A novel technique of low molecular weight dextran infusion followed by catheter push (D-PUSH) for optical coherence tomography

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This paper also includes supplementary data published online at: https://eurointervention.pcronline.com/doi/10.4244/EIJ-D-20-00996

Introduction

Despite the established usefulness of optical coherence tomography (OCT) guidance in percutaneous coronary intervention (PCI), the quality of the OCT images obtained is sometimes poor due to inadequate clearance of blood flow in cases involving extremely tight stenotic lesions. Increasing the volume of contrast media, generally used for blood flow clearance, is also a problem. A novel OCT procedure, the "low molecular weight dextran (LMWD) infusion followed by catheter push (D-PUSH)" procedure, in which an OCT catheter is advanced from the proximal to distal target lesion segment after initiating LMWD infusion from a guiding catheter, may improve image quality compared with conventional OCT procedures. The aims of the current study were to evaluate image quality obtained by the D-PUSH procedure compared with the conventional OCT procedure in patients with acute coronary syndrome (ACS).

Methods

STUDY POPULATION

A total of 50 ACS patients who underwent the novel D-PUSH OCT procedure by pre-specified operators (Y. Shibata and H. Okazaki) were prospectively enrolled. These two operators had previously performed the D-PUSH procedure 10 times and thus were well trained. Patient enrolment details are shown in **Supplementary Figure 1**.

ANGIOGRAPHIC ANALYSIS

Qualitative coronary angiographic analyses were performed for the initial coronary angiography to evaluate lesion location, lesion complexity, and Thrombolysis In Myocardial Infarction (TIMI) flow grade. After obtaining a TIMI flow grade of ≥2, quantitative coronary angiography (QCA) analyses were performed to measure variables, including lesion length, minimal lumen diameter (MLD), reference vessel diameter, % diameter stenosis, and TIMI flow grade.

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OCT PROCEDURE

For cases with initial coronary angiography TIMI flow grades <2, we first performed intracoronary thrombectomy before OCT examination. The OCT imaging of the culprit lesion was acquired by frequency-domain OCT (Abbott Vascular, Santa Clara, CA, USA) after administering intracoronary nitroglycerine. First, we performed the novel OCT procedure, D-PUSH, followed by the conventional OCT procedure. When performing D-PUSH and conventional procedures, "flush mediums" on the OCT system (OPTIS™ mobile; Abbott Vascular) were set to "1:1 (contrast:saline)" where the refractive index was 1.393, and "contrast" where the refractive index was 1.449. **Supplementary Figure 2** and **Moving image 1** show a representative case where the middle portion of the right coronary artery lesion **(Supplementary Figure 2A)** was evaluated by D-PUSH and conventional OCT procedures. The D-PUSH procedure involves four steps: i) an OCT catheter is placed proximal to the lesion **(Supplementary Figure 2B, Moving image 2)**; ii) LMWD is infused via an automated injector (Zone Master SR Fusion; Sugan Co. Ltd., Osaka, Japan) into the right coronary artery at a rate of 3 mL/s for 6 seconds from the guiding catheter and, if the culprit lesion is in the left coronary artery, LMWD is infused at a rate of 4 mL/s for 6 seconds; iii) two seconds after initiating infusion, the catheter is advanced distal to the lesion **(Supplementary Figure 2C, Moving image 2)**; and iv) the optical lens is then automatically pulled back proximally from distal to the lesion for 75 mm at 36 mm/s (0.2 mm/frame). Conventional OCT examination was performed following the D-PUSH procedure using the current protocol. An OCT catheter has already been placed distal to the lesion **(Supplementary Figure 2D, Moving image 3)**, after which an optical lens is automatically pulled from the distal to proximal sections of the lesion for 75 mm at 36 mm/s (0.2 mm/frame) while infusing contrast media into the right coronary artery at a rate of 3 mL/s for 4 seconds **(Supplementary Figure 2E, Moving image 3)**. In the case of a left coronary artery lesion, contrast media is infused from the guiding catheter at a rate of 4 mL/s for 4 seconds. Lesions were examined using both the D-PUSH and conventional procedures up to two times each at the operator's discretion.

OCT IMAGE ANALYSIS

All OCT images were analysed by an independent cardiologist (N. Kobayashi) who was blinded to the clinical presentation and OCT procedure protocols. An analysed vessel was divided into five segments, as shown in **Supplementary Figure 2A**. We performed further quantitative OCT analyses to compare the image quality of D-PUSH with conventional OCT examination. **Supplementary Figure 2F** and **Moving image 4**, and **Supplementary Figure 2G** and **Moving image 5** demonstrate representative OCT images obtained by D-PUSH and conventional procedures, respectively. Degrees of visualisable arcs were assessed every 1 mm, and the average degree of visualisable arc in each segment was compared between D-PUSH and conventional procedures **(Supplementary Figure 2H)** for each patient using the paired Wilcoxon signed-rank

non-parametric test. Cases where the average visualisable arc of the distal lesion segment was ≥45° wider in the D-PUSH procedure compared with the conventional procedure were defined as D-PUSH-preferred cases.

