TABLE 4. Risk Models of Postoperative Occurrences After ADP Surgery

Variable	Septic Shock	Any Systemic Sepsis	Progressive Renal Insufficiency	Acute Renal Failure	On Ventilator > 48 Hours	Pneumonia	CVA/ Stroke	SSI Any
Demographics								
Age 60–75	1.144	1.095	1.105	1.144	1.16	1.214	1.174	1.04
Males		1.153			1.13	1.317		
Preoperative risk assessment								
General								
ADL totally dependent	1.178				1.399		1.426	
ADL partially dependent		1.175	1.23			1.278		
ASA class 4 and class 5	3.635	2.993	3.147	3.474	3.341	2.321	3.433	1.705
ASA class 3	1.77	1.888	1.957	1.922	2.066	1.837	1.691	1.347
Body mass index $\geq 30\,kg/m^2$					1.567			
Body mass index $\geq 26\,kg/m^2$			1.438	1.614	1.224			1.274
Alcohol drinking (at times/ occasional)			1.181	1.256		1.206		1.118
Brinkmann index ≥ 600	1.199				1.217			
Brinkmann index ≥ 400		1.162						
>10% loss body weight in last 6 months								1.561
Respiratory								
Ventilator dependent	1.519	1.404	1.305		2.734		2.035	
Current pneumonia		1.35	1.667	1.704	1.89	4.994	1.599	
History of severe COPD	1.371				1.472	1.403		
Respiratory failure	1.236					1.292		
Cardiovascular								
Congestive heart failure			1.501		1.331			
Hypertension requiring medication		1.119	1.199		1.235			
Hypertension without treatment								
Renal								
Acute renal failure	1.471	1.258	2.975	3.869	1.26	1.504		
Cerebral nervous system								
CVA/Stroke		1.346		1.675	1.376	1.631	1.826	
Cerebrovascular disease within 14 days		1.933					3.406	
Cerebrovascular disease	1.373					1.421		
Hematological								
Bleeding disorder without treatment	1.437	1.494		1.471	1.377	1.289	1.92	
Bleeding disorder			1.361					
Blood transfusions	1.511	1.556	1.514	1.61	1.887	1.546	1.432	1.17
Preoperative transfusion of ≥ 1 unit of RBCs			1.303		1.369			1.355
Infectious disorder								
Systemic Sepsis	2.821	4.086	1.974	2.035	2.092	1.901	1.776	1.824
Oncological								
Other than cancer surgery	0.734		0.803					
Other								
Open wound		1.469						2.186
Steroid use for chronic condition	1.486		1.585		1.586	1.545		1.507
Ascites without control		1.17						
Esophageal varices without control					1.846			
Preoperative laboratory value								
WBC < 3500/mL	1.989	1.462	1.318	1.55	1.553		1.428	1.225
Hematocrit over 48% (male), 42% (female)	1.441	1.334		1.52	1.493			
Plate count < 150,000/mL		1.175	1.192					
Plate count < 50,000/mL	1.741							
Serum albumin < 3.5 g/dL		1.286			1.153			1.162
Serum albumin < 2.5 g/dL	1.267					1.18	1.251	
Serum albumin < 2.0 g/dL		1.287	1.403		1.606	1.255		1.227

Variable	Septic Shock	Any Systemic Sepsis	Progressive Renal Insufficiency	Acute Renal Failure	On Ventilator > 48 Hours	Pneumonia	CVA/ Stroke	SSI Any
SGOT ≥ 40 U/L							1.252	
SGOT ≥ 35 U/L	1.272	1.198	1.4	1.454	1.281			
Bilirubin < 0.2 mg/dL						2.611		
Serum creatinine ≥ 3.0 mg/dL							1.626	
Serum creatinine ≥ 2.0 mg/dL		1.233	1.637					
Serum creatinine ≥ 1.2 mg/dL	1.454		1.721	1.566	1.202		1.31	
BUN ≥ 60 mg/dL				1.388				
BUN ≥ 25 mg/dL			1.362	1.43				
BUN ≥ 20 mg/dL	1.355	1.357	1.344		1.404	1.278	1.415	1.156
Serum sodium < 130 mEq/L		1.233						
Serum sodium ≥ 146 mEq/L		1.482	1.432	1.586	1.68	1.501	1.499	
Alkaline phosphatase < 110 mEq/L								1.487
CRP > 10 mg/dL								1.353
INR of PT values ≥ 1.67	1.44	1.239						
PT < 10 s						1.232		1.157
PTT < 30 s	1.181							1.137

