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The First-in-Man Technique of Drug Eluting and Perfusion Therapy for Left Main Coronary Artery Disease

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ABSTRACT

Background: Treating ostial left circumflex artery (LCx) lesions in percutaneous coronary intervention (PCI) for left main disease (LMD) remains a challenge. Despite recent recommendations for the use of drug-coated balloon (DCB) in this lesion, there are concerns about crossover-stenting from the left main trunk (LMT) to the left anterior descending artery (LAD). Specifically, isolated DCB treatment for the ostial LCx lesion may induce carina shift, while conventional kissing balloon technique (C-KBT) with a standard balloon and a DCB may prolong LMT occlusion, leading to hemodynamic instability.

Objectives: This study aimed to evaluate the safety and feasibility of a novel double-effect KBT (W-KBT) using a perfusion balloon (PB) for the LMT-LAD and a DCB for the LMT-LCx, allowing prolonged inflation while maintaining coronary perfusion.

Methods: This single-center prospective study enrolled consecutive patients with de-novo LMD and ostial LCx lesions, requiring crossover-stenting from the LMT to the LAD followed by proximal optimization technique and C-KBT. After confirming optimal PCI, W-KBT was performed.

Results: Among 12 enrolled patients (mean age 73.8 ± 7.2, 91.7% men), procedural success, defined as device delivery and W-KBT time ≥ 30 s, was achieved in all cases via the transradial approach. W-KBT inflation-time was consistently 60 s; ST changes occurred in 50% (no ST-elevation); mean ST-change time was 41.2 ± 7.1 s; mean delta-blood pressure was -13.7 ± 11.4 mmHg; mean delta-heart rate was -3.4 ± 5.9 bpm; and no inotropes or mechanical cardiac support were needed.

Conclusion: Within the limited sample size of this pilot study, the safety and feasibility of the first-in-man W-KBT were suggested.

Summary: This pilot study evaluated the safety and feasibility of a novel double-effect kissing balloon technique (W-KBT) in percutaneous coronary intervention for left main coronary artery disease, realized by the combined use of a perfusion balloon and a drug-coated balloon. Among 12 patients, device delivery was successful via a transradial approach using a 7 Fr guiding catheter. The W-KBT was maintained for 60 s without hemodynamic instability, providing adequate drug application to the ostial left circumflex artery lesion. Furthermore, no ST-elevation or periprocedural myocardial infarction was observed, highlighting the safety and feasibility of this technique.

Abbreviations: DCB, drug-coated balloon; IVUS, intravascular ultrasound; KBT, kissing balloon technique; LAD, left anterior descending artery; LCx, left circumflex artery; LMD, left main disease; LMT, left main trunk; PB, perfusion balloon; PCI, percutaneous coronary intervention; POT, proximal optimization technique.

1 | Introduction

Percutaneous coronary intervention (PCI) for left main coronary artery disease (LMD) has been established as an alternative treatment strategy to coronary artery bypass grafting [1–3]. A recent analysis demonstrated significant clinical benefits from revascularization for LMD over medical therapy alone, even in the contemporary medicine era, with the risk reduction rate of more than 50% [4]. However, despite advances in procedural techniques (including proximal optimization technique [POT]), technologies (such as new generation drug-eluting stents, intravascular imaging, and coronary physiology), and pharmacotherapies, cardiovascular events arising from the ostial lesions of the left circumflex artery (LCx) remains an issue, associated with increased unplanned repeat revascularization up to 15% in a year [5, 6]. Recent expert recommendations suggest the use of drug-coated balloon (DCB) for the ostial lesion of the side-branch including ostial LCx [7, 8]. However, the optimal timing and method for DCB use in PCI for LMD (LM-PCI) are not well specified. Furthermore, concerns exist regarding cases of crossover-stenting from the left main trunk (LMT) to the left anterior descending artery (LAD) and the kissing balloon technique (KBT). Specifically, using a DCB for the ostial LCx before stenting raises concerns that the subsequent KBT may dislodge the drug applied to the ostial LCx, potentially reducing the efficacy of the DCB. Utilizing a DCB in isolation for the ostial LCx after stenting with POT and KBT may result in additional carina shift. The combination of a conventional balloon for the LMT-LAD and a DCB for the LMT-LCx in KBT could potentially cause hemodynamic instability due to prolonged occlusion time for the entire left coronary artery system. Of note, current DCBs should be inflated for at least 30 s to ensure adequate drug delivery, and longer inflation times was demonstrated to be associated with improved clinical outcomes [9, 10]. In this context, a new technique is needed to safely and effectively apply a DCB to the ostial LCx lesion. Therefore, we sought to evaluate the safety and feasibility of a novel approach: double-effect KBT (W-KBT) in LM-PCI.

2 | Methods

2.1 | Study Population

This was a single-center prospective observational study: JDEPTH-LM Pilot study (Japanese Coronary Intervention using Drug Eluting and Perfusion Therapy for Left Main Disease). We enrolled consecutive patients of de-novo LMD with ostial LCx lesions, requiring crossover-stenting from the LMT to the LAD followed by POT and conventional KBT (C-KBT). As per our clinical practice in LM-PCI, POT is routinely performed in all cases, while the decision to perform C-KBT depends on the operator's discretion. Patients with ST-segment elevation myocardial infarction (STEMI) or cardiogenic shock, those requiring mechanical circulatory support for the procedure, those requiring a two-stent technique for LMD, those who did not achieve TIMI 3 flow in the LCx after C-KBT, and individuals who underwent ad-hoc LM-PCI without being informed about the study were excluded. Written informed consent was obtained from all participants. The study was approved by the ethics committees of our institution and conducted in compliance with the principles outlined in the Declaration of Helsinki.