Results

Of 50 enrolled patients, 84% were male. The median age was 69 years and median creatinine level on admission was 0.83 mg/dL. Detailed baseline clinical characteristics and laboratory data are shown in **Supplementary Table 1**. There was no statistical difference between creatinine levels before and after the procedures (median 0.83 mg/dL vs 0.74 mg/dL, p=0.069). Among the 50 enrolled cases, analysable OCT images could be obtained in 45 cases **(Supplementary Figure 1)**. On average, we performed D-PUSH and conventional procedures 1.2 and 1.3 times per patient, respectively. Angiography and OCT findings are shown in **Supplementary Table 2**. Of the 45 lesions, we were unable to use either D-PUSH or conventional procedures to evaluate plaque morphologies (i.e., ruptured or unruptured) in two cases due to massive residual thrombi. Of the remaining 43 lesions, plaque morphologies in 11 lesions could not be assessed by the conventional procedure whereas D-PUSH was able to assess all cases (23 were plaque rupture and 20 were non-plaque rupture). A comparison of OCT image quality between D-PUSH and conventional procedures is shown in **Table 1**. Average visualisable arcs evaluated by D-PUSH were wider compared with conventional procedure in proximal (p=0.023) and distal (p<0.001) lesion segments, as well as in distal reference segments (p<0.001). Receiver operating characteristic (ROC) curve analysis showed a required MLD cut-off value of 0.49 mm to predict D-PUSH-preferred cases **(Supplementary Figure 3)**.

Table 1. Comparisons of average visualisable arcs between D-PUSH and conventional OCT procedures.

Average of visualisable arc (°)	D-PUSH (n=45)	Conventional (n=45)	p-value
Proximal reference segment	360 (360, 360)	360 (360, 360)	0.239
Proximal lesion segment	360 (360, 360)	360 (360, 360)	0.023
Minimum lumen area site	360 (360, 360)	360 (360, 360)	0.083
Distal lesion segment	360 (360, 360)	331 (224, 360)	<0.001
Distal reference	360 (360, 360)	273 (68, 360)	<0.001

D-PUSH: low molecular weight dextran infusion followed by catheter PUSH; OCT: optical coherence tomography

Discussion

OCT exhibits superior axial resolution compared with intravascular ultrasound. Conversely, OCT has disadvantages, such as requiring complete blood clearance from the lumen for imaging, as well as increased amounts of contrast media to eliminate blood. Contrast media infused from the guiding catheter fails to eliminate blood flow in cases of severely stenotic lesions,

e.g., lesions with an MLD ≤0.49 mm, due to the OCT catheter becoming wedged in the lesion. OCT-guided PCI is not recommended for patients with unknown renal function, as it requires additional contrast media. Therefore, in these cases, we recommend the novel OCT procedure, D-PUSH, which more reliably eliminates blood flow and avoids using large volumes of contrast media. A recent report described the safety of OCT-guided PCI using LMWD compared with intravascular ultrasound guidance on renal function[1]. Because LMWD and contrast media have different refractive properties, the flush medium setting on the OCT system is changed if available. If a change of setting is not available, area and length measurements of images acquired with LMWD are corrected by multiplying by 1.117 and 1.057, respectively[2].

In real clinical practice, contrast media infusion followed by catheter push (C-PUSH) can be applied to patients with tight stenotic lesions, who do not exhibit renal insufficiency **(Supplementary Figure 4, Supplementary Figure 5, Moving image 6–Moving image 12)**. Because understanding the catheter advancement timing is comparatively easier in C-PUSH than D-PUSH, C-PUSH can be an initial step for D-PUSH training.

Limitations

This study demonstrated the usefulness of D-PUSH in a limited number of ACS subjects. Lesions with severe calcification or tortuosity, as well as patients with critical conditions, were excluded. Currently, the reproducibility of the D-PUSH procedure for stable (non-thrombotic) lesions remains uncertain. In addition, the advantage of using LMWD instead of contrast media to avoid renal damage was not proven in the current study.

Conclusions

OCT image quality obtained by D-PUSH was higher compared with conventional procedures, particularly in cases involving extremely tight stenotic lesions with an MLD ≤0.49 mm.

