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Routine intracoronary imaging-guided left main coronary intervention

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Left main (LM) percutaneous coronary intervention (PCI) with routine intracoronary imaging guidance is recommended; however, its real-world effectiveness remains unclear. A total of 743 consecutive patients undergoing drug-eluting stent implantation for de novo unprotected LM lesions across 19 Japanese National Hospital Organization hospitals where routine imaging guidance was adopted were analyzed. The primary endpoint was 1-year major adverse cardiovascular and cerebrovascular events (MACCE), comprising all-cause death, cerebrovascular disorder, clinical-driven revascularization, and myocardial infarction. In this cohort, acute coronary syndrome was present in 31.2%, with 39.3% classified as Canadian Cardiovascular Society functional angina (CCS) class ≥ III. LM bifurcation lesions were observed in 78.0%, with two-stent implantation in 8.8%. MACCE occurred in 17.5%, with target lesion revascularization and cardiac death rates of 2.0% and 3.4%, respectively. Independent risk factors for MACCE included two-stent implantation (hazard ratio [HR], 2.49), mechanical cardiac support device use (HR, 2.17), CCS class ≥ III (HR, 2.07), 10% increase in left ventricular ejection fraction (HR, 0.72), and radial access (HR, 0.62). Routine imaging-guided LM-PCI is associated with favorable low rate of target lesion revascularization and cardiac death. However, severe left ventricular dysfunction and LM bifurcation treated with two-stent implantation increase risks, requiring more comprehensive management.

Keywords Left main coronary artery, Percutaneous coronary intervention, Intracoronary imaging, Major adverse cardiovascular and cerebrovascular events

Intracoronary imaging guidance is recommended for left main (LM) percutaneous coronary intervention (PCI) [1,2], which has a higher risk of hemodynamic collapse or fatal events during and after the PCI owing to a

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large perfusion territory. Imaging guidance reduces mortality and target lesion revascularization[3–10] which is associated with sufficient stent expansion with less malapposition owing to optimal device selection and swift detection of stent failure or deformation[11,12]. Additionally, imaging-guided bifurcation intervention is useful for the prediction of side branch (SB) compromise[11] and prevention of unnecessary aggressive SB treatments, such as two-stent deployment or oversized SB dilation, leading to overtreatment regardless of uncertain angiographic findings in the bifurcation [13].

A meta-analysis of 11 randomized control trials comparing LM-PCI and coronary artery bypass graft (CABG), including 11,518 patients, demonstrated similar rates of all-cause mortality when the Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score was < 32[14]. Therefore, the guidelines have been changed so that LM-PCI is ranked in class I treatment, similar to CABG, when the SYNTAX score is < 22, which indicates that anatomical lesion complexity is low[1,2].

Intracoronary imaging guidance has become more popular in Japan than in other countries because of reimbursement of intracoronary imaging devices through social insurance. Intracoronary imaging guidance was used in 95% of all PCIs in the nationwide survey in 2014[15]. In the Japanese Circulation Society 2018 Guidelines on Revascularization of Stable Coronary Artery Disease, intravascular ultrasound (IVUS) guidance is strongly recommended as class I in LM-PCI, and optical coherence tomography (OCT)/optical frequency-dependent imaging (OFDI) guidance is also recommended as class IIa in bifurcation PCI[2]. However, most of the evidences are derived from small-scale randomized trials comparing imaging guidance and angio-guidance or propensity-match comparison in large-scale registries, in which more complex lesions are selected according to the cases treated under imaging guidance[5]. Therefore, the efficacy of routine intracoronary imaging for LM-PCI in daily practice has not yet been clarified. We aimed to investigate the clinical outcomes of LM-PCI in a large cohort of the Japanese National Hospital Organization (LM-JANHO) group, where intracoronary imaging guidance is routinely used.

Methods

Study population and design

The LM-JANHO is a multicenter, retrospective, observational registry study. In total, 806 consecutive patients who underwent LM-PCI with a drug-eluting stent (DES) between January 2016 and December 2020 were retrospectively enrolled from 19 institutes in the Japanese National Hospital Organization group.

The inclusion criteria were as follows: (1) de novo LM lesions including significant stenosis in the LM (≥ 50%) and/or daughter branches (≥ 75%) within a distance of 5 mm from the carina, which were treated with DES implantation in LM or crossover from LM to daughter branches; (2) suitable lesion for DES implantation in the LM; (3) patient age > 20 years; and (4) tolerability of dual antiplatelet therapy for > 6 months. The exclusion criteria were as follows: (1) in-stent restenosis lesions; (2) chronic total occlusion in the LM or adjusting branches; (3) the left anterior descending artery (LAD) and/or left circumflex artery (LCX) protected by prior CABG; (4) female with possible or definite pregnancy; (5) unsuitable candidate as judged by the responsible doctor, and (6) refusal to provide personal information for the study after receiving study information, in accordance with the opt-out system.

After the exclusion of 38 patients (inclusion criteria unmet in 26, lost to follow-up in 11, physician's decision in one) and 25 patients with any deficit of 1-year follow-up data, the data of 743 patients were analyzed (Fig. 1). The study protocol was approved by the central ethics committee of the Japanese National Hospital Organization headquarters and each institution's ethical committee. This study was conducted using an opt-out system and was disclosed to the patients and requirement for informed consent was waived. The study protocol was developed

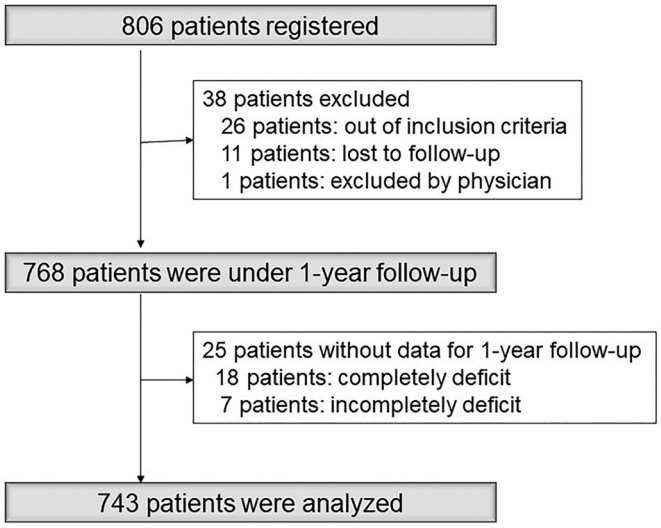

Fig. 1. Study flow of the extraction of the analyzed patients.

in accordance with the Declaration of Helsinki and registered in the University Hospital Medical Information Network (ID: UMIN 000,037,332) prior to the initiation of enrollment.

