ORIGINAL RESEARCH

Procedural Volume and Outcomes After Percutaneous Coronary Intervention for Unprotected Left Main Coronary Artery Disease—Report From the National Clinical Data (J-PCI Registry)

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BACKGROUND: There is a limited evidence base to support the volume-outcome relationship in patients undergoing percutaneous coronary intervention (PCI) for unprotected left main coronary artery disease (UPLMD). This study aimed to evaluate the relationship between institutional and operator volume and in-hospital outcomes in patients undergoing PCI for unprotected left main coronary artery disease.

METHODS AND RESULTS: We analyzed characteristics and clinical outcomes of 24 320 patients undergoing PCI for unprotected left main coronary artery disease at 1102 hospitals by 7244 operators using data from the Japanese nationwide J-PCI Registry (National PCI Data Registry) between January 2014 and December 2017. We classified institutions and operators into quartiles based on the mean annual volume of PCI. A generalized linear mixed-effects model was used to evaluate the association between institutional and operator PCI volume and in-hospital outcomes. Among the 24 320 patients, 4027 (16.6%), 6147 (25.3%), and 14 146 (58.2%) presented with ST-segment–elevation myocardial infarction, non–ST-segment–elevation acute coronary syndrome, and stable ischemic heart disease; their crude in-hospital mortality was 15%, 3.1%, and 0.3%, respectively. Compared with patients in the lowest quartile of institutional volume (1–216 PCIs/y), the adjusted odds ratio of in-hospital death in patients in the second (217–323 PCIs/y), third (324–487 PCIs/y), and fourth (488–3015 PCIs/y) quartile of institutional volume was 0.75 (95% CI, 0.51–1.10; *P*=0.14), 0.87 (95% CI, 0.57–1.34; *P*=0.54), and 0.51 (95% CI, 0.30–0.86; *P*=0.01), respectively. These findings were consistent in rates of in-hospital death or any complication. Conversely, operator PCI volume was not significantly associated with in-hospital outcomes.

CONCLUSIONS: Institutional rather than operator-based PCI volume was associated with better in-hospital outcomes in patients undergoing PCI for unprotected left main coronary artery disease.

Key Words: mortality/survival ■ percutaneous coronary intervention ■ revascularization ■ unprotected left main coronary artery disease ■ volume-outcome relationship

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See Editorial by Saad and Brilakis

Recently, the short- and long-term outcomes of patients undergoing percutaneous coronary intervention (PCI) for unprotected left main coronary artery disease (UPLMD) have improved substantially, predominantly attributable to advances in interventional techniques, devices, and patient selection.[1–3] Consequently,

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Nonstandard Abbreviations and Acronyms

NSTE-ACS	non–ST-segment–elevation acute coronary syndrome
PCI	percutaneous coronary intervention
SIHD	stable ischemic heart disease
STEMI	ST-segment–elevation myocardial infarction
UPLMD	unprotected left main coronary artery disease

current European and Japanese clinical practice guidelines recommend both PCI and coronary artery bypass grafting for UPLMD patients with low or intermediate complexity,[4,5] and now an increasing number of PCIs for patients with UPLMD have been performed by many operators in various hospitals. Institutional and operator PCI volumes play important roles in quality assessment in patients undergoing PCI.[6–10] Patients undergoing PCI for UPLMD with ST–segment-elevation myocardial infarction (STEMI) or non–ST-segment–elevation acute coronary syndrome (NSTE-ACS) remain at high risk of in-hospital death.[11,12] Hence, better understanding of the PCI volume-outcome relationship has become crucial in efforts to improve outcomes in these patients. A retrospective single-center study reported that patients undergoing PCI for UPLMD performed by high-volume operators had lower short- and long-term mortality.[13] Despite the fact that the study had a limited number of patients, clinical practice guideline recommendations

have solely referred to these data to outline the volume-outcome relationship of PCI for UPLMD, which is recommended to be performed by trained operators with an annual volume of ≥25 PCIs for left main coronary artery disease.[4]

The purpose of this study was to examine the relationship between institutional and operator volumes of PCI and in-hospital outcomes in patients with UPLMD, using a nationwide PCI registry in Japan.

METHODS

The data, analytic methods, and study materials will not be made publicly available to other researchers for the purpose of reproducing the results or replicating the procedure.

J-PCI Registry and Study Design

The J-PCI registry (National PCI Data Registry), administered by the Japanese Association of Cardiovascular Intervention and Therapeutics, is a prospective Japanese nationwide multicenter registry that has been previously described.[7,14,15] Briefly, it was designed to collect data on clinical characteristics and in-hospital outcomes from patients undergoing PCI at >1000 hospitals in Japan (≈85% of all PCIs). Data were collected from the National Clinical Database website using an electronic data capture system. Participating sites are randomly selected for annual audits by members of the Japanese Association of Cardiovascular Intervention and Therapeutics registry subcommittee. The study protocol of the J-PCI registry was approved by the Institutional Review Board Committee of the Network for Promotion of Clinical Studies (a specified nonprofit organization affiliated with Osaka University Graduate School of Medicine, Osaka, Japan) and complied with the principles contained within the Declaration of Helsinki. Written informed consent was waived because of the retrospective and observational nature of the study.

