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Full Length Article

Drug-Coated Balloon Only Percutaneous Coronary Intervention for De-Novo Chronic Total Occlusion: Insights From the Multicenter International CTO-DENOVO Registry

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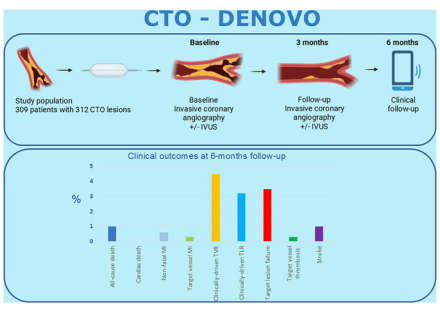
We aimed to assess the clinical, angiographic, and outcome profiles of patients undergoing chronic total occlusion (CTO) percutaneous coronary intervention (PCI) with the use of drug-coated balloon (DCB)-only approach in a retrospective multicenter international registry. Data from 309 patients with 312 CTO lesions undergoing successful CTO PCI with DCB-only approach at 42 sites were collected. Angiographic and clinical follow-up was performed at 3 and 6 months, respectively. The primary endpoint was target lesion failure (TLF), defined as composite of cardiac death, target vessel myocardial infarction, or clinically-driven target lesion revascularization (TLR). Secondary endpoints included binary restenosis (≥50% stenosis) and late lumen loss (LLL) on angiography. The mean age was 67 ± 10 years, and 58.9% patients were male. The main indication for DCB was small vessel disease (37.1%), and most CTO were recanalized with intraplaque wiring (93%). TLF was 3.5% with no cardiac death at 6 months. Of 157 CTO with angiographic follow-up (50.3%) at a median of 99 days (IQR: 85 to 136 days), the LLL was −0.1 mm (IQR: −0.3 to 0.3 mm), and 47.8% vessels showed positive remodelling. Binary restenosis and re-occlusion were 24.2% and 4.0%, respectively. Coronary CTO with binary restenosis had significantly higher residual stenosis directly post-PCI (p <0.001) than CTO without restenosis. In conclusion, treatment of CTO with a DCB-only approach is safe, with a low number of TLF at 6-month follow-up. In selected population with angiographic follow-up, suboptimal predilatation result was associated with an increased rate of restenosis and warrants further investigation.



Central illustration

Data from randomized clinical trials support the role of percutaneous revascularization of coronary chronic total occlusions (CTO) in improving the quality of life.[1–3] Yet percutaneous management of CTO––often involving long, calcified lesions with diffuse distal disease––is still associated with higher risk of stent failure and potentially increased rates of major adverse cardiac events compared with subtotal stenoses.[4] This has prompted a growing interest in the "leave-nothing-behind" strategies based upon the use of drug-coated balloons (DCB) as an alternative for metallic stents in CTO percutaneous coronary intervention (PCI).[5,6] Particularly germane to this concept, DCB can preserve coronary vasomotor function, promote late lumen enlargement, and potentially reduce the risk of restenosis and thrombosis.[7–9] Although clinical data support DCB safety and efficacy for in-stent restenosis,[10] de novo small vessel disease,[11] and high bleeding risk patients,[12] evidence for a DCB-only approach in de-novo CTO is still limited to small and mostly single-center studies.[13–15] In this multicenter international registry, we aimed to assess: 1) target lesion failure at 6 months and 2) detailed angiographic outcomes at 3 months in patients undergoing successful CTO recanalization with the use of DCB-only approach.

Methods

Study design and population

The CTO-DENOVO study (www.clinicaltrials.gov identifier, NCT05977842) is a multicenter retrospective registry of consecutive

patients who underwent successful CTO PCI using a DCB-only strategy between December 2012 and June 2024 (42 sites, Supplementary Table 1). Exclusion criteria were: in-stent CTO and de novo coronary CTO undergoing successful recanalization with the use of drug-eluting stent (DES) at the occlusion site. The use of DES ≥5 mm outside of the occlusion site was not deemed as the exclusion criterion. Study design is presented in Figure 1. The study was conducted in accordance with the Declaration of Helsinki, and institutional review board approval was obtained at the participating centers. The study informed consent was waived based on the retrospective nature of the study.

