Propensity score matching in younger (<60 years of age) and older (≥60 years of age) patients

There were significant differences between the RT and MS groups in regard to the operative, cardiopulmonary bypass, and aortic cross-clamp times regardless of being divided into younger (<60 years of age) and older (≥60 years of age) age groups (Table 3). On the other hand, there was no significant difference in regard to the incidence of reexploration for bleeding between the two groups when only younger patients were analyzed, whereas reexploration for bleeding occurred significantly more often in the RT group

Table 3 Postoperative outcomes of the propensity score matching analysis in younger (<60 years of age) and older (≥60 years of age) patients

	Younger cohort			Older cohort		
	RT group ($n = 425$)	MS group ($n = 443$)	p value	RT group ($n = 325$)	MS group ($n = 307$)	p value
Operation time (min)	324 ± 86	277 ± 74	<0.01	307 ± 82	266 ± 67	<0.01
CPB time (min)	199 ± 68	144 ± 49	<0.01	179 ± 58	137 ± 43	<0.01
Cross-clamp time (min)	138 ± 51	104 ± 38	<0.01	122 ± 44	98 ± 32	<0.01
30-day mortality	0	0	NS	2 (0.6 %)	0	NS
In-hospital mortality	0	0	NS	4 (1.2 %)	2 (0.7 %)	NS
Reoperation for bleeding	7 (1.6 %)	6 (1.4 %)	NS	15 (4.6 %)	3 (1.0 %)	<0.01
Cardiac tamponade	1 (0.2 %)	3 (0.7 %)	NS	2 (0.6 %)	4 (1.3 %)	NS
Stroke	2 (0.5 %)	3 (0.7 %)	NS	4 (1.2 %)	3 (1.0 %)	NS
Deep sternal infection	0	1 (0.2 %)	NS	0	1 (0.2 %)	NS
Other infection	2 (0.5 %)	0	NS	1 (0.3 %)	0	NS
Sepsis	0	1 (0.2 %)	NS	1 (0.3 %)	1 (0.3 %)	NS
Prolonged ventilation	9 (2.1 %)	4 (0.9 %)	NS	11 (3.4 %)	6 (2.0 %)	NS
Renal failure	4 (0.9 %)	3 (0.7 %)	NS	4 (1.2 %)	8 (2.6 %)	NS
New onset of AF	50 (11.8 %)	62 (14.0 %)	NS	76 (23.4 %)	77 (25.1 %)	NS
ICU stay	1.9 ± 2.0	2.3 ± 1.8	<0.01	2.6 ± 6.4	2.6 ± 1.9	NS
Time to discharge	13 ± 8	16 ± 8	<0.01	16 ± 14	18 ± 10	<0.01

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

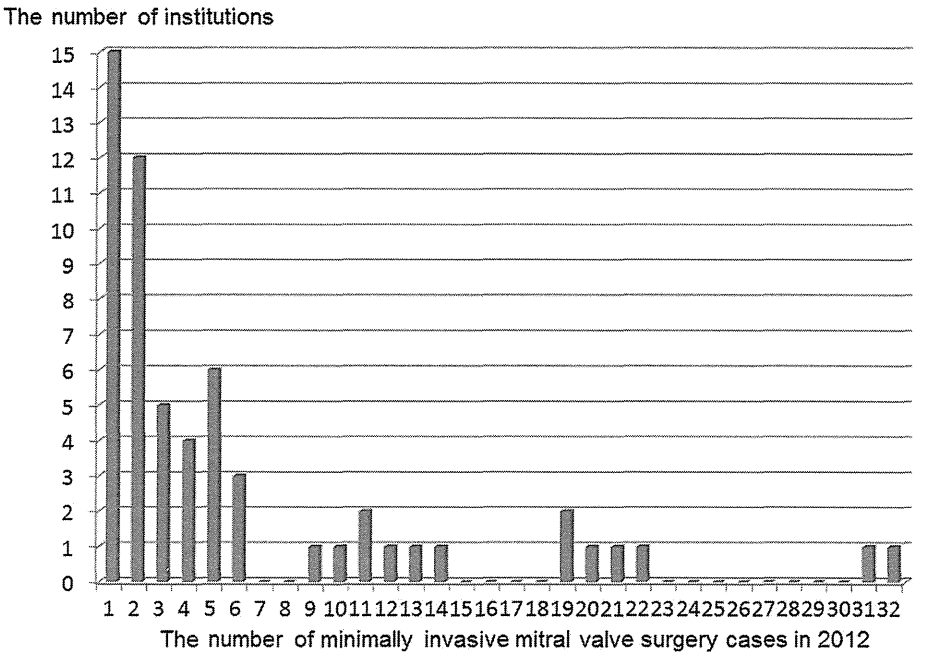

Fig. 2 Distribution of the number of MICS-mitral cases. Many low-volume institutions performed fewer than 10 cases per year

Table 4 Postoperative outcomes of MICS-mitral patients between high- (≥10 cases per year) and low- (<10 cases per year) volume institutions

	High-volume ($n = 497$, 13 institutions)	Low-volume ($n = 259$, 46 institutions)	p value
Operation time	309 ± 80	329 ± 91	<0.01
CPB time (min)	197 ± 67	176 ± 58	<0.01
Cross-clamp time (min)	136 ± 51	122 ± 42	<0.01
Transfusion	160 (32 %)	107 (41 %)	<0.05
30-day mortality	0	2 (0.8 %)	NS
In-hospital mortality	0	4 (1.5 %)	<0.05
Reoperation for bleeding	10 (2 %)	12 (5 %)	NS
Cardiac tamponade	1 (0.2 %)	2 (0.8 %)	NS
Stroke	4 (0.8 %)	2 (0.8 %)	NS
Deep sternal infection	0	0	NS
Other infection	1 (0.2 %)	2 (0.8 %)	NS
Sepsis	0	1 (0.4 %)	NS
Prolonged ventilation	3 (0.6 %)	17 (6.6 %)	<0.01
Renal failure	2 (0.4 %)	6 (2.3 %)	<0.05
New onset of AF	84 (17 %)	42 (16 %)	NS
PMI	4 (0.8 %)	2 (0.8 %)	NS
ICU stay	1.5 ± 1.1	3.5 ± 7.3	<0.01
Time to discharge	13 ± 10	17 ± 13	<0.01

AF atrial fibrillation, *CPB* cardiopulmonary bypass, *ICU* intensive care unit, *PMI* perioperative myocardial infarction

when only older patients were included in the analysis. No mortality occurred in the younger patients in the RT group, and the ICU length of stay and days to discharge were also shorter for younger patients in the RT group.

Hospital volume and outcomes of MICS-mitral

The distribution of MICS-mitral cases is shown in Fig. 2. A comparison of the outcomes between the low-volume (<10 cases/year, 46 institutions) and high-volume (≥10 cases/year, 13 institutions) institutions revealed significant differences in regard to the postoperative complications (Table 4). While there were no deaths in the high-volume group, the 30-day and in-hospital mortality rates in the low-volume group were 0.8 and 1.5 %, respectively. The incidence of reexploration for bleeding was also more frequent in the low-volume group. Furthermore, the operative time, cardiopulmonary bypass time, aortic cross-clamping time, postoperative ventilation time, length of ICU stay, and days to discharge were significantly shorter in the high-volume group.

Discussion

The advantage of MICS-mitral has been highlighted in recent years. Several meta-analyses revealed lower rates of reoperation for postoperative hemorrhage, as well as a trend toward a decreased hospital length of stay, reduced postoperative bleeding, faster times to extubation, less pain, and a more swift return to regular activity [20, 21]. On the other hand, another review noted that minimally invasive mitral valve surgery was not without risk, as the rates of stroke (2.1 vs. 1.2 %), aortic dissection (0.2 vs. 0 %), groin complications (2 vs. 0 %), and phrenic nerve palsy (3 vs. 0 %) were significantly increased [22].

Although several comparative studies have previously been conducted to compare MICS-mitral and conventional median sternotomy procedures, only a few propensity-matched comparisons of the two techniques have been conducted [16–18], which showed similarly excellent outcomes for both types of operations, with no apparent disadvantages of the MICS-mitral approach. However, those reports were from a single institution and data from a propensity-matched analysis based on a multicenter analysis are scarce. To overcome selection bias, it is important to evaluate the results of MICS-mitral in a multicenter cohort. The study population was derived from a national database that includes all cardiovascular surgical institutions in Japan and the results reflect real-world data obtained from Japanese patients. As a result, we consider that the findings of our study provide useful information regarding MICS-mitral procedures and can help to determine the appropriate indication.

Mortality

The present findings demonstrate an excellent surgical outcome for isolated mitral valve repair. In Japan, the 30-day

and in-hospital mortality rates following such a procedure are similar to those in Western countries and better in younger patients, as no deaths occurred in our MICS-mitral patients younger than 60 years of age. We found several factors for treatment allocation bias in regard to the preoperative condition, indicating that patient selection for the MICS-mitral procedure was well conducted. We considered the overall better outcomes as compared to previously reported results. In essence, the reason for the excellent results achieved by Japanese cardiac surgeons appears to be multifactorial [23]. Although previous studies also showed excellent results with a low 30-day mortality rate of approximately 1.0 % [9, 18, 24], those results were from single institutions. The present results were obtained from multiple centers throughout Japan and show the safety of MICS-mitral for patients with isolated mitral valve regurgitation.

Perioperative outcomes

There are several concerns regarding the widespread adoption of MICS-mitral surgery, mainly in regard to the perioperative outcomes. Prolonged cardiopulmonary bypass and ischemic times are one of the major issues related to MICS-mitral. As also shown in previous studies [16, 25], the present findings revealed a nearly 30-min longer operation-related time. Another concern is the rate of reexploration for bleeding, which was more frequent in the MICS-mitral patients. Because the ratio of cardiac tamponade was higher in the MS group, this suggests that most of the bleeding incidents occurred in the chest cavity. A third concern is postoperative stroke. Previous reports showed that the risk of stroke was significantly increased for RT as compared with MS [22, 25]. Furthermore, two different propensity comparison studies showed a significant increase in stroke in association with a minimally invasive procedure as compared with a conventional median sternotomy approach (1.9 vs. 0.9 %) [16, 17]. On the other hand, several reports found no difference in stroke between these two groups [9, 24]. The present results also failed to show a significant difference between the RT and MS groups, which may have been due to the low overall incidence of stroke in both groups. Nevertheless, stroke is not a concern related to MICS-mitral in Japan. We also found no significant differences in postoperative renal failure, insufficiency pneumonia, pleural effusion, pneumothorax, pneumonia, or overall pulmonary complications between the RT and MS groups.