Study Population

For the present study, we analyzed the data of patients registered in the J-PCI between January 2014 and December 2017 (n=941 516). We excluded patients <18 years or >100 years of age (n=351), and those with missing data regarding sex (n=3403) or in-hospital death and/or complications (n=1150). To restrict the data to patients undergoing PCI for UPLMD, we also excluded patients without left main coronary artery disease (n=881 924), those with missing angiographic characteristics (n=17 886), those who did not undergo PCI for UPLMD (n=9728), and those with a history of prior coronary artery bypass grafting (n=2754). Ultimately, the remaining 24 320 patients were included in this study (Figure 1).
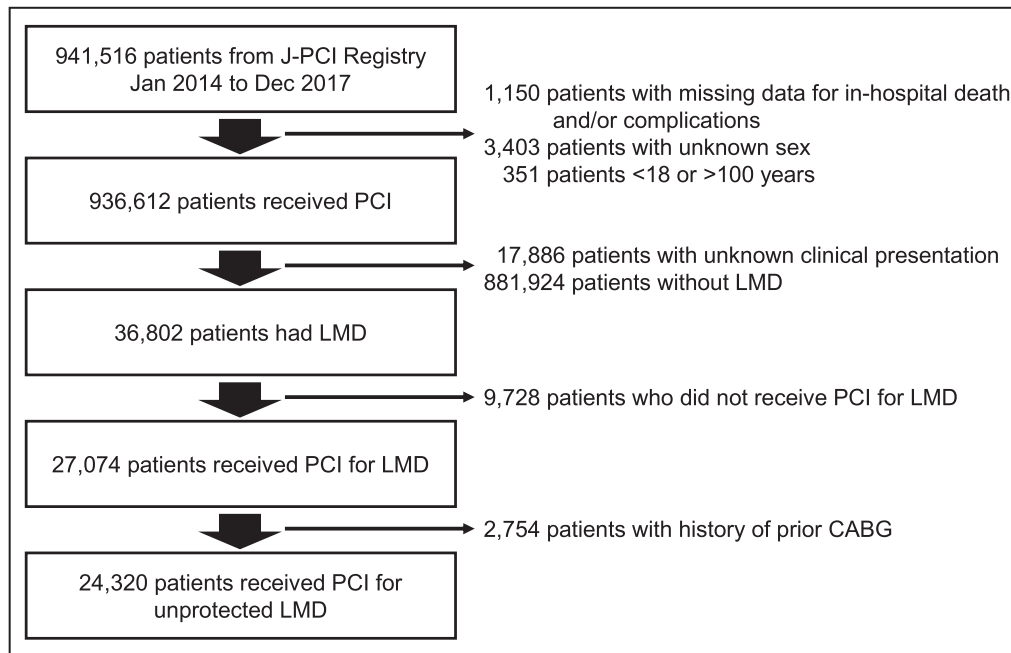
Figure 1.   Flow diagram for identifying study population.
CABG indicates coronary artery bypass grafting; LMD, left main coronary artery disease; and PCI, percutaneous coronary intervention.

Annual Institutional and Operator Volumes of PCI

A mean annual institutional PCI volume was calculated by dividing the hospital's total number of PCIs between January 2014 and December 2017 by 4. Because the J-PCI registry uses a unique operator identifier that carries across hospitals, each operator's volume of PCI could be counted as long as the PCI was performed in hospitals participating in the J-PCI registry (≈90% of those in the nation). Thus, a mean annual operator PCI volume was also calculated by dividing the operator's total number of PCIs during the study period by 4.

Definition of Variables

According to the J-PCI protocol, patients with NSTE-ACS included those with non–ST-segment–elevation myocardial infarction (NSTEMI) and unstable angina; and patients with stable ischemic heart disease (SIHD) included those with stable angina, old myocardial infarction, and silent ischemia.

Cardiogenic shock was defined as a sustained episode of systolic blood pressure <80 mm Hg, cardiac index <1.8 L/min per m^2 determined to be secondary to cardiac dysfunction, and/or the requirement for a parenteral inotropic or vasopressor agent or mechanical support, including an intra-aortic balloon pump, to maintain blood pressure and cardiac index above the specified levels within 24 hours before the PCI procedure.

Acute heart failure was defined as symptoms of heart failure within 24 hours before the PCI procedure, including dyspnea on mild activity, orthopnea, body fluid retention, moist rales, neck vein distention, and pulmonary edema, which were equivalent to congestive heart failure of New York Heart Association functional classification class IV.

Chronic kidney disease in this registry was defined as the presence of proteinuria, serum creatinine ≥1.3 mg/dL or estimated glomerular filtration rate ≤60 mL/min per 1.73 m^2, according to guidelines from the Japanese Society of Nephrology (https://cdn.jsn.or.jp/guideline/pdf/CKDguide2012.pdf).

Successful PCI was defined as achievement of Thrombolysis in Myocardial Infarction flow grade III with residual stenosis ≤25% in the target lesion.

Clinical Outcomes

The primary outcome was in-hospital mortality, defined as the rate of death before hospital discharge or within 30 days after PCI, in case of excessive hospitalization over 30 days after PCI. The secondary outcome was a composite of in-hospital death and periprocedural complications, including cardiac tamponade, cardiogenic shock requiring mechanical and/or inotropic support, stent thrombosis ("definite" in the definition of the Academic Research Consortium),[16] emergency surgery, and bleeding requiring blood transfusion. The J-PCI registry collects in-hospital death and these complications separately in each patient, which allowed us to avoid double counting of events.

Statistical Analysis

Continuous variables are presented as mean±SD. Categorical variables are presented as frequencies and percentages and were compared using the chi-square test. The primary prespecified analysis examined the association between institutional or operator procedural volume and in-hospital mortality. Mean annual institutional and operator volumes of PCI were divided into quartiles based on the total number of PCIs for ease of interpretation. The trend of crude in-hospital outcomes across PCI volume quartiles in each stratum was assessed using the Cochran–Armitage trend test with Bonferroni adjustment for multiple comparisons.

A generalized linear mixed-effects model with an unstructured covariance matrix was developed to identify independent predictors of the primary and secondary outcomes. A 3-level hierarchical structure was constructed, in which hospitals and operators were included as random intercepts in the mixed-effects models to account for clustering of patient outcomes within hospitals and operators. Covariates for adjustment in the model were selected on the basis of clinical relevance,[6,7,17] including the following variables: age, sex, hypertension, diabetes mellitus, hyperlipidemia, smoking status, chronic kidney disease, dialysis, chronic lung disease, peripheral arterial disease, history of PCI, history of myocardial infarction, history of heart failure, clinical presentation (SIHD versus NSTE-ACS versus STEMI), cardiac arrest, cardiogenic shock, acute heart failure, anginal symptom within 1 month, weekend versus weekday PCI, emergency/urgent versus elective PCI, arterial access site (femoral versus radial versus others), and teaching hospitals with on-site cardiac surgery. The associations between in-hospital outcomes and covariates were expressed as adjusted odds ratios with 95% CIs. Furthermore, the relative importance of institutional and operator volumes modeled as continuous variables in relation to outcomes was assessed using generalized linear mixed-effects models. In these models, institutional and operator volumes were corrected for skewness using log transformation, and the effect of a linear interaction term (log [institutional volume]×log [operator volume]) on outcomes was also tested.