CTO PCI

CTO PCI was performed in accordance with standard guidelines by experienced CTO PCI operators acquainted with all crossing strategies (antegrade wiring, antegrade dissection and re-entry, retrograde wiring and retrograde dissection and re-entry). After successful CTO recanalization, lesion preparation with a balloon-to-artery ratio of approximately 1:1 was performed, followed by DCB delivery and inflation for at least 30 seconds.[16] A DCB strategy was preferred provided a satisfactory angioplasty result after lesion preparation was achieved including the following criteria: 1) a fully inflated balloon of the correct size for the vessel[17]; 2) Thrombolysis in Myocardial Infarction (TIMI) flow grade 2 or 3[18,19]; 3) <40% residual stenosis; and 4) the absence of a flow-limiting dissection.[17,19] Bail-out stenting and use of intravascular ultrasound (IVUS) were at the operator's discretion. A subgroup of patients with successful DCB use at the intended CTO lesion, and without the need for bail-out stenting were invited to undergo follow-up invasive coronary angiography (ICA) with optional IVUS at 3 months at discretion of the operator and irrespective of whether it was clinically indicated by the presence of symptoms.

Quantitative coronary angiography

Baseline and follow-up angiograms were analyzed offline by an experienced reader (M.D.) blinded to IVUS measurements using a dedicated software tool (Medis Medical Imaging, Leiden, The Netherlands). Angiographic end-diastolic frames from the region of interest were selected for analysis. The reference diameter of the vessel was determined by marking segments with minimal coronary atherosclerosis within 5 mm of the occlusion site. The coronary artery was automatically delineated, and manual correction was applied if necessary. Proximal and distal markers of the lesion were aligned with the corresponding locations of the DCB-treated segments. The minimal lumen diameter (MLD) was measured and residual percent diameter stenosis was calculated. Acute recoil was defined as the difference between balloon diameter and post-procedural MLD (balloon diameter—postprocedural MLD), whereas late lumen loss (LLL) was defined as a difference between post-procedural and follow-up MLD (post-procedural MLD—follow-up MLD).[17]

IVUS imaging

Baseline and follow-up IVUS were analyzed by an experienced reader (M.D.) using the CAAS IntraVascular software (Pie Medical Imaging BV, Maastricht, The Netherlands). Proximal and distal reference segments were selected according to the procedural ICA images as adjacent to the location of the DCB inflation. In each cross-sectional image, the external elastic lamina and the lumen area were manually traced. For each lesion, the minimal lumen area (MLA) was measured. Plaque burden was defined as plaque and media cross-sectional area divided by the external elastic lamina cross-sectional area. Remodeling was defined as vessel cross-sectional area at the lesion divided by the vessel cross-sectional area at the reference segment. IVUS-defined LLL was calculated using the following formula: (post-procedural MLA—MLA at follow-up) / post-procedural MLA.

Definitions and study endpoints

Coronary CTO was defined as a complete luminal occlusion on ICA with TIMI flow grade 0 lasting ≥3 months.[20] TIMI flow grade was assessed as previously defined.[18] The CTO PCI difficulty was assessed using J-CTO score as previously described.[21] CTO crossing success was defined as angiographic confirmation of guidewire placement in the true lumen beyond the occluded segment according to the coronary CTO Academic Research Consortium.[19]

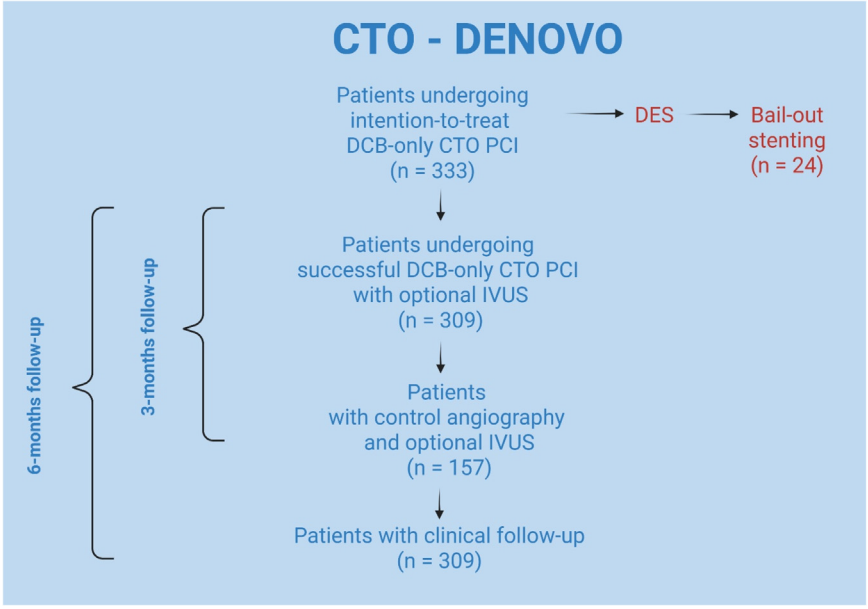


Figure 1. Study flow chart. CTO = chronic total occlusion; DCB = drug coated balloon; DES = drug eluting stent; IVUS = intravascular ultrasound.