2.2 | Study Devices

There were two DCBs available in Japan in the study period: Agent (Boston Scientific, Natick, MA, USA) and SeQuent Please Neo (B. Braun, Melsungen, Germany). Both of them were Paclitaxel-coated balloons and there were no criteria applied for selecting DCBs in this study. The shortest lengths of both DCBs were 15 mm and nominal pressures for both DCBs was set at 6 atm, with a minimum inflation time of 30 s to ensure adequate drug delivery. A perfusion balloon (PB) (Ryusei, Kaneka Medix, Osaka, Japan) is a dedicated special semi-compliant balloon which enables distal coronary perfusion during balloon inflation, as it is equipped with multiple holes both in the proximal and distal parts of the balloon (Figure 1). The length of this balloon is exclusively 20 mm, and the nominal pressure is also 6 atm.

2.3 | W-KBT Procedure

Standard LM-PCI was performed according to the recent treatment guidelines and expert recommendations, including the use of intravascular ultrasound (IVUS) [11–13]. After confirming the achievement of optimal left main PCI by IVUS, W-KBT was additionally performed. The W-KBT was named after the drug-eluting and perfusion therapy ("double-effect") achieved by dedicated devices (DCB and PB), as well as the initial of the interventional cardiologist who innovated this technique (Dr. "W"). This technique involved the use of a PB for the LMT-LAD and a DCB for the LMT-LCx, sized in a 1:1 ratio to the balloons used in the C-KBT, and inflated at nominal pressures simultaneously. A side-by-side comparison of W-KBT and C-KBT is illustrated in Figure 2. Figure 3 demonstrates the preservation of distal coronary blood flow into the LAD despite the occlusive status of the LMT during W-KBT in an actual case.

2.4 | Study Endpoints

The primary endpoint was the procedural success, defined as the achievement of device delivery and balloon inflation time (W-KBT time) $\geq$ 30 s. Secondary endpoints included the total W-KBT time, the incidence of ischemic ST-changes, time to ST-change (ST-change time), changes in blood pressure and heart rate (delta-BP and delta-HR, respectively), and the frequency of use of inotrope and mechanical circulatory support following W-KBT. Ischemic ST change was defined as a transient ST elevation of 0.1 mV or more, an ST depression of 0.1 mV or more, or new appearance of negative U waves, recorded in at least two contiguous leads on the 12-lead ECG.

2.5 | Statistical Analysis

Categorical data are expressed as numbers and percentages. Continuous variables are expressed as mean and (±) standard deviation or as median accompanied by interquartile range (IQR) as appropriate. Continuous variables were compared with Student *t* or Mann–Whitney *U* tests, and categorical

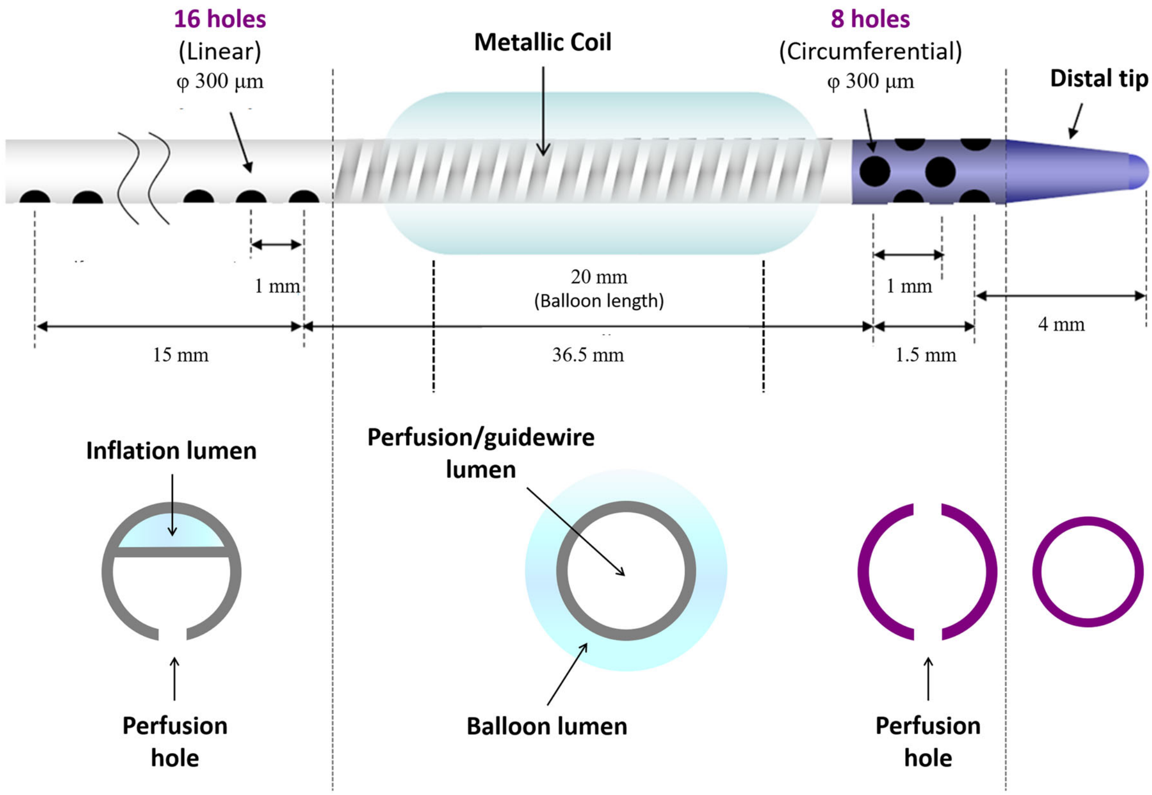


FIGURE 1 | Structure of Perfusion Balloon. The perfusion balloon used in this study equipes with 16 proximal and 8 distal perfusion holes (φ300 μm), which allow coronary blood flow to pass from the proximal to the distal segment through the balloon shaft. [Color figure can be viewed at wileyonlinelibrary.com]

variables with chi-square or Fisher exact tests, as appropriate. For paired pre- and post-procedural comparisons (e.g., systolic blood pressure and heart rate), mean differences and their 95% confidence intervals (CI) were calculated using the paired *t*-test and the *t*-distribution. All probability values were two-sided, and *p* values < 0.05 were considered statistically significant. All the statistical analysis was performed using R version 4.1.2 (R Foundation for Statistical Computing, Vienna, Austria).