ADL = activities of daily living; ASA = American Society of Anesthesiologists Physical Status; AST = aspartate amino transferase; BUN = blood urea nitrogen; COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; CVA = cerebrovascular accident; WBC = white blood cell.

risk factors of mortality in patients with ADP.[15] Preoperative variables associated with organ dysfunction tended to be included as risk factors in most of the risk models: preoperative ventilation/pneumonia, acute renal failure, bleeding disorders, low white blood cell count, low albumin level, and elevation of blood urea nitrogen.[15] High serum sodium levels, indicative of severe dehydration in patients, were also identified. In contrast, the risk model for SSI, which was poorly associated with mortality ($r = 0.107$), showed a relatively low C-index (0.688) compared with the other risk models. Risk factors such as pulmonary, renal, and cerebral disorders were not included in the risk model. The key part of these risk models is that variables

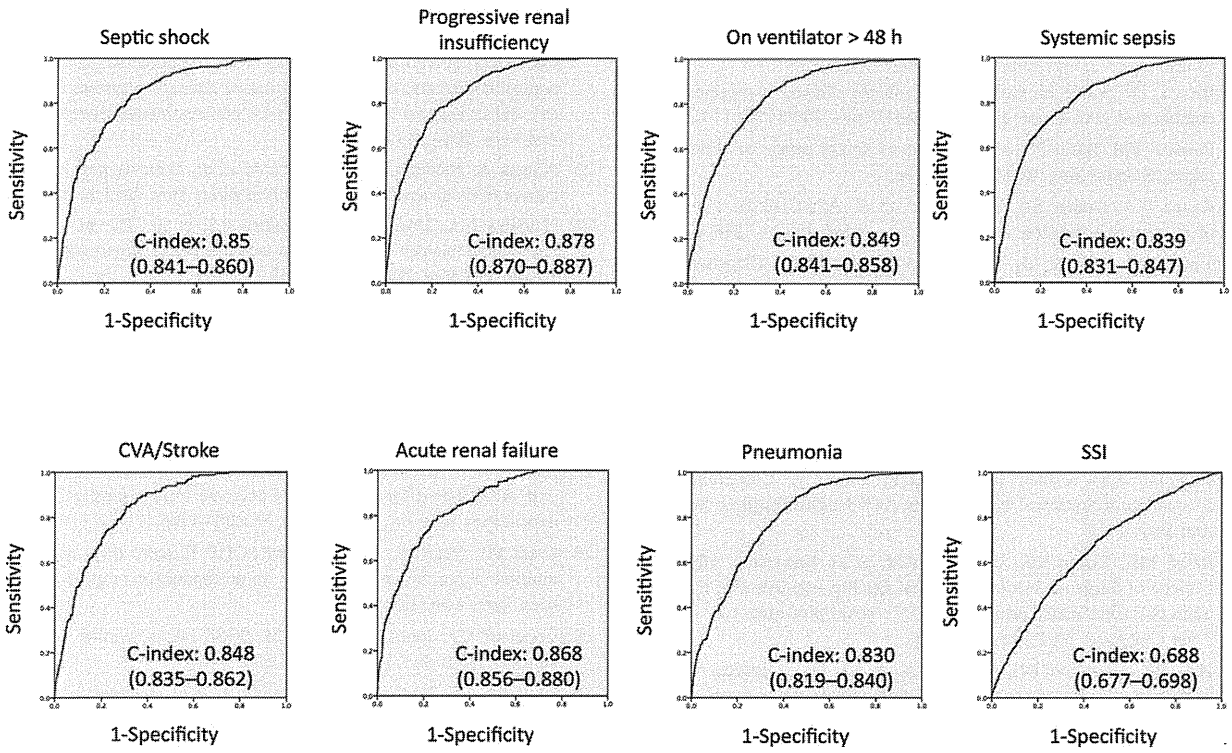

FIGURE 1. Receiver operating characteristic (ROC) curves of each postoperative complication was shown with the C-indices and 95% CIs of each occurrence. ROC = receiver operating characteristic, CIs = confidence intervals.

that were not included as risk factors of mortality were picked up as predictors of morbidities leading to mortality. This will help to improve the postoperative management of patients with ADP.

There are several limitations to this study. First, although these risk models for morbidities effectively predicted their occurrence based on preoperative variables, the source of infection and degree of its control would affect mortality and morbidity. These intraoperative parameters will be evaluated in a future study. Second, in the NCD data-entry system, the final outcome of each morbidity, whether it improved, was unresolved, led to death, and was not recorded. It is not possible to relate each morbidity directly to mortality, although most fatal cases feature multiple organ failure at the end.