Sensitivity analyses were performed using a generalized additive mixed model, which have the potential to model nonlinear trends between outcomes and continuous variables (ie, age and institutional and operator volumes) without making strong assumptions about the parametric form of these trends. Smoothing spline curves were similar to the curves in generalized linear mixed-effects models, supporting the validity of our primary analyses. A *P* value of <0.05 was considered statistically significant.

Statistical analyses were performed using R version 3.6.1 (R Foundation for Statistical Computing, Vienna, Austria) and Python version 3.7.0 (available at https://www.python.org/).

RESULTS

Population Characteristics

Among the 24 320 patients undergoing PCI for UPLMD performed at 1102 institutions by 7244 operators in Japan, 4027 (16.6%) had STEMI, 6147 (25.3%) had NSTE-ACS, and 14 146 (58.2%) had SIHD. The baseline patient characteristics are shown in Table 1. The mean age of the patients was 72.4±10.4 years, and 19 035 (78%) were men. Hypertension and hyperlipidemia predominated in each stratum. Diabetes mellitus, prior history of PCI, myocardial infarction, and heart failure were less frequent in patients with STEMI. Acute heart failure, cardiogenic shock, and cardiac arrest within 24 hours of PCI and weekend PCI were more frequent in patients with STEMI. Femoral access was more frequent than radial access in patients with STEMI (66% versus 29%) or NSTE-ACS (50% versus 44%). Drug-eluting stents were predominantly used in each stratum. Thrombus aspiration was more frequently performed in patients with STEMI than in those with NSTE-ACS or SIHD (39% versus 6.5% versus 1.0%, respectively). Rotational atherectomy was performed in 9.0% of patients with SIHD, 5.7% of those with NSTE-ACS, and 2.1% of those with STEMI. Compared with high-volume operators, low-volume operators more frequently performed PCI for UPLMD in patients with STEMI. Similarly, PCI in patients with STEMI was more frequently performed at low-volume hospitals than at high-volume hospitals.

In-Hospital Outcomes

In-hospital outcomes in patients undergoing PCI for UPLMD are shown in Table 2. Crude mortality rate was higher in patients with STEMI (15%) than in those with NSTE-ACS (3.1%) or SIHD (0.3%). Regarding PCI-related complications, cardiogenic shock requiring mechanical and/or inotropic support was more frequent in patients with STEMI (13%) than in those with NSTE-ACS (3.8%) or SIHD (1.0%). Bleeding requiring blood transfusion was also more frequent in patients with STEMI (3.3%) than in those with NSTE-ACS (1.0%) or SIHD (0.4%).

After adjustment for baseline characteristics, adjusted odds ratio of in-hospital death was 7.2-fold higher in patients with STEMI (95% CI, 4.11–12.62; *P*<0.001) and 3.3-fold higher in those with NSTE-ACS (95% CI, 1.92–5.71; *P*<0.001) than in those with SIHD (Figure 2A). Adjusted odds ratio of in-hospital death or

Table 1. Baseline Characteristics

Variable	Missing	SIHD (n=14 146)	NSTE-ACS (n=6147)	STEMI (n=4027)
Age, y	0 (0)	72.3 (9.7)	73.7 (10.8)	70.9 (11.9)
Male	0 (0)	11 258/14 146 (80)	4631/6147 (75)	3146/4027 (78)
History				
Hypertension	1029 (4.2)	10 977/13 749 (80)	4633/5868 (79)	2569/3674 (70)
Diabetes mellitus	1029 (4.2)	6956/13 749 (51)	2721/5868 (46)	1516/3674 (41)
Hyperlipidemia	1029 (4.2)	9670/13 749 (70)	3761/5868 (64)	1989/3674 (54)
Current/recent smoker (within 1 y)	1029 (4.2)	3873/13 749 (28)	1709/5868 (29)	1335/3674 (36)
Chronic kidney disease	1029 (4.2)	2859/13 749 (21)	1493/5868 (25)	883/3674 (24)
Dialysis	1029 (4.2)	1142/13 749 (8.3)	482/5868 (8.2)	137/3674 (3.7)
Chronic lung disease	1029 (4.2)	339/13 749 (2.5)	182/5868 (3.1)	103/3674 (2.8)
Peripheral arterial disease	1029 (4.2)	1574/13 749 (11)	597/5868 (10)	215/3674 (5.9)
Prior PCI	421 (1.7)	8742/13 794 (63)	2475/6112 (40)	769/3993 (19)
Prior myocardial infarction	573 (2.4)	3812/13 733 (28)	1228/6063 (20)	587/3951 (15)
Prior heart failure	780 (3.2)	2655/13 586 (20)	1194/6034 (20)	439/3920 (11)
Preprocedural characteristics				
Cardiac arrest within 24 h	565 (2.3)	42/13 663 (0.3)	325/6092 (5.3)	1039/4000 (26)
Cardiogenic shock within 24 h	570 (2.3)	103/13 663 (0.8)	764/6090 (13)	2061/3997 (52)
Acute heart failure within 24 h	583 (2.4)	179/13 664 (1.3)	1008/6088 (17)	1890/3985 (47)
Anginal symptom within 1 mo	0 (0)	8711/14 146 (62)	6145/6147 (100)	4023/4027 (100)
Procedure day	19 (<0.01)			
Weekday		13 849/14 134 (98)	5474/6144 (89)	2934/4023 (73)
Weekend		285/14 134 (2.0)	670/6144 (11)	1089/4023 (27)
Procedural characteristics				
Emergency/urgent PCI	0 (0)	440/14 146 (3.1)	3070/6147 (50)	3609/4027 (90)
Arterial access site	0 (0)			
Femoral		6577/14 146 (46)	3067/6147 (50)	2657/4027 (66)
Radial		6728/14 146 (48)	2735/6147 (44)	1150/4027 (29)
Others		841/14 146 (5.9)	345/6147 (5.6)	220/4027 (5.5)
Type of device used	0 (0)			
Bare-metal stent		191/14 146 (1.4)	161/6147 (2.6)	215/4027 (5.3)
Drug-eluting stent		13 129/14 146 (93)	5655/6147 (92)	3472/4027 (86)
Rotational atherectomy		1271/14 146 (9.0)	349/6147 (5.7)	85/4027 (2.1)
Directional coronary atherectomy		134/14 146 (0.9)	14/6147 (0.2)	1/4027 (0.02)
Filter-based distal protection		162/14 146 (1.1)	158/6147 (2.6)	197/4027 (4.9)
Thrombus aspiration		147/14 146 (1.0)	400/6147 (6.5)	1571/4027 (39)
Fluoroscopy time, min	2994 (12.3)	38.2 (25.2)	40.8 (26.7)	42.1 (25.4)
Hospital characteristics				
Teaching hospitals with on-site cardiac surgery	0 (0)	9882/14 146 (70)	3964/6147 (64)	2727/4027 (68)
Mean annual institutional PCI volume	0 (0)			
First quartile (1–216)		2337/14 146 (17)	1303/6147 (21)	876/4027 (22)
Second quartile (217–323)		2956/14 146 (21)	1421/6147 (23)	1053/4027 (26)
Third quartile (324–487)		3809/14 146 (27)	1673/6147 (27)	1183/4027 (29)
Fourth quartile (488–3015)		5044/14 146 (36)	1750/6147 (28)	915/4027 (23)
Operator characteristics				
Mean annual operator PCI volume	0 (0)			
First quartile (1–40)		2269/14 146 (16)	1179/6147 (19)	1022/4027 (25)
Second quartile (41–64)		3013/14 146 (21)	1470/6147 (24)	1048/4027 (26)