Impact on daily practice

When performing primary PCI for patients with kidney disease or unknown renal function, D-PUSH OCT is useful to evaluate tight stenotic lesions without the use of large volumes of contrast media. The biggest advantage of D-PUSH is obtaining information from the distal part of the lesion, which helps operators when deciding PCI strategies, e.g., stent length and diameter.

Conflict of interest statement

The authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Figure 1. Patient enrolment.
Supplementary Figure 2. A representative case of the D-PUSH procedure and evaluation of OCT image quality.
Supplementary Figure 3. ROC curve analyses for MLD on QCA and MLA on OCT.
Supplementary Figure 4. The C-PUSH procedure performed for the partially tortuous right coronary artery.
Supplementary Figure 5. The C-PUSH procedure performed on the left anterior descending artery with long, tandem, partially calcified lesions.
Supplementary Table 1. Baseline clinical characteristics and laboratory data.
Supplementary Table 2. Angiography and OCT findings.
Moving image 1. Angiography image from severely tight stenotic lesion in the middle portion of the right coronary artery.
Moving image 2. Angiography image from the D-PUSH OCT procedure.
Moving image 3. Angiography image from the conventional OCT procedure.
Moving image 4. OCT image for severely tight stenotic right coronary artery lesion obtained by the D-PUSH OCT procedure.
Moving image 5. OCT image for severely tight stenotic right coronary artery lesion obtained by the conventional OCT procedure.
Moving image 6. Angiography image from severely tight stenotic lesion in the distal portion of the right coronary artery with partial tortuousness.
Moving image 7. Angiography image from the C-PUSH OCT procedure.
Moving image 8. Angiography image from the conventional OCT procedure.
Moving image 9. OCT image for the stenotic and tortuous right coronary artery lesion obtained by the C-PUSH OCT procedure.
Moving image 10. OCT image for the stenotic and tortuous right coronary artery lesion obtained by the conventional OCT procedure.
Moving image 11. Angiography image from the C-PUSH OCT procedure for long, tandem, partially calcified lesions in the middle portion of the left anterior descending artery.
Moving image 12. OCT image of long, tandem left anterior descending artery obtained by the C-PUSH procedure.

The supplementary data are published online at:
https://eurointervention.pcronline.com/
doi/10.4244/EIJ-D-20-00996

Supplementary data
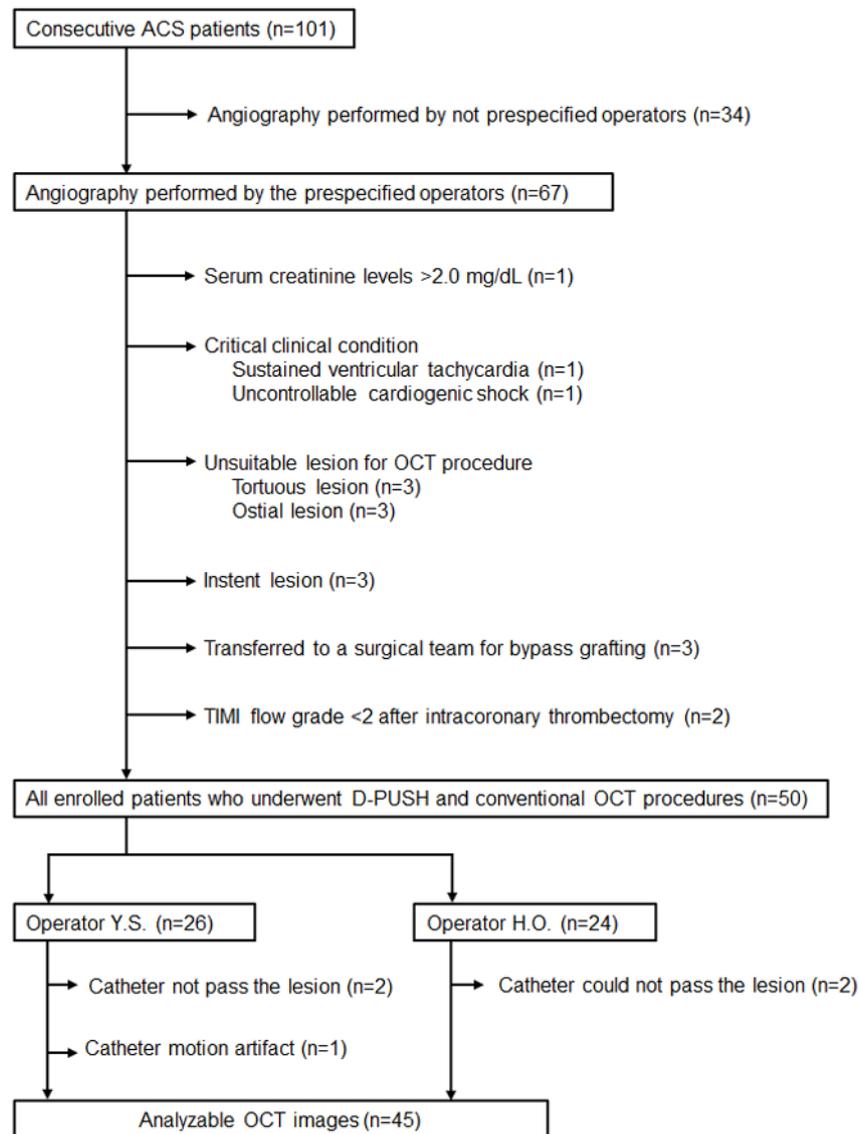
Supplementary Figure 1. Patient enrolment.