Device success was defined as successful delivery and inflation of the allocated DCB at the intended target lesion within 30 to 60 seconds during a first-use attempt (DCB not previously used), successful withdrawal of the device system, and attainment of TIMI grade 2 or 3 antegrade flow with a final in-segment or in-lesion residual stenosis <40%. [17,19] Procedure success was defined as device success and both, freedom from in-hospital cardiovascular death, peri-procedural myocardial infarction, target lesion revascularization, any stroke, Bleeding Academia Consortium Scale 3 to 5 bleeding and freedom from bail-out stenting.[17]

The primary endpoint was target lesion failure defined as a composite of cardiac death, target vessel-related myocardial infarction or clinically-driven target lesion revascularization at 6-months. Target lesion was considered as the DCB-treated coronary segment plus 1 mm proximal and distal to the balloon.[17] Myocardial infarction was defined using the fourth universal definition of myocardial infarction.[22] The clinical endpoints were derived from patient records and via a phone contact if necessary. The secondary endpoints were assessed at 3-months and included: binary restenosis (≥50% degree of stenosis in the target segment), LLL, target lesion closure, ICA-driven target lesion revascularization, and MLA on IVUS.

Statistical analysis

Data are presented as mean with standard deviation or median with interquartile range (IQR) for continuous variables and frequency (percentage) for categorical variables. A paired sample T test was used for comparison of normally distributed data, while non-normally distributed continuous data were compared using the Wilcoxon signed-rank test. Categorical data were analyzed using the Fisher's exact test, excluding cases with missing data for the variable of interest. Statistical significance was defined as a p-value of <0.002 after Bonferroni correction for comparison between coronaries with versus without ≥50% diameter stenosis at follow-up. A p-value of <0.05 was considered statistically significant for all other analyses. Analyses were performed using SPSS software, version 29 (IBM Corp., Armonk, NY, USA).

Results

Baseline clinical characteristics

Of the 333 patients with 336 lesions receiving intention-to-treat DCB-based CTO PCI at the 42 centers, 24 patients required bail-out stenting (7.2%). Consequently, a total of 309 patients with 312 CTO lesions who underwent CTO PCI using a DCB-only approach were included in the final analysis (Figure 1). The mean age was 67 ± 10 years, and 58.9% were male. The prevalence of diabetes and chronic kidney disease were 36% and 16.9%, respectively. The most common indication for DCB use was small vessel disease (37.1%), followed by diffuse coronary artery disease (34.2%). Baseline clinical characteristics are presented in Table 1.

Table 1
Clinical characteristics.

Baseline clinical characteristics	N = 309
Age, years	67 ± 10
Male	182 (58.9%)
BMI, kg/m^2	29.1 ± 4.6
Diabetes mellitus	111 (36%)
Diabetes mellitus on insulin	38 (12.4%)
Hypertension	264 (85.6%)
Dyslipidaemia	266 (86.2%)
Current smoker	53 (17.5%)
Family history of coronary artery disease	57 (18.4%)
Prior myocardial infarction	119 (38.4%)
Prior percutaneous coronary intervention	141 (45.6%)
Prior coronary artery bypass grafting	13 (4.2%)
Prior stroke	19 (6.1%)
Heart failure	119 (38.4%)
Chronic kidney disease	52 (16.9%)
Left ventricular ejection fraction, %	50.4 ± 11.2
Clinical presentation	
Stable angina	254 (82.2%)
Unstable angina	10 (3.2%)
NSTEMI	24 (7.8%)
Silent ischemia	21 (6.8%)
Symptoms	
CCS I	58 (18.8%)
CCS II	128 (41.4%)
CCS III	43 (13.5%)
CCS IV	21 (6.8%)
Major reason for DCB PCI	
Small vessel	115 (37.1%)
Diffuse disease	106 (34.2%)
Not planned but stent-like result after predilatation	42 (13.8%)
High bleeding risk	11 (3.6%)
Bifurcation CTO	20 (6.6%)
Aneurysmatic vessel	3 (1%)
Usual practice for all comer CTO PCI	8 (2.6%)