(Continued)

Table 1. Continued

Variable	Missing	SIHD (n=14 146)	NSTE-ACS (n=6147)	STEMI (n=4027)
Third quartile (65–94)		3955/14 146 (28)	1713/6147 (28)	1088/4027 (27)
Fourth quartile (95–578)		4909/14 146 (35)	1785/6147 (29)	869/4027 (22)

Data are expressed as mean (standard deviation) or n/N (%) of patients. NSTE-ACS indicates non-ST–segment elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.

any complication was also higher in patients with STEMI (odds ratio, 2.64; 95% CI, 2.00–3.49; P<0.001) or NSTE-ACS (odds ratio, 1.44; 95% CI, 1.12–1.86; P=0.005) than in those with SIHD (Figure 2B). Advanced age, female sex, chronic kidney disease, peripheral arterial disease, cardiac arrest within 24 hours of PCI, cardiogenic shock within 24 hours of PCI, acute heart failure within 24 hours of PCI, and emergency or urgent PCI were associated with a higher odds ratio of in-hospital death. The radial approach was associated with a lower odds ratio of in-hospital death than the femoral approach (odds ratio, 0.49; 95% CI, 0.38–0.64; P<0.001).

Annual Institutional PCI Volume and Outcomes

The relationships between mean annual institutional PCI volumes and in-hospital outcomes are shown in Table 3. Crude mortality rate was significantly lower in higher quartiles of institutional volume in patients with STEMI (P<0.001). Crude mortality and complication rates were significantly lower in higher quartiles of institutional volume in each stratum (P<0.001 for all). The relationship between institutional volume quartile and in-hospital outcomes was partly attenuated after adjusting for potential confounders (Figures 2 and 3). Compared with patients in the lowest quartile of institutional volume (1–216 PCIs/y), the odds ratio of in-hospital death in patients in the second (217–323 PCIs/y), third (324–487 PCIs/y), and fourth (488–3015 PCIs/y) quartile of institutional volume

was 0.75 (95% CI, 0.51–1.10; P=0.14), 0.87 (95% CI, 0.57–1.34; P=0.54), and 0.51 (95% CI, 0.30–0.86; P=0.01), respectively (Figure 2A). Similarly, the odds ratio of in-hospital death or any complication in patients treated in the second, third, and fourth quartiles of institutional volume was 0.96 (95% CI, 0.73–1.26; P=0.78), 0.88 (95% CI, 0.65–1.21; P=0.44), and 0.64 (95% CI, 0.44–0.93; P=0.02), respectively, as compared with patients in the lowest quartile of institutional volume (Figure 2B). A higher institutional volume was marginally associated with a lower odds ratio of in-hospital death (odds ratio, 0.76 per log increase; 95% CI, 0.58–1.00; P=0.052) and in-hospital death or any complication (odds ratio, 0.83 per log increase; 95% CI, 0.68–1.00; P=0.054). There was no significant interaction between institutional and operator volume in in-hospital death (P=0.44 for interaction) and in-hospital death or any complication (P=0.48 for interaction). Adjusted rate of in-hospital death in patients treated in the first, second, third, and fourth quartiles of institutional volume was 3.9%, 3.3%, 3.7%, and 1.7%, respectively. Similarly, the adjusted rate of in-hospital death or any complication in patients in the first, second, third, and fourth quartiles of institutional volume was 7.5%, 7.6%, 6.8%, and 3.6%, respectively.

Annual Operator PCI Volume and Outcomes

Table 4 shows the relationship between mean annual operator PCI volumes and in-hospital outcomes.