Among 101 consecutive patients with ACS transferred to the emergency department of Nippon Medical School Chiba Hokusoh Hospital, 67 patients underwent emergency coronary angiography by pre-specified operators (Y. Shibata and H. Okazaki) who were well trained in the D-PUSH OCT procedure. Among them, 17 patients were excluded based on pre-determined exclusion criteria: one patient exhibited serum creatinine levels >2.0 mg/dL, two exhibited critical clinical conditions (sustained ventricular tachycardia or uncontrollable cardiogenic shock), six had unsuitable lesion morphologies for OCT procedures (three exhibited tortuous lesions, and three exhibited ostial lesions), three demonstrated in-stent lesions, three were transferred to a surgical team to undergo coronary artery bypass grafting, and two failed to achieve a TIMI flow grade of ≥2 after intracoronary thrombectomy. The remaining 50 ACS patients were enrolled in the current study. Among these 50 patients, 26 and 24 underwent OCT procedures by Y. Shibata and H. Okazaki, respectively. Of the four cases where the catheter was unable to pass the lesion, two were

attempted by Y. Shibata and two by H. Okazaki. One case examined by Y. Shibata could not be analysed due to severe motion artefacts. The success rates of the D-PUSH procedure between operators were comparable (88% and 92%; p=0.706). The remaining 45 cases examined by D-PUSH and conventional OCT procedures were able to be analysed.

ACS: acute coronary syndrome; D-PUSH: low molecular weight dextran infusion followed by catheter push; OCT: optical coherence tomography; TIMI: Thrombolysis In Myocardial Infarction
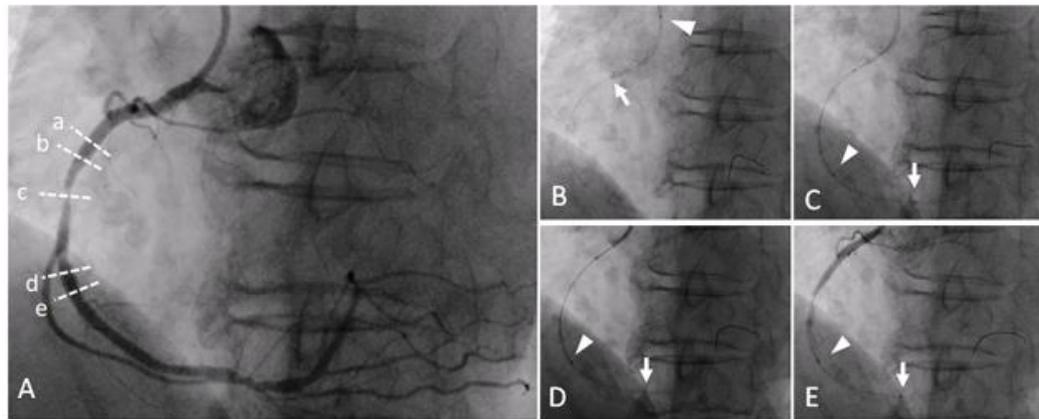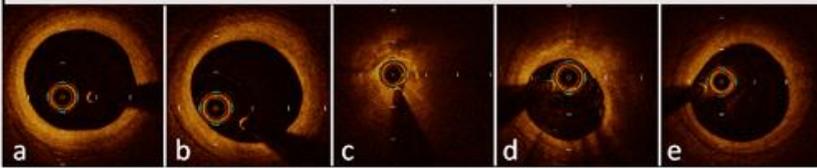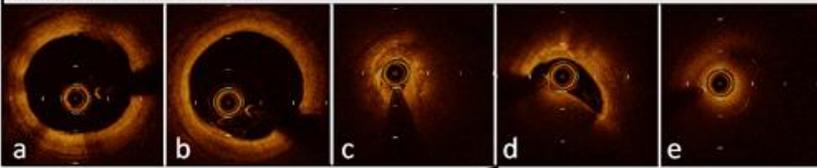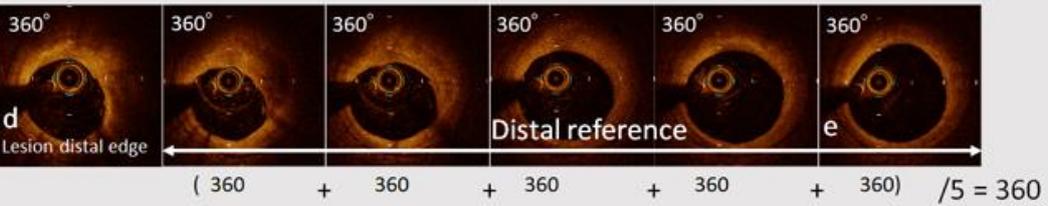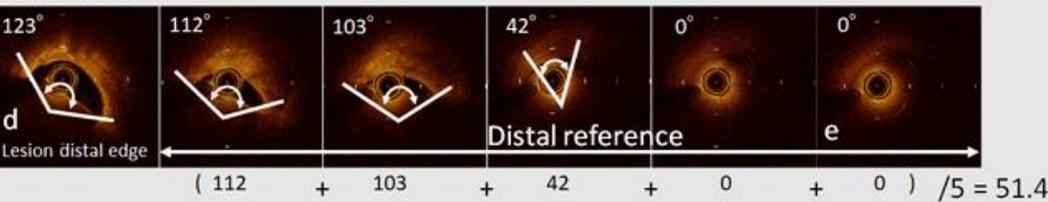
Supplementary Figure 2. A representative case of the D-PUSH procedure and evaluation of OCT image quality.

