted and outcome based to improve the quality of surgical care [6]. Development of the NCD allows risk-adjusted analysis in Japan.

The NCD continuously recruits individuals to approve the input data from members of several 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 inspecting randomly chosen institutions. All variables, definitions, and inclusion criteria regarding the NCD are accessible to all the participating institutions from the website (http://www.ncd.or.jp/) and are also intended to support an e-learning system in order for participants to input consistent data. The NCD also provides answers to all queries regarding data entry (approximately 80,000 inquiries in 2011) and regularly includes some of the queries as frequently asked questions on the website.

In the gastrointestinal surgery section, all surgical cases are registered and require detailed input items for eight procedures representing the performance of surgery in each specialty (low anterior resection, right hemicolectomy, hepatectomy, total gastrectomy, partial gastrectomy, pancreatoduodenectomy, esophagectomy, and surgery for acute diffuse peritonitis). Risk models for predicting surgical outcome have been created for the mortality of each procedure [7–13]. A total of 120,000 cases collected from the eight procedures in 2011 were then analyzed in each procedure. Data were randomly assigned into two subsets that were split as follows—80 % for model development and 20 % for validation. The two sets of logistic models (30-day mortality and operative mortality) were constructed for dataset development using a step-wise selection of predictors. Potential independent variables included patient demographics, pre-existing comorbidities, preoperative laboratory values, and operative data. Furthermore, multiple significant risk factors were identified in each procedure—age, American Society of Anesthesiologists class, respiratory distress, body mass index, platelet count, Brinkman index, etc. As a performance parameter of the risk model, the C-indices of the 30-day and operative mortality calculated from all models were >0.7; in particular, the indices of total gastrectomy [11], right hemicolectomy [9], and surgery for acute diffuse peritonitis [13] were >0.8, suggesting that the area under the receiver operating characteristics curves results were good. This is considered as proof of the efficacy and reliability of these risk models. These models could be available for participating institutes and would be useful for benchmark performance and decision making by surgeons as well as informed consent for patients. The NCD is currently planning to provide feedback on severity-adjusted clinical performance through a web-based program. Real-time feedback through the web provides an opportunity to observe changes within facilities and shifts in clinical performance [3].

The benefits of the NCD for patients include their ability to receive high-quality healthcare through the improvement of the medical service—fewer complications, shorter hospital stay, and better outcomes. Patients can also select hospitals that suit their preferences by choosing among board-certified surgeons in a relevant field. The benefits for surgeons who use the NCD include receiving better data for more targeted decision-making and disciplined reports that provide performance information useful for surgery and the ability to identify one's position among peers to allow strategic planning.

Current activities of site-specific cancer registries

The site-specific cancer registries in Japan are conducted by academic societies or research organizations specializing in cancers of different origin. Many institutes nationwide are included and collect detailed clinical information based on the general rules of the Japanese classification of cancer [2]. The first site-specific cancer registry was launched in 1952 to collect data about gynecological cancer. In the field of gastroenterological surgery, gastric cancer (1963), esophageal cancer (1965), and hepatic cancer (1965) registries were launched as pioneers in developing site-specific cancer registries; colorectal, pancreatic, and biliary cancer registries were established in the 1980s. Each registry has released the original investigation report based on the specificity of each site. In the Japan pancreatic cancer registry, >350 leading institutions voluntarily contributed their information and periodic follow-up. Several reports on the overall survival and prognostic factors of pancreatic cancer in Japan have been published. A continuous survey on pancreatic cancer could indicate that the improvement of the survival of patients with invasive cancer can be attributed to the introduction of effective chemotherapies, regionalization, and earlier diagnosis and treatment [14–16]. For instance, the Japanese Society for Cancer of the Colon and Rectum (JSCCR), a nationwide database, covers approximately 10 % of all patients with colorectal cancer in Japan [17]. The JSCCR provided important information in establishing general rules for the Japanese classification of colorectal cancer and published clinical guidelines for the treatment of colorectal cancer. It has been evaluated that the publication of the guidelines has accelerated the spread of surgical standards [18]. As described, site-specific cancer registries, which register in-depth information in contrast to population-based and hospital-based cancer registries, have played a major role in the development of the cancer treatment program.

In contrast, there are several limitations to site-specific cancer registries. First, incomplete follow-up data is a serious issue; the data collection system at the institute needs to be improved. Second, management infrastructure systems are unstable as a whole in site-specific cancer registries. Third, inadequate standardization in the registration procedure is present in these registries. Furthermore, the registration forms of each registry and even the basic parameters for cancer registration are different. As a whole, in site-specific cancer registries, the databases have a lower cover rate (number of registration/estimated morbidity) that is not a complete enumeration.