Table 2. In-Hospital Clinical Outcomes

	SIHD (n=14 146)	NSTE-ACS (n=6147)	STEMI (n=4027)	P Value
In-hospital death	44 (0.3)	193 (3.1)	615 (15)	<0.001
Any complication	249 (1.8)	424 (6.9)	947 (24)	<0.001
Cardiac tamponade	33 (0.2)	17 (0.3)	14 (0.3)	0.45
Shock requiring mechanical and/or inotropic support	145 (1.0)	234 (3.8)	518 (13)	<0.001
Stent thrombosis	19 (0.1)	19 (0.3)	32 (0.8)	<0.001
Requirement for emergency surgery	15 (0.1)	14 (0.2)	21 (0.5)	<0.001
Bleeding requiring blood transfusion	57 (0.4)	63 (1.0)	131 (3.3)	<0.001
Radial access site bleeding	4 (0.03)	10 (0.2)	8 (0.2)	<0.001
Femoral or other access site bleeding	32 (0.2)	26 (0.4)	65 (1.6)	<0.001
Non–access site bleeding	22 (0.2)	28 (0.5)	71 (1.8)	<0.001

Data are expressed as N (%) of patients. NSTE-ACS indicates nonST-segment–elevation acute coronary syndrome; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.
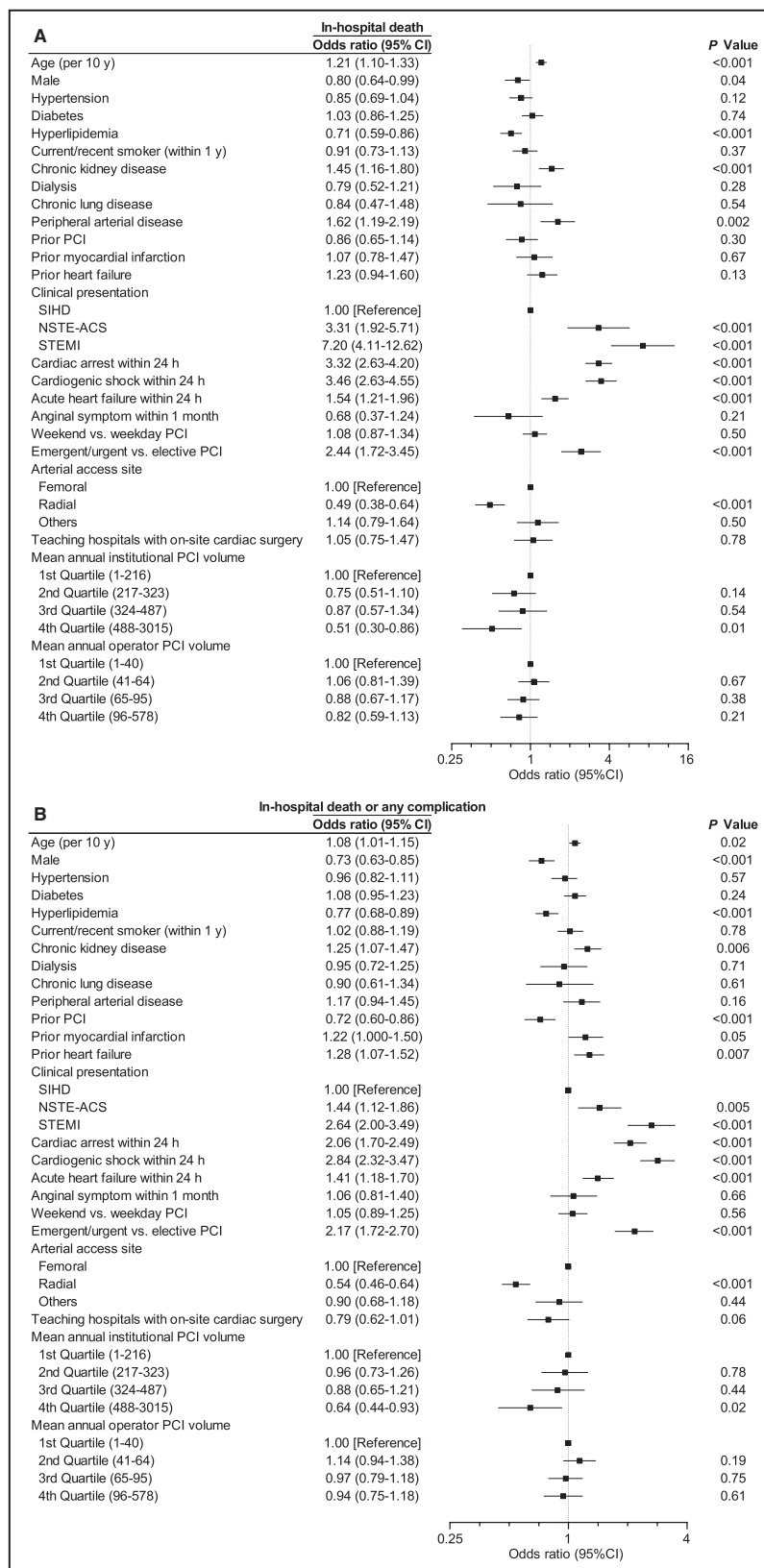
A — In-hospital death

	Odds ratio (95% CI)	P Value
Age (per 10 y)	1.21 (1.10-1.33)	<0.001
Male	0.80 (0.64-0.99)	0.04
Hypertension	0.85 (0.69-1.04)	0.12
Diabetes	1.03 (0.86-1.25)	0.74
Hyperlipidemia	0.71 (0.59-0.86)	<0.001
Current/recent smoker (within 1 y)	0.91 (0.73-1.13)	0.37
Chronic kidney disease	1.45 (1.16-1.80)	<0.001
Dialysis	0.79 (0.52-1.21)	0.28
Chronic lung disease	0.84 (0.47-1.48)	0.54
Peripheral arterial disease	1.62 (1.19-2.19)	0.002
Prior PCI	0.86 (0.65-1.14)	0.30
Prior myocardial infarction	1.07 (0.78-1.47)	0.67
Prior heart failure	1.23 (0.94-1.60)	0.13
Clinical presentation		
SIHD	1.00 [Reference]	
NSTE-ACS	3.31 (1.92-5.71)	<0.001
STEMI	7.20 (4.11-12.62)	<0.001
Cardiac arrest within 24 h	3.32 (2.63-4.20)	<0.001
Cardiogenic shock within 24 h	3.46 (2.63-4.55)	<0.001
Acute heart failure within 24 h	1.54 (1.21-1.96)	<0.001
Anginal symptom within 1 month	0.68 (0.37-1.24)	0.21
Weekend vs. weekday PCI	1.08 (0.87-1.34)	0.50
Emergent/urgent vs. elective PCI	2.44 (1.72-3.45)	<0.001
Arterial access site		
Femoral	1.00 [Reference]	
Radial	0.49 (0.38-0.64)	<0.001
Others	1.14 (0.79-1.64)	0.50
Teaching hospitals with on-site cardiac surgery	1.05 (0.75-1.47)	0.78
Mean annual institutional PCI volume		
1st Quartile (1-216)	1.00 [Reference]	
2nd Quartile (217-323)	0.75 (0.51-1.10)	0.14
3rd Quartile (324-487)	0.87 (0.57-1.34)	0.54
4th Quartile (488-3015)	0.51 (0.30-0.86)	0.01
Mean annual operator PCI volume		
1st Quartile (1-40)	1.00 [Reference]	
2nd Quartile (41-64)	1.06 (0.81-1.39)	0.67
3rd Quartile (65-95)	0.88 (0.67-1.17)	0.38
4th Quartile (96-578)	0.82 (0.59-1.13)	0.21