Percutaneous coronary intervention protocol

All patients were treated with sufficient periprocedural heparin and dual antiplatelet therapy with aspirin (100 mg) and either clopidogrel (50–75 mg) or prasugrel (3.75 mg), which was continued for at least 6 months. In cases with deficits in PCI initiation, the procedure was performed after administering the loading dose (aspirin 200 mg, clopidogrel 300 mg, and prasugrel 20 mg). Imaging was strongly recommended before PCI to assess the lesion and select the optimal therapeutic device and after the PCI procedure for its optimization. The use of IVUS or OCT/OFDI was at the operator's discretion. If any stent failure (stent malapposition > 400 μm, insufficient stent expansion [< 80%] compared with the mean value of proximal and distal references, and stent deformation) or serious dissection in the SB or stent proximal and/or distal edges was observed on imaging, prompt additional treatment was performed. The proximal optimal technique (POT), using a short balloon according to the LM vessel size, was recommended; however, its use relied on the operator's discretion after the imaging assessment for LM stent expansion. After LM crossover stenting to the LAD or LCX, opposite branch ostial dilation and the choice of method (kissing balloon inflation [KBI] or opposite branch dilation alone) were also dependent on the operator's discretion.

Data collection

Patient background, lesion characteristics, on-site visual assessment of coronary angiography, PCI procedure, medical treatment, and clinical outcome at 1-year follow-up were registered from each hospital to the REDCap system, a web-based application designed for streamlined data collection and management, in Osaka Metropolitan University Hospital center for clinical research and innovation.

Endpoint

Major adverse cardiovascular and cerebrovascular events (MACCE) were defined as composite endpoints of the following at 1-year follow-up: all-cause death, cerebrovascular disorder, any clinically driven revascularization, and myocardial infarction.

In this study, cardiac death was defined as death due to cardiac diseases, including heart failure, fatal arrhythmia, and sudden death. Target lesion revascularization (TLR) was defined as any revascularization by PCI or CABG in the treated LM and adjusting proximal LAD and LCX within 5 mm from the branch ostium. Target vessel revascularization (TVR) was defined as revascularization of the LM, LAD, or LCX. Clinically driven revascularization included TVR and non-TVR. Stent thrombosis included definite and probable stent thrombosis as defined by the Academic Research Consortium. Cerebrovascular disorders included stroke with any new-onset neurological deficit due to the occlusion of the cerebrovascular artery and cerebrovascular hemorrhage, except for traumatic hemorrhage. Successful PCI was defined as the achievement of Thrombolysis in Myocardial Infarction flow grade III with residual stenosis of ≤ 25% in the target lesion[16]. Downstream disease was defined as LM lesion with ≥ 75% stenosis in both the mid-LAD and mid-LCX, or in either vessel.

Statistical analyses

Continuous variables are expressed as mean ± standard deviation. Categorical variables are presented as percentages. Cox proportional hazard models were constructed to evaluate the association between each patient background, lesion characteristics, PCI procedures, and MACCE. Hazard ratios (HRs) and 95% confidence intervals (CIs) were calculated. All variables were included in the multivariate analysis to control confounders. The rates of MACCE and all-cause death incidences between patient background, legion characteristics, PCI procedures were compared by estimating cumulative incidence functions against the days from PCI. All reported p-values were determined by two-sided analysis, and p-values < 0.05 were considered significant. Analyses were performed using the R software (version 4.2.2) (R Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline patient characteristics

Baseline patient characteristics are summarized in Table 1. Increased prevalence rates of male sex (78.7%), dyslipidemia (71.0%), diabetes mellitus (49.3%), prior myocardial infarction (25.2%), and prior PCI or CABG (43.6%) were observed. The mean left ventricular ejection fraction was 56 ± 15%. Acute coronary syndrome (ACS) was observed in 31.2% of the patients, and a severe hemodynamic collapse state (cardiogenic shock, cardiopulmonary arrest, and pulmonary edema) was observed in 2.4–6.1% of the patients. Canadian Cardiovascular Society (CCS) class ≥ 3 was observed in 39.3% of the patients. The characteristics of the patients with and without ACS are summarized in the supplement Table 1. Patients with ACS had lower prevalences of comorbidities, including hypertension (66.7% vs. 78.2%), dyslipidemia (65.4% vs. 73.7%), peripheral artery disease (7.8% vs. 13.4%), and prior MI (16.5% vs. 29.3%). However, patients with ACS were more likely to present with CCS class ≥ III angina (85.5% vs. 18.7%) and lower LVEF (52 ± 15 vs. 58 ± 15). They also had higher rates of hemodynamic instability, including cardiogenic shock (19.0% vs. 0.2%), cardiopulmonary arrest (7.8% vs. 0%), and pulmonary edema (13.4% vs. 2.8%).