The main advantages of this approach are related to the reduced rate of transfusion [18, 26, 27], fewer severe infections [22], and shorter length of ICU or hospital stay [18, 25, 27]. Our findings from the overall matched analysis support a lower rate of mediastinitis and shorter ICU or in-hospital stay, although there was no significant difference in the rate of transfusion between the groups. None of the patients who underwent MICS-mitral experienced postoperative mediastinitis, which is considered to be one of the most important advantages of the procedure. Although the ICU length of stay was significantly shorter in the RT group, there was also significant heterogeneity for this outcome.

Age and postoperative outcomes of MICS

There are few data available to discuss the effect of age in regard to MICS-mitral, thus the present results are interesting. Our propensity-matched analysis of the younger age group (<60 years of age) revealed no mortality in the RT group in this younger cohort, although the operative, cardiopulmonary bypass, and aortic cross-clamping times remained longer in the RT group, whereas the incidence of reexploration for bleeding was similar between the two groups. There were no disadvantages regarding postoperative complications in the RT group and all disadvantages of MICS-mitral were observed in older patients (≥60 years of age). Most previous studies found that older age was not a contraindication for the MICS-mitral approach in regard to mortality and morbidity, which are consistent with our results [16, 22, 28]. However, an important finding in our study is that a higher rate for reexploration for bleeding was only seen in older patients. We speculated that the reason for a higher incidence of reexploration for bleeding in the older cohort was due to tissue fragility in the thoracic cavity. Therefore, MICS-mitral can be safely used, especially in younger cases.

Effects of hospital volume

Most previous papers that reported excellent outcomes for MICS-mitral were from institutions with a large number of patients [8, 9, 16, 18]. The volume of operations performed is generally considered to affect the operative results in cardiac surgery [23]. However, several institutions that perform this procedure have a relatively small number of MICS-mitral patients. The learning curve is also considered to have effects on various factors related to minimally invasive cardiac surgery in previous reports [8, 29]. Therefore, it is important to examine the effects of hospital volume on the outcomes of the procedure. Our results revealed that hospital volume correlated with both operative mortality and morbidity. In addition, we found longer CPB and cross-clamp times in the high-volume group, which may be related to the higher incidence of complex mitral valve repair in those patients. However, despite those longer time periods, the operative time was shorter in that group. This may have been due to shorter set-up and chest closing times

because the surgeons and staff in the high-volume group had much experience in performing MICS-mitral repair procedures via right mini-thoracotomy. Because the MICS-mitral operation requires special settings and instruments, it remains unknown whether the potential benefits, such as reduced respiratory support and lower risk of wound infections, outweigh the potential drawbacks of an initially higher complication rate. Considering our results showed an apparent relationship between the hospital volume and outcome, it may be necessary to consider the effects of hospital volume and adjust the number of institutions performing MICS-mitral procedures. As previous reports have noted, a clear tendency for better results was observed if the surgeon performed MICS-mitral at least twice per week [8], thus it may be better for this procedure to be restricted to high-volume centers with a relatively large and stable number of mitral valve operations. We will continue to investigate this issue because there are many MICS-mitral training programs and the opportunities to become exposed to the procedure as a resident are increasing. In addition, careful patient selection should be implemented during the initial phase of the program, especially in low-volume institutions.

Study limitations

There are several limitations associated with the present study, including its retrospective design. Our investigation was primarily focused on detailed, short-term outcomes and did not include any long-term results because the data used were an accumulation of the clinical results from 210 cardiac surgical units located throughout Japan. Thus far, 100 % data submission to the JACVSD under third-party surveillance has only been achieved for short-term results. In addition, patients selected for minimally invasive mitral surgery tend to be less sick, have fewer comorbidities, and are often earlier in the course of disease. Although propensity score matching helps account for such bias, it selects patients with intermediate risk because patients on either end of the probability spectrum are typically unmatchable. To the best of our knowledge, this is one of the largest propensity score-matched comparisons of mitral valve repair via right mini-thoracotomy and conventional sternotomy to date. Nevertheless, because the study population was derived from a single reference health system, external validity is partially limited at the expense of enhancing internal validity. Moreover, the data reported cannot be construed to be equivalent to those obtained from a large randomized controlled trial, which may not be ethically feasible.

Furthermore, important data are lacking, including factors related to the quality of mitral valve repair, such as the incidence of conversion from mini-thoracotomy to full sternotomy and from mitral reconstruction to replacement with a prosthesis, as well as detailed echocardiographic data and long-term outcomes. These are major limitations in this large national database. Those limitations are important since the minimally invasive approach may potentially compromise the quality of valve repair, especially when it is performed by less-experienced surgeons. Unfortunately, the JCVSD does not include factors related to the conversion rate, detailed echocardiographic data, or long-term results, thus it is impossible to evaluate these factors. However, the JCVSD includes all cardiovascular surgical institutions in Japan and the results reflect real-world data obtained from Japanese patients. As a result, we believe that the shortcomings of the data are outweighed by the nature of the national database, which presents current surgical results of mitral valve surgery procedures performed in Japan and includes data from top-rated institutions as well as those with lower surgical volumes.

In conclusion, MICS-mitral procedures via RT were successfully performed without compromising the clinical outcomes. Although the procedure time and incidence of postoperative bleeding should be improved, a right mini-thoracotomy approach can be safely used in appropriately selected patients, especially those younger than 60 years of age, and when performed in high-volume institutions. Although the recent statement from the International Society of Minimally Invasive Coronary Surgery assigned a class IIb recommendation for minimally invasive surgery for mitral valve disease [30], this comprehensive multicenter analysis can provide variable information for an appropriate indication for MICS-mitral and may influence future applications of this procedure.

Conflict of interest None.

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Real-World Use and Appropriateness of Coronary Interventions for Chronic Total Occlusion (from a Japanese Multicenter Registry)

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Little is known about the outcomes and indications of chronic total occlusion percutaneous coronary intervention (CTO-PCI), other than in high-volume centers. We sought to provide a real-world overview of the clinical outcomes and appropriateness of PCI for CTO. The analysis included 4,950 consecutive PCIs for nonacute indications registered in the multicenter Japanese PCI registry in collaboration with the US National Cardiovascular Data Registry (Cath-PCI). Data included demographics, clinical outcomes (procedural success and complication rates), and the indication appropriateness, based on the 2012 appropriate use criteria for revascularization. The overall procedural success and major adverse cardiac event rates of 501 cases with CTO-PCI (10.1%) were 76% and 3.2%, respectively. Based on the criteria, mapping failures occurred in 2,521 procedures; the remaining 2,429 PCIs were successfully mapped. The CTO-PCIs were performed for more appropriate indications than PCIs for lesions without CTO. The rate of inappropriate indications was significantly lower in CTO-PCIs than in non–CTO-PCIs (23.0% vs 31.4%, p = 0.04). Only 17% of CTO-PCIs were directly assigned to CTO-specific scenarios because such scenarios are only intended for "Lone" CTO; the rest of the CTO-PCI cases were secondarily mapped to non-CTO–specific scenarios. In conclusion, as many as 10% of the elective PCIs were performed for CTO lesions in a contemporary multicenter Japanese PCI registry; CTO-PCI was associated with lower procedural success and higher complication rates than non–CTO-PCI. Its indication was relatively appropriate; however, our findings emphasize the need for more rigorous evaluation in terms of the present insufficient CTO-related clinical scenarios. © 2015 Elsevier Inc. All rights reserved. **(Am J Cardiol 2015;116:858–864)**

The prevalence of chronic total occlusion (CTO), a coronary lesion that is completely occluded for >3 months, is reportedly 18% to 52% in large registries.[1–3] Despite the development of novel equipment and techniques, percutaneous coronary intervention (PCI) for lesions with CTO is technically challenging and often referred to as "the last frontier" for interventional cardiologists; favorable success rates of CTO-PCIs ranging from 82.9% to 87.9% have been previously reported on the basis of data from high-volume centers or operators.[4–8] However, real-world data and outcomes of contemporary CTO-PCIs in institutes other than high-volume centers have been limited[9]; despite the benefits associated with successful CTO-PCIs, it has been performed relatively infrequently in average-sized centers, mostly because of historically low success rates and fear of procedure-related complications. Therefore, an understanding of the patients' backgrounds and complication rates is needed for the real-world implementation of CTO-PCIs. Furthermore, the appropriateness of CTO-PCI has not been investigated using internationally derived criteria. Appropriate use criteria (AUC) for revascularization was recently developed by the American College of Cardiology Foundation and 5 other societies in response to increasing momentum toward compliance with appropriate procedural indications.[10,11] These AUC have been applied to various registries, the results of which indicate a strong possibility of PCI overuse in real-world practice.[12–15] The indications for PCI should be rigorously considered, particularly when used for CTO, given the relatively high incidence of complications (1.8% to 3.1%) and risk of exposure to contrast media or radiation.[4,5,7,16] The purpose of the present study was to clarify the outcomes of CTO-PCIs in real-world practice in Japan and to evaluate the appropriateness of PCI indications

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See page 863 for disclosure information.

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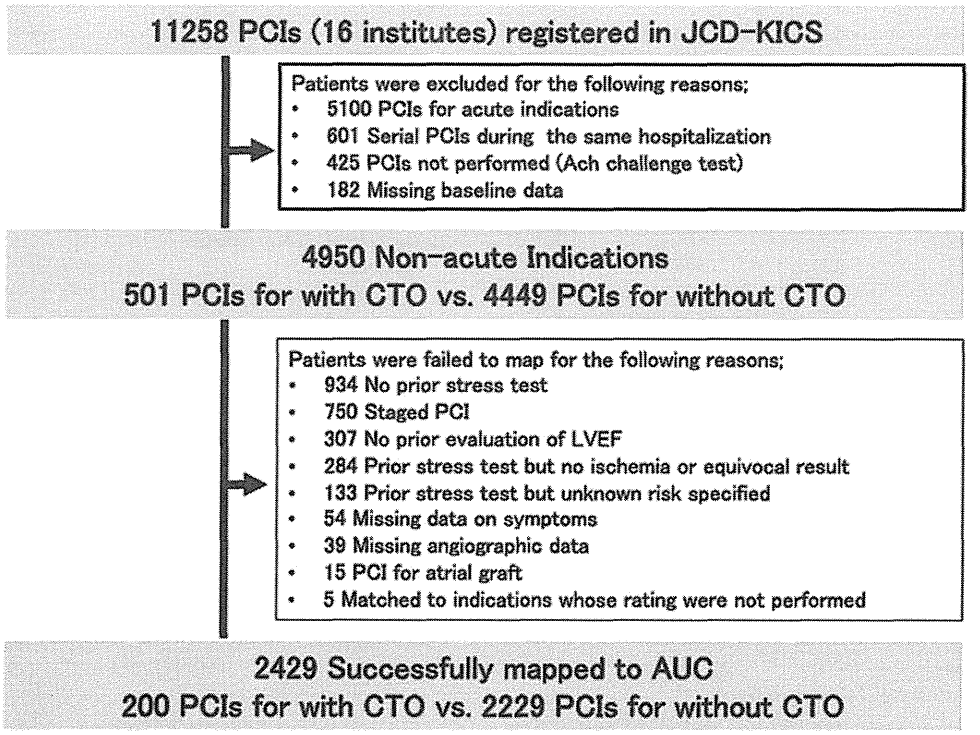

Figure 1. Flowchart of the process to identify the cohort of patients who underwent PCI procedures for nonacute indications. Ach = acetylcholine; LVEF = left ventricular ejection fraction.

based on the US AUC in an effort to identify the gap between demographic and outcome information between CTO-PCIs performed in high-volume and average-sized centers and to determine whether registered CTO-PCI procedures are considered appropriate under validated standards and, conversely, whether the provided scenarios in these standards adequately cover "real-world" PCI cases.

