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ORIGINAL RESEARCH

CORONARY

Procedural Impact of Advanced Calcific Plaque Modification Devices Within Percutaneous Revascularization of Chronic Total Occlusions

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ABSTRACT

BACKGROUND Significant calcifications within a coronary chronic total occlusion (CTO) increase procedural complexity and the risk for complications. Expert consensus documents recommend the use of advanced calcific plaque modification devices (ACPMDs) for calcified CTO percutaneous coronary intervention (PCI), whereas data on their procedural impact are limited.

OBJECTIVES The aim of this study was to describe trends, settings, and outcomes of PCI of severely calcified CTO performed with and without ACPMDs.

METHODS Data from 15,329 CTO PCIs enrolled in the ERCTO (European Registry of Chronic Total Occlusion) between 2021 and 2023 were analyzed. On the basis of the presence of severe calcifications within the CTO, the study population was divided into 2 groups: nonsevere (n = 12,289) and severe (n = 3,040) calcium. Then, the severe group was divided into non-ACPMD (n = 2,253) and ACPMD (n = 787), according to the use of ACPMDs.

RESULTS Compared with the non-ACPMD group, the ACPMD group had higher rates of antegrade wiring (77.9% vs 49.2%; $P < 0.001$) and technical success (97.6% vs 79.1%; $P = 0.001$) and lower rates of periprocedural and in-hospital major adverse cardiac and cerebrovascular events (MACCE) (1.8% vs 3.5%; $P = 0.001$). A severe amount of calcium was independently associated with technical failure (OR: 3.13; 95% CI: 2.43-4.09; $P < 0.001$) but not with MACCE (OR: 0.88; 95% CI: 0.58-1.35; $P = 0.15$). Furthermore, extraplaque crossing was independently associated with MACCE (antegrade dissection and re-entry without retrograde contribution: OR: 3.12; 95% CI: 1.79-4.20; $P < 0.001$; antegrade dissection and re-entry with retrograde contribution: OR: 3.12; 95% CI: 1.67-4.11; $P = 0.049$; retrograde dissection and re-entry: OR: 1.90; 95% CI: 1.25-2.86; $P = 0.002$).

CONCLUSIONS Applying ACPMDs in severely calcified CTO to PCI was associated with higher technical success and lower MACCE rates. The presence of severe coronary calcification on coronary angiography was a marker of clinical and procedural complexity and was associated with technical failure but not with MACCE. (JACC Cardiovasc Interv. 2025;18:1376–1390) © 2025 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

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Expert interventional operators are faced with severe coronary calcifications during chronic total occlusion (CTO) percutaneous coronary intervention (PCI) in up to 50% of procedures, according to worldwide CTO PCI registries.[1,2] The presence of relevant coronary calcifications within a CTO was associated with lower rates of technical success and a higher risk for periprocedural complications.[3] Furthermore, evidence of significant coronary calcifications within a CTO lesion, as assessed using coronary angiography, is one of the most important factors included in different dedicated CTO PCI risk scores to anticipate the procedural complexity and potentially associated complications.[4-7]

Recent state-of-the-art papers and expert consensus documents have emphasized that a systematic approach to treating patients with severely calcified coronary lesions is crucial to improve the performance of such procedures, which are increasingly common in daily practice.[8-10] This approach should include the use of dedicated devices to modify calcific plaque, along with comprehensive multi-imaging assessments of the amount and distribution of coronary calcifications.

However, data on the procedural impact of so called advanced calcific plaque modification devices (ACPMDs), including intracoronary atherectomy and lithotripsy, during CTO PCI are very limited. Furthermore, despite the high rate of severe coronary calcification in CTOs, estimated at 18%, ACPMDs have been used in only 25% of these patients during CTO PCI in the ERCTO (European Registry of Chronic Total Occlusion).[11]

The aim of the present study was to investigate current trends, settings, and procedural outcomes of PCI of severely calcified CTO performed with and without ACPMDs in the contemporary ERCTO.

METHODS

In this cross-sectional study, data from 15,899 CTO PCIs enrolled in ERCTO between January 2021 and December 2023 were analyzed.

ERCTO is an electronically based retrospective, nonrandomized, observational all-comers multicenter registry, including consecutive patients undergoing CTO PCI. The ERCTO registry was developed by the EURO CTO nonprofit association to collect data from patients treated using CTO PCI by expert operators at referral centers across Europe, the United Kingdom, Switzerland, and Turkey. The registry was carried out according to the principles of the Declaration of Helsinki and international data protection laws and was ethically approved. Patients' data were anonymized and managed according to the data safety protocols of the participating centers.