A) Severely tight stenotic lesion in the middle portion of the right coronary artery (Moving image 1). Segments of the proximal reference (a–b), the proximal lesion (b–c), the minimum lumen site (c), the distal lesion (c–d) and the distal reference (d–e) are shown.

B) & C) Angiography images from the D-PUSH OCT procedure (Moving image 2). Both the distal tip (arrows) and optical lens (arrowheads) were placed proximal to the lesion before LMWD infusion (B), and both distal tip (arrows) and optical lens (arrowheads) were advanced distal to the lesion two seconds after initiating LMWD infusion (C).

D) & E) Angiography images from the conventional OCT procedure (Moving image 3). Both distal tip (arrows) and optical lens (arrowheads) were placed distal to the lesion before (D) and after (E) initiating contrast media infusion.

F) & G) Representative OCT images at the proximal edge of the proximal reference (a), proximal edge of the lesion (b), minimum lumen site (c), distal edge of the lesion (d), and distal edge of the distal reference (e) obtained by D-PUSH (F, Moving image 4) and conventional (G, Moving image 5) procedures, respectively.

H) Comparison of OCT image quality in the distal reference segment (d–e) between D-PUSH and conventional procedures. Degrees of visualisable arcs were assessed every 1 mm and averaged in the segment.

D-PUSH: low molecular weight dextran infusion followed by catheter push; LMWD: low molecular weight dextran; OCT: optical coherence tomography
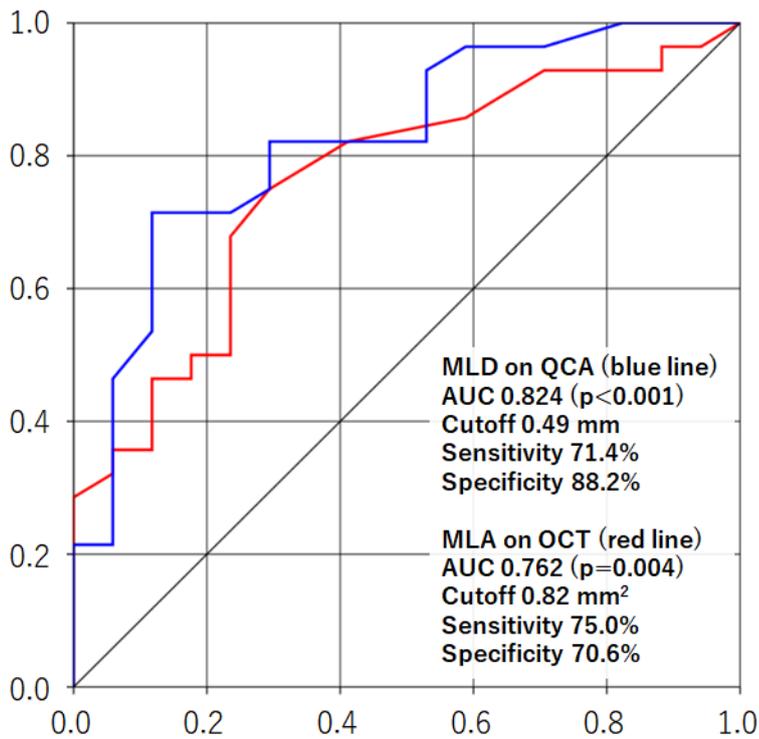
Supplementary Figure 3. ROC curve analyses for MLD on QCA and MLA on OCT.