BMI = body mass index; CCS = Canadian cardiovascular society; CTO = chronic total occlusion; DCB = drug coated balloon; NYHA = New York Heart Association; NSTEMI = Non-ST elevated myocardial infarction; PCI = percutaneous coronary intervention

Baseline angiographic and procedural characteristics

The majority of patients had single-vessel disease (36.6%). The most common target CTO vessel was the left anterior descending artery (37.9%), followed by the right coronary artery (36.2%), and the left circumflex artery (25.9%). The mean J-CTO score was 1.5 ± 1.1. The vast majority of CTO treated with a DCB-only approach were recanalized using the antegrade wiring or retrograde wiring strategies (93%), and IVUS guidance was utilized in 32.1% of cases. In almost half of the cases, single access (48.1%) was used, while single CTO wire was sufficient to recanalize CTO in 34.4% of cases. The use of cutting and/or scoring balloons was 18.1%, while mechanical atherectomy was applied in 4.2% of cases. The median number of DCB per CTO lesion was 1 (IQR: 1 to 2), while the mean DCB diameter and the mean DCB length were 2.7 ± 0.4 mm and 29.7 ± 7.7 mm, respectively. The most frequently used DCB was Sequent Please Neo (59.9%). At the end of CTO PCI, 52.9% of the vessels had angiography-detected dissections (Table 2). The device success was 81.7%.

Primary endpoint: in-hospital and intermediate-term outcomes

The median length of hospital stay was 2 (IQ: 1 to 4) days including 1 (IQ: 1 to 2) day post-CTO PCI. The in-hospital complications included coronary artery perforation (2.4%), pericardiocentesis (0.8%), periprocedural myocardial infarction (0.4%), and acute kidney injury (0.8%), and neither death nor stroke were reported.

At 6-months, the all-cause mortality was 1.0% with no reported cases of cardiac death. Target-vessel myocardial infarction was 0.3%, while clinically-driven target vessel revascularization and clinically-driven target lesion revascularization were 4.5% and 3.2%, respectively. The overall rate of target lesion failure was 3.5%, and target vessel thrombosis was 0.3% (Table 3).

Secondary endpoint: follow-up quantitative coronary angiography

Follow-up ICA was performed in 157 patients with 157 CTO vessels (50.3%) after the median time of 99 days (IQR: 85 to 136 days). Late lumen loss was −0.1 mm (IQR: −0.3 to 0.3 mm) with 75 CTO lesions (47.8%) showing late lumen gain. The re-occlusion and binary restenosis occurred in 6 CTO vessels (4%) and 38 CTO vessels (24.2%),

Table 2
Angiographic and procedural characteristics

Baseline angiographic characteristics	N = 312
Number of diseased vessels	
One-vessel disease	114 (36.6%)
Two-vessel disease	104 (33.3%)
Three-vessel disease and/or left main coronary artery	94 (30.1%)
Target CTO vessel	
Left anterior descending coronary artery	118 (37.9%)
Left circumflex coronary artery	81 (25.9%)
Right coronary artery	113 (36.2%)
Target CTO vessel characteristics	
Blunt stump	91 (29.2%)
Any calcium within CTO segment	126 (40.4%)
Bending ≥45° within CTO segment	61 (19.5%)
Lesion length ≥20mm	142 (45.5%)
Re-try lesion	14 (4.5%)
J-CTO Score	
0	60 (19.2%)
1	65 (20.8%)
2	68 (21.8%)
3	43 (17.2%)
4	13 (5.2%)
5	1 (0.3%)
Access site	
Single access	150 (48.1%)
Radial	135 (43.3%)
Double access	126 (40.3%)
Biradial	68 (21.8%)
Bifemoral	8 (2.5%)
Radial and femoral	43 (13.8%)
Sheath size	
6 Fr	42 (13.4%)
7 Fr	196 (62.8%)
8 Fr	5 (1.6%)
Successful final strategy	
Antegrade wiring	283 (90.7%)
Retrograde wiring	7 (2.3%)
Antegrade dissection and re-entry	21 (6.7%)
Retrograde dissection and re-entry	1 (0.3%)
CTO wire number	
1	107 (34.4%)
2	62 (19.9%)
3	37 (11.8%)
≥4	36 (11.5%)
CTO lesion modification	
Semi-compliant balloon only	67 (21.4%)
Non-compliant balloon	241 (77.4%)
Scoring and/or cutting balloon	57 (18.1%)
Intracoronary lithotripsy	6 (1.9%)
Coronary atherectomy	13 (4.2%)
Largest pre-dilatation balloon diameter	2.8 ± 0.5
Any dissection	155 (52.9%)
Drug-coated balloon	
Paclitaxel-coated balloon	275 (91.9%)
Sirolimus-coated balloon	24 (8.1%)
DCB type	
Sequent Please Neo	180 (59.9%)
Pantera Lux	33 (11.1%)
Agent	14 (4.7%)
RX Essential Pro	22 (7.4%)
Selution	11 (3.7%)
Magic Touch	12 (4.0%)
Prevail	8 (2.4%)
Biostream	11 (3.7%)
Restore	2 (0.6%)
Elutax	1 (0.3%)
Ever Flow	1 (0.3%)
Protege	1 (0.3%)
Sequent SCB	1 (0.3%)
Number of DCB used	1 (1–2)
DCB diameter (mm)	2.7 ± 0.4
DCB to reference vessel ratio	1.3 ± 0.3
DCB length (mm)	29.7 ± 7.7
Procedural details	
Fluoroscopic time (min)	28.1 (17.0–49.5)
Contrast volume (ml)	200 (149–266)
Total absorbed dose (mGy)	1463.3 ± 1092.7
Total radiation Dose Area Product (μGy*m2)	6605 (1340–12088)