The decision to treat patients with CTOs using PCI was based on clinical decision making during routine clinical care and according to international guidelines on myocardial revascularization.[12] The sequence of wiring techniques and guidewire selection was left entirely to the operator's discretion.

ABBREVIATIONS AND ACRONYMS

ACPMD = advanced calcific plaque modification device

ADR-R = antegrade dissection and re-entry with retrograde contribution

AW-0 = antegrade wiring without retrograde contribution

CTO = chronic total occlusion

IVL = intravascular lithotripsy

IVUS = intravascular ultrasound

MACCE = major adverse cardiac and cerebrovascular event(s)

PCI = percutaneous coronary intervention

RDR = retrograde dissection and re-entry

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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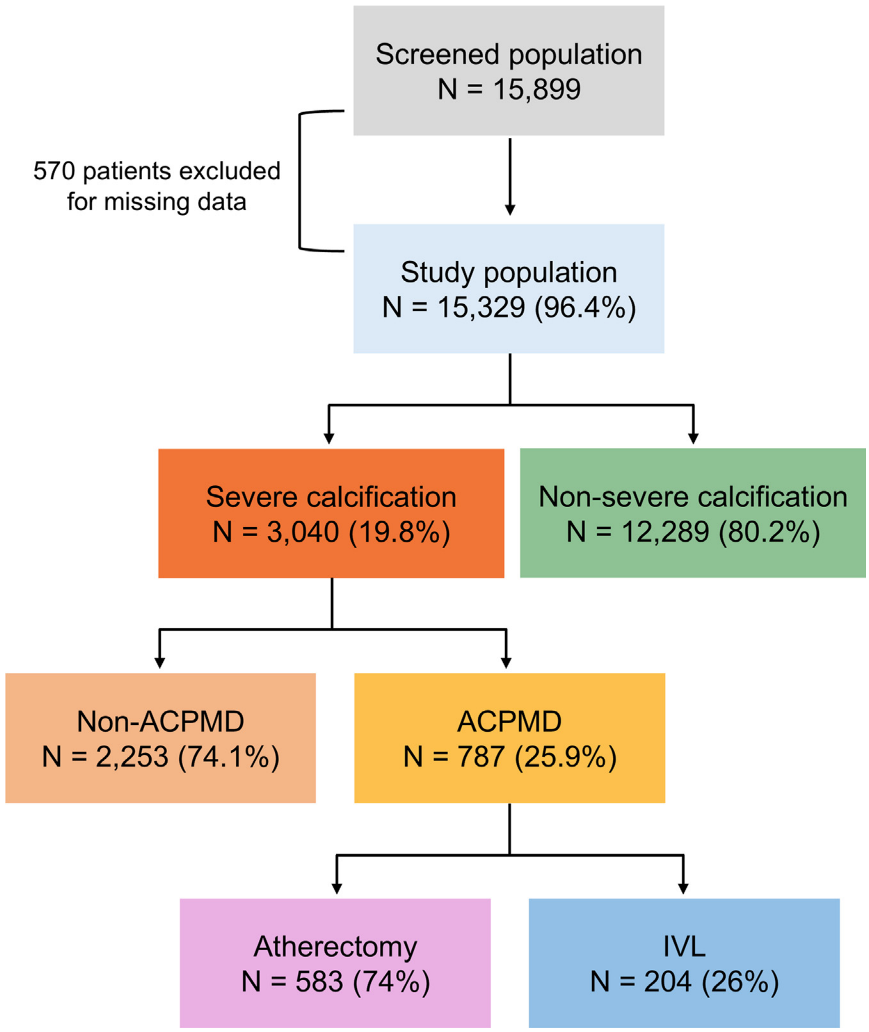
FIGURE 1 **Study Flowchart**



ACPMD = advanced calcific plaque modification device; IVL = intravascular lithotripsy.

The assessment of coronary calcification was based on coronary angiography. Coronary calcification was graded according to evidence of severe coronary calcification and nonsevere calcification. The latter was made up of patients with none, mild, and moderate evidence of calcification. Thereafter, the severely calcified group was separately analyzed on the basis of whether an ACPMD was applied or not. ACPMDs included the following plaque modification techniques: 1) coronary atherectomy by rotational or orbital atherectomy; and 2) intravascular lithotripsy (IVL).