Methods

Data were obtained from the Japan Cardiovascular Database Keio Inter-hospital Cardiovascular Studies (JCD-KICS) PCI registry, which is a prospective, multicenter registry designed to collect clinical variables and outcome data on consecutive patients with PCI, with dedicated clinical research coordinators assigned to each site.[15,17] In this registry, 16 teaching hospitals within the metropolitan Tokyo area participated in and registered all PCI procedures performed during the study period, including failure cases, using an Internet-based interface. The annual average number of PCIs for each institution was 153. Approximately, 200 variables were collected for each patient; clinical variables and inhospital outcomes in the JCD-KICS were defined in accordance with the National Cardiovascular Data Registry (NCDR) version 4.1.[18,19]

The data were checked for completeness and internal consistency. Quality assurance was achieved through automatic system validation and reporting of data completeness and through education and training for dedicated clinical research coordinators specifically trained for the present PCI registry. The senior study coordinator (IU) and exclusive onsite auditing by the investigators (SK and AK) ensured proper registration of each patient.

A total of 11,258 consecutive patients who underwent PCI procedures from September 2008 to March 2013 for acute and nonacute indications were registered in the database. Of these, 6,308 patients were excluded because they underwent PCIs for acute indications (n = 5,100), underwent serial PCIs during the same hospitalization (n = 601), underwent an acetylcholine challenge test (n = 425), or had insufficient baseline data (n = 182). CTO was defined as angiographic evidence of a total occlusion of Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow for an estimated duration of at least 3 months based on the first onset of angina pectoris, a history of myocardial infarction in the target vessel territory, or comparison with a previous angiogram. In this study, cases with unknown occlusion duration were also identified as CTO. On the basis of this definition, CTO should not be the culprit lesion of ACS; therefore, we excluded the acute cases from this analysis. The remaining 4,950 patients underwent PCI for nonacute indications were included in the analysis (Figure 1).

Procedural success was defined as successful CTO recanalization with achievement of <50% residual stenosis within the treated segment and restoration of Thrombolysis In Myocardial Infarction grade 3 anterior flow. Inhospital major adverse cardiac events (MACE) included any of the following adverse events before hospital discharge: myocardial infarction, recurrent angina requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass surgery, tamponade requiring pericardiocentesis or surgery, or death from any cause. Bleeding was defined as follows: (1) occurring at the percutaneous entry site, during or after the catheterization laboratory visit until discharge, which may be external or a hematoma >10 cm for

Table 1
Demographics of patients undergoing percutaneous coronary intervention for non-acute indications

Variables	Chronic Total Occlusion		*P* value
	Yes (N=501)	No (N=4449)	
Mean age (years)	66.6±10.8	68.4±9.6	<0.001
Body mass index (kg/m^2)	24.7±3.7	24.4±3.5	0.103
Men	429 (85.6%)	3577 (80.4%)	0.005
Smoker	157 (31.3%)	1338 (30.1%)	0.573
Hypertension	382 (76.2%)	3492 (78.5%)	0.253
Dyslipidemia	366 (73.1%)	3206 (72.1%)	0.674
Diabetes mellitus	219 (43.7%)	2109 (47.4%)	0.119
Previous heart failure	62 (12.4%)	495 (11.1%)	0.412
Previous myocardial infarction	188 (37.5%)	1514 (34.0%)	0.124
Previous percutaneous coronary intervention	230 (45.9%)	2393 (53.8%)	0.001
Previous coronary bypass	41 (8.2%)	296 (6.7%)	0.191
Hemodialysis	20 (4.0%)	229 (5.1%)	0.331
Previous cerebrovascular disease	55 (11.0%)	400 (9.0%)	0.143
Previous peripheral artery disease	62 (12.4%)	463 (10.4%)	0.193
Previous chronic obstructive pulmonary disease	15 (3.0%)	141 (3.2%)	1
Canadian cardiovascular society class			
Asymptomatic	247 (49.3%)	1912 (43.0%)	0.109
I	58 (11.6%)	635 (14.3%)	
II	120 (24.0%)	1251 (28.1%)	
III	48 (8.9%)	420 (9.4%)	
IV	8 (1.6%)	72 (1.6%)	
Unknown	16 (3.2%)	112 (2.5%)	
Laboratory findings			
Creatinine (mg/dl)	0.9 (0.5-1.3)	0.9 (0.6-1.2)	0.813
Hemogrobin (g/dl)	13.2±1.9	13.2±2.1	0.985
Preprocedural computed tomography angiography	209 (41.7%)	1366 (30.7%)	<0.001
Preprocedural myocardial perfusion imaging	138 (27.5%)	1267 (28.5%)	0.087
Mild	15 (3.0%)	239 (5.4%)	0.081
Moderate	66 (13.2%)	553 (12.4%)	
Severe	26 (5.2%)	162 (3.6%)	
Unknown	31 (6.2%)	287 (6.5%)	
Chronic total occlusion site			
Left anterior descending	176 (35.1%)	Not applicable	
Left circumflex	109 (21.8%)		
Right coronary artery	216 (43.1%)		
Prescription at discharge			
Aspirin	491 (98.0%)	4372 (98.3%)	0.126
Clopidogrel	420 (83.8%)	4002 (90.0%)	<0.001
Ticlopidine	27 (5.4%)	223 (5.0%)	0.66
Cilostazole	22 (4.4%)	110 2.5%)	0.044
Warfarin	57 (11.4%)	396 (8.9%)	0.227
Angiotensin-converting enzyme inhibitor	317 (63.3%)	2763 (62.1%)	0.76
Angiotensin receptor blocker			
Beta-blocker	362 (72.3%)	2864 (64.4%)	0.004
Calcium blocker	164 (32.7%)	1729 (38.9%)	0.026
Statin	435 (86.8%)	3637 (81.7%)	0.027

femoral, >5 cm for brachial, or >2 cm for radial access; (2) retroperitoneal; (3) gastrointestinal; (4) genitourinary; or (5) other/unknown origin during or after the catheterization laboratory visit until discharge. Only bleeding events requiring a transfusion and/or with a decrease in hemoglobin >3.0 g/dl were included. This bleeding criterion is also consistent with Bleeding Academic Research Consortium grade 3A to C.[20] The definition of these complications was in accordance with the NCDR Cath-PCI registry, and any additional data elements and definitions can be found at their Web site.[21]

Table 2
Clinical outcomes of percutaneous coronary intervention for with and without chronic total occlusion

	Chronic total occlusion		*P* value
	Yes (N=501)	No (N=4449)	
Procedural Success	381 (76.0%)	4295 (96.5%)	<0.001
Major adverse cardiac events	16 (3.2%)	112 (2.5%)	0.371
Tamponade	4 (0.8%)	3 (0.1%)	0.003
Urgent Revascularization	1 (0.2%)	5 (0.1%)	0.473
Post-procedural myocardial infarction	11 (2.2%)	101 (2.3%)	1
In-hospital Death	3 (0.6%)	9 (0.2%)	0.114
Coronary Dissection	10 (2.0%)	51 (1.1%)	0.129
Coronary Perforation	20 (4.0%)	39 (0.9%)	<0.001
Cardiogenic Shock	8 (1.6%)	28 (0.6%)	0.025
Heart Failure	3 (0.6%)	16 (0.4%)	0.432
Stroke	2 (0.4%)	8 (0.2%)	0.269
Contrast Volume	230 (72 - 388)	160 (81 - 239)	<0.001
Hemodialysis	2 (0.4%)	7 (0.2%)	0.229
Bleeding Complication	25 (5.0%)	76 (1.7%)	<0.001
Transfusion	14 (2.8%)	46 (1.0%)	0.002
Fluoroscopy time (minute)	59.6±36.1	28.7±19.8	<0.001

The method to develop the AUC for coronary revascularization has been previously described.[10,11] The AUC was originally developed through a collaboration of 6 American professional organizations (American College of Cardiology Foundation, Society for Cardiovascular Angiography and Intervention, Society of Thoracic Surgeons, American Association for Thoracic Surgery, American Heart Association, and American Society of Nuclear Radiology) in 2009 and updated in 2012. We used an algorithm to map PCIs in the JCD-KICS PCI registry to the updated 2012 AUC to rate the procedures as appropriate, uncertain, or inappropriate. This algorithm, which was validated in a previous study, enabled the mapping to be performed in an efficient manner.[13] All the definitions in our study were identical to those in the AUC.

Baseline characteristics and clinical outcomes, including the technical success rate and inhospital MACE, as well as the appropriateness ratings were compared between the PCIs for lesions with and without CTO using the chi-square test or Fisher's exact test for categorical variables and the Student unpaired *t* test or Wilcoxon rank-sum test for continuous variables. Data were analyzed using SPSS version 22 (IBM Corp, Armonk, New York). All p values were 2 sided, and significance was defined as $p < 0.05$ for all analyses.

Results

In the 4,950 elective PCIs, CTO-PCI was performed for 501 cases (10.1%). Table 1 lists the demographics of the patients. The patients with CTO lesions were likely to be

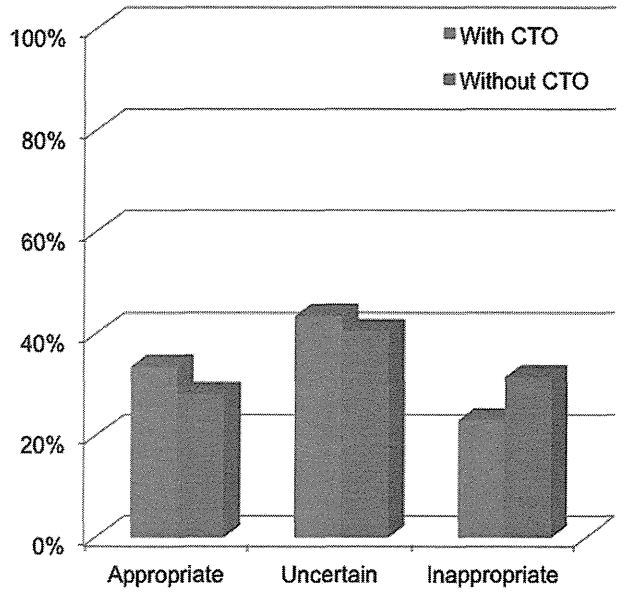

Figure 2. Appropriate use ratings of PCIs for lesions with and without CTO.