Vessel disease was defined by the presence of ≥50% diameter stenosis in major coronary arteries. CTO = chronic total occlusion; DCB = drug coated balloon; J-CTO score = Japan Chronic Total Occlusion score

respectively, while the rate of ICA-driven target lesion revascularization was 14%.

Diameter stenosis at follow-up was significantly higher than the diameter stenosis immediately post-PCI with DCB (36.4 ± 21.3 and 28 ± 13%, respectively, p <0.001, Table 4). This was driven by a similar MLD immediately post-DCB and at follow-up (1.7 ± 0.6 and 1.7 ± 0.7 mm, respectively, p = 0.743), together with an increased distal reference vessel diameter at follow-up as compared with the index procedure (2.4 ± 0.7 and 2.2 ± 0.7 mm, respectively, p <0.001, Table 4). The quantitative angiographic analysis of paired cases is presented in Supplementary Table 2.

CTO vessels with ≥50% diameter stenosis showed significantly higher final residual diameter stenosis directly post-PCI (30.8 ± 16.6% vs 28.1 ± 12.3%, p <0.001) as compared with CTO with <50% diameter stenosis (Table 5).

Secondary endpoint: IVUS findings

IVUS data was available in 52 cases and 29 cases of the index and follow-up procedures, respectively. The final median MLA was 2.3 mm^2 (IQR: 1.6 to 4.5 mm^2) at the index procedure, and increased to 4.6 mm^2 (IQR: 3.3 to 9.9 mm^2; *p* <0.001) at follow-up. The final index maximal plaque burden at the site of in-segment CTO was 75.6% (IQR: 66.5 to 81.2%), and significantly decreased to 63.2% (IQR: 18.5 to 68.4%, p = 0.001) at follow-up. Overall, the LLL was −0.64 ± 0.67 (Table 6). The sub analysis of the 29 IVUS paired cases showed consistent results (Supplementary Figure 1).

Discussion

This multicenter international registry evaluated the clinical, angiographic, and outcome profiles of patients undergoing DCB-only angioplasty for de-novo coronary CTO. The main findings of the present study are the following: 1) most CTO patients had small vessel and/or diffuse coronary artery disease; 2) the difficulty level of DCB-treated CTO lesions was in the intermediate range (as per J-CTO score) with a predominant use of intraplaque wiring strategy (93%); 3) intraprocedural complications and 6-month clinically-indicated target lesion failure were low, and 4) in the selected population with

Table 3
Clinical outcomes at 6 months follow-up

Clinical outcomes at 6-months follow-up	n = 309
All-cause death	3 (1%)
Cardiac death	0%
Non-fatal myocardial infarction	2 (0.6%)
Target vessel myocardial infarction	1 (0.3%)
Clinically-driven target vessel revascularization	14 (4.5%)
Clinically-driven target lesion revascularization	10 (3.2%)
Target lesion failure	11 (3.5%)
Target vessel thrombosis	1 (0.3%)
Stroke	3 (1%)

Values represent a per-patient analysis. Target lesion failure comprised cardiac death, target vessel myocardial infarction or clinically-driven target lesion revascularization.