Lesion background

The backgrounds of the lesions are shown in Table 1. LM bifurcation was observed in 78.0% of the patients, and the most prevalent Medina classification was 1–1-0 lesion (30.1%) and true bifurcation lesion, which included significant stenosis in both the main vessel (MV) and SB, accounted for 34.7%. Patients with ACS had more true bifurcation lesion than those without (supplement Table 1, 41.7% vs. 31.2%). Angiographically

Patient background		
Age	years	73.0 ± 10.1
Male	n, (%)	583 (78.7)
Hypertension	n, (%)	553 (74.6)
Dyslipidemia	n, (%)	526 (71.0)
Diabetes	n, (%)	365 (49.3)
Smoking	n, (%)	237 (32,0)
Hemodialysis	n, (%)	34 (4.6)
Chronic obstructive pulmonary disease	n, (%)	17 (2.3)
Peripheral artery disease	n, (%)	86 (11.6)
Prior myocardial infarction	n, (%)	187 (25.2)
Prior PCI/CABG	n, (%)	323 (43.6)
Family history	n, (%)	95 (12.8)
Left ventricular ejection fraction	%	56 ± 15
Clinical presentation		
Stable angina	n, (%)	290 (39.2)
Old myocardial infarction	n, (%)	38 (5.1)
Silent myocardial ischemia	n, (%)	145 (19.6)
Acute coronary syndrome	n, (%)	231 (31.2)
Cardiogenic shock	n, (%)	45 (6.1)
Cardio-pulmonary arrest	n, (%)	18 (2.4)
Pulmonary edema	n, (%)	45 (6.1)
CCS classification		
I	n, (%)	288 (39.1)
II	n, (%)	158 (21.5)
III	n, (%)	100 (13.6)
IV	n, (%)	189 (25.7)
Pre-PCI		
Total cholesterol	mg/dL	169.4 ± 42.5
Trigriceride	mg/dL	130.7 ± 82.6
High density lipoprotein cholesterol	mg/dL	49.0 ± 13.7
Low density lipoprotein cholesterol	mg/dL	98.6 ± 36.8
Hemoglobin A_1C	%	6.6 ± 1.2
Serum creatinine	mg/dL	1.27 ± 1.38
Estimated glomerular filtration ratio	mL/min/1.73 m^2	58 ± 23
Lesion background		
Bifurcation lesion	n, (%)	573 (78.0)
Medina 1–0-0	n, (%)	54 (9.4)
Medina 1–1-0	n, (%)	173 (30.1)
Medina 1–1-1	n, (%)	139 (24.2)
Continued		

Patient background		
Medina 1–0-1	n, (%)	31 (5.4)
Medina 0–1-0	n, (%)	136 (23.7)
Medina 0–1-1	n, (%)	29 (5.1)
Medina 0–0-1	n, (%)	12 (2.1)
True bifurcation lesion	n, (%)	199 (34.7)

Table 1. Patient and lesion background. PCI, percutaneous coronary intervention; CABG, coronary artery bypass graft; CCS, Canadian Cardiovascular Society functional angina classification. Acute coronary syndrome included acute myocardial infarction accompanied by elevated cardiac biomarker levels with or without ST elevation on electrocardiography and unstable angina, defined as new-onset or increased-severity angina within 1 month, resting angina, and postinfarction angina without elevated cardiac biomarker levels. Stable angina was defined as stable symptoms during high exertion, with no chest pain at rest in the past month. Silent myocardial ischemia was defined as the objective evidence of myocardial ischemia without evident chest symptoms. Cardiogenic shock was defined as a sustained episode of systolic blood pressure <80 mmHg and cardiac index <1.8 L/min m^2, determined to be secondary to cardiac dysfunction, and/or the requirement of a parenteral inotropic or vasopressor agent or mechanical support to maintain blood pressure and cardiac index within 24 h before PCI. Pulmonary edema was equivalent to "Congestive Heart Failure" in the New York Heart Association functional classification class IV (reference 16).

nonsignificant LM lesions (Medina 0-x-x) were included in 30.9% of the patients owing to the identification of LM atherosclerotic plaques on intracoronary imaging.

PCI procedures

The PCI procedures details are presented in Table 2. Radial access was frequently used in 70.1% of the patients, and most patients were treated with 6- and 7-Fr guiding systems (51.9% and 41.8%, respectively). Imaging guidance was routinely performed (97.7%), and IVUS and OCT/OFDI were performed in 86.5% and 12.2% of the patients, respectively. A current-generation DES was implanted in all patients, except for one in which a bare metal stent was used according to the physician's discretion. Two-stent deployment in the LM bifurcation was performed in 8.8% of the patients, and elective procedure was performed in only 14 patients (1.9% of the entire cohort). The stenting technique was performed in the sequence of culottes, T-stenting, and crush stenting. The POT was performed in 53.1% of the patients treated with one-stent deployment. KBI or SB dilation alone was performed in 75.0% of the patients. A mechanical cardiac support device was used in 16.4% of the patients (intra-aortic balloon pumping, 15.8%; extracorporeal membrane oxygenation, 2.7%). Modification of calcified lesions was performed using rotational or orbital atherectomy (9.2%) and a scoring balloon (19.7%). MV stent size was 3.5–4.0 mm in 63.0% and 3.0–3.5 mm in 30.8% of the patients, and SB stent size was 3.0–3.5 mm in 41.0% and 2.5–3.0 mm in 34.9% of the patients. The PCI success rate was 98.6%.

Adverse events at 1-year follow-up

Adverse events at the 1-year follow-up are shown in Table 3. The rates of all-cause death, cerebrovascular disorders, clinically driven revascularization, and myocardial infarction were 8.9%, 1.2%, 8.2%, and 1.9%, respectively. MACCE, which were a composite of these events, were observed in 17.5% of the patients. TLR and cardiac death occurred in 2.0% and 3.4% of the patients, respectively. The cumulative curve of MACCE showed a gradual increase (Fig. 2), whereas that of all-cause death peaked within 30 days and plateaued at 1 year (Fig. 3).

Risk in major adverse cardiovascular and cerebrovascular events

The cumulative curve of MACCE showed higher rates of mechanical cardiac support device use (Fig. 2b), CCS classes III and IV (Fig. 2c), two-stent implantation (Fig. 2d), nonradial access (Fig. 2e), ACS (Fig. 2g) and existence of downstream disease (Fig. 2h). True bifurcation lesions did not lead to significant impact on MACCE rate (Fig. 2f). The cumulative curve of all-cause death showed higher rates of mechanical cardiac support device use (Fig. 3b), CCS class IV (Fig. 3c), nonradial access (Fig. 3e), and ACS (Fig. 3g) which peaked within 30 days. True bifurcation lesions (Fig. 3f) and existence of downstream disease (Fig. 3h) also showed significant higher rates with gradual increase after 30 days. However, two-stent implantation (Fig. 3d) had no significant impact.