3 | Results

3.1 | Study Population and Procedural Details

Between January 2023 and December 2023, 12 patients were included among 75 patients with LMD who underwent PCI during this study period (Figure 4). The mean age was 73.8 ± 7.2 years (91.7% male). The mean SYNTAX score was 29 (IQR: 26.3−34.5) and mean percent diameter stenosis on quantitative coronary angiography was 67.0 ± 13.1%. Dominance of left coronary artery was observed in 75% of cases. Details of patient and vessel/lesion characteristics are provided in Table 1.

Regarding PCI procedures, transradial approach was utilized in all cases with a 7 Fr guiding catheter via a 7 Fr Glidesheath Slender (TERUMO, Tokyo, Japan), of which outer diameter was comparable to that of a conventional 6 Fr sheath. According to IVUS guidance, stent size was appropriately selected for the crossover-stenting from the LMT to the LAD (≥3.5 mm). POT was performed in all cases and C-KBT was performed with non-compliant balloons in both vessels, the LMT-LAD and LMT-LCx. Accordingly, W-KBT was performed with a PB and a DCB, of which sizes were comparable to those in the C-KBT. Agent was more frequently used as a DCB (91.7%). Details of the devices used are shown in Table 2. To provide a practical illustration of the procedural steps and angiographic findings, a representative case is presented in Figure 5.

3.2 | Primary and Secondary Outcomes

Procedural success, defined as the device delivery and W-KBT time ≥ 30 s, was achieved in 100% of cases (12/12). Median W-KBT time was 60 s (IQR: 60−60). The incidence of ischemic ST-changes was 50% (6/12), without cases experiencing ST-elevation. Mean ST-change time was 41.2 ± 7.1 s. Notably, while the time to ST-depression resolution after balloon deflation was 5.8 ± 6.5 in four cases, ST-depression resolution was observed in approximately 10 s in two cases despite occlusive status of the LMT by W-KBT (9 s and 11 s, respectively). Regarding hemodynamic changes, baseline BP and HR before W-KBT were 139.9 ± 23.2 mmHg and 76.5 ± 18.0 bpm, respectively. Then, mean delta-BP was −13.7 ± 11.4 (95% CI: −20.9 to −6.4) mmHg and mean delta-HR was −3.4 ± 5.9 (95% CI: −7.2 to +0.3) bpm, which resulted in no use of inotrope or mechanical circulatory support during or after W-KBT (Table 3).