Table 4
Quantitative coronary angiography

Final result of the index CTO PCI	n = 312
Proximal reference diameter, mm	2.3 ± 0.6
Distal reference diameter, mm	2.2 ± 0.7
Mean reference diameter, mm	2.3 ± 0.7
Minimum lumen diameter, mm	1.7 ± 0.6
Residual stenosis, %	28 ± 13.3
Angiographic follow-up	**n = 157**
Proximal reference diameter, mm	2.8 ± 2.2
Distal reference diameter, mm	2.4 ± 0.7
Mean reference diameter, mm	2.6 ± 0.9
Minimum lumen diameter, mm	1.7 ± 0.7
Residual stenosis, %	36.4 ± 21.3

Values represent a per-lesion analysis.
CTO = chronic total occlusion; PCI = percutaneous coronary intervention.

Table 5
Comparison of coronary arteries with ≥50% versus <50% diameter stenosis at follow-up

	Diameter stenosis <50% n = 119	Diameter stenosis ≥50% n = 38	p-value
Clinical information			
Age (years)	65 ± 10	67 ± 10	0.751
Sex male	83 (69.7%)	24 (63.1%)	0.477
Diabetes	39 (32.7%)	13 (34.2%)	0.839
Chronic kidney disease	17 (14.3%)	5 (13.1%)	1.000
Smoker	23 (19.3%)	10 (26.3%)	0.353
Lesion characteristics			
LAD lesion	47 (39.4%)	13 (34.2%)	0.296
Diffuse disease	63 (53%)	31 (80.7%)	0.013
Distal reference vessel diameter (mm)	2.26 ± 0.66	2.33 ± 0.74	0.851
Small vessel by operator	23 (27.7%)	12 (46.1%)	0.095
Small vessel <2.75 mm	23 (27.7%)	8 (21%)	0.579
Occlusion length ≥20 mm	56 (54.4%)	11 (34.2%)	0.310
Any calcium	49 (41.2%)	20 (52.6%)	0.160
J-CTO ≥2	53 (44.4%)	19 (50%)	0.551
Immediate angiographic results			
Post-PCI MLD	1.68 ± 0.54	1.64 ± 0.75	0.114
Post-PCI diameter stenosis (%)	28.1 ± 12.3	30.8 ± 16.6	<0.001
Maximal balloon size (mm)	2.85 ± 0.54	2.75 ± 0.49	0.357
Cutting and/or scoring balloon	11 (9.2%)	10 (26.3%)	0.010
Paclitaxel-coated balloon	95 (78.9%)	27 (71.0%)	0.837
Dissection and re-entry techniques	4 (3.3%)	3 (7.8%)	0.356
Acute recoil (mm)	1.08 ± 0.57	0.87 ± 0.83	0.149
Angiographic dissection			
None	55 (46.2%)	13 (34.2%)	0.219
Dissection type A-B	51 (42.9%)	22 (57.9%)	0.109
Dissection type ≥C	13 (10.9%)	3 (7.9%)	1.000

Values represent a per-lesion analysis. A p-value of <0.002 was considered significant after Bonferroni correction.
J-CTO score = Japan Chronic Total Occlusion score, LAD = left anterior descending artery, MLD = minimal lumen diameter, PCI = percutaneous coronary intervention.

Table 6
Intravascular ultrasound results

Baseline IVUS	n = 52
Remodeling index	0.64 ± 0.39
Proximal reference	
Mean vessel diameter, mm	3.3 ± 0.9
Plaque burden, %	38.0 ± 12.4
CTO lesion	
MLA, mm^2	2.3 (1.6 to 4.5)
Minimal lumen diameter, mm	1.6 ± 0.6
Maximal plaque burden, %	75.6 (66.5 to 81.2)
Distal reference	
Mean vessel diameter, mm	2.2 ± 0.6
Plaque burden, %	35.9 ± 13.7
Follow-up IVUS	**n = 29**
Remodeling index	0.64 ± 0.45
Proximal reference	
Mean vessel diameter, mm	3.4 ± 0.5
Plaque burden, %	27.3 ± 14.9
CTO lesion	
MLA, mm^2	4.6 (3.3 to 9.9)
Minimal lumen diameter, mm	2.5 ± 0.6
Maximal plaque burden, %	63.2 (18.5 to 68.4)
Distal reference	
Mean vessel diameter, mm	2.6 ± 0.3
Plaque burden, %	31.1 ± 9.2

Values represent a per-lesion analysis.
CTO = chronic total occlusion; IVUS = intravascular ultrasound; MLA = minimal lumen area.

control angiography, despite negative LLL, the rates of binary restenosis and target lesion revascularization were non-negligible and warrant further investigation.