ADP is a clinically distinct entity requiring life-saving emergency surgery and intensive care. We created risk models for morbidities in critically ill patients with ADP, using variables recorded by the NCD comparable to those of the ACS-NSQIP, and these models performed well. These models could be formatted to feed information back to the NCD and can be expected to improve the quality of the surgical and postoperative care of patients with ADP.

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ORIGINAL ARTICLE

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

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

Keywords Mitral valve · Surgery · Valvular diseases

Introduction

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

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

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

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

Patients and methods

Japan Adult Cardiovascular Surgery Database

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

Study population

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

Study design

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

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

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

Statistical analysis

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

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

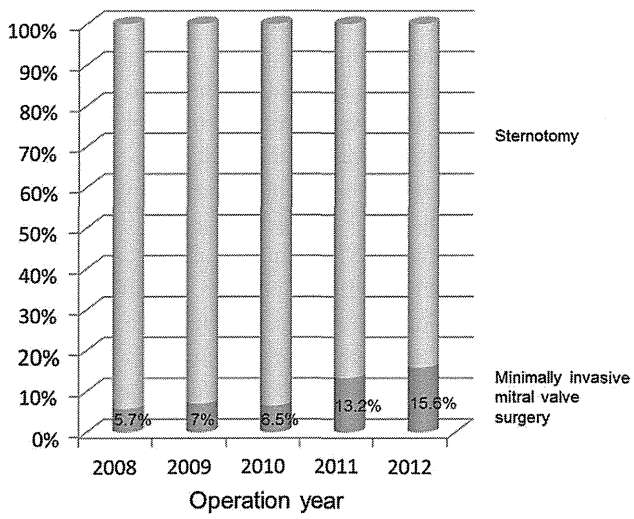

Fig. 1 Ratio of MICS-mitral in patients who underwent isolated mitral valve repair between 2008 and 2012. The ratio within the overall cohort gradually increased over time