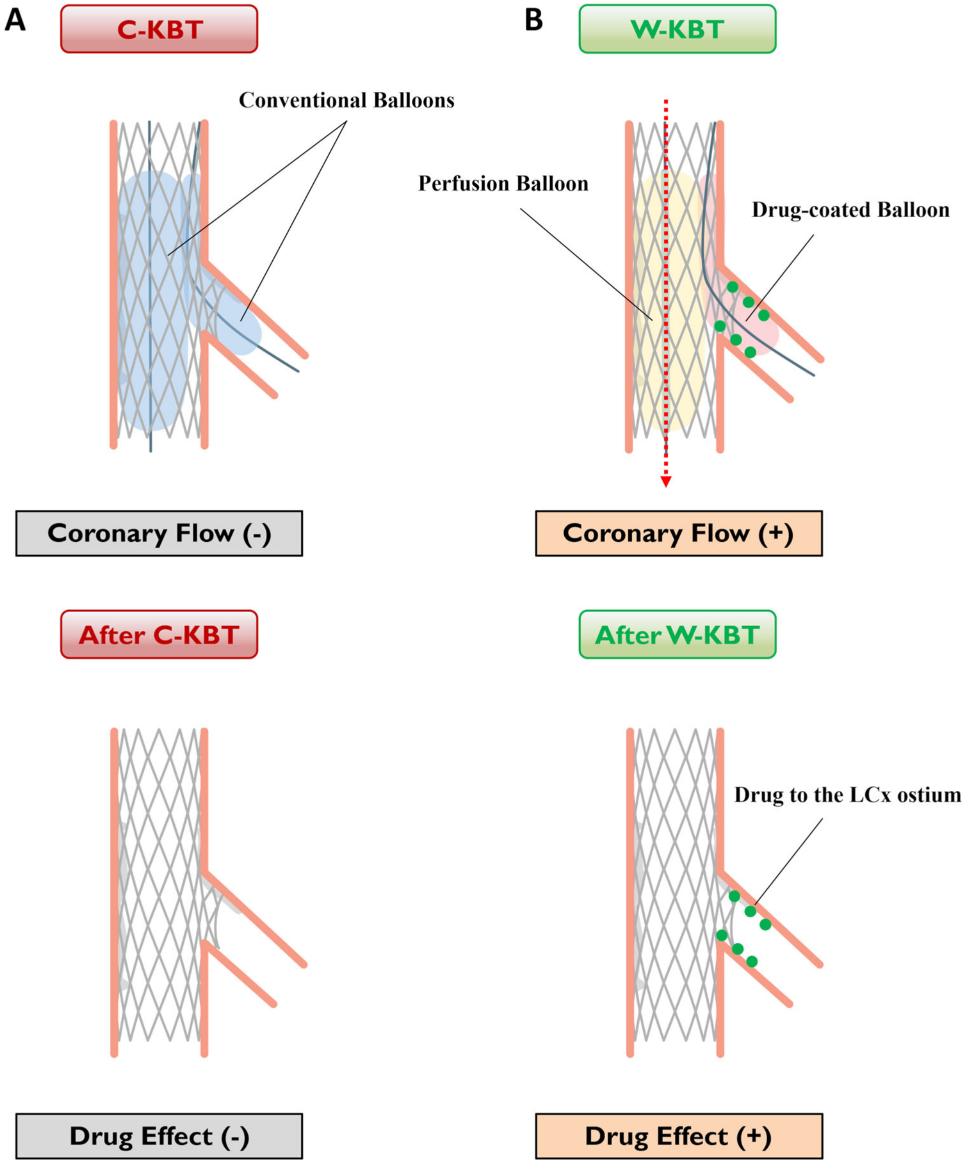


FIGURE 2 | Comparative Schema between C-KBT and W-KBT. In performing KBT with conventional balloons (C-KBT) for the left main bifurcation lesion, prolonged inflation may not be feasible due to the full-occlusion of the LMT with the risk of hemodynamic instability. Following C-KBT, no drug is delivered to the LCx ostial lesion (A). The novel W-KBT utilizes a PB for the LMT-LAD and a DCB for the LMT-LCx, which allows a prolonged inflation safely without hemodynamic instability, because of the preserved coronary blood flow through the perfusion holes of the balloon, potentially enhancing drug delivery to the ostial lesion of the LCx. Following W-KBT, the effect of drug is expected to reduce adverse cardiovascular events arising from LCx ostial lesion (B). C-KBT, conventional kissing balloon technique; DCB, drug-coated balloon; LAD, left anterior descending artery; LCx, left circumflex artery; LMT, left main trunk; PB, perfusion balloon; PCI, percutaneous coronary intervention; W-KBT, double-effect kissing balloon technique. [Color figure can be viewed at wileyonlinelibrary.com]

3.3 | Clinical Outcomes

Although this study aimed to assess only procedural safety and feasibility endpoints, we conducted clinical follow-up as part of our routine practice. Among patients who presented with stable angina pectoris ($n = 11$) with a pre-procedural cardiac troponin T level of 0.035 ± 0.04 ng/mL, a slight increase in the post-procedural cardiac troponin T level was observed (0.073 ± 0.06 ng/mL) ($p = 0.09$). One-year follow-up was conducted through direct hospital visits and no cardiovascular events were observed, including ischemia-driven target lesion revascularization arising from the ostial lesion of the LCx.

4 | Discussion

This pilot study evaluated the safety and feasibility of a novel technique of the W-KBT in LM-PCI. Our main findings are as follows. Firstly, despite the bulky device profiles of the currently available PB and DCB, device delivery was achieved in all cases via the transradial approach with 7 Fr guiding catheters. Secondly, despite the semi-occlusion of the LMT during W-KBT, this technique was maintained for 60 s in all cases without hemodynamic instability, providing sufficient time to apply the drug to the ostial lesion of the LCx. Lastly, ST-elevation was not observed during procedure and periprocedural MI was not

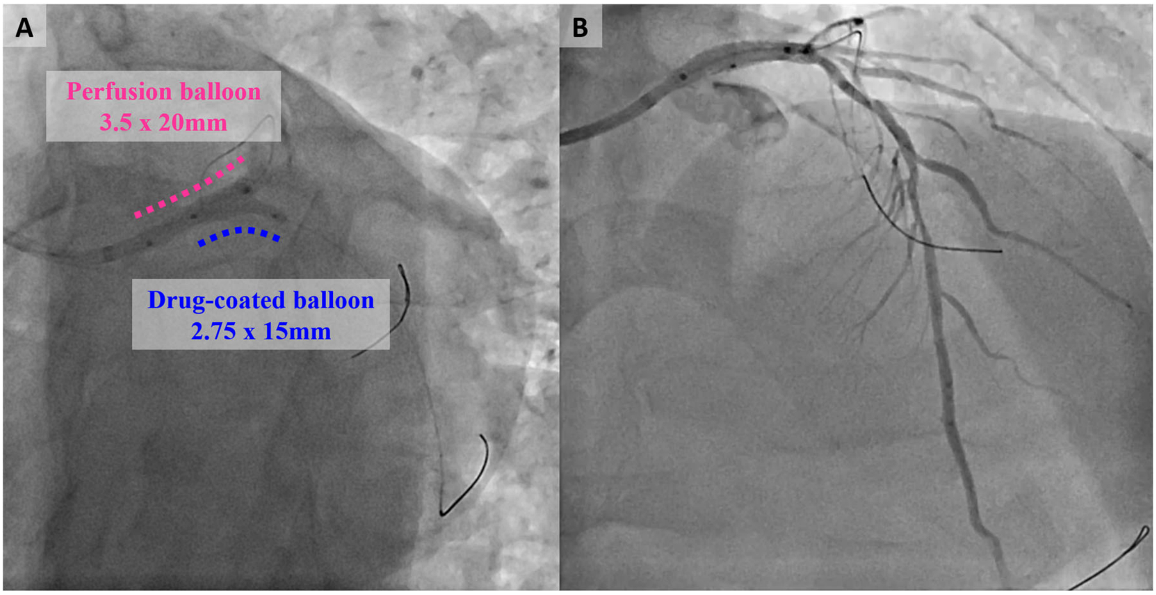


FIGURE 3 | Demonstration of Preserved Coronary Flow in LAD during W-KBT. (A) Simultaneous balloon inflation with a 3.5 mm PB for the LMT-LAD and a 2.75 mm DCB for the LMT-LCx (Caudal view). (B) Contrast media passing through the distal LAD can be observed during W-KBT, despite the semi-occlusive status of the LMT (Cranial view). Abbreviations as in Figure 2. [Color figure can be viewed at wileyonlinelibrary.com]