ROC curves of MLD on QCA (blue line) and MLA on OCT (red line) in the adoption of D-PUSH rather than conventional OCT procedures. AUC values for MLD and MLA were 0.824 (p<0.001) and 0.762 (p=0.004), respectively. Cut-off values of MLD 0.49 mm (sensitivity 71.4% and specificity 88.2%) and MLA 0.82 mm² (sensitivity 75.0% and specificity 70.6%) were required to predict D-PUSH-preferred cases (i.e., cases where the average visualisable arc of the distal lesion segment was ≥45° wider in the D-PUSH procedure compared with the conventional procedure).

AUC: area under the curve; D-PUSH: low molecular weight dextran infusion followed by catheter push; MLA: minimum lumen cross-sectional area; MLD: minimum lumen diameter; OCT: optical coherence tomography; QCA: quantitative coronary angiographic analyses; ROC: receiver operating characteristic
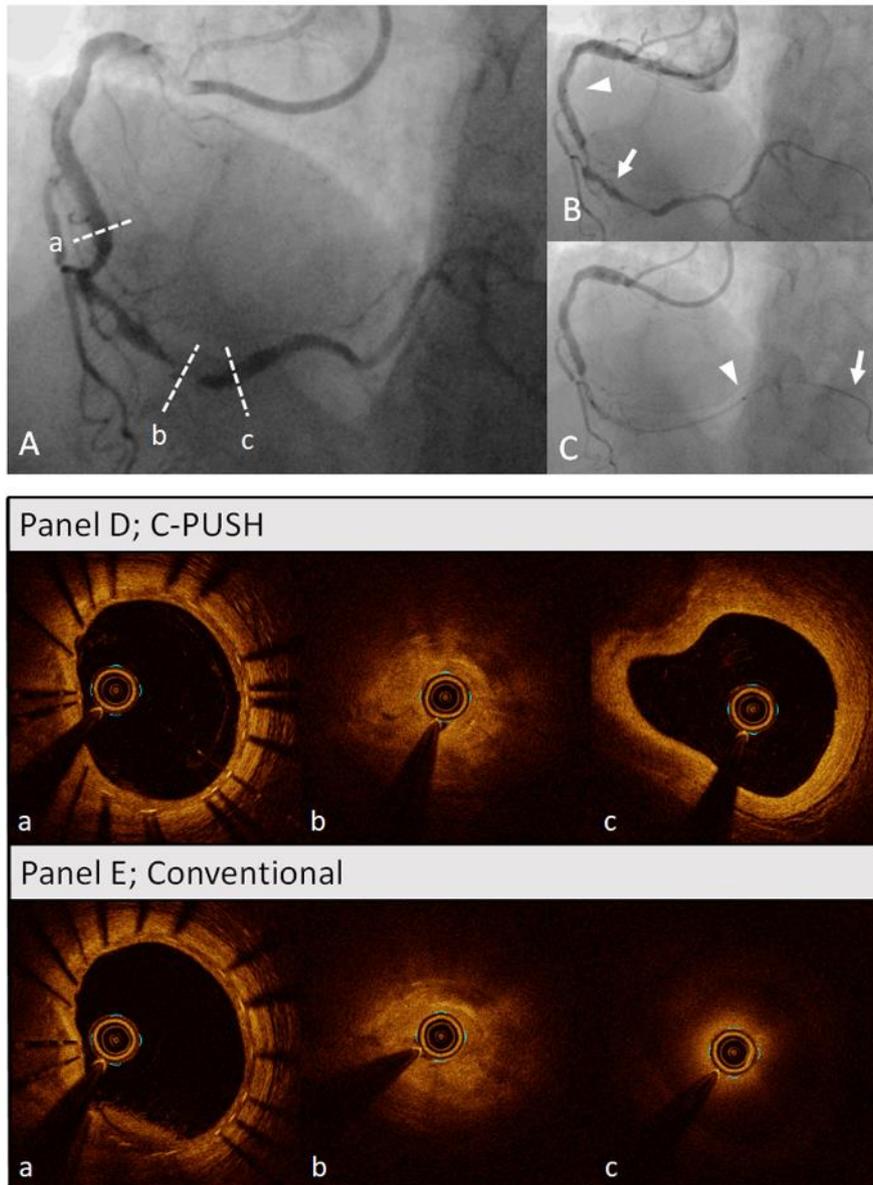
Supplementary Figure 4. The C-PUSH procedure performed for the partially tortuous right coronary artery.