Odds ratio (95%CI)

B — In-hospital death or any complication

	Odds ratio (95% CI)	P Value
Age (per 10 y)	1.08 (1.01-1.15)	0.02
Male	0.73 (0.63-0.85)	<0.001
Hypertension	0.96 (0.82-1.11)	0.57
Diabetes	1.08 (0.95-1.23)	0.24
Hyperlipidemia	0.77 (0.68-0.89)	<0.001
Current/recent smoker (within 1 y)	1.02 (0.88-1.19)	0.78
Chronic kidney disease	1.25 (1.07-1.47)	0.006
Dialysis	0.95 (0.72-1.25)	0.71
Chronic lung disease	0.90 (0.61-1.34)	0.61
Peripheral arterial disease	1.17 (0.94-1.45)	0.16
Prior PCI	0.72 (0.60-0.86)	<0.001
Prior myocardial infarction	1.22 (1.000-1.50)	0.05
Prior heart failure	1.28 (1.07-1.52)	0.007
Clinical presentation		
SIHD	1.00 [Reference]	
NSTE-ACS	1.44 (1.12-1.86)	0.005
STEMI	2.64 (2.00-3.49)	<0.001
Cardiac arrest within 24 h	2.06 (1.70-2.49)	<0.001
Cardiogenic shock within 24 h	2.84 (2.32-3.47)	<0.001
Acute heart failure within 24 h	1.41 (1.18-1.70)	<0.001
Anginal symptom within 1 month	1.06 (0.81-1.40)	0.66
Weekend vs. weekday PCI	1.05 (0.89-1.25)	0.56
Emergent/urgent vs. elective PCI	2.17 (1.72-2.70)	<0.001
Arterial access site		
Femoral	1.00 [Reference]	
Radial	0.54 (0.46-0.64)	<0.001
Others	0.90 (0.68-1.18)	0.44
Teaching hospitals with on-site cardiac surgery	0.79 (0.62-1.01)	0.06
Mean annual institutional PCI volume		
1st Quartile (1-216)	1.00 [Reference]	
2nd Quartile (217-323)	0.96 (0.73-1.26)	0.78
3rd Quartile (324-487)	0.88 (0.65-1.21)	0.44
4th Quartile (488-3015)	0.64 (0.44-0.93)	0.02
Mean annual operator PCI volume		
1st Quartile (1-40)	1.00 [Reference]	
2nd Quartile (41-64)	1.14 (0.94-1.38)	0.19
3rd Quartile (65-95)	0.97 (0.79-1.18)	0.75
4th Quartile (96-578)	0.94 (0.75-1.18)	0.61

Odds ratio (95%CI)

Figure 2. Adjusted odds ratio for (A) in-hospital death and (B) in-hospital death or any complication.
NSTE-ACS indicates non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.

Table 3. Mean Annual Institutional PCI Volume and Outcomes

	Mean Annual Institutional PCI Volume					P for Trend*
	Overall	First Quartile (1–216)	Second Quartile (217–323)	Third Quartile (324–487)	Fourth Quartile (488–3015)	
Crude in-hospital death						
SIHD	44/14 146 (0.3)	9/2337 (0.4)	14/2956 (0.5	12/3809 (0.3)	9/5044 (0.2)	0.04
NSTE-ACS	193/6147 (3.1)	45/1303 (3.5)	48/1421 (3.4)	60/1673 (3.6)	40/1750 (2.3)	0.08
STEMI	615/4027 (15.3)	163/876 (18.6)	154/1053 (14.6)	209/1183 (17.7)	89/915 (9.7)	<0.001
Crude in-hospital death or any complication						
SIHD	249/14 146 (1.8)	52/2337 (2.2)	82/2956 (2.8)	64/3809 (1.7)	51/5044 (1.0)	<0.001
NSTE-ACS	424/6147 (6.9)	99/1303 (7.6)	116/1421 (8.2)	130/1673 (7.8)	79/1750 (4.5)	<0.001
STEMI	947/4027 (23.5)	243/876 (27.7)	251/1053 (23.8)	304/1183 (25.7)	149/915 (16.3)	<0.001

Data are expressed as n/N (%) of patients. NSTE-ACS indicates non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.

*P<0.017 was considered statistically significant after Bonferroni adjustment for multiple comparisons.

Crude mortality rate was significantly lower in higher quartiles of operator volume in patients with NSTE-ACS (P<0.001). Crude mortality and complication rates were also significantly lower in higher quartiles of operator volume in patients with NSTE-ACS or STEMI (P<0.001 and P=0.007, respectively). However, the relationship between operator volume and in-hospital outcomes did not reach statistical significance after adjusting for potential confounders and institutional volume (Figure 2). These results were consistent when operator volume was included as a continuous variable in the models of in-hospital death (odds ratio, 0.92 per log increase; 95% CI, 0.78–1.09; P=0.35) and in-hospital death or any complication (odds ratio, 0.98 per log increase; 95% CI, 0.87–1.11; P=0.76). Adjusted rate of in-hospital death in patients in the first (1–40 PCIs/y), second (41–64 PCIs/y), third (65–95 PCIs/y), and fourth (96–578 PCIs/y) quartile of operator volume was 4.1%, 3.8%, 3.0%, and 1.9%, respectively. Similarly, adjusted rate of in-hospital death or any complication in patients in the first, second, third, and fourth quartile of operator volume was 7.7%, 7.5%, 6.0%, and 4.2%, respectively.