Results

Overall cohort

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

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

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

Propensity score matching

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

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

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

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

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

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

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

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

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

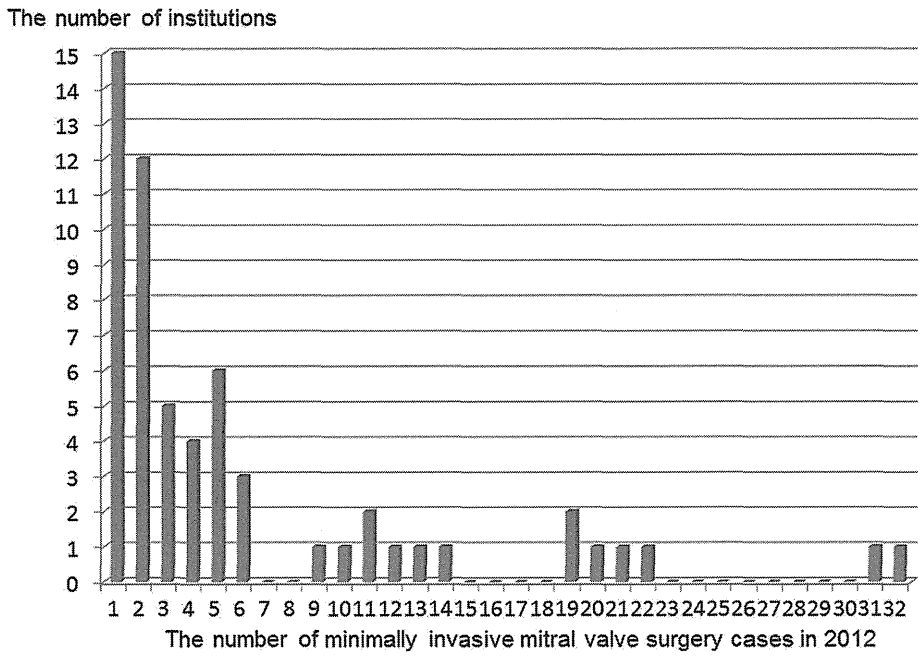

Fig. 2 Distribution of the number of MICS-mitral cases. Many low-volume institutions performed fewer than 10 cases per year

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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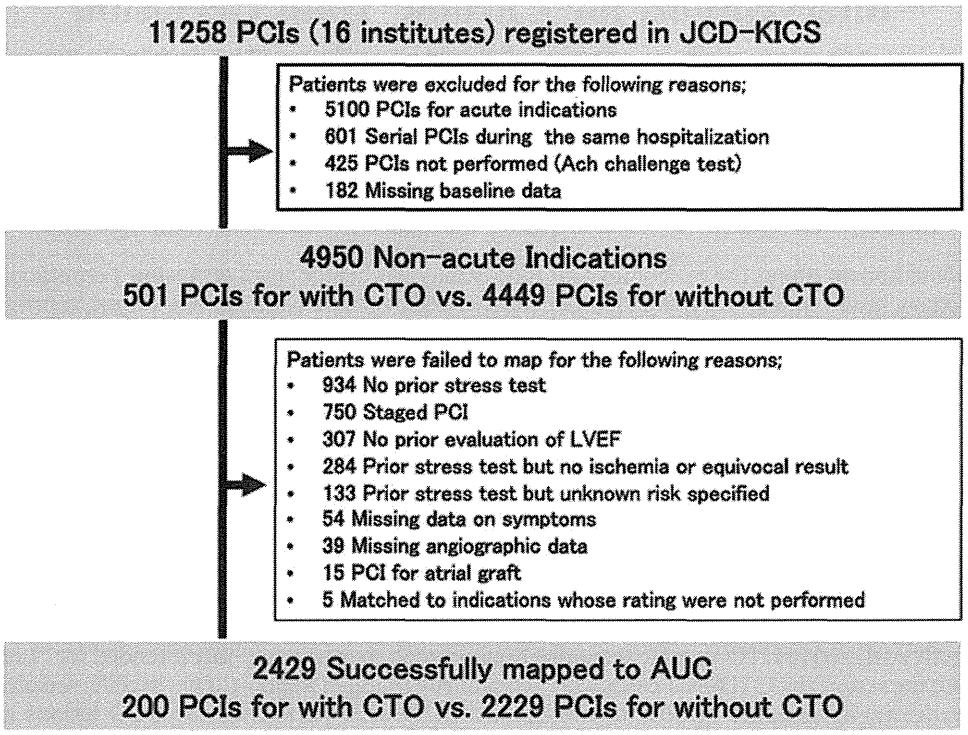

Figure 1. Flowchart of the process to identify the cohort of patients who underwent PCI procedures for nonacute indications. Ach = acetylcholine; LVEF = left ventricular ejection fraction.