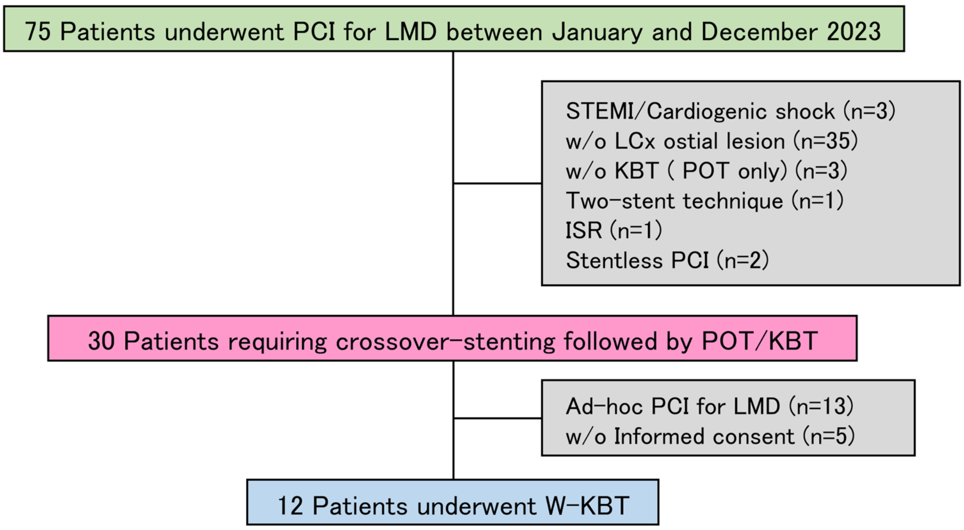


FIGURE 4 | Study flow. Within a year, 12 patients were included in this study. ISR, in-stent restenosis; LMD, left main coronary artery disease; POT, proximal optimization technique; STEMI, ST-elevation myocardial infarction. Other abbreviations as in Figure 2. [Color figure can be viewed at wileyonlinelibrary.com]

documented afterward, further highlighting the feasibility and safety of this technique (Central Illustration 1).

4.1 | Who Will Benefit From W-KBT?

Patients with LMD involving the ostial disease of the LCx may particularly benefit from W-KBT following POT and C-KBT. Although C-KBT is not an essential component of provisional stenting in bifurcation lesions in general, recent studies suggested that it might reduce the incidence of target vessel myocardial infarction and target lesion revascularization [14]. In real-world practice, the decision to perform C-KBT is left to operator discretion, as was the case in the present study. As shown in Table 1, we included patients with a certain degree of disease burden in the LCx. That is, the study population consisted of patients with substantial plaque burden or high-grade stenosis at the LCx ostium—lesions that are likely to contribute to late major adverse cardiovascular events.

Treatment of ostial lesions in the LCx remains challenging and is often referred to as the "Achilles' heel of PCI." The outcomes of two-stent techniques for LMD have been suboptimal and are not recommended except in selected cases [12, 13]. Specifically, one registry-based observational study ($n = 937$) comparing single- and two-stent techniques for LMD concordantly demonstrated significantly higher rate of repeat revascularization in two-stent strategy up to 25% at median follow-up of 4.4 years, despite similar mortalities among strategies [5]. This study also reported that main cause of repeat revascularization was restenosis of ostial lesion of

TABLE 1 | Patient and vessel/lesion characteristics.

Patient characteristics ($n = 12$)	
Age, years	73.8 ± 7.2
Male	11 (91.7)
Clinical presentation	
Stable AP	11 (91.7)
unstable AP	0
NSTEMI	1 (8.3)
Hypertension	11 (91.7)
Dyslipidemia	12 (100)
Diabetes mellitus	8 (66.7)
Chronic kidney disease	5 (41.7)
Hemodialysis	1 (8.3)
ex-Smoker	7 (58.3)
Family history of CAD	4 (33.3)
Previous MI	4 (33.3)
Ejection fraction, %	64.8 ± 8.7
Vessel and lesion characteristics ($n = 12$)	
SYNTAX Score	29 (26.3-34.5)
Right dominant	3 (25.0)
Other diseased vessels	
Mid-distal LAD	10 (83.3)
Mid-distal LCx	3 (25.0)
RCA	3 (25.0)
With CTO	1 (8.3)
Left main disease type	
Ostium	2 (16.7)
Body	3 (25.0)
Distal	12 (100)
Medina classification	
(1,1,1)	10 (83.3)
(1,0,1)	2 (16.7)
(0,1,1)	0 (0)
(0,0,1)	0 (0)
Quantitative coronary angiography	
LM-LAD: diameter stenosis, %	67.0 ± 13.1
LM-LAD: lesion length, mm	18.8 ± 3.6
LM-LCx: diameter stenosis, %	68.6 ± 16.2
LM-LCx: lesion length, mm	14.4 ± 1.8

Note: Values are mean ± SD, median (interquartile range), and *n* (%).
Abbreviations: AP, angina pectoris; CAD, coronary artery disease; CTO, chronic total occlusion; EF, ejection fraction; LAD, left anterior descending artery; LCx, left circumflex artery; LM, left main; MI, myocardial infarction; NSTEMI, non-ST elevation myocardial infarction; RCA, right coronary artery; SYNTAX, Synergy Between PCI With Taxus and Cardiac Surgery.