Cooperation with the NCD and site-specific cancer registries

In order to solve several problems with site-specific cancer registries, it has been planned that the NCD generalizes site-specific cancer registries. Approximately 610,000 surgical cases were registered in the NCD in one year, including approximately 220,000 cases for the treatment of malignant tumors. The cover rate (number of registration/estimated morbidity) of the NCD is higher than that of site-specific cancer registries and glanularity is higher compared with that of other registries (Fig. 1). Breast cancer registration of the Japanese Breast Cancer Society was combined with the NCD in 2012. The Japan pancreatic cancer registry was also combined with the NCD in 2012. In addition, the liver cancer study group of Japan has just transferred its registration system into the NCD. Information required for the Japanese lung cancer registry is now mostly input into the NCD. At present, the NCD not only has the role of being a surgical database but also of being a database for several cancer registries. With cooperation between the NCD and high-precision site-specific cancer registries, it should be possible to build the basic framework to evaluate healthcare quality in the cancer control plan. Moreover, by assessing the performance of board-certified physicians for cancer treatment according to a guideline, it would be possible to identify the strategy towards the standardization of cancer treatment in Japan.

To assure the success of this cooperation, several issues should be solved. Data should be appropriately collected and should follow an exact baseline assessment. In particular, exhaustive and reliable information and a follow-up survey of a long-term prognosis are indispensable for the survival rate of cancer patients. The lack of long-term prognosis information has been an issue in site-specific cancer registries. The deviation of a participating institution and a registration case and the defect of a follow-up survey serve as bias; therefore, their influence on the interpretation of a result represents a major problem. The collection of the prognosis information in the NCD could allow the evaluation of a short-term prognosis on the basis of a 30-day postoperative outcome. A follow-up survey at 1, 5, and 10 years, based on the clinical feature of each cancer will be designed in the near future. The data quality and compatibility of the NCD are also continuously verified.

In contrast, several cancer registries and case registration systems are processed in parallel for a follow-up survey of cancer prognosis. Furthermore, the efficiency of data collection is also an important issue. Cooperation with the NCD and other cancer registries is essential to avoid inaccurate follow-up data. The government has started promoting and supporting the cancer registration plan based on the Cancer Registration Act of 2013. With this promotion and mandatory feedback to each department, prognosis information of cancer patients arranged by population- and hospital-based cancer registries can help in efficient data accumulation for the NCD. Fig. 2 shows the cooperation and integration of cancer registration systems.

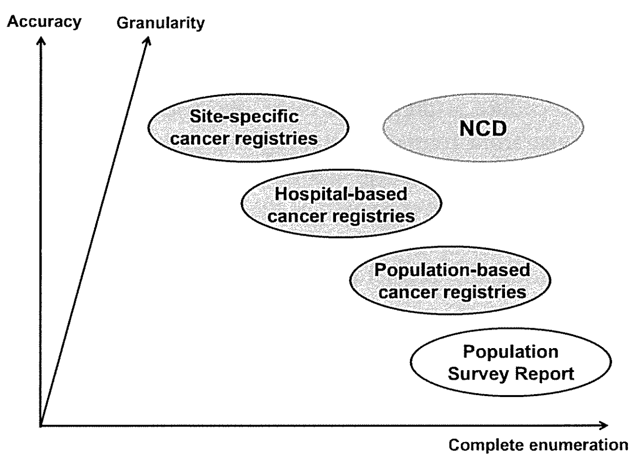
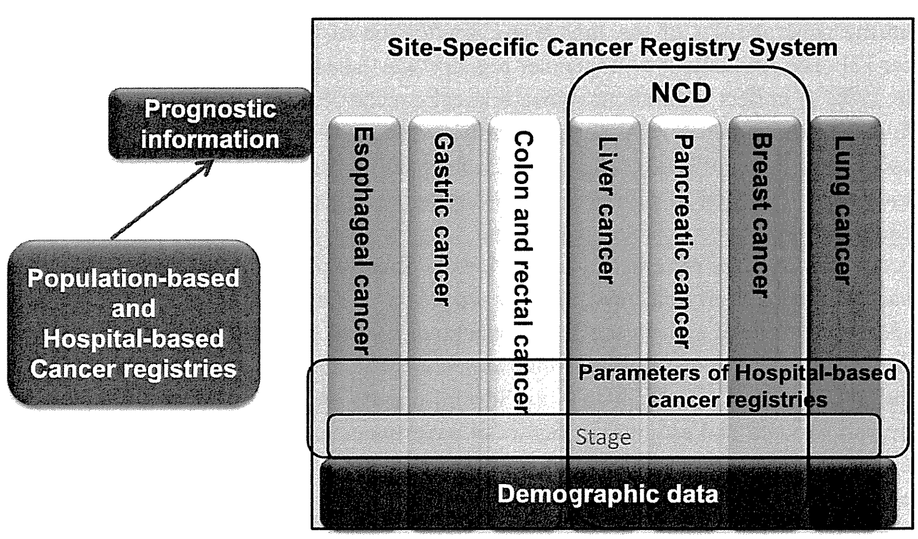