Multivariate analysis of the risk of MACCE is shown in Table 4. Independent factors that elevated the risk included CCS ≥ class III (HR, 2.07; 95% CI, 1.39–3.07; $p < 0.001$), mechanical cardiac support device use (HR, 2.17; 95% CI, 1.43–3.30; $p < 0.001$), and two-stent implantation (HR, 2.49; 95% CI, 1.48–4.18; $p < 0.001$). Factors that reduced the risk were left ventricular ejection fraction – 10% increase (HR, 0.72; 95% CI, 0.52–0.99; $p = 0.041$) and radial access (HR, 0.62; 95% CI, 0.42–0.91; $p = 0.015$).

Discussion

In the LM-JANHO study on routine imaging-guided unprotected LM-PCI, including acute coronary syndrome, 17.5% of the patients experienced composite endpoints (comprising all-cause death, cerebrovascular disorder, any clinically driven revascularization, and myocardial infarction) at the 1-year follow-up. Notably, the study reported a low incidence of TLR (2.0%) and cardiac death (3.4%). Risk factors for the composite endpoints

Access		
Radial	n, (%)	519 (70.1)
Femoral	n, (%)	198 (26.8)
Brachial	n, (%)	23 (3.1)
System		
6 Fr	n, (%)	383 (51.9)
7 Fr	n, (%)	309 (41.8)
8 Fr	n, (%)	47 (6.4)
Imaging guide	n, (%)	726 (97.7)
Intravascular ultrasound	n, (%)	636 (86.5)
Intravascular ultrasound	n, (%)	636 (85.6)
Optical coherence tomography	n, (%)	83 (11.2)
Both imaging devices usage	n, (%)	7 (1.0)
Drug-eluting stent		
First generation	n, (%)	0 (0)
Current generation	n, (%)	742 (99.9)
Two-stent implantation	n, (%)	65 (8.8)
Elective	n, (%)	14 (21.5)
Culotte	n, (%)	26 (40.0)
Crush	n, (%)	16 (24.6)
T-stenting	n, (%)	21 (32.3)
Proximal optimization technique	n, (%)	333 (53.1)
Side branch dilation in 1-stent	n, (%)	472 (75.0)
Kissing balloon inflation	n, (%)	390 (62,0)
Side branch dilation alone	n, (%)	82 (13.0)
Mechanical cardiac support device	n, (%)	122 (16.4)
Intra-aortic balloon pumping	n, (%)	117 (15.8)
Extracorporeal membrane oxygenation	n, (%)	20 (2.7)
Lesion modification		
Rotational/Orbital atherectomy	n, (%)	68 (9.2)
Directional coronary atherectomy	n, (%)	10 (1.4)
Scoring balloon	n, (%)	145 (19.7)
Main vessel stent		
Size: ≥ 4.0 mm	n, (%)	117 (16.0)
3.5–4.0 mm	n, (%)	390 (53.3)
3.0–3.5 mm	n, (%)	187 (25.5)
2.5–3.0 mm	n, (%)	33 (4.5)
< 2.5 mm	n, (%)	5 (0.7)
Length	mm	23.0 ± 8.5
Product		
Xience	n, (%)	359 (49.4)
Synergy/Promus	n, (%)	129 (17.8)
Resolute Integrity/Onyx	n, (%)	79 (10.9)
Ultimaster	n, (%)	106 (14.6)
Nobori/BioFreedom	n, (%)	38 (5.2)
Orsilo	n, (%)	14 (1.9)
Bare metal stent	n, (%)	1 (0.1)
Side branch		
Size: ≥ 4.0 mm	n, (%)	4 (4.8)
3.5–4.0 mm	n, (%)	7 (8.4)
3.0–3.5 mm	n, (%)	34 (41.0)
2.5–3.0 mm	n, (%)	29 (34.9)
< 2.5 mm	n, (%)	9 (10.8)
Length	mm	21.6 ± 7.8
Product		
Xience	n, (%)	34 (41.0)
Synergy/Promus	n, (%)	16 (19.3)
Continued		

Access		
Resolute Integrity/Onyx	n, (%)	13 (15.7)
Ultimaster	n, (%)	17 (20.5)
Nobori/BioFreedom	n, (%)	1 (1.2)
Orsilo	n, (%)	2 (2.4)
Bare metal stent	n, (%)	0 (0)
Procedural success	n, (%)	730 (98.6)

Table 2. Procedures of left main percutaneous coronary intervention.

Adverse events		frequency
All-cause death	n (%)	66 (8.9)
Cardiac death	n (%)	25 (3.4)
Cerebrovascular disorder	n (%)	9 (1.2)
Clinically driven revascularization	n (%)	61 (8.2)
Target vessel revascularization	n (%)	34 (4.6)
Target lesion revascularization	n (%)	15 (2.0)
Stent thrombosis	n (%)	2 (0.3)
Myocardial infarction	n (%)	14 (1.9)
Worsening renal function	n (%)	12 (1.6)
Major adverse cardiovascular and cerebrovascular events	n (%)	130 (17.5)

Table 3. Clinical outcomes at the 1-year follow-up.

included CCS class ≥ III, use of a mechanical cardiac support device, and two-stent implantation, while a 10% increase in left ventricular ejection fraction and radial access were associated with a reduced risk.

Imaging guidance in LM-PCI demonstrated a lower incidence of composite endpoints of all-cause death, restenosis, or definite stent thrombosis (HR, 0.65; 95% CI, 0.50–0.84) and all-cause death alone (HR, 0.62; 95% CI, 0.47–0.82) in 2468 patients of the Swedish Coronary Angiography and Angioplasty Registry, in which IVUS guidance was used in 25.2% of the patients[4]. In 11,264 unprotected LM-PCI procedures performed in England and Wales, analysis of 5056 pairs of imaging- and angio-guided PCIs after propensity matching showed that the imaging-guided PCI presented a lower incidence of 12-month mortality than the angio-guided PCI (odds ratio [OR], 0.660; 95% CI, 0.57–0.77)[9]. A meta-analysis of comparison between IVUS guidance (2096 patients) and angio-guidance (1984 patients) in LM-PCI also exhibited a lower incidence of all-cause death (OR, 0.46; 95% CI, 0.30–0.71), cardiac death (OR, 0.47; 95% CI, 0.29–0.77), and composite endpoints, including stent thrombosis, myocardial infarction, cardiac death, and all-cause death (OR, 0.42; 95% CI, 0.26–0.67)[5]. However, imaging guidance was employed for complex lesions in these studies, and the efficacy of routine imaging in every LM-PCI has not been elucidated.