Table 3
Chronic total occlusion specific scenarios

Indication Nos. (Appropriateness use criteria)	No. of cases	Clinical Scenarios
26	22 (11%)	Chronic total occlusion of 1 major epicardial artery without other stenoses Intermediate-risk findings on noninvasive testing No or minimal anti-ischemic medical therapy
28	6 (3.0%)	Chronic total occlusion of 1 major epicardial artery without other stenoses High-risk findings on noninvasive testing No or minimal anti-ischemic medical therapy
24	5 (2.5%)	Chronic total occlusion of 1 major epicardial artery without other stenoses Low-risk findings on noninvasive testing No or minimal anti-ischemic medical therapy
29	12 (6.0%)	Chronic total occlusion of 1 major epicardial artery without other stenoses High-risk findings on noninvasive testing A course of maximal anti-ischemic medical therapy

younger, male, and to have a lower prevalence of a previous history of PCI compared with patients without CTO. There were also differences in the preprocedural evaluation pattern between the patients with and without CTO lesions; in patients with CTO lesions, computed tomography angiography (CTA) was more frequently performed, whereas the use of myocardial perfusion imaging (MPI) was similar between the 2 groups. Furthermore, implementation of medical therapy at discharge was also different between the patients with and without CTO lesions; in patients with CTO lesions, optimal medical therapy, including the use of β blockers and statins, was more frequently implemented compared with patients without CTO. Notably, the prescription rate of

Table 4
Non chronic total occlusion scenarios applied in mapping patients with percutaneous coronary intervention for chronic total occlusion in the setting of multivessel disease

Indication Nos. (Appropriateness use criteria)	No. of cases	Clinical scenarios
20	81 (40.5%)	One- or 2-vessel coronary artery disease without involvement of proximal left anterior descending No noninvasive testing performed
16	18 (9.5%)	One- or 2-vessel coronary artery disease without involvement of proximal left anterior descending Intermediate-risk findings on noninvasive testing Receiving no or minimal anti-ischemic medical therapy
48	13 (6.5%)	Three-vessel coronary artery disease (no left main) Abnormal LV systolic function
44	12 (6.0%)	Three-vessel coronary artery disease (no left main) Low-risk findings on noninvasive testing Receiving no or minimal anti-ischemic medical therapy
38	9 (4.5%)	Two-vessel coronary artery disease involving the proximal left anterior descending Intermediate-risk findings on noninvasive testing Receiving no or minimal anti-ischemic medical therapy

clopidogrel was significantly lower and tended to be replaced with other antiplatelet/anticoagulant agents such as cilostazole or warfarin in patients with CTO.

Table 2 provides the clinical outcomes, including the rates of procedural success and complications. Overall success rate of CTO-PCI was 76.0%. The incidence of MACE was not significantly different between the 2 groups (3.2% for CTO-PCIs vs 2.5% for PCIs for lesion without CTO, $p = 0.371$), but tamponade, coronary perforation, cardiogenic shock after procedure, and bleeding were more frequently observed in CTO-PCIs. In addition, a greater amount of contrast media was used for CTO-PCIs.

In the 4,950 elective PCIs, a rating could not be determined for 2,521 PCIs (Figure 1) mainly because of one of the following reasons: no previous stress test performed ($n = 934$), staged PCI ($n = 750$), no previous evaluation of left ventricular systolic function ($n = 307$), or previous stress test with no ischemia or equivocal result ($n = 284$). Of the 2,429 PCIs that were rated, CTO-PCIs were performed for fewer inappropriate indications than PCIs for lesions without CTO (23.0% vs 31.4%, $p = 0.04$; Figure 2). However, because cases with multiple stenotic lesions were excluded from ratings in all CTO-specific scenarios (Table 3), the vast majority of CTO-PCIs could not be related directly to CTO-specific scenarios. Therefore, in the present study, only PCIs for "Lone" CTO, which accounted for 17% of all CTO-PCIs, were successfully assigned

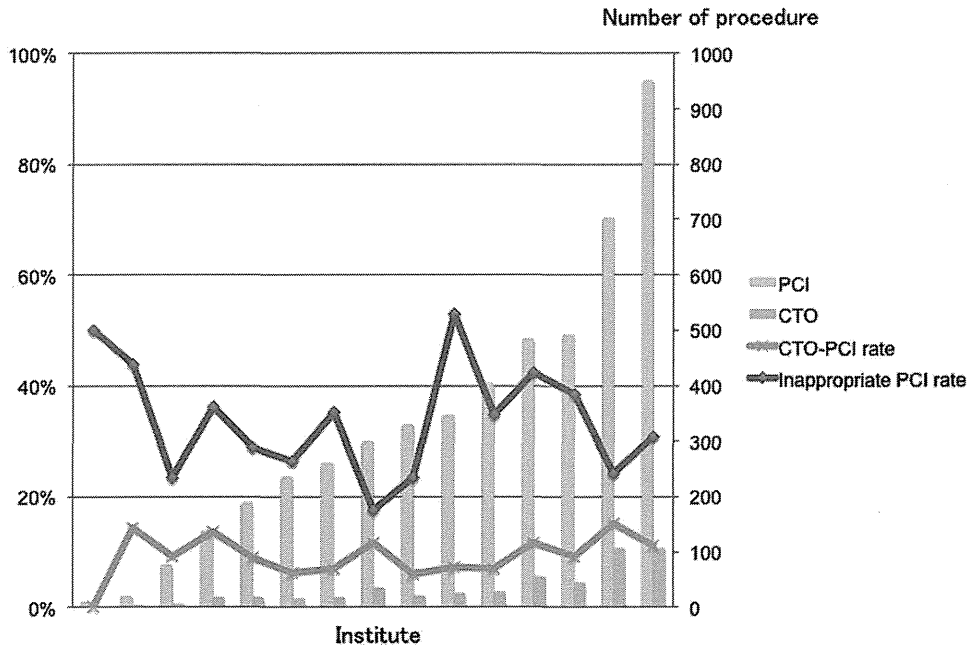

Figure 3. Association between procedural volume by institute and the rates of CTO-PCI or inappropriate PCI. *Light blue bar*, all procedural numbers by institute; *orange bar*, number of CTO-PCI by institute; *green line*, ratio of CTO-PCI to all procedures by institute (percentage); *purple line*, percentage of inappropriate PCI by institute.

directly to CTO-specific scenarios, and the remaining CTO-PCIs were mapped secondarily to non-CTO–specific scenarios (Table 4).

The association between procedural volume by institute and rates of CTO-PCI or inappropriate PCI is described in Figure 3. Regardless of procedural volumes, the CTO-PCI rates were consistent among institutes. Although the rates of inappropriate PCI were 18% to 53% among institutes, they were not correlated with PCI volumes.

Discussion

In JCD-KICS, approximately 10% of the PCIs were CTO related, and the overall success rate and inhospital clinical outcomes were comparable with previously published studies,[15] despite a higher rate of specific complications such as coronary perforation compared with non-CTO cases. Notably, relatively favorable appropriateness ratings of CTO-PCIs were observed; however, because most of the CTO-PCIs could not be assigned to CTO-specific scenarios because of the significant limitation in the current AUC, further effort is needed to refine the current criteria for more rigorous evaluations.

Because of the advent of newly developed devices and techniques, sufficient procedural success and acceptable complication rates have been achieved. Although, from the NCDR Cath-PCI registry in which CTO-PCI represented 3.8% of the total PCI volume, the procedural success rate bottomed out at a relatively low level (59%),[9] a meta-analysis of studies regarding CTO-PCIs published from 2000 to 2011 reported pooled estimates for procedural success and MACE of 77% and 3.1%, respectively.[16] From the latest reports of various CTO registries, which were mostly derived from high-volume centers, procedural success and MACE rates were 82.9% to 87.9% and 1.8% to 1.9%, respectively.[4,5,7,8] In the present study, although CTO-PCI was associated with lower procedural success and higher complication rates than non–CTO-PCI, its procedural success and complication rates were comparable with those of previously published studies even in real-world practice and primarily in average-sized centers.

Previous reports have demonstrated that greater procedural volumes of the institute and operator were associated with better success rates.[16] The procedural volume per institute in the present registry was low compared with high-volume centers, where the annual numbers of CTO-PCI were 0 to 47 cases (median 8 cases). However, in the real world, most CTO cases are medically managed, and only a few cases undergo PCI,[2] as indicated in the NCDR Cath-PCI registry, where ~3% of elective PCIs were for CTO.[22] The results of the present study appear to indicate that CTO-PCI can be safely implemented with realistic indications and application.

PCIs for lesions with CTO were performed under more rigorous indications than those without CTO. Following the application of the most recent AUC (2012 version)[10,11] in various registries, the rate of inappropriate PCIs was 11.6% to 17.0% based on the original 2009 criteria[12–14,23] and 23.2% based on the revised 2012 criteria,[14] which is consistent with our results.[15] The appropriateness ratings are based on different combinations of clinical presentation, symptom severity (Canadian Cardiovascular Society class), ischemia severity, and the implementation of optimal medical therapy. The lower rating of inappropriate indications might have resulted from that the patients who underwent CTO-PCI were more likely to have moderate-to-severe ischemia.

Notably, most patients with CTO lesions and collateral circulation experience ischemia owing to inadequate perfusion distal of the occlusion, and a previous study demonstrated that a 12.5% ischemic burden at baseline was an optimal threshold to identify patients who are likely to benefit from CTO-PCI in terms of reduced ischemic burden.[24] Therefore, ischemic burden should be evaluated before CTO-PCI, especially in asymptomatic patients. From this aspect, it is important to assess the appropriateness of CTO-PCI on the basis of AUC, which places considerable emphasis on a preprocedural ischemic evaluation.

Conversely, the present study highlights a significant discrepancy between real-world practice and the criteria. In the current AUC, CTO-specific clinical scenarios are only intended for "Lone" CTO, and CTO with other stenotic lesions could not be properly assigned using such scenarios. However, about 3/4 of patients with CTO reportedly have multivessel lesions,[2] which was consistent with our cohort. Furthermore, in patients with 2- or 3-vessel disease who underwent revascularization, CTO-PCI was attempted in only 22% of cases, and coronary artery bypass surgery was the overwhelming procedure for CTO vessel revascularization.[25] Therefore, the appropriate rating for CTO lesions might differ according to the number of diseased vessels.