A) Severely tight stenotic lesion in the distal portion of the right coronary artery with partial tortuousness (Moving image 6). The proximal lesion segment (a–b), the minimum lumen site (b), and the distal lesion segment (b–c) are shown.

B) Angiography image from the C-PUSH OCT procedure (Moving image 7). Both the distal tip (arrows) and optical lens (arrowheads) were placed proximal to the lesion shortly after initiating contrast media infusion (3 mL/s for four seconds).

C) Angiography image from the conventional OCT procedure (Moving image 8). Both distal tip (arrows) and optical lens (arrowheads) were placed distal to the lesion before initiating contrast media infusion (3 mL/s for 4 seconds).

D) & E) OCT images at the proximal edge of the lesion (a), minimum lumen site (b), and distal edge of the lesion (c) obtained by C-PUSH (D, Moving image 9) and conventional (E, Moving image 10) procedures, respectively. In both the C-PUSH and conventional OCT procedures, an optical lens is automatically pulled from the distal to proximal sections of the lesion for 75 mm at 36 mm/s (0.2 mm/frame) while infusing contrast media into the right coronary artery at a rate of 3 mL/s for 4 seconds.

C-PUSH: contrast media infusion followed by catheter push; OCT: optical coherence tomography
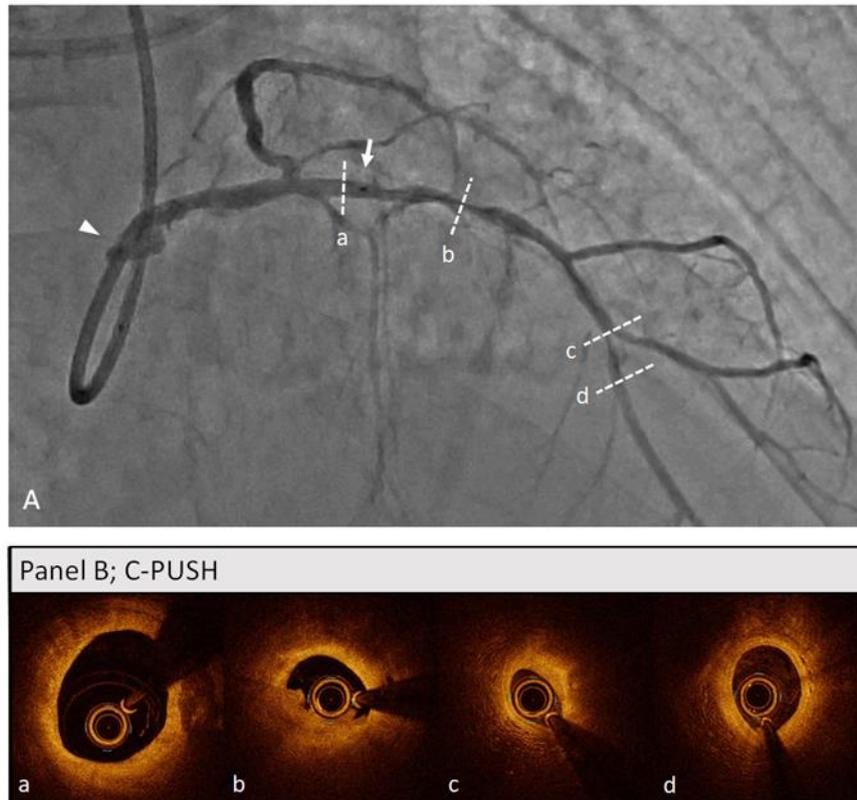
Supplementary Figure 5. The C-PUSH procedure performed on the left anterior descending artery with long, tandem, partially calcified lesions.

A) Angiography image from the C-PUSH OCT procedure for long, tandem, partially calcified lesions in the middle portion of the left anterior descending artery (Moving image 11). Lesion proximal edge (a), proximal stenotic site (b), distal minimum lumen site (c), and lesion distal edge (d) are shown. Both the distal tip (arrows) and optical lens (arrowheads) were placed proximal to the lesion shortly after initiating contrast media infusion (4 mL/s for 4 seconds).