The present study included cases with acute myocardial infarction and cardiogenic shock that were excluded in the other previous studies of the imaging-guided LM-PCI[5,7–9,17]. Therefore, all-cause death (8.9% vs. 2.5–9.0%) and cardiac death at 1 year (3.4% vs. 0.8–2.4%) were observed more frequently in the present study than in previous studies. However, there was a similar incidence rate of TVR (4.6% vs. 4.2–6.7%) and lower incidence rates of TLR (2.0% vs. 2.7–7.7%), stent thrombosis (0.3% vs. 0.5–1.7%), and myocardial infarction (1.9% vs. 1.5–11.2%), indicating that optimal PCI was induced by imaging guidance in survivors after acute coronary events. The following factors contribute to the efficacy of routine imaging guidance in LM-PCI: first, the optimal device selection in terms of size and length was based on pre-PCI imaging, which decreased additional stenting due to overdilation or inappropriate positioning of the balloon or stent in the plaque-rich area. Information concerning plaque morphology, thrombus burden, and intracoronary calcification severity was also useful for appropriate preparation before stenting. Second, some atherosclerotic plaques were identified by intracoronary imaging in the angiographically insignificant LM lesions, which increased LM crossover stenting in the Medina (0-x-x) lesions. In this study, this type of lesion was observed in 30.9% of the patients, whereas in previous studies with limited use of imaging, it was observed in 0–21.5% of the patients[18–21]. Third, more appropriate PCI optimization for sufficient stent expansion, less stent malapposition or deformation, and navigation of optimal SB guidewire crossings were promoted. Accurate assessment of SB dissection or stenosis after balloon dilation on intracoronary imaging resulted in a decrease in two-stent deployment in this study (8.8%). Elective two-stent deployment was performed in only 1.9% of the patients, and fewer escalations from provisional stenting (6.9%) were noted. Thus, local effectiveness of imaging-guided PCI on LM lesion was prominent in less TLR (2.0%) and cardiac death (3.4%) in this study compared with the prior Japanese registry study (AOI registry) (TLR: 9.1% [bifurcation]/11.0% [non-bifurcation], cardiac death: 6.6%/5.0%[19]) or randomized studies comparing provisional and elective two stenting with the limited use of imaging guidance (EBC MAIN, TLR: 6.1% [provisional stent]/9.3% [two stents][21]; DK Crush V, TLR: 10.7%/5.0%, cardiac death: 1.3%/2.1%[20]).

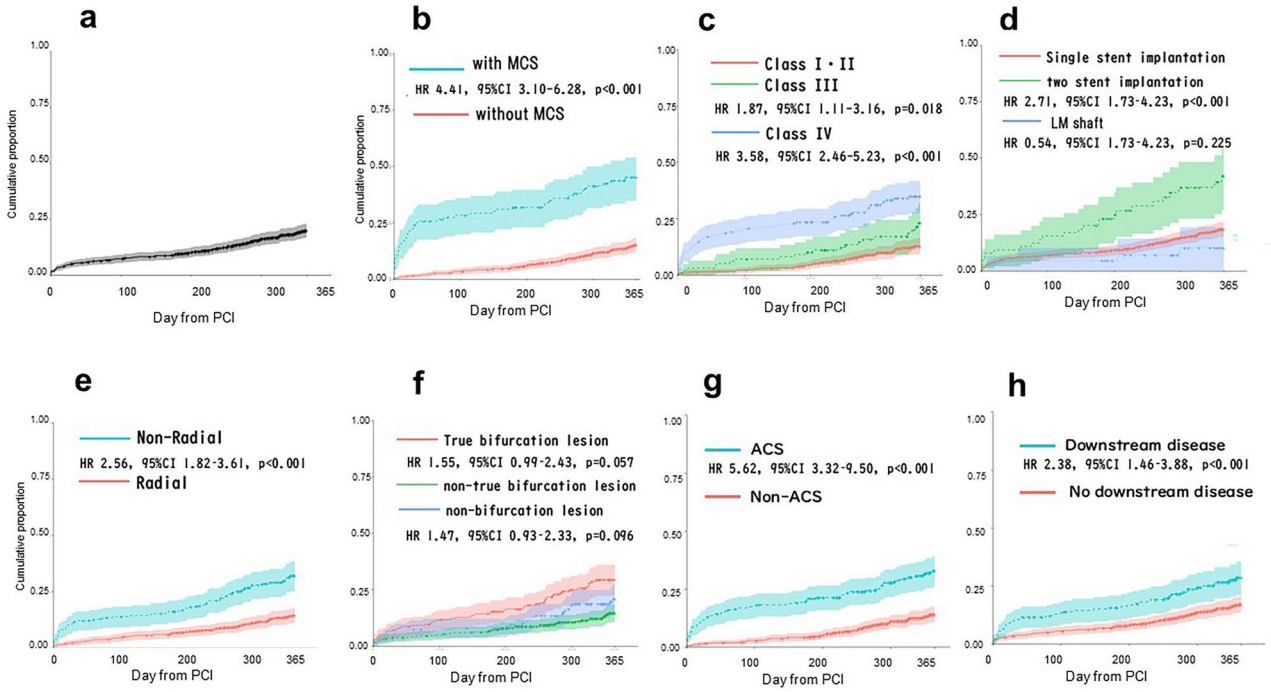

Fig. 2. Cumulative curve of major adverse cardiovascular and cerebrovascular events. (**a**) Entire group. (**b**) The groups using or not using a mechanical cardiac support device (MCS). Hazard ratios (HR) were calculated in comparison to the non-MCS group. CI: coefficient interval. (**c**) Canadian Cardiovascular Society functional angina classification. HRs were calculated in comparison to Class I and II group. (**d**) The groups treated with a single stent, two stents, and left main shaft stenting alone. HRs were calculated in comparison to single stent group. (**e**) The groups of radial and nonradial access. HR was calculated in comparison to nonradial access group. (**f**) The groups of true bifurcation lesion, non-true bifurcation lesion, and non-bifurcation lesion. HRs were calculated in comparison to non-true bifurcation group. (**g**) The groups of acute coronary syndrome (ACS) and non-ACS. HR was calculated in comparison to non-ACS group. (**h**) The groups of existence or none of downstream disease defined as left main lesion with ≥75% stenosis in both the middle left anterior descending artery and middle left circumflex artery, or in either vessel. HR was calculated in comparison to no downstream disease group.