DISCUSSION

In this prospective nationwide multicenter registry, we demonstrated that higher institutional PCI volume rather than operator PCI volume could be a significant determinant of lower rate of in-hospital adverse outcomes in patients who undergo PCI for UPLMD. Our findings extend previous studies[6,7,10] demonstrating an inverse volume-outcome relationship of PCI, to further understand how institutional PCI volume affects PCI for UPLMD. To our knowledge, this study represents one of the largest multicenter registries focusing on the volume-outcome relationship of PCI for UPLMD.

The significant association between institutional PCI volume and outcomes in patients with UPLMD provides additional support for volume-based referral strategies. A volume-outcome relationship has been demonstrated in a variety of procedures, such as transcatheter aortic valve replacement[18] and other surgical procedures.[19] High-volume hospitals may have sufficient human resources and experiences, resulting in proper treatment and adequate care (ie, "practice makes perfect"), and their better outcomes may attract more patients (ie, "selective referral").[20] PCI for UPLMD is a relatively rare procedure because the frequency of PCI for UPLMD in this cohort was 2.6% (24 320/936 612 PCIs in 4 years). Given the low frequency of PCI for UPLMD overall, a substantial annual number of PCI cases for UPLMD may be required to achieve proper treatment and adequate care during and after PCI procedures. In this study, the highest quartile of institutional PCI volume (488–3015 PCIs/y) had a significantly lower odds ratio of in-hospital mortality than that in the lowest quartile (Figure 2A). Our findings support the recommendation in the 2018 European Society of Cardiology and European Association for Cardio-Thoracic Surgery guidelines that an annual institutional volume of >400 PCIs is considered the optimal threshold for PCI for acute coronary syndrome.[4]

In contrast to a previous report from a single-center study,[13] there was no significant relationship between operator PCI volume and outcomes after PCI for UPLMD. Xu et al reported that patients treated by high-volume UPLMD PCI operators (≥15 PCI for UPLMD annually) had lower 30-day mortality after PCI for UPLMD (adjusted hazard ratio, 0.22; 95% CI, 0.09–0.59; P=0.003) than those treated by low-volume operators.[13] Badheka et al, using data from the National Inpatient Sample in the United States between 2005 and 2009,[6] and Fanaroff et al, using the data from the NCDR (National Cardiovascular Data Registry) CathPCI
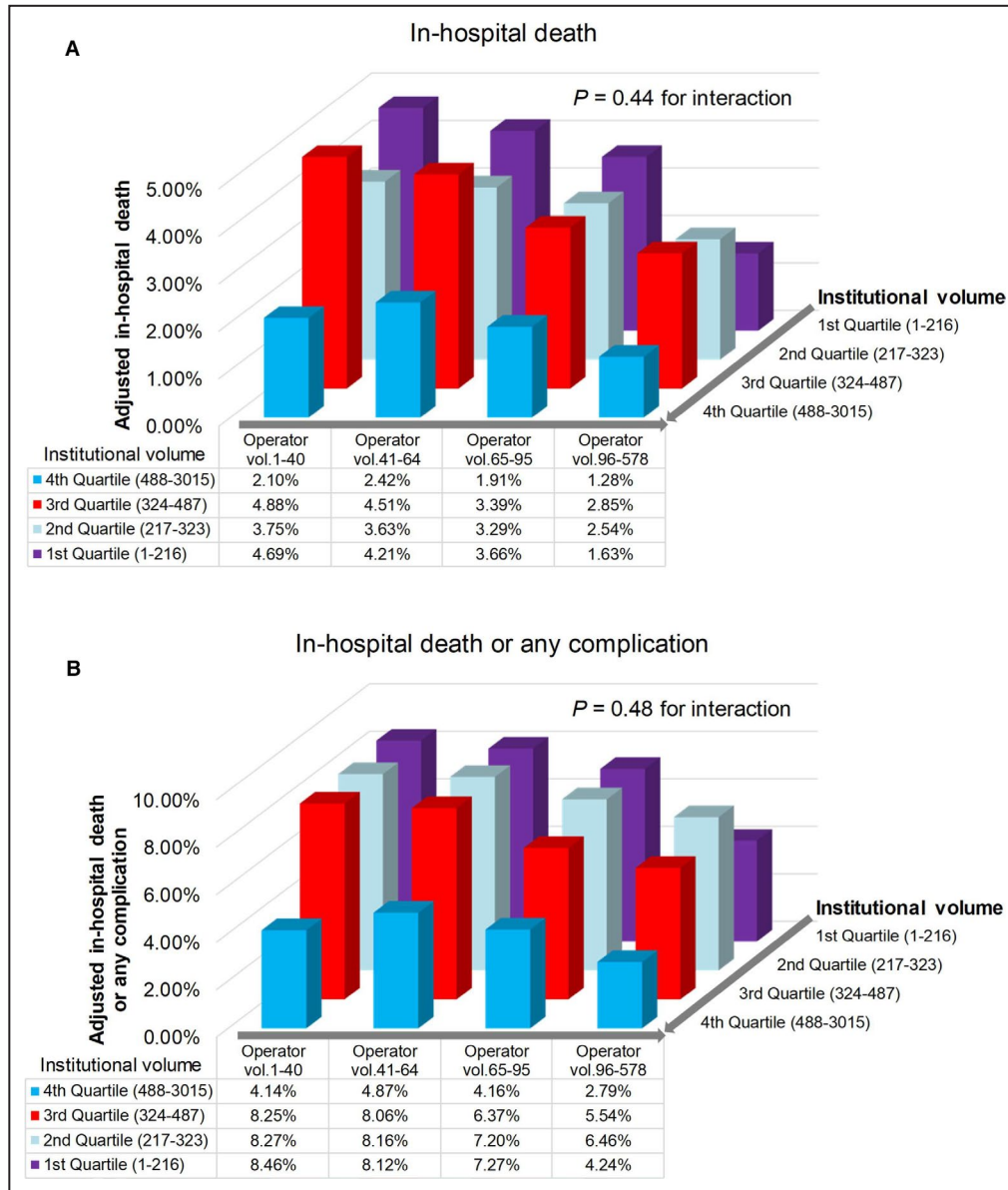
Figure 3. Adjusted event rates for in-hospital outcomes according to mean annual institutional and operator percutaneous coronary intervention (PCI) volumes.