We previously reported a growing disconnect between the AUC and current methods for pre-PCI evaluation,[15] which have changed from a focus on MPI- to CTA-based assessment because of the technological evolution of cardiovascular imaging. Because the current AUC assign considerable value to functional information in reflection of a strong tilt toward physiologic assessment of ischemia in the United States, the use of CTA might result in an increased rate of inappropriate PCIs because CTA provides only anatomic information, which is not recognized as pre-PCI evaluation in the current criteria. Moreover, marked variation in ratings between individual physicians and the AUC Technical Panel has been reported.[26] The discrepancy between physician ratings of AUC scenarios and the actual AUC ratings reflects a gap in the practice of ideal care, and our study findings emphasize the need for more rigorous evaluation in terms of the present insufficient CTO-related clinical scenarios.

For a thorough understanding of our results, several limitations should be acknowledged. First, not all hospitals that perform PCI in Japan participate in our registry. However, the registry consists of multiple centers and includes a relatively large number of procedures. Therefore, we believe this is one of the most representative Japanese databases to include PCI patients and that our results comprise the most complete assessment of current practice patterns throughout Japan. Second, although the lesion must have been present for longer than 3 months to be classified as a CTO, the period for which a CTO has been present is difficult to determine with complete certainty because the estimation is based on clinical history and a previous angiogram. In the present study, cases with unknown occlusion duration were also considered to have CTO, which could have resulted in overestimation of the CTO incidence. Third, angiographic features and technical factors, which have been associated with the procedural success of CTO-PCI,[27] were lacking in this study because this registry was defined in collaboration with the NCDR Cath-PCI registry and did not provide specific information for CTO-PCI. However, analysis of the angiographic and technical details was not within the scope of the present study because it focused on the overall results of CTO-PCI in real-world practice and the appropriateness of indications. Finally, although we demonstrated an association between procedural volume by institute and the rates of inappropriate PCI, the correlation between annual PCI volumes by operator and the rates of inappropriate procedure could not be evaluated because of the limited number of CTO-PCIs included in the analysis. Further investigations will be required to clarify this association.

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Disclosures

The authors have no conflicts of interest to disclose.

Supplementary Data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.amjcard.2015.06.008.

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ORIGINAL ARTICLE

Risk Model for Distal Gastrectomy When Treating Gastric Cancer on the Basis of Data From 33,917 Japanese Patients Collected Using a Nationwide Web-based Data Entry System

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Objective: To establish a risk model for distal gastrectomy in Japanese patients with gastric cancer.

Background: Risk stratification for distal gastrectomy in Japanese patients with gastric cancer improves surgical outcomes.

Methods: The National Clinical Database was constructed for risk determination in gastric cancer-related gastrectomy among Japanese individuals. Data from 33,917 gastric cancer cases (1737 hospitals) were used. The primary outcomes were 30-day and operative mortalities. Data were randomly assigned to risk model development (27,220 cases) and test validation (6697 cases) subsets. Stepwise selection was used for constructing 30-day and operative mortality logistic models.

Results: The 30-day, in-hospital, and operative mortality rates were 0.52%, 1.16%, and 1.2%, respectively. The morbidity was 18.3%. The 30-day and operative mortality models included 17 and 21 risk factors, respectively. Thirteen variables overlapped: age, need for total assistance in activities of daily living preoperatively or within 30 days after surgery, cerebrovascular disease history, more than 10% weight loss, uncontrolled ascites, American Society of Anesthesiologists score (≥ class 3), white blood cell count more than 12,000/μL or 11,000/μL, anemia (hemoglobin: males, <13.5 g/dL; females, <12.5 g/dL; or hematocrit: males, <37%; females <32%), serum albumin less than 3.5 or 3.8 g/dL, alkaline phosphatase more than 340 IU/L, serum creatinine more than 1.2 mg/dL, serum Na less than 135 mEq/L, and prothrombin time-international normalized ratio more than 1.25 or 1.1. The C-indices for the 30-day and operative mortalities were 0.785 (95% confidence interval, 0.705–0.865; $P < 0.001$) and 0.798 (95% confidence interval, 0.746–0.851; $P < 0.001$), respectively.

Conclusions: The risk model developed using nationwide Japanese data on distal gastrectomy in gastric cancer can predict surgical outcomes.

Keywords: distal gastrectomy, gastric cancer, National Clinical Database, risk model of mortality, surgical outcome

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Age-adjusted mortality of gastric cancer has decreased in most countries; however, it remains the fourth most common cause of cancer death worldwide.[1] Treatment for gastric cancer has received special consideration in East Asia because of its high incidence.[2] Surgery is the most effective treatment approach for gastric cancer. According to the Japanese gastric cancer treatment guidelines, standard surgery for curable advanced gastric cancer is more than two-thirds (subtotal) gastrectomy with D2 dissection.[3] This procedure has been performed without pancreatosplenectomy, which has been shown to be responsible for high mortality and morbidity.[4] In general, the gastrectomy procedures, including lymphadenectomy for early and advanced gastric cancer, have been accepted and performed as standard procedures in most hospitals that participate in the Japanese Gastric Cancer Association.[5] The Japanese Gastric Cancer Association collected data regarding the survival outcomes of 13,626 patients with primary gastric cancer treated at 208 participating hospitals in 2002 and showed that the direct death rate (30-day mortality) was 0.48%.[5] In addition, a nationwide survey by the Japanese Society of Gastrointestinal Surgery (JSGS), which included 24,100 cases treated at 1775 institutions in 2006 and 2007, found that the mortality rates varied from 0.4% to 1.1% depending on the hospital volume.[6] The outcomes appear to be better than those reported in Western countries[7–10]; however, further improvement is still possible.

The National Clinical Database (NCD), which commenced patient registration in January 2011, is a web-based data entry system linked to the surgical board certification in Japan. In this study, we focused on the NCD division of gastrointestinal surgery,[11–13] which uses patient variables and definitions that are almost identical to those used by the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP).[14] Traditionally, various governing bodies, including ACS-NSQIP, have used the 30-day patient mortality as a benchmark to assess the quality of both hospital and surgeon performances in virtually all major surgical procedures. However, we recently reported that mortality based only on known data at 30 days is misleading, and it greatly underestimates the actual perioperative mortality by up to 50% compared with that at 90 days for various procedures (eg, pancreaticoduodenectomy, hepatectomy, and total gastrectomy).[11–13] Thus, the risks for 30- and 90-day in-hospital mortalities should be analyzed together with parameters similar to those used in ACS-NSQIP for patients undergoing distal gastrectomy. To formulate risk models for the 30-day and operative mortalities associated with distal gastrectomy, we evaluated data from 33,917 gastric cancer cases entered in NCD and tested the performance of the model for open and laparoscopic gastrectomy.

METHODS

Study Population

NCD is a nationwide project performed with the cooperation of the board certification system for surgery in Japan. Submission of cases to NCD is a prerequisite for all member institutions of both the Japan Surgical Society and the JSGS, and only registered cases can be used for board certification.[15] Information related to more than 1,200,000 surgical cases treated at more than 3500 hospitals was

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collected in 2011. The common input items in the JSGS guidelines have been registered from 2045 institutions. To ensure data traceability, NCD staff work with individuals who approve the data, those in the departments responsible for the annual reporting of case data, and individuals who enter the data via a web-based data management system. The staff also validates data consistency consecutively based on random inspections of the institutions.

In this study, we focused on the specific NCD section for gastrointestinal surgery, which uses variables and definitions that are almost identical to those employed by ACS-NSQIP (http://site.acsnsqip.org/wp-content/uploads/2013/10/ACSNSQIP.PUF_.UserGuide.2012.pdf#search = 'user+guide+for+the+2012+ACS+NSQIP'). Briefly, potential independent variables included patient demographics, pre-existing comorbidities, preoperative laboratory values, and operative data. The demographic variables of age, sex, smoking status, and alcohol drinking status were considered. The patients were categorized according to whether they were transferred directly by ambulance or not. General factors such as preoperative functional status [independent, partially dependent, and totally dependent based on a patient's ability to perform activities of daily living (ADL) at 30 days and immediately before surgery] and body mass index were also considered. The American Society of Anesthesiologists (ASA) physical status classification system was evaluated. We also considered pre-existing comorbidities, including cardiovascular status (eg, congestive heart failure, coronary diseases, hypertension, previous cardiac surgery, and peripheral vascular disease), respiratory status (eg, dyspnea, ventilator dependence, pneumonia, and chronic obstructive pulmonary disease), renal status (eg, acute renal failure and dialysis), hematological status (eg, bleeding disorders and preoperative blood transfusion), oncological status (eg, disseminated cancer, chemotherapy, and radiotherapy), preoperative blood transfusion, chronic corticosteroid use, ascites, sepsis, diabetes, presence of an open wound, and pregnancy. The laboratory parameters included in the analysis were white blood cell count, hemoglobin level, hematocrit, platelet count, prothrombin time-international normalized ratio, and activated partial thromboplastin time, as well as the serum levels of albumin, total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, urea nitrogen, creatinine, sodium, hemoglobin A_{1c}, and C-reactive protein.

This study focused on 30-day outcomes (if a patient had been discharged after their initial admission) based on a direct 30-day time point assessment. The outcomes included 23 rigorously defined morbidities (including the following categories: wound, respiratory system, urinary tract, central nervous system, cardiac, and other preoperative conditions) as well as mortality. NCD registered the surgical cases from each department in the gastroenterological surgery section, which required the detailed input of items for 8 procedures that represented the performance of surgery in each specialty. All the variables and definitions, as well as the inclusion criteria for NCD, are accessible on the NCD Web site (http://www.ncd.or.jp/). NCD supports an E-learning system to ensure consistent data entry by participants. The NCD staff also answers all inquiries regarding data entry (approximately 80,000 inquiries in 2011) and regularly lists some of these as "Frequently Asked Questions" on the Web site.

The presence of distal gastrectomy in patients with gastric cancer was performed between January 1, 2011 and December 31, 2011 at 1737 institutions in Japan. The NCD records of patients who did not give permission to use their records were excluded from this analysis. Records with missing data in terms of age, sex, or status at 30 days after surgery were also excluded. We selected patients who had undergone distal gastrectomy for gastric cancer, including those who underwent cholecystectomy during the same operation. The exclusion criteria were any other associated surgeries that affected the outcomes based on the surgical criteria for distal gastrectomy applied in Japan after distal gastrectomy and/or gall bladder cancer (Fig. 1). Data were excluded for 41 patients who had undergone simultaneous distal pancreatectomy and 87 patients who had undergone splenectomy (30-day mortalities, 0% and 3.4%, respectively). After data cleaning, the data from 33,917 patients with gastric cancer treated at 1737 hospitals throughout Japan were used to develop the risk model (Fig. 1).