In the analysis of risk of MACCE in the present study, CCS class ≥ III and mechanical cardiac support device use were directly related to the severe hemodynamic collapse state, which might result in cardiac death in acute phase. As nonradial access was adopted more frequently in an unstable hemodynamic state with weak pulsation of the radial artery, it was also associated with the risk of cardiac death. In fact, the group with these factors had elevated mortality within 30 days and reached a plateau at 1 year (Fig. 3). Even with technical improvements in LM-PCI under imaging guidance, the initial myocardial damage induced by LM ischemia cannot be effectively relieved.

Lower left ventricular ejection fraction was identified as an independent risk factor for MACCE. This was a result of LM ACS that led to severe left ventricular damage or ischemic cardiomyopathy that had already presented with multiple-vessel diseases, including LM lesions. A lower left ventricular ejection fraction was associated with heart failure recurrence, fatal arrhythmic events, and more frequent coronary revascularization.

Two-stent deployment was also an independent risk factor for MACCE. Higher risk[18,19,22,23] of two-stent deployment was demonstrated in previous studies in which first-generation DES were mainly used. However, similar[21,23] or superior clinical outcomes[20,24] compared with provisional stenting have been reported in recent studies that used current-generation DES. In the present study, two-stent deployment was used in a limited manner for more complex lesions (8.8%). In other studies, escalation to provisional two stenting was observed in 22–47% of the patients owing to suboptimal findings in the SB, primarily assessed by angiographic diameter stenosis[25]. However, these assessments have overestimated the severity of physiologically insignificant stenoses in 30% of cases[26]. In this study, SB lesions were generally unstented if imaging confirmed no signs of vessel occlusion threatening conditions, including intimal flaps, hematoma progression, or insufficient lumen dilation with significant plaque burden. True bifurcation lesions were not identified as risk factors for MACCE. As the use of two-stent techniques increased in cases involving diffuse downstream disease, the need for vessel revascularization also rose. However, it did not significantly impact all-cause mortality, likely due to PCI optimization with imaging guidance. Therefore, comprehensive management strategies that consider plaque debulking, aggressive medical therapy, and switching to CABG after lesion assessment using intracoronary imaging are required.

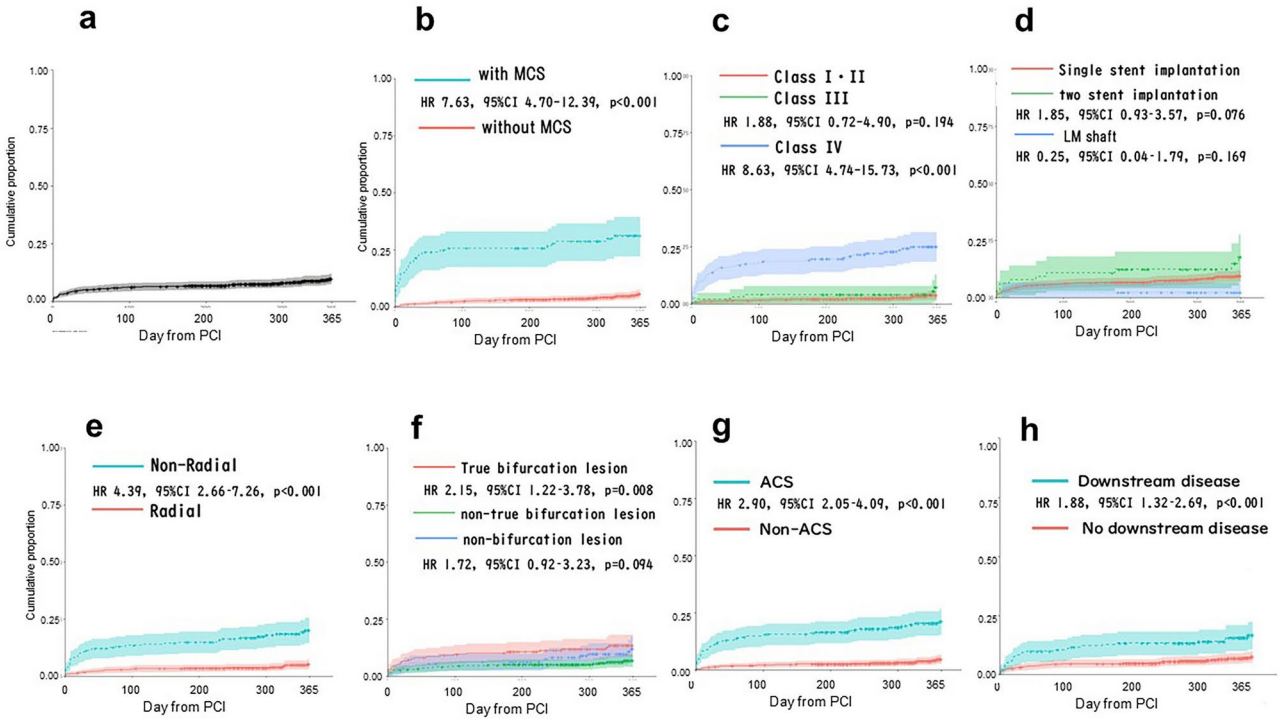

Fig. 3. Cumulative curve of all-cause mortality. (**a**) Entire group. (**b**) The groups using or not using a mechanical cardiac support device (MCS). (**c**) Canadian Cardiovascular Society functional angina classification. (**d**) The groups treated with a single stent, two stents, and left main shaft stenting alone. (**e**) The groups of radial and nonradial access. (**f**) The groups of true bifurcation lesion, non-true bifurcation lesion, and non-bifurcation lesion. (**g**) The groups of acute coronary syndrome (ACS) and non-ACS. (**h**) The groups of existence or none of downstream disease. HR calculations for each group consistent with those indicated in Fig. 2.