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

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

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]

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

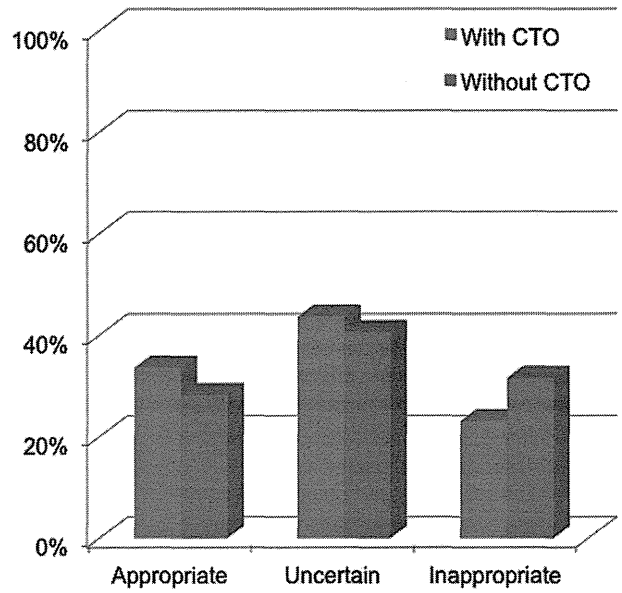

Figure 2. Appropriate use ratings of PCIs for lesions with and without CTO.

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

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

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 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

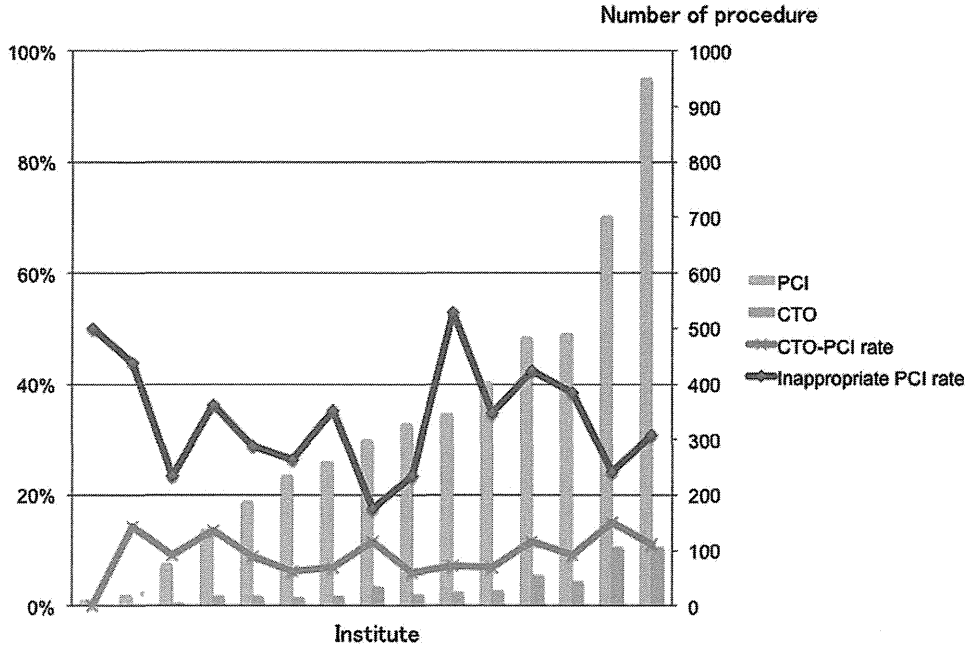

Figure 3. Association between procedural volume by institute and the rates of CTO-PCI or inappropriate PCI. *Light blue bar*, all procedural numbers by institute; *orange bar*, number of CTO-PCI by institute; *green line*, ratio of CTO-PCI to all procedures by institute (percentage); *purple line*, percentage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