Prior studies reported the mean age of patients undergoing de-novo CTO PCI with DCB-only approach between 56 and 68 years with a predominance of male (76 to 85.7%), and a prevalence of diabetes ranging from 23.5% to 45%.[13–15] Our findings are broadly consistent, with a mean age of 67 years and diabetes in over one-third of patients. Indeed, the relatively high prevalence of diabetes in patients referred to DCB-only angioplasty may reflect diffuse coronary artery disease with small reference segments, consistent with the main indications for DCB in our cohort (small vessel disease followed by diffuse coronary disease).

Although DCB use in CTO PCI is rapidly increasing and reached 15% in Europe in 2023,[5] angiographic and procedural features of DCB-only PCI for de-novo CTO have been described only in a few small and mostly single-center studies. While in the studies by Köln et al[13] and Jun et al[14] the most common target CTO vessel for DCB-only angioplasty was the left anterior descending artery (up to 48.4%), Terashita et al[15] reported predominant DCB use in the right coronary artery CTO. Of interest, we observed an equal distribution of the left anterior descending artery and the right coronary artery CTO vessels treated with DCB, potentially reflecting changing temporal trends in CTO interventions. The mean CTO difficulty in our cohort was intermediate (J-CTO score 1.5 ± 1.1) and matched prior reports (J-CTO score 1.4 ± 0.6 and 1.7 ± 0.9).[14,15] Indeed, this finding suggests that DCB-only approach is mainly applied to less complex lesions, as reflected by frequent intraplaque wiring (93%) and common single access use (48.1%) in our study. In addition, our mean DCB diameter (2.7 mm) was comparable to prior reports (range between 2.55 and 2.78 mm)[13–15] and corresponds well to small vessels per the DCB Academic Research Consortium.[17] Despite recommendations for liberal use of modified balloons in DCB-only PCI to achieve sufficient luminal enlargement and reduce vessel recoil by creating effective incisions in the atherosclerotic plaque,[17] cutting or scoring balloon use was low in our study.

At 6-month follow-up, target lesion failure was relatively low, with no cardiac death, target vessel myocardial infarction in 0.3%, and a clinically-indicated target lesion revascularization in 3.2%. These results are consistent with previous CTO studies on DCB-only approach.[5,6,14,15] Furthermore, the rate of target vessel thrombosis was marginal in our study (0.3%) and corresponds to the rate of definite or probable stent thrombosis (0.4%) at 12-months in the EURO-CTO trial.[1] Overall, our data suggest a favorable safety profile of DCB-only angioplasty in coronary CTO at intermediate follow-up, and large-scale randomized studies comparing DCB with drug-eluting stents in CTO now appear warranted.

Among the 51% of our patients with 3-month angiographic follow-up, binary restenosis occurred in 24.2% of CTO vessels. This rate of restenosis is numerically higher than in the prior reports using current generation of drug-eluting stents (20 to 21%)[23,24] and DCB-only approach (15 to 19%),[13–15] and might be explained by several factors. First, the adoption of modified balloons and long DCB per CTO lesion was lower in our cohort as compared to prior reports.[13–15] Second, only our study included CTO treated with dissection and re-entry techniques (7% of all procedures), leading to DCB application in the extraplaque space––a phenomenon that yields non-homogenous transfer of the antiproliferative agent in the layers of the coronaries.[7] Third, in this study recoil of 40% by visual assessment was allowed after DCB-only PCI which is above the <30% consensus threshold.[16] Notably, restenosis at 3-months was associated with greater residual stenosis post-PCI, underscoring the need for optimal lesion preparation before DCB delivery. Importantly, the increased restenosis rate did not translate into an excess of target lesion revascularization, possibly due to limited symptoms in patients with borderline restenosis.

Intravascular ultrasound provides key insights into arterial healing after DCB-only CTO PCI. In lesions with IVUS data, we observed an approximate two-fold increase in MLA and a reduction in maximal plaque burden at 3 months, translating into negative luminal loss. While both vessel enlargement and plaque regression were recently shown as potential causes of late lumen enlargement after DCB in non-CTO lesions,[7] our findings demonstrate similar IVUS patterns for the first time in a CTO population.