A, Adjusted rates for in-hospital death. **B**, Adjusted rates for in-hospital death or any complication.

(Catheterization Percutaneous Coronary Intervention) registry in the United States between 2009 and 2015, reported a similar inverse relationship between operator PCI volume and in-hospital outcomes in the general population undergoing PCI. However, contradictory data have been published in other PCI registries.[7,21,22] Hannan et al analyzed data from the New York State's Percutaneous Coronary Intervention Reporting System in 1998 to 2000 (n=107 713) and found that in-hospital mortality in patients undergoing PCI performed by lower-volume operators (<75 PCI annually) was varied but not significantly different from that with higher-volume operators.[22]

There are several possible explanations for the nonsignificant relationship between operator PCI volume and in-hospital mortality in the present study. First, the majority (60%–70%) of PCIs for UPLMD were performed in teaching hospitals with on-site cardiac surgery; therefore, low-volume operators could perform PCI under the close supervision of experienced operators with on-site surgical backup. The lifetime PCI experience of each operator is also important[23,24] because older experienced operators seem to perform fewer on-call (urgent or emergency) PCIs than younger operators, which may result in a meaningful variation in in-hospital mortality among patients treated by

Table 4. Mean Annual Operator PCI Volume and Outcomes

| | Mean Annual Operator PCI Volume | | | | | |
	Overall	First Quartile (1–40)	Second Quartile (41–64)	Third Quartile (65–95)	Fourth Quartile (96–578)	P for Trend*
Crude in-hospital death						
SIHD	44/14 146 (0.3)	6/2269 (0.3)	9/3013 (0.3)	19/3955 (0.5)	10/4909 (0.2)	0.70
NSTE-ACS	193/6147 (3.1)	48/1179 (4.1)	61/1470 (4.1)	51/1713 (3.0)	33/1785 (1.8)	<0.001
STEMI	615/4027 (15.3)	169/1022 (16.5)	173/1048 (16.5)	156/1088 (14.3)	117/869 (13.5)	0.03
Crude in-hospital death or any complication						
SIHD	249/14 146 (1.8)	40/2269 (1.8)	64/3013 (2.1)	71/3955 (1.8)	74/4909 (1.5)	0.16
NSTE-ACS	424/6147 (6.9)	104/1179 (8.8)	117/1470 (8.0)	122/1713 (7.1)	81/1785 (4.5)	<0.001
STEMI	947/4027 (23.5)	252/1022 (24.7)	274/1048 (26.1)	245/1088 (22.5)	176/869 (20.3)	0.007

Data are expressed as n/N (%) of patients. NSTE-ACS indicates non–ST-segment–elevation acute coronary syndrome; PCI, percutaneous coronary intervention; SIHD, stable ischemic heart disease; and STEMI, ST-segment–elevation myocardial infarction.

*P<0.017 was considered statistically significant after Bonferroni adjustment for multiple comparisons.

low-volume operators including inexperienced fellows and seasoned operators. Our results also underscore the relative importance of institutional volume compared with operator volume in patients undergoing PCI for UPLMD.

There is no standardized PCI protocol for UPLMD, including the duration of dual antiplatelet therapy, stent type and size, and PCI strategies. Although not the primary focus of this analysis, it is noteworthy that a rate of radial approach in PCI was low in both patients with STEMI and patients with NSTE-ACS, whereas the radial approach was significantly associated with low in-hospital mortality after adjusting for potential confounders. Recent studies also suggested that the radial approach is associated with lower mortality and access site complication rate than the femoral approach in patients with STEMI or NSTE-ACS attributable to UPLMD.[12] Although cardiogenic shock or cardiac arrest attributable to UPLMD may preclude the radial approach for PCI, the transradial intervention should be considered as the first choice in patients undergoing PCI[25] even for UPLMD.

Limitations

The J-PCI registry is a large nationwide multicenter registry collecting clinical, procedural, and institutional data elements at participating centers via a web-based interface; however, the auditing procedures are under development. Therefore, the accuracy of data heavily depends on each hospital and operator, and in-hospital outcomes may be underreported. Coronary angiography and procedural details, such as the culprit lesion morphology, TAXUS Drug-Eluting Stent Versus Coronary Artery Bypass Surgery for the Treatment of Narrowed Arteries score, stent type, single or double stenting for bifurcation lesions, and intravascular imaging use, were not available; nonetheless, the selected variables included all predictors

of in-hospital mortality using a previously published PCI risk score model.[17] Although having a large number of institutions providing primary PCI may contribute to better outcomes, especially for patients with STEMI in rural areas, we could not prove this because the door-to-balloon time or onset-to-balloon time was not included in this analysis. Finally, we do not have long-term follow-up data, and thus further studies are needed to determine whether high-volume hospitals lead to better long-term outcomes in patients undergoing PCI for UPLMD.

CONCLUSIONS

In this prospective nationwide multicenter registry, we demonstrated that higher institutional PCI volume could be a determinant of better patient outcomes following PCI for UPLMD. Higher operator PCI volume was also associated with lower crude mortality rate in patients with NSTE-ACS; however, this relationship was attenuated after adjusting for potential confounders and institutional PCI volume.

Impact on Daily Practice

In this prospective nationwide multicenter registry, we demonstrated that higher institutional PCI volume rather than operator PCI volume could be a significant determinant of lower rate of in-hospital adverse outcomes in patients who undergo PCI for unprotected left main coronary artery disease. The adjusted odds ratio for in-hospital mortality was significantly lower in the highest quartile of institutional volume compared with the lowest quartile (adjusted odds ratio, 0.51; 95% CI, 0.30–0.86; P=0.01). Our findings may help to further understand how institutional PCI volume affects PCI for unprotected left main coronary artery disease.

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