LCx. Furthermore, neither crossover-stenting from the LMT to the LCx nor isolated stenting solely from the ostium into the LCx has yielded optimal results, reporting an adverse event rate of 24.5% at 3 years with these strategies [6].

TABLE 2 | Procedural characteristics.

Procedural characteristics ($n = 12$)	
Access	
Radial	12 (100)
Brachial	0 (0)
Femoral	0 (0)
Guiding catheter size (Fr)	
6	0 (0)
7	12 (100)
8	0 (0)
Guiding catheter type	
SL3.5	10 (83.3)
EBU3.5	1 (8.3)
IL	1 (8.3)
Crossover stent size	
4.0 mm	1 (8.3)
3.5 mm	11 (91.7)
Balloon sizes for W-KBT (PB/DCB)	
3.5/3.0	1 (8.3)
3.5/2.75	3 (25.0)
3.5/2.5	6 (50.0)
3.5/2.25	1 (8.3)
3.0/2.5	1 (8.3)
DCB type	
SeQuent Please NEO	1 (8.3)
Agent	11 (91.7)

Note: Values are *n* (%).
Abbreviations: DCB, drug-coated balloon; PB, perfusion balloon; W-KBT, double-kissing balloon technique.

Consequently, rather than deploying stents, the use of DCBs has been advocated for side-branch ostial lesions, including those in the LCx [7, 8]. A recent trial, DCB-BIF (Comparison of Noncompliant Balloon With DCB Angioplasties for Side Branch After Provisional Stenting for Patients With True Coronary Bifurcation Lesions), supports their efficacy in such scenarios, showing that stenting the main-branch with a DCB for a compromised side-branch results in a lower 1-year risk of major adverse cardiac events compared with that with conventional balloon (7.2% vs. 12.5%; HR: 0.56; 95% CI: 0.35–0.88; $p = 0.013$) [15]. However, in the context of LMD, the efficacy of DCB treatment specifically targeting the LCx ostium has not been evaluated.

Thus, the clinical rationale for performing W-KBT as the final step in LM bifurcation PCI lies in the possibility of minimizing LCx-related adverse cardiovascular events through targeted application of a DCB, thereby improving the overall procedural outcome of LM-PCI.

4.2 | Value of This New Approach

The W-KBT offers a novel procedural refinement in LM-PCI, enabling safe and effective DCB delivery to the LCx ostium without