End Points

The primary outcome measures were the 30-day and operative mortalities. "Operative mortality" was defined as death during the index hospitalization, regardless of the length of hospital stay (≤90 days), as well as death after hospital discharge and 30 days or less from the surgery date.

Statistical Analysis

We used SPSS (version 20; IBM Corp., Armonk, NY) for the data analyses. Data were randomly divided into 2 subsets with a split of 80/20, where 1 set was used for model development (27,220 cases) and the other for validation (6697 cases). There were no significant differences in the profiles of the variables between the model development and validation sets, according to univariate analysis using Fisher exact tests and unpaired Student t tests. The 2 sets of logistic models (30-day mortality and operative mortality) were constructed for data set development using forward stepwise selection of predictors with a $P < 0.05$ for inclusion. A goodness-of-fit test was performed to assess how well the model could discriminate between patient survival and death. The receiver operating characteristic (ROC) curves for 30-day and operative mortalities were created for the validation data set. An ROC curve is a plot of a test's true positive rate (sensitivity) versus its false-positive rate (1 − specificity). Each point on the ROC curve indicates a pair of false- and true-positive rates that is achieved using a particular threshold to dichotomize the predicted probabilities. Model calibration (the degree to which the observed outcomes matched the predicted outcomes from the model across a group of patients) was

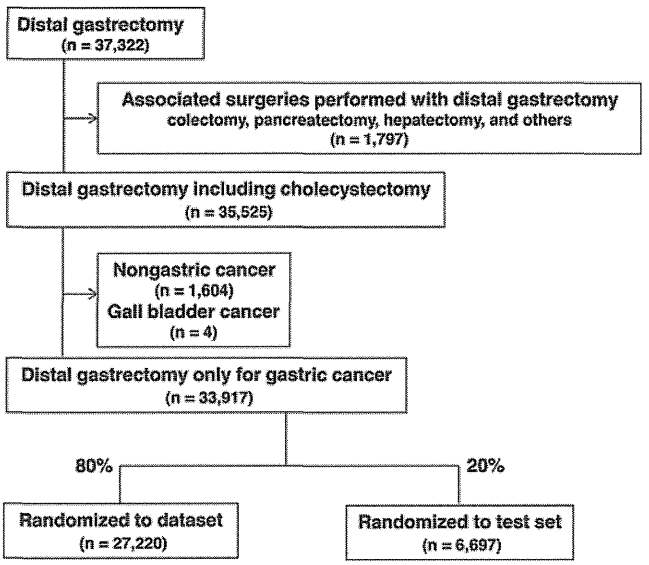

FIGURE 1. Study population selection process. We selected cases where the patients underwent distal gastrectomy for gastric cancer, including patients who simultaneously underwent cholecystectomy. The exclusion criteria were any other associated surgery that could affect the outcomes after distal gastrectomy and/or gall bladder cancer.

examined by comparing the observed and predicted averages with each of 10 equally sized subgroups, which were arranged in order of increasing patient risk.

RESULTS

Risk Profile of the Study Population

The NCD patient population (patients with gastric cancer who underwent distal gastrectomy: n = 33,917) had a mean age of 69.0 (standard deviation = 11.8) years, and 66.5% of the patients were males. Among this population, 1.4% of the patients arrived at the hospital by ambulance and 0.9% required emergency surgery. An abbreviated risk profile of the study population is shown in Table 1. In brief, 8.9% of the patients had an ASA classification of 3 to 5; 0.7% and 0.8% had total dependency during ADLs within 30 days after surgery or preoperatively, respectively; 4.7% needed some assistance with ADLs before surgery; 18.2% had a body mass index more than 25 kg/m^2; and 4.7% had experienced weight loss more than 10%. In terms of pre-existing comorbidities, 33.3% of the patients had hypertension, 15.1% had diabetes mellitus, 3.6% had chronic obstructive pulmonary disease, 0.8% required preoperative dialysis, 3.9% had cerebrovascular disease, 1.1% had ascites, and 2.8% required blood transfusion. Distal gastrectomy with associated cholecystectomy was performed in 10.3% of the patients.

Outcome Rates

The 30-day, in-hospital, and operative mortality rates for distal gastrectomy in the treatment of gastric cancer among the 2011 NCD population were 0.52%, 1.16%, and 1.2%, respectively.

The postoperative morbidities are summarized in Table 2. The overall morbidity in the distal gastrectomy population was 18.3%, and grade II or higher complications, as defined by the Clavien–Dindo Classification of Surgical Complications system,[16] were observed in 11.5% of the patients. Surgical complications included surgical site infection in 4.3% of the patients, anastomotic leakage in 2.1%, and pancreatic fistula (grades A, B, and C) in 1.6%. Nonsurgical complications included pneumonia in 2.0% of the patients, acute renal failure in 0.3%, central nervous system events in 0.5%, and cardiac events in 0.3%.

The following variables were significantly more frequent in the 30-day and operative mortality groups compared with the nonmortality group: reoperation within 30 days, overall complications, surgical complications (except bile leakage in the 30-day mortality group), and nonsurgical complications. In the 30-day mortality group, the incidences of unplanned intubation, pulmonary embolism, cardiac events, and septic shock were increased compared with those in the operative mortality group. In contrast, the incidence of postoperative infectious complications (ie, surgical site infection, bile leakage, pneumonia, and urinary tract infection) increased in the operative mortality group.

Model Results and Performance

Two different risk models were developed. The final logistic models with odds ratios (ORs) and 95% confidence intervals (CIs) are shown in Table 3. The scoring system for the mortality risk models based on the logistic regression equation was as follows:

$$\text{Predicted mortality} = e(\beta 0 + \sum \beta i Xi)/1 + e(\beta 0 + \sum \beta i Xi),$$

where βi is the coefficient of the variable Xi in the logistic regression equation provided in Table 3 for 30-day mortality and 90-day in-hospital mortality. Xi = 1 if a categorical risk factor is present and 0 if it is absent. For the age categories, Xi = 1, if the patient age is less than 59 years; Xi = 2, for 60 to 64 years; Xi = 3, for 65 to 69 years; Xi = 4, for 70 to 74 years; Xi = 5, for 75 to 79 years; and Xi = 6, for 80 years or more. The 2 groups shared 13 overlapping variables: age, need for total assistance in ADL before surgery or within 30 days after surgery, history of cerebrovascular disease, weight loss more than 10%, uncontrolled ascites, ASA score class 3 or more, white blood cell count more than 12,000/μL or 11,000/μL, anemia (hemoglobin: males, <13.5 g/dL; females, <12.5 g/dL; or hematocrit: males <37%; females <32%), serum albumin less than 3.5 or 3.8 g/dL, alkaline phosphatase more than 340 IU/L, serum creatinine more than 1.2 mg/dL, serum Na less than 135 mEq/L, and prothrombin time-international normalized ratio more than 1.25 or 1.1. The independent variables for only 30-day mortality were habitual alcohol consumption, preoperative pneumonia, history of myocardial infarction, and untreated bleeding disorder. The independent variables for only operative mortality were the presence of respiratory distress, disseminated cancer, chronic corticosteroid use, emergency surgery, low platelet count (<12 × 10^4/μL), aspartate aminotransferase more than 40 IU/L, increased level of total bilirubin (>2 mg/dL), and activated partial thromboplastin time more than 40 seconds.

Model Performance

To evaluate the model performance, we evaluated the area under the ROC curve (AUC) and the model calibration across risk groups. The ROC curves for both models are shown in Figure 2. The AUC was 0.785 for the 30-day mortality [95% confidence interval (CI), 0.705–0.865; $P < 0.001$] and 0.798 for the overall operative mortality (95% CI, 0.746–0.851; $P < 0.001$). Figure 3 shows the calibration of the models, which illustrates how well the rates for the predicted events matched those of the observed events among the patient risk subgroups.

We evaluated the model performance in open and laparoscopic distal gastrectomy cases (n = 22,039 and 11,878 cases, respectively). The preoperative risk factors were significantly higher in open cases than those in laparoscopic cases (Table 4; Supplemental Digital Content available at http://links.lww.com/SLA/A750). The 30-day and operative mortalities in the open cases were significantly high than those in the laparoscopic cases (Table 5; Supplemental Digital Content available at http://links.lww.com/SLA/A751). This was also the case with morbidity. The ROC curves obtained when both models were applied to the open and laparoscopic cases are shown in Figure 4 (Supplemental Digital Content available at http://links.lww.com/SLA/A752). The AUC was 0.746 for the 30-day mortality (95% CI, 0.628–0.863; $P < 0.001$) and 0.787 for the overall operative mortality (95% CI, 0.717–0.856; $P < 0.001$) in the laparoscopic cases. The AUC was 0.791 for the 30-day mortality (95% CI, 0.756–0.827; $P < 0.001$) and 0.831 for the overall operative mortality (95% CI, 0.808–0.853; $P < 0.001$) in the open cases.

DISCUSSION

The nationwide database used in this study was constructed from the data related to 33,917 cases treated at 1737 hospitals, which comprise most of the Japanese institutions that perform gastric cancer surgery. In this study, the postoperative morbidity, 30-day mortality, and postoperative mortality were 18.3%, 0.52%, and 1.2%, respectively. This is the first report in Japan to present 30-day and operative mortality risk models for distal gastrectomy, which were developed using data from the nationwide web-based data entry system of NCD. The variables examined were selected from among those considered in ACS-NSQIP. The 30-day and operative mortality models included 17 and 21 significant variables, respectively, and the C-indices for the 30-day and operative mortalities in the validation sets were 0.785 and 0.798, respectively, thereby supporting the good predictive abilities of the models.