B) Representative OCT images at the proximal edge of the lesion (a), proximal stenotic site (b), distal minimum lumen site (c), and distal edge of the lesion (d) obtained by C-PUSH (Moving image 12). An optical lens is automatically pulled from the distal to proximal sections of the lesion for 75 mm at 36 mm/s (0.2 mm/frame) while infusing contrast media into the right coronary artery at a rate of 4 mL/s for 4 seconds.

C-PUSH: contrast media infusion followed by catheter push; OCT: optical coherence tomography

Supplementary Table 1. Baseline clinical characteristics and laboratory data.

	n=50
Patient characteristics	
Male	42/50 (84%)
Age, years	69 (57, 76)
Diabetes mellitus	21/50 (42%)
Hypertension	39/50 (78%)
Dyslipidaemia	32/50 (64%)
Prior myocardial infarction	7/50 (14%)
Systolic blood pressure, mmHg	149 (123, 160)
Diastolic blood pressure, mmHg	84 (70, 96)
Heart rate, /minute	78 (64, 94)
Electrocardiography findings	
ST-segment elevation	34/50 (68%)
Non-ST-segment elevation	16/50 (32%)
Acute coronary syndrome type	
Myocardial infarction	49/50 (98%)
Unstable angina pectoris	1/50 (2%)
Killip class	
I	35/50 (70%)
II, III, IV	8/50 (16%)
IV	7/50 (14%)
Laboratory data*	
Creatinine on admission, mg/dL	0.83 (0.69, 0.96)
Creatinine after procedure, mg/dL[†]	0.74 (0.65, 0.95)
Blood glucose, mg/dL	149 (119, 197)
Low-density lipoprotein cholesterol, mg/dL	123 (117, 131)
High-density lipoprotein cholesterol, mg/dL	45 (40, 51)
Triglyceride, mg/dL	122 (81, 199)
Haemoglobin A1c, %	6.2 (5.7, 6.8)
C-reactive protein, mg/dL	0.20 (0.08, 0.83)
B-type natriuretic peptide, pg/mL	45 (23, 148)
High-sensitivity cardiac troponin T, ng/mL	0.117 (0.032, 0.432)
Creatine kinase-MB on admission, U/L	18 (13, 30)
Peak creatine kinase-MB, U/L[‡]	98 (40, 312)

Values are shown as median (interquartile range) or n (%). *Peripheral blood samples were obtained on admission. †Serum creatinine values were examined on admission and within 24 hours after primary PCI. ‡To evaluate peak CK-MB values, blood samples were obtained serially every 6 hours after ED presentation until the CK-MB value began to decline.

Supplementary Table 2. Angiography and OCT findings.

Angiography findings	(n=50)
Multivessel disease[*]	30/50 (60%)
Culprit artery	
Right coronary artery	13 (26%)
Left anterior descending artery	30 (60%)
Left circumflex artery	7 (14%)
Initial TIMI flow grade	
0 or 1	27 (54%)
2	6 (12%)
3	17 (34%)
ACC/AHA classification type B2/C	48/50 (96%)
Post-thrombectomy/pre-OCT angiography analyses	(n=50)
Lesion length, mm	21.1 (15.0, 26.0)
Minimum lumen diameter, mm	0.50 (0.37, 0.70)
Reference vessel diameter, mm	2.63 (2.29, 3.14)
Diameter stenosis, %	81.8 (73.0, 88.1)
TIMI flow grade	
0 or 1	0 (0%)
2	15 (30%)
3	35 (70%)
Initial/post-thrombectomy OCT findings	(n=45)
Lesion length, mm	23.3 (19.7, 29.9)
Length of distal reference, mm	5.0 (5.0, 5.0)
Length of proximal reference, mm	5.0 (5.0, 5.0)
Length from lesion distal edge to MLA site, mm	12.9 (8.8, 18.3)
Length from MLA site to lesion proximal edge, mm	11.1 (9.3, 14.2)
Minimum lumen CSA, mm^2	0.83 (0.79, 1.10)
Distal reference lumen CSA, mm^2	3.99 (2.89, 6.02)
Proximal reference lumen CSA, mm^2	6.72 (4.70, 9.13)
Plaque rupture/non-plaque rupture/massive thrombi	23 (51%)/20 (44%)/2 (4%)
Thrombus	41/45 (91%)
Red thrombus/white thrombus	22 (54%)/19 (46%)

Values are shown as median (interquartile range) or n (%).

[*] Defined as the presence of two or more diseased vessels (diameter stenosis ≥50%).

ACC: American College of Cardiology; AHA: American Heart Association; CSA: cross-sectional area; OCT: optical coherence tomography; TIMI: Thrombolysis In Myocardial Infarction