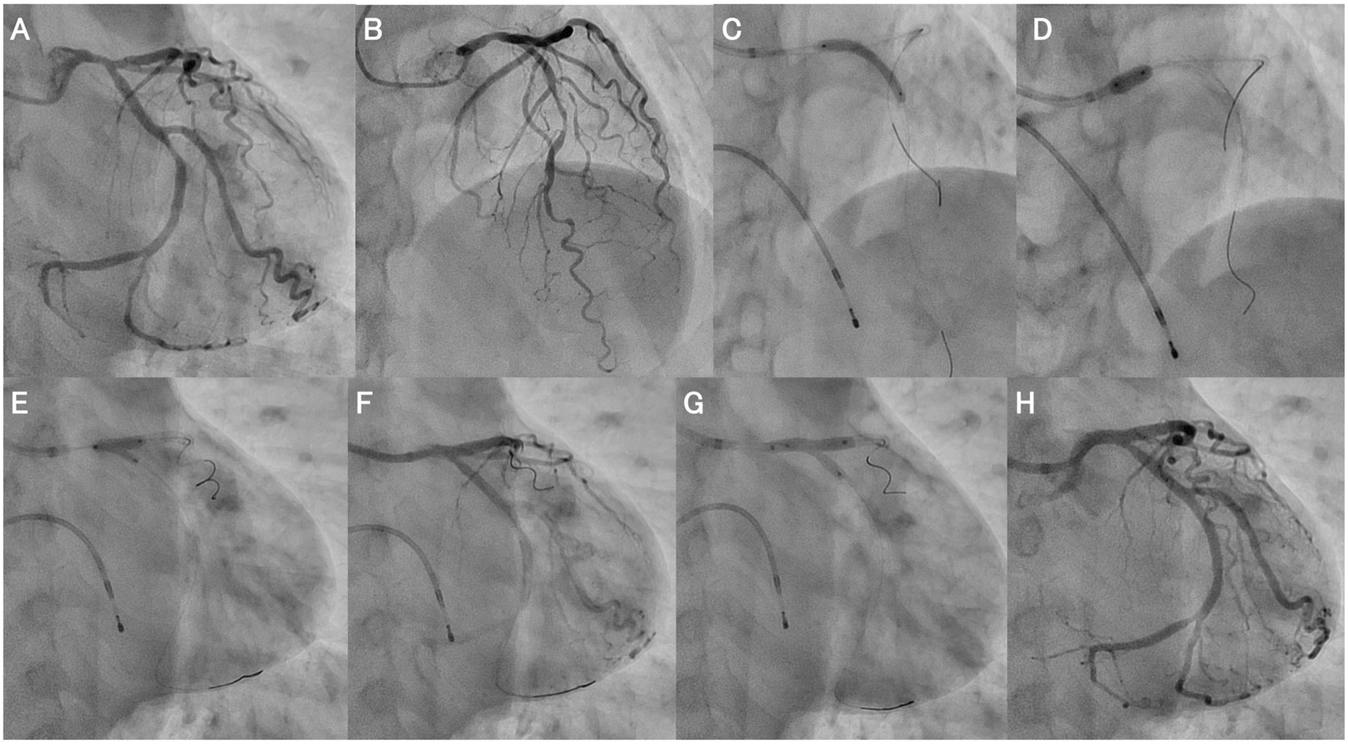


FIGURE 5 | Representative Case undergoing W-KBT. A patient with stable angina pectoris and an anatomically hypoplastic right coronary artery (left-dominant circulation) underwent PCI for a left main bifurcation lesion. Initial angiography revealed moderate stenoses in the mid-LAD and LCx (A, B). After stenting of the mid-LAD and LCx and appropriate lesion preparation for the LMD, crossover-stenting from the LMT to the LAD was performed (C), followed by POT (D) under IVUS guidance. C-KBT was then carried out (E). After confirming optimal LM-PCI results by IVUS and angiography (F), W-KBT was additionally performed (G). Final angiography demonstrated a successful result (H). A temporary pacemaker was placed during the procedure due to the left-dominant coronary anatomy. IVUS, intravascular ultrasound. Other abbreviations as in Figure 2 and Figure 4.

TABLE 3 | Procedural feasibility and safety endpoints.

Primary endpoint	
Procedural success (%)	100
Secondary endpoints	
W-KBT time (sec)	60 (60-60)
No ST-change (%)	50
ST-depression (%)	50
ST-elevation (%)	0
ST-change time (sec)	41.2 ± 7.1
Brood Pressure Change (mmHg)	−13.7 ± 11.4
Heart Rate Change (bpm)	−3.4 ± 5.9
Use of Inotrope (%)	0
Use of MCS (%)	0

Note: Values are mean ± SD, median (interquartile range), and %.
Abbreviations: Bpm, beats per minutes; MCS, mechanical circulatory support.
Other abbreviations as in Table 2.

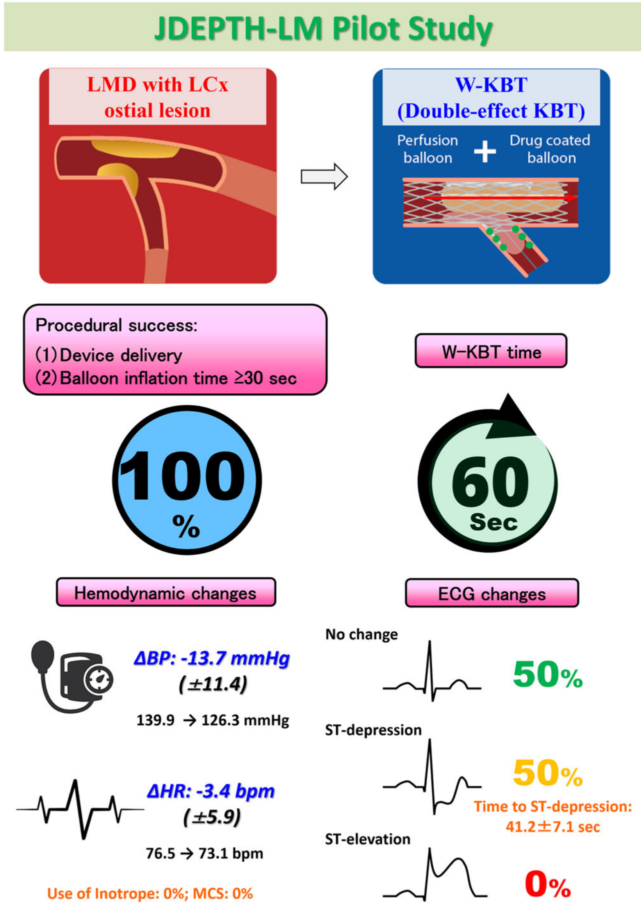
compromising the structural integrity of the main-branch stent. Unlike sequential DCB inflation—which may require repeat POT or C-KBT to correct stent distortion—W-KBT allows for prolonged and targeted DCB application while preserving LAD perfusion. This is especially important given that current DCBs require at least 30 s of inflation for optimal drug transfer, and longer inflation durations was reported to be associated with better clinical outcomes [9, 10].

In the present study, we employed the KBT utilizing the unique properties of PB and DCB as a final step in LM-PCI. Traditionally, PB has been used to maintain distal myocardial perfusion during hemostatic procedures in cases of coronary artery perforation [16]. Recently, their utility has been demonstrated in dilating unstable lesions in the setting of acute coronary syndromes including STEMI, while preventing distal embolization [17, 18]. However, the use of PB in the LMD or in the stable coronary artery disease without a well-developed collateral network has not been evaluated. We have recently reported that even in stable coronary artery disease involving the LMT, PB inflation can maintain moderate coronary blood flow [19]. As suggested in that report, the semi-occlusive status induced by balloon inflation may promote collateral recruitment, and since antegrade flow is not completely interrupted, a minimal level of myocardial perfusion is achieved. Therefore, we considered that prolonged LMT dilation using a PB could be performed without compromising hemodynamics. In this study, indeed, we successfully performed 60-s inflations in all cases without any significant hemodynamic changes or ST-segment elevation. Furthermore, in two of the six cases with ST-segment depression, ST resolution before balloon deflation was observed, likely due to reduced ischemia from collateral network formation. A very recent report further reinforced the safety of this technique, demonstrating that when coronary vasodilators such as nicorandil were administered during balloon inflation, their effects were clearly observed distal to the PB via its perfusion holes, leading to resolution of even transient ST-segment elevation [20].

retracting the guidewire just proximal to the perfusion holes can increase coronary flow by approximately 1.5-fold and may help resolve transient ischemia during balloon inflation [17].

Although procedural success in LM-PCI is known to be influenced by operator experience [21, 22], this study did not evaluate differences related to operator proficiency. Since both PB and DCB have relatively bulky profiles, device delivery can be challenging in some cases, and further evaluation of their practical applicability for general interventional cardiologists is warranted.