TABLE 1. Key Preoperative Risk Factors and Surgical Outcomes

	Entire Study Population (n = 33,917)		Distal Gastrectomy Outcome Groups: 30-d Mortality (n = 176)			Distal Gastrectomy Outcome Groups: Operative Mortality (n = 409)		
Characteristics	**n**	**%**	**n**	**%**	***P***	**n**	**%**	***P***
Demographics								
Age, mean (SD), yr	69 (11.8)		76.4 (11.2)		<0.001	76.4 (11.2)		<0.001
Males	22,558	66.5	130	73.9	0.039	301	73.6	0.002
Ambulance transport	474	1.4	12	6.8	<0.001	33	8.1	<0.001
Preoperative risk assessment								
General								
ADL before 30 d: total assistance	227	0.7	12	6.8	<0.001	27	6.6	<0.001
Preoperative ADL: total assistance	264	0.8	14	8.0	<0.001	33	8.1	<0.001
Preoperative ADL: any assistance	1604	4.7	45	25.6	<0.001	121	29.6	<0.001
Body mass index >25 kg/m^2	6153	18.2	28	15.9	0.49	60	14.7	0.07
Habitual alcohol consumption	8113	23.9	41	23.3	0.92	75	18.3	0.008
Current smoker (within a year)	6721	19.8	32	18.2	0.63	75	18.3	0.49
Brinkman index >400	9201	27.1	43	24.4	0.44	104	25.4	0.47
Diabetes	5131	15.1	43	24.4	0.001	84	20.5	0.003
Pulmonary								
Preoperative pneumonia	147	0.4	9	5.1	<0.001	17	4.2	<0.001
Chronic obstructive pulmonary disease	1206	3.6	14	8.0	0.006	41	10.0	<0.001
Respiratory distress	743	2.2	18	10.2	<0.001	51	12.5	<0.001
Cardiac								
Congestive heart failure	262	0.8	8	4.5	<0.001	15	3.7	<0.001
Myocardial infarction	188	0.6	7	4.0	<0.001	13	3.2	<0.001
Angina pectoris	442	1.3	9	5.1	<0.001	20	4.9	<0.001
Previous percutaneous coronary intervention	846	2.5	16	9.1	<0.001	30	7.3	<0.001
Previous cardiac surgery	408	1.2	6	3.4	0.02	13	3.2	0.002
Previous peripheral vascular disease surgery	169	0.5	5	2.8	0.002	9	2.2	<0.001
Hypertension	11,293	33.3	75	42.6	0.010	165	40.3	0.003
Renal								
Acute renal failure	23	0.1	0	0.0	1.00	2	0.5	0.003
Preoperative dialysis	268	0.8	7	4.0	<0.001	15	3.7	<0.001
Central nervous system								
Previous cerebrovascular disease	1329	3.9	28	15.9	<0.001	53	13.0	<0.001
Nutritional/immune/other								
Weight loss >10%	1599	4.7	34	19.3	<0.001	80	19.6	<0.001
Ascites	372	1.1	15	8.5	<0.001	34	8.3	<0.001
Ascites without control	298	0.9	13	7.4	<0.001	29	7.1	<0.001
Disseminated cancer	584	1.7	16	9.1	<0.001	46	11.2	<0.001
Chronic steroid use	287	0.8	1	0.6	1.00	13	3.2	<0.001
Bleeding disorder without treatment	148	0.4	7	4.0	<0.001	13	3.2	<0.001
Preoperative transfusions	944	2.8	26	14.8	<0.001	51	12.5	<0.001
Chemotherapy	453	1.3	4	2.3	0.30	8	2.0	0.27
Radiotherapy	45	0.1	0	0.0	1.00	1	0.2	0.42
Sepsis	57	0.2	3	1.7	0.003	7	1.7	<0.001
Emergent surgery	316	0.9	16	9.1	<0.001	35	8.6	<0.001
ASA ≥Grade 3	3008	8.9	62	35.2	<0.001	152	37.2	<0.001
ASA Grade 5	33	0.1	2	1.1	0.013	3	0.7	0.007
Cholecystectomy	3499	10.3	15	8.5	0.528	43	10.5	0.879
Preoperative laboratory data								
White blood cells								
>9000/mL	1933	5.7	29	16.5	0.015	66	16.1	<0.001
>11,000/mL	601	1.8	16	9.1	<0.001	32	7.8	<0.001
Hemoglobin, males: <13.5 g/dL; females: <12.5 g/dL	14,642	43.2	129	73.3	<0.001	294	71.9	<0.001
Hematocrit, males: <37% females: <32%	10,467	30.9	108	61.4	<0.001	250	61.1	<0.001
Platelets								
<8 × 10^4/mL	175	0.5	5	2.8	0.029	9	2.2	<0.001
<12 × 10^4/mL	932	2.7	13	7.4	0.001	38	9.3	<0.001
Serum albumin <3.8 g/dL	8730	25.7	99	56.3	<0.001	255	62.3	<0.001

(*Continues*)

TABLE 1. Key Preoperative Risk Factors and Surgical Outcomes (*Continued*)

			Distal Gastrectomy Outcome Groups					
	Entire Study Population (n = 33,917)		30-d Mortality (n = 176)			Operative Mortality (n = 409)		
Characteristics	**n**	**%**	**n**	**%**	***P***	**n**	**%**	***P***
AST >40 IU/L	2064	6.1	20	11.4	0.007	56	13.7	<0.001
ALP >340 IU/L	2540	7.5	30	17.0	<0.001	61	14.9	<0.001
Total bilirubin >2 mg/dL	285	0.8	2	1.1	0.66	10	2.4	0.003
BUN >20 mg/dL	5201	15.3	52	29.5	<0.001	135	33.0	<0.001
Creatinine >1.2 mg/dL	2231	6.6	32	18.2	<0.001	76	18.6	<0.001
Serum Na								
<130 mEq/L	179	0.5	11	6.3	0.061	19	4.6	<0.001
<135 mEq/L	1068	3.1	32	18.2	<0.001	70	17.1	<0.001
Hemoglobin A_{1c} >6.5%	2035	6.0	8	4.5	0.520	20	4.9	0.40
CRP >1.0 mg/dL	2696	7.9	44	25.0	<0.001	118	28.9	<0.001
PT-INR								
>1.1	4748	14.0	63	35.8	<0.001	142	34.7	<0.001
>1.25	966	3	21	12	<0.001	42	10	<0.001
APTT > 40 seconds	902	2.7	13	7.4	<0.001	39	9.5	<0.001

ALP indicates alkaline phosphatase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; PT-INR, prothrombin time-international normalized ratio; SD, standard deviation.

TABLE 2. Prevalence of Morbidity With Distal Gastrectomy Outcomes

			Distal Gastrectomy Outcome Groups					
	Entire Study Population (n = 33,917)		30-d Mortality (n = 176, 0.52%)			Operative Mortality (n = 409, 1.2%)		
Postoperative Outcomes	**n**	**%**	**n**	**%**	***P***	**n**	**%**	***P***
Readmission within 30 d	553	1.6	3	1.7	0.765	7	1.7	0.843
Reoperation within 30 d	633	1.9	29	16.9	<0.001	80	19.6	<0.001
Postoperative complications								
Overall	6193	18.3	148	84.1	<0.001	329	80.4	<0.001
≥Grade II	3893	11.5	138	78.4	<0.001	303	74.1	<0.001
Surgical complications								
Surgical site infection	1458	4.3	31	17.6	<0.001	89	21.8	<0.001
Superficial incisional	668	2.0	9	5.1	0.008	42	10.3	<0.001
Deep incisional	288	0.8	8	4.5	<0.001	35	8.6	<0.001
Organ space	910	2.7	27	15.3	<0.001	72	17.6	<0.001
Wound dehiscence	182	0.5	6	3.4	<0.001	26	6.4	<0.001
Anastomotic leak	696	2.1	25	14.2	<0.001	73	17.8	<0.001
Pancreatic fistula	542	1.6	17	9.7	<0.001	37	9.0	<0.001
Bile leakage	102	0.3	2	1.1	0.099	13	3.2	<0.001
Nonsurgical complications								
Pneumonia	687	2.0	35	19.9	<0.001	122	29.8	<0.001
Unplanned intubation	293	0.9	77	43.8	<0.001	136	33.3	<0.001
Prolonged ventilation >48 hr	299	0.9	59	33.5	<0.001	129	31.5	<0.001
Pulmonary embolism	26	0.1	4	2.3	<0.001	5	1.2	<0.001
Acute renal failure	89	0.3	25	14.2	<0.001	55	13.4	<0.001
Urinary tract infection	150	0.4	5	2.8	0.001	21	5.1	<0.001
Events in central nervous system	164	0.5	32	18.2	<0.001	60	14.7	<0.001
Cardiac events	118	0.3	75	42.6	<0.001	88	21.5	<0.001
Septic shock	138	0.4	38	21.6	<0.001	75	18.3	<0.001

Many studies have aimed to develop methods that predict the risk of perioperative mortality following gastric resection in the Western hemisphere[17–20] and in Asian countries.[21] All these previous studies used data from either a single institution or a nationwide database.[17–21] The most commonly used nationwide databases in the Western hemisphere are the population-based National Inpatients Sample[17,18] and ACS-NSQIP.[20] However, the National Inpatients Sample data set is an administrative data set, which lacks operative factors such as the procedure duration, bleeding volume, and extent of lymph node resection, and it also lacks other important factors such as ASA status, preoperative nutritional status, extent of weight loss, palliative versus curative resection, and use of neoadjuvant therapy. The risk models created using ACS-NSQIP variables have been shown to be quite effective for predicting mortality in

TABLE 3. Risk Models for 30-Day Mortality and Operative Mortality After Distal Gastrectomy

	30-d Mortality					Operative Mortality				
Variables	**b Coefficient**	**Odds Ratio**	**95% CI**		***P***	**b Coefficient**	**Odds Ratio**	**95% CI**		***P***
Age category	0.184	1.202	1.062	1.361	0.004	0.283	1.327	1.217	1.446	<0.001
ADL										
Before 30 d: total assistance	1.083	2.955	1.418	6.159	0.004					
Preoperative: total assistance						1.099	3.001	1.856	4.852	<0.001
Habitual alcohol consumption	0.453	1.573	1.047	2.362	0.029					
Preoperative pneumonia	1.019	2.769	1.171	6.549	0.02					
Respiratory distress						0.869	2.385	1.634	3.482	<0.001
Myocardial infarction	1.14	3.127	1.282	7.63	0.012					
Previous cerebrovascular disease	0.734	2.084	1.248	3.48	0.005	0.575	1.777	1.228	2.572	0.002
Weight loss >10%	0.82	2.271	1.437	3.589	<0.001	0.785	2.192	1.592	3.018	<0.001
Ascites without control	1.091	2.978	1.404	6.315	0.004	1.018	2.767	1.638	4.674	<0.001
Disseminated cancer						1.063	2.896	1.897	4.42	<0.001
Chronic steroid use						1.026	2.789	1.454	5.35	0.002
Bleeding disorder without treatment	1.17	3.223	1.205	8.622	0.02					
Emergent surgery						0.618	1.856	1.026	3.357	0.041
ASA ≥class 3	0.668	1.95	1.288	2.953	0.002	0.648	1.912	1.453	2.518	<0.001
White blood cells										
>11,000/mL						0.934	2.545	1.591	4.071	<0.001
>12,000/mL	1.299	3.666	1.837	7.314	<0.001					
Hemoglobin										
Males: <13.5 g/dL females: <12.5 g/dL	0.596	1.814	1.136	2.897	0.013					
Hematocrit										
Males: <37% females: <32%						0.364	1.439	1.089	1.901	0.01
Platelets $<12 \times 10^4$/mL						0.696	2.006	1.3	3.093	0.002
Serum albumin										
<3.5 g/dL	0.395	1.485	0.979	2.252	0.063					
<3.8 g/dL						0.555	1.741	1.303	2.326	<0.001
Aspartate aminotransferase >40 IU/L						0.416	1.516	1.06	2.169	0.023
Alkaline phosphatase >340 IU/L	0.772	2.164	1.384	3.386	0.001	0.442	1.556	1.113	2.173	0.01
Total bilirubin >2 mg/dL						0.969	2.634	1.204	5.764	0.015
Creatinine >1.2 mg/dL	0.573	1.773	1.124	2.796	0.014	0.59	1.803	1.328	2.448	<0.001
Serum Na <135 mEq/L	0.908	2.48	1.528	4.025	<0.001	0.812	2.251	1.612	3.146	<0.001
PT-INR										
>1.1						0.423	1.527	1.175	1.985	0.002
>1.25	0.708	2.03	1.162	3.549	0.013					
APTT > 40 seconds						0.455	1.576	1.05	2.366	0.028
Intercept	−7.393				<0.001	−6.996				<0.001

APTT indicates activated partial thromboplastin time; PT-INR, prothrombin time-international normalized ratio.