Our study has several limitations. First, it is a retrospective registry of patients selected for DCB-only approach at the operators' discretion, introducing potential selection bias. Yet, our study represents the largest pooled cohort, and may help in generating hypotheses for future randomized trials. Second, the low use of dedicated plaque modification devices (cutting/scoring balloons, atherectomy, intravascular lithotripsy) may have influenced outcomes. Third, angiographic follow-up was performed in half of patients before clinical outcome ascertainment, and could have prompted revascularization based on imaging rather than symptoms, inflating non–clinically driven target lesion revascularization.[25] Moreover, operator-driven decisions for repeat angiography may have led to overestimation of restenosis, particularly in lesions with suboptimal results. The relatively low rate of follow-up IVUS limits the generalizability but reflects real-world imaging use in a retrospective registry. In addition, the predominance of paclitaxel-coated balloons, the absence of a standardized 12-month follow-up and the lack of data on clinical patient improvement represent further limitations for comparison with other studies. Finally, reported bailout stenting rates are restricted to cases after DCB use and do not account for coronary dissections or hematomas occurring immediately after lesion predilatation.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Dr. Opolski received research grant from B. Braun. Dr. Woitek received lecture fees and served as a consultant for Abbott, Boston Scientific, Biotronik/Teleflex and Shockwave Medical, and reports a relationship with TU Dresden that includes: consulting or advisory. Other authorsdeclare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Maksymilian P. Opolski: Writing – original draft, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Magdalena M. Dobrolinska:** Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis. **Sina Porouchani:** Writing – review & editing, Resources, Methodology. **Grzegorz Sobieszek:** Writing – review & editing, Investigation. **Bartosz Zieba:** Writing – review & editing, Investigation. **Felix J. Woitek:** Writing – review & editing, Investigation. **Michal Kryjak:** Writing – review & editing, Investigation. **Mihajlo Kovacic:** Writing – review & editing, Investigation. **Umberto Barbero:** Writing – review & editing, Investigation. **Zoltán Ruzsa:** Writing – review & editing, Investigation. **Kornél Kákonyi:** Writing – review & editing, Investigation. **Ilya Litovchik:** Writing – review & editing, Investigation. **Jakub Drozd:** Writing – review & editing, Investigation. **David Neves:** Writing – review & editing, Investigation. **Ignacio Amat-Santos:** Writing – review & editing, Investigation. **Mihnea T. Nichita-Brendea:** Writing – review & editing, Investigation. **Claudiu Ungureanu:** Writing – review & editing, Investigation. **Sylwia Iwanczyk:** Writing – review & editing, Investigation. **Vojtěch Novotný:** Writing – review & editing, Investigation. **Alexander Geppert:** Writing – review & editing, Investigation. **Paul Felix Harbich:** Writing – review & editing, Investigation. **Sanghoon Shin:** Writing – review & editing, Investigation. **Mauro Gitto:** Writing – review & editing, Investigation. **Gabriele Gasparini:** Writing – review & editing, Investigation. **Stefan Harb:** Writing – review & editing, Investigation. **Michele Cacia:** Writing – review & editing, Investigation. **Wojciech Zimoch:** Writing – review & editing, Investigation. **Mihai Cocoi:** Writing – review & editing, Investigation. **Daniel Rzeznik:** Writing – review & editing, Investigation. **Paweł Kleczynski:** Writing – review & editing, Investigation. **Roman Stipal:** Writing – review & editing, Investigation. **Rocco Giunta:** Writing – review & editing, Investigation. **Mateusz Tajstra:** Writing – review & editing, Investigation. **Lukasz Pyka:** Writing – review & editing, Investigation. **Leszek Bryniarski:** Writing – review & editing, Investigation. **Pavol Tomasov:** Writing – review & editing, Investigation. **Piotr Wanczura:** Writing – review & editing, Investigation. **Wojciech Stecko:** Writing – review & editing, Investigation. **Slawomir Golebiewski:** Writing – review & editing, Investigation. **Piotr Pawluczuk:** Writing – review & editing, Investigation. **Grzegorz Horszczaruk:** Writing – review & editing, Investigation. **Marin Postu:** Writing – review & editing, Investigation. **Tibor Szük:** Writing – review & editing, Investigation. **Rostislav Prog:** Writing – review & editing, Investigation. **Olli-Pekka Piira:** Writing – review & editing, Investigation. **Pawel Radecki:** Writing – review & editing, Investigation. **Marcin Makowski:** Writing – review & editing, Investigation. **Szymon Glodala:** Writing – review & editing, Investigation. **Marek Jankiewicz:** Writing – review & editing, Investigation. **Bilal Iqbal:** Writing – review & editing, Methodology, Investigation. **Tuomas T. Rissanen:** Writing – review & editing, Supervision, Investigation.

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Supplementary materials

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