	Univariate			Multivariate		
Variables	**Hazard ratio**	**95% CI**	**P value**	**Hazard ratio**	**95% CI**	**P value**
Age (10 years increase)	1.11	0.92–1.32	0.272	1.00	0.79–1.27	0.979
Male	1.07	0.70–1.64	0.751	1.13	0.71–1.81	0.597
Smoker	1.23	0.86–1.75	0.263	1.31	0.89–1.93	0.178
Body mass index (1 kg/m^2 increase)	1.03	1.00–1.04	0.008	1.04	0.95–1.14	0.372
eGFR (10 mL/min/1.73 m^2 increase)	0.85	0.79–0.92	< 0.001	0.84	0.67–1.04	0.107
Left ventricular ejection fraction (10% increase)	0.75	0.85–0.66	< 0.001	0.72	0.52–0.99	0.041
Dyslipidemia	0.76	0.53–1.10	0.143	0.90	0.60–1.33	0.592
Hypertension	1.07	0.71–1.61	0.753	1.19	0.76–1.86	0.438
Diabetes mellitus	1.08	0.77–1.52	0.661	0.99	0.68–1.43	0.952
CCS ≥ class III	2.92	2.05–4.18	< 0.001	2.07	1.39–3.07	< 0.001
Residual significant stenosis after PCI	1.34	0.91–1.98	0.138	1.31	0.85–2.00	0.221
Radial access	0.39	0.27–0.54	< 0.001	0.62	0.42–0.91	0.015
Mechanical cardiac support device	4.39	3.08–6.26	< 0.001	2.17	1.43–3.30	< 0.001
Lesion modification: rotational or orbital atherectomy	1.30	0.76–2.22	0.341	1.40	0.78–2.53	0.260
Left main stent size ≥ 3.5 mm	0.71	0.50–1.03	0.068	0.75	0.51–1.10	0.140
Two-stent implantation	2.80	1.79–4.36	< 0.001	2.49	1.48–4.18	0.001
True bifurcation lesion	2.00	1.40–2.84	< 0.001	0.91	0.55–1.48	0.693
Proximal optimization technique	0.78	0.55–1.10	0.156	0.89	0.62–1.29	0.542

Table 4. Univariate and multivariate analysis of the risk of major adverse cardiovascular and cerebrovascular events. CI, confidence interval; eGFR, estimated glomerular filtration ratio; CCS, Canadian Cardiovascular Society functional angina classification.

The present study included several contemporary PCI techniques which might influence on the clinical outcome.

Radial access

Radial access was used in 70.1% of the patients using a 6- or 7-Fr guiding catheter. Radial access was first approached in elective cases, and the introduction of a slender system with a thinner outer sheath by 1 Fr than the conventional system allowed for increased use of a 7-Fr guiding catheter, which enabled complex PCI procedures to be performed with greater ease. Radial access is associated with less bleeding (OR, 0.43; 95% CI, 0.27–0.69; p = 0.0004) and lower in-hospital mortality rate (OR, 0.49; 95% CI, 0.31–0.79; p = 0.004) in a meta-analysis of LM-PCI including 17,258 patients[27].

POT

In the present study, POT was performed in 53.1% of the patients, which was not as in randomized trials[10,20,21], but more frequent than in other registry studies[8,19,28]. The POT provides sufficient stent expansion and less stent malapposition in the proximal MV, and re-POT is recommended after SB dilation to correct stent deformation[28–30]. In the present study, the more frequent KBI (62%) might have resulted in sufficient stent expansion with less malapposition in the LM, and confirmation by imaging led to a lower performance of POT or re-POT. However, it is crucial to determine the optimal size of the balloon for the POT according to the LM vessel size in the pre-PCI imaging and to confirm sufficient stent expansion in the LM, including the polygon confluence without any significant stent malapposition in the post-PCI imaging[31].

SB dilation under the imaging guidance

Any SB dilation was performed more frequently (75%) in the present study than in other registry studies[26,28,32,33]. The LCX ostial area is larger than that of other SBs in non-LM bifurcations and is covered with more jailing struts[34]. The success rate of optimal SB wiring was lower in LM bifurcation than in non-LM bifurcation under angio-guidance (55% vs. 75%), and more incomplete strut apposition was observed in LM bifurcation[34]. Incomplete removal of jailing struts in the LCX ostium due to suboptimal SB wiring or inappropriate balloon dilation leads to clustering of jailing struts at the rim of the LCX ostium, which may be associated with thrombus attachment or restenotic reaction[35–37]. More suboptimal SB wiring and subsequent SB dilation than expected would have occurred in previous studies due to the limited use of imaging. Leaving the LCX without any dilation after LM-LAD crossover stenting has a sufficiently higher survival rate from cardiac events in cases with high FFR values in the jailed LCX[32]. In contrast, there are reports of non-fenestration-related restenosis due to intimal coverage of the jailing struts at the LCX ostium and very late stent thrombosis on the jailing struts in an autopsy study of sudden cardiac death of patients after LM-PCI[37]. In the e-Ultimaster bifurcation substudy, which demonstrated the efficacy of the POT but not that of KBI, the least and most prevalent target lesion failures were found in cases with both POT and KBI performed and those without either of them, which indicates that leaving the SB untouched without any optimization in the proximal MV or SB is associated with worse clinical outcomes[28]. Imaging-guided optimal SB treatment and POT are crucial to reduce procedure-related events.