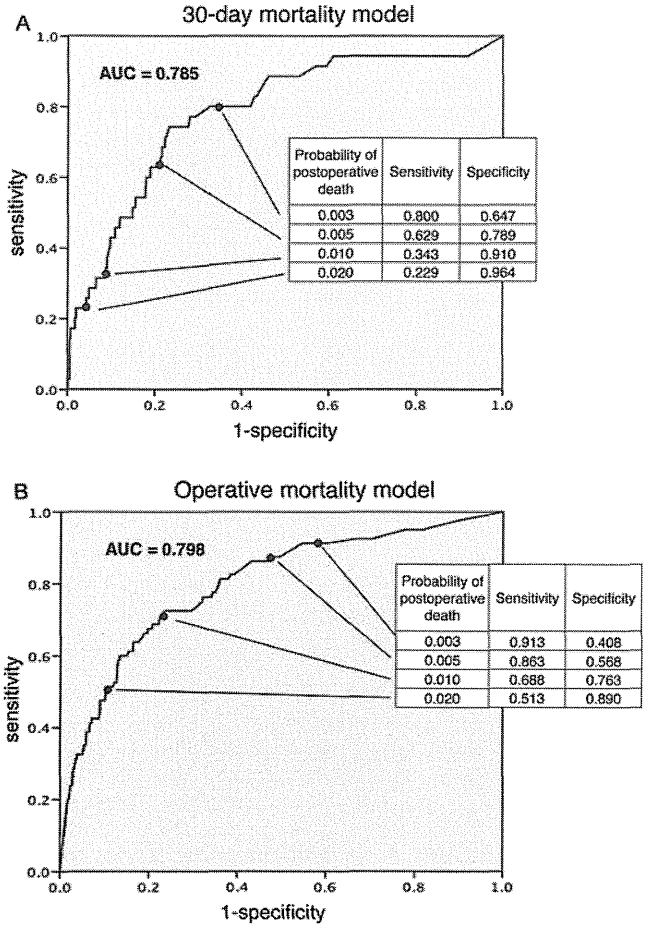

FIGURE 2. ROC curves of the (A) 30-day mortality model and (B) operative mortality model. The AUC was 0.785 for the 30-day mortality (95% CI, 0.705–0.865; $P < 0.001$) and 0.798 for the overall operative mortality (95% CI, 0.746–0.851; $P < 0.001$).

various procedures and for improving surgical quality in participating hospitals.[14] However, Borja-Cacho et al[22] showed that the current ACS-NSQIP variables do not have a good predictive capacity for major complications after major oncological resection, and thus they advocated the use of additional disease-specific and operation-specific variables to obtain more accurate predictions of the 30-day postoperative outcome. NCD uses variables similar to those employed in ACS-NSQIP but with some modifications that allow it to represent not only the 30-day mortality but also the in-hospital mortality 90 days or less after surgery. The Japanese system of universal health care allows most patients who undergo surgery to be cared for in the same hospital that performed the operation until the patient can independently function in terms of ADL.[23,24] With this adjustment to include longer-term mortality, the operative mortality rate of patients treated by distal gastrectomy increased to twice the 30-day mortality rate (1.2% vs 0.52%, respectively).

There are 2 major distinct gastrectomy procedures: distal and total gastrectomy. The surgical procedures for resection and anastomosis are quite different, and the outcomes of the respective procedures are reported in the JSGS annual report (30-day mortality/operative mortality: subtotal gastrectomy, 0.6%/1.3%; total gastrectomy, 1.0%/2.3%).[25] In this study, we focused only on patients who had undergone distal gastrectomy for gastric cancer. Out of the 17 and 21 risk factors in the 30-day and operative mortality models, respectively, 13 variables shared similar characteristics. Previously, many of these factors have been shown to affect perioperative mortality in patients who undergo gastric resections for malignancy.[17–22] The results of our study clearly showed that common and independent variables affected the mortality risk in the early (30-day mortality) and late (90-day in-hospital mortality) postoperative periods. The variables that predicted the 30-day mortality only and not the operative mortality comprised those that influence relatively early death after surgery, such as habitual alcohol consumption, preoperative pneumonia, myocardial infarction, and untreated bleeding disorder. The variables that predicted operative mortality only are those that influence late death after surgery, such as any respiratory distress, disseminated cancer, chronic corticosteroid use, emergency surgery, low platelet count, and high levels of aspartate aminotransferase, total bilirubin, and activated partial thromboplastin time. The variables that predicted both the 30-day and operative mortalities are those that influence both early and late death after surgery. In particular, the laboratory variables (eg, white blood cell count, serum albumin, and prothrombin time-international normalized ratio) that captured the risk of both early and late mortality appeared to be related to substantially abnormal levels in the 30-day mortality group. Further analysis is needed to determine the variables that are relevant to the respective morbidities leading to mortality, but these results provide insight into the specific preoperative risk variables responsible for the early or late mortality of patients who undergo distal gastrectomy.

This study had several limitations, which need to be addressed in future studies. First, the reported mortality and morbidity rates in our study would have been influenced by cancer stage, extent of lymphadenectomy (eg, D1, D1, and D2),[8,9,10,26–28] curative ability of the surgery,[29,30] hospital volume,[31,32] and institutional experience.[33] In addition, we only analyzed the variables that could be obtained before surgery. Although these risk models predicted the mortality well for open or laparoscopic approaches, the effects of these variables on outcomes should be assessed in a future study using a propensity score matching system. Second, some reports have described preoperative scoring systems that predict surgical risks, such as the Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity and the Estimation of Physiologic Ability and Surgical Stress for general surgery.[34,35] However, although these systems are useful for general surgery, some modifications would be required for specific operative procedures.[36] The NCD is currently being used to investigate the accuracy of these models for Japanese patients who undergo gastrectomy. Third, although our analysis used the nationwide database, the study population was limited to a single race. Therefore, our results should be evaluated on the basis of comparisons with patients from other countries using the same variables and definitions. Thus, we are currently planning a mutual collaboration with ACS-NSQIP.

CONCLUSIONS

We report the first risk stratification study based on the NCD for distal gastrectomy in cancer treatment. The NCD database allowed us to determine interinstitutional differences in outcomes and the factors that affect these differences. This system will contribute to an improved quality control in surgical practice and it should also be useful in counseling and for obtaining informed consent from patients.

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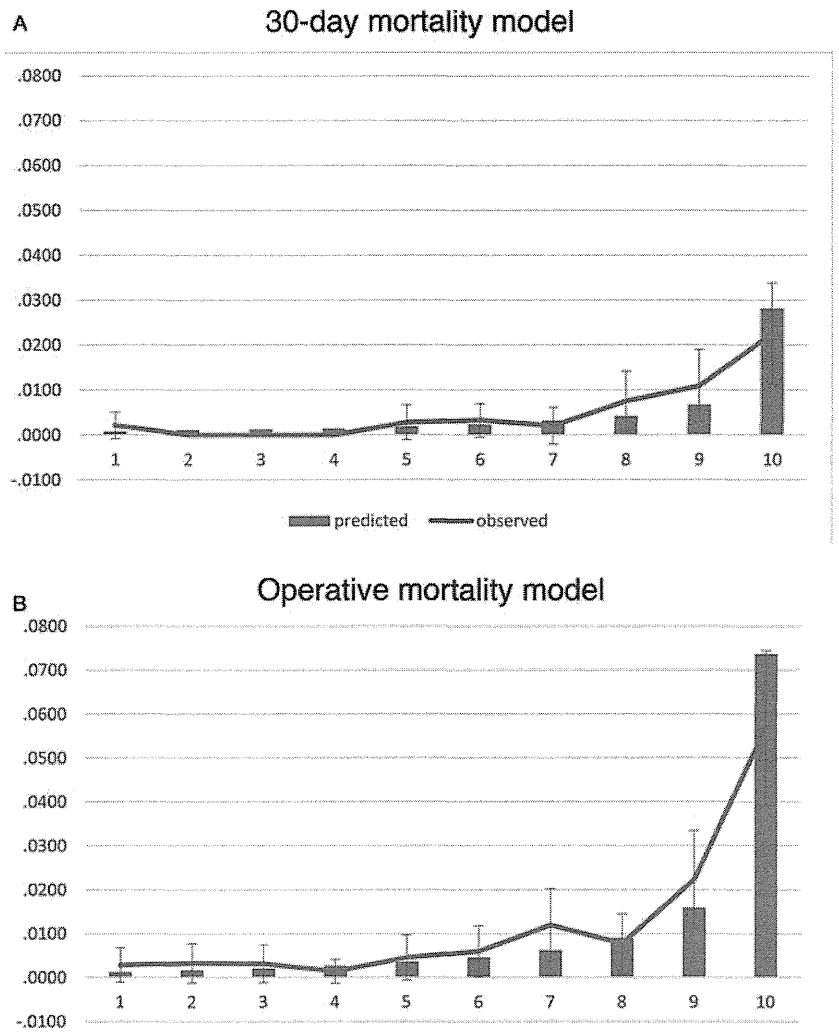

FIGURE 3. Calibrations of the 30-day mortality model (A) and operative mortality model (B). The calibrations of the models illustrate how well the rates of the predicted events matched those of the observed events among the patient risk subgroups. The error bar represents 95% confidence interval.

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