Importantly, W-KBT is intended as an optional technique for delivering effective drug to the LCx ostial lesions without deforming the optimized stent configuration achieved by C-KBT. The goal is to achieve safe balloon inflation for at least 30 s, ensuring sufficient drug delivery while maintaining procedural safety during KBT.



CENTRAL ILLUSTRATION 1 | In this pilot study assessing the safety and feasibility of W-KBT in PCI for LMD with the ostial lesion of the LCx, procedural success was achieved in 100% and the W-KBT was maintained for 60 seconds without hemodynamic instability and ST-elevation, providing adequate drug application to the ostial LCx lesion. [Color figure can be viewed at wileyonlinelibrary.com]

4.3 | Technical Consideration

As suggested in international treatment guidelines and expert recommendations, IVUS-guided device sizing is particularly important in LM-PCI [11, 12]. In W-KBT, we used the same balloon sizes as determined for C-KBT based on IVUS measurements. Because LMD are located proximally, the guiding catheter and devices are in close proximity. As shown in Figure 1, the proximal perfusion holes of the PB are located within 15 mm from the balloon's proximal edge. If the guiding catheter overlaps these holes during balloon inflation, coronary flow may be significantly limited. Therefore, once W-KBT (i.e., simultaneous inflation of PB and DCB) is initiated, it is crucial to promptly disengage the guiding catheter from the LMT to avoid covering the perfusion holes (Figure 5G, Supporting Information S1: Video 1).

In the present study, no clinically significant hemodynamic deterioration or ST-segment elevation was observed as shown in Table 3. Nevertheless, close monitoring of vital signs, ECG changes, and patient symptoms is essential during W-KBT. Intravenous injection of vasopressors such as norepinephrine and intracoronary injection of coronary vasodilators like nicorandil may be considered as needed [20]. As demonstrated in a bench model, temporarily

4.4 | Future Perspective

To validate the findings suggested in this pilot study and to further explore unresolved aspects of the W-KBT, a nation-wide prospective registry is currently underway in Japan (NCT06436092) [12]. The Japanese Coronary Intervention Using Drug-Eluting and Perfusion Therapy for LMD Registry (JDEPTH-LM Registry) is designed to assess the safety and efficacy of W-KBT in a real-world setting. This multicenter observational study, involving 32 institutions and aiming to enroll 280 patients with stable angina, unstable angina, or non-ST-elevation myocardial infarction, will focus on patients with LMD involving the LCx ostium. All patients will undergo a standardized procedural sequence consisting of provisional crossover-stenting from LMT to LAD, POT, C- KBT, and a final W-KBT using a PB for the LAD and a DCB for the LCx ostium, with inflation maintained for ≥30 s. The co-primary endpoints are procedural success (safety) and the 12-month incidence of major adverse cardiovascular events (efficacy). Secondary endpoints include ECG changes, hemodynamic parameters (BP and HR), and total inflation time during W-KBT. Predefined subgroup analyses will examine procedural and clinical outcomes in relation to a variety of clinical and procedural factors, including wedge pressure using a pressure-wire during W-KBT, the presence and characteristics of ST-segment changes during W-KBT, the incidence of periprocedural myocardial infarction by different definitions [23], degree of stent deformation following W-KBT on IVUS, LCx ostial lesion morphology, patient symptoms during W-KBT, left ventricular ejection fraction, operator experience with LM-PCI, as well as angiographic and ischemia assessment findings at follow-up. These analyses are expected to provide a deeper understanding of the mechanisms and applicability of W-KBT in real-world settings and potentially help define its role as an adjunctive strategy in contemporary LM-PCI.

4.5 | Study Limitations

This study has several limitations. First, it was a single-center pilot study with a small sample size, which limits the generalizability of its findings. Second, this was neither a study assessing clinical outcomes, nor comparing between W-KBT and C-KBT. Third, although 75% of cases in this study exhibited left coronary artery dominance, the safety of W-KBT in patients with anatomically hypoplastic right coronary arteries, where myocardial perfusion relies predominantly on the left coronary system, was not thoroughly evaluated. Fourth, similarly, the safety of this technique in patients with reduced left ventricular function was not assessed. Furthermore, due to the limited lengths of the device currently available (PB: 20 mm and DCBs: ≥ 15 mm), the form of W-KBT may not be ideal as the KBT in some cases as demonstrated in Figure 3. The impact of such device profile limitation on the stent eccentricity required further evaluation by intracoronary imaging. These unresolved issues are being systematically addressed in the aforementioned nationwide registry. Finally, practical considerations regarding device cost and availability outside Japan must be acknowledged. The reimbursed prices in Japan for the devices additionally used in W-KBT are approximately $1000 for the Ryusei PB catheter and $1200 for the DCB. If clinical benefit is demonstrated, these costs may be justifiable for selected cases. Moreover, with future improvements in device deliverability, it may become feasible to complete LM-PCI using only POT followed by W-KBT, potentially omitting C-KBT. Although the Ringer PB catheter (Teleflex, Wayne, PA, USA) is available outside Japan, it remains uncertain whether the structural properties of this device allow for the same W-KBT as described in the present study [24].

5 | Conclusions

Within the limited sample size of this pilot study, the safety and feasibility of the novel W-KBT were suggested. Further investigations are warranted to assess the clinical applicability and utility of W-KBT, as well as its impact on long-term outcomes in patients undergoing LM-PCI in real-world practice.

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Conflicts of Interest

T.W. has received speaker fee from Abbott Medical Japan, Boston Scientific Japan, and KANEKA Medix. The other authors declare no conflicts of interest.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.