Fig. 1 Characteristics of cancer registries. Granularity and degree of complete enumeration are different among registries

Future direction of the NCD and site-specific cancer registries

The coordination of a nationwide and advanced cancer registry, such as the combination between the NCD and site-specific cancer registry could positively impact society through their activities. In order to accomplish the same, the NCD needs to make progress by continuously evaluating this database. As mentioned above, the NCD is now planning to give feedback based on a rich store of clinical data. Similarly, in the cardiac surgery field, a web-based program provides feedback on severity-adjusted clinical performance [19]. The report is prepared by highlighting the patient characteristics. By utilizing the risk model, users would be able to predict the estimated mortality through entering the system on the web. ‘Surgical Risk Calculator’ developed by ACS-NSQIP

Fig. 2 Cooperation and integration of cancer registration systems. The prognostic information arranged by population-based and hospital based cancer registries are returned to the hospital which offered information. The information is then reflected through each hospital to the NCD and site-specific cancer registries



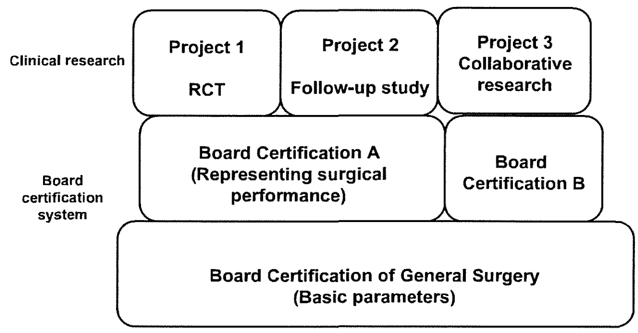


Fig. 3 Utilization possibilities for the NCD. The basic society (Japan Surgical Society) supports the basic case registration system for board certification in the NCD. It is also constituted by an individual clinical research project representing each specialized society

(http://riskcalculator.facs.org/) is a similar feedback system. Furthermore, real-time and useful feedback is essential in developing a large-scale database. For instance, ACS-NSQIP indicates that surgical outcomes improve in participating hospitals; 66 % of hospitals showed improved risk-adjusted mortality and 82 % showed improved risk-adjusted complication rates. NSQIP hospitals appear to be avoiding substantial numbers of complications, improving care, and reducing costs [20]. The NCD is a platform of databases which would allow collaboration among institutes in Japan to provide an opportunity for clinical research based on a large-scale database and to produce novel evidence (Fig. 3).

International collaboration is important to evaluate the quality of medical care and to provide meaningful improvement. However, international comparisons of general surgery and outcomes using nationwide clinical registry data have not been accomplished. There is little information on the outcomes of Japanese patients undergoing gastroenterological surgery and its comparison with those of other countries. Furthermore, the application of predictive models for clinical risk stratification has not been internationally evaluated. The NCD in Japan collaborates with the ACS-NSQIP, which shares a similar goal of developing a standardized surgery database for quality improvement. The NCD implemented the same variables used by the ACS-NSQIP to facilitate international cooperative studies, which have recently started [21]. This collaboration is expected to provide a global benchmark and to evaluate and improve clinical care by comparing the treatment practices among countries using nationwide cancer registries.

Conclusions

Cooperation between the NCD and site-specific cancer registries can establish a valuable platform to develop a cancer care plan in Japan. Studies are in progress to improve the quality control of surgical procedures using the NCD. Furthermore, clinical research and evidence-based policy recommendations from accurate data of a nationwide database may positively impact the public.

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Conflict of interest The authors declare that they have no conflict of interest.

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