Mechanical cardiac supporting device

In the present study, intra-aortic balloon pumping was used in 15.8% of the patients, and extracorporeal membrane oxygenation was used in 2.7% of the patients. As Impella had not been introduced in Japan at the start of the study period and had limited use for cardiogenic shock in licensed institutes, there were no cases with Impella support in this study. As the inefficacy of intra-aortic balloon pumping or extracorporeal membrane oxygenation on long-term survival has been reported[38,39] a higher rate of cardiac death in patients using a mechanical cardiac support device was demonstrated in this study. Improvement of the survival rate after LM-related ACS has been reported in Impella support due to early unloading of the left ventricle, prevention of its remodeling, and subsequent multiple organ failure[40]. Improvement in mortality is expected using Impella support; however, further studies are warranted to investigate its efficacy in LM-related ACS in East Asian races, which have shown a higher bleeding risk than Caucasian races[41].

The present study had some limitations. 1) The study did not adopt a randomized trial design, with 97.7% of cases treated under imaging guidance. Consequently, the study design does not facilitate a direct assessment of the efficacy of imaging guidance in comparison with angio-guidance. Instead, efficacy was established by comparing the results with those from previous reports. The efficacy of routine imaging guidance as compared to that of angiography-guidance or selective imaging-guidance should be investigated in ongoing or future randomized trials. 2) As consecutive cases of LM-PCI were enrolled, this study included cases of acute myocardial infarction or cardiogenic shock, which were excluded in previous studies. This may have led to an increase in clinical events, particularly in terms of mortality. 3) Because this was a retrospective study, there were no standardized criteria for optimal PCI results in intracoronary imaging among the participating institutes, except for the general recommendations of a stent expansion index > 80%, minimal stent malapposition, and confirmation of the SB wiring site. 4) LM-PCI techniques have not been standardized across the centers, potentially introducing some bias and had impact on the results. 5) The enrollment of LM-PCI or CABG in LM-related diseases varied among the participating institutes, and the expertise and skills of operators performing LM-PCI also differed. These variations may have influenced the study outcomes. 6) A lower, non-standard dose of P2Y12 inhibitors was used in the Japanese population, more prone to bleeding compared to Caucasians, as per Japanese guidelines[2]. No increase in thromboembolic or bleeding events was observed.

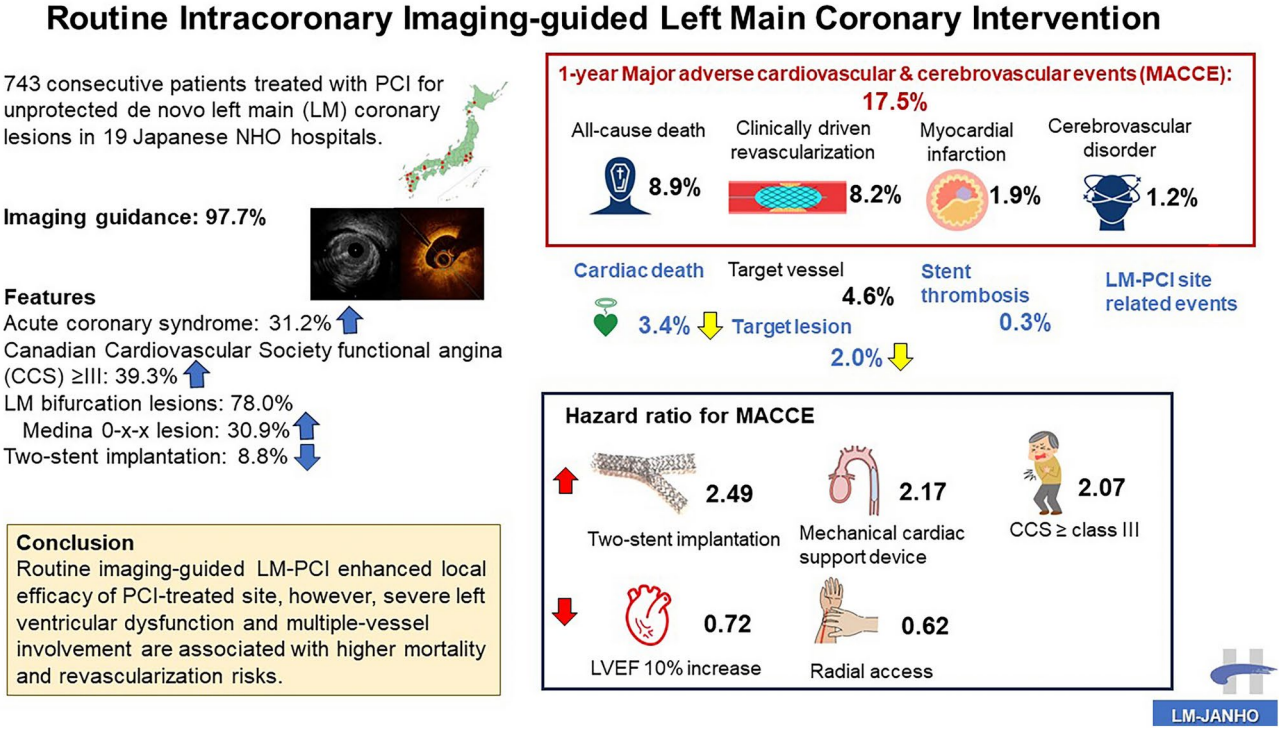

Fig. 4. Graphic abstract of Routine intracoronary imaging-guided left main coronary intervention.

Conclusion

This study clarifies the clinical outcomes of left main coronary intervention guided by routine intracoronary imaging, revealing a low frequency of target lesion revascularization and cardiac death. Despite the favorable local efficacy of imaging guidance, patients with severe left ventricular dysfunction and multi-vessel disease remain at higher risk of mortality and revascularization, underscoring the need for comprehensive management strategies for these complex cases. (Fig. 4: graphic abstract).

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Author contributions

Y. Murasato: Conceptualization, Investigation, Formal analysis, Writing—Original Draft, Project administration, Funding acquisition. H. N., H. S., M. A., F. M, Y. U., K. M., M. A., T. K., M. S., K. F., T. S., S. I., T. T., Y. Morita, K. K., A. T., Y. O., and A. F.: Investigation, Writing – Review & Editing. H. Y.: Formal analysis, Data Curation, Writing—Review & Editing.

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Declarations

Competing interests

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Additional information

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