DEFINITIONS. The following definitions were adopted from the CTO-ARC (Chronic Total Occlusions Academic Research Consortium) recommendations.[13] CTO was defined as the absence of antegrade flow through the lesion with a presumed or documented duration of >3 months, with TIMI flow grade 0. The present analysis referred only to the final CTO crossing strategies, as recently outlined.[14]

Technical success was defined as the successful recanalization of the CTO vessel with <30% residual stenosis and final TIMI flow grade 3. This definition is slightly different from the CTO-ARC definition, which includes technical success even in those cases with final TIMI flow grade 2. Procedural success was defined as technical success in the absence of major adverse cardiac and cerebrovascular events (MACCE), a composite of death, myocardial infarction, stroke,

TABLE 1 Baseline Characteristics

	Overall Population (N = 15,329)			
		Severe Calcification (n = 3,040)		
	Nonsevere Calcification (n = 12,289)	Non-ACPMD (n = 2,253)	ACPMD (n = 787)	*P* Value
Patient characteristics				
Age, y	64.6 ± 10.4	68.9 ± 9.4	71.4 ± 9.2	**<0.001**
Men	1,0315 (83.9)	1,888 (83.8)	653 (83)	0.772
BMI, kg/m^2	28.4 ± 4.6	28.5 ± 4.8	28.4 ± 4.7	0.540
Hypertension	9,049 (73.6)	1,846 (81.9)	672 (85.4)	**<0.001**
Dyslipidemia	8,625 (70.2)	1,754 (77.9)	649 (82.5)	**<0.001**
Diabetes mellitus	3,523 (28.7)	818 (36.3)	321 (40.8)	**<0.001**
Current smokers	2,871 (23.4)	387 (17.2)	95 (12.1)	**<0.001**
Ex-smokers	3,449 (28.1)	706 (31.3)	236 (30)	
Never smokers	5,969 (48.5)	1,160 (51.5)	456 (57.9)	
COPD	673 (5.5)	153 (6.8)	37 (4.7)	**0.023**
Previous MI	4,107 (33.4)	782 (34.7)	226 (28.7)	**<0.001**
Prior stroke	385 (3.1)	91 (4)	48 (6.1)	**<0.001**
Previous CABG	1,237 (10.1)	479 (21.3)	187 (23.8)	**<0.001**
Previous PCI	6,113 (49.7)	1,127 (50)	398 (50.6)	0.886
Atrial fibrillation	632 (5.1)	169 (7.5)	88 (11.2)	**<0.001**
eGFR, mL/min	71.3 ± 24.4	70.3 ± 22.4	69.1 ± 24	**0.014**
On dialysis at baseline	142 (1.2)	60 (2.7)	18 (2.3)	**<0.001**
LVEF ≥50%	8,527 (69.4)	1,441 (64)	537 (68.2)	**<0.001**
LVEF ≥35%-<50%	2,884 (23.5)	601 (26.6)	171 (21.8)	
LVEF <35%	878 (7.1)	211 (9.4)	79 (10)	
Lesion characteristics				
Target vessel				
LMT	26 (0.2)	18 (0.8)	12 (1.5)	**<0.001**
LAD	3,316 (27)	581 (25.8)	222 (28.2)	
LCx	1,943 (15.8)	257 (11.4)	117 (14.9)	
RCA	6,590 (53.6)	1,353 (60.1)	416 (52.9)	
SB	388 (3.2)	41 (1.8)	17 (2.2)	
Bypass	26 (0.3)	3 (0.1)	3 (0.4)	
CTO length, mm	25.8 ± 15.6	27 ± 16	32.7 ± 19.7	**<0.001**
CTO diameter, mm	2.99 ± 0.7	3.03 ± 0.9	3.11 ± 0.6	**<0.001**
Complexity				
J-CTO score	2.05 ± 1.2	3.19 ± 1	2.68 ± 1	**<0.001**
EURO CTO score	1.98 ± 1.1	3.23 ± 1	2.94 ± 1	**<0.001**
Stump:				**<0.001**
Tapered	5,440 (44.3)	635 (28.2)	356 (45.2)	
Blunt	4,661 (37.9)	1,131 (50.2)	302 (38.4)	
Lesion length >20 mm	6,740 (54.8)	1,497 (66.4)	406 (51.6)	**<0.001**
Tortuosity (severe)	278 (2.3)	133 (5.9)	23 (2.9)	**<0.001**
Previous attempts ≥1	2,510 (20.4)	584 (25.9)	196 (24.9)	**<0.001**

Values are mean ± SD or n (%). *P* values refer to 3-group comparison; *P* values in **bold** denote statistical significance.

ACPMD = advanced calcific plaque modification device; BMI = body mass index; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; CTO = chronic total occlusion; eGFR = estimated glomerular filtration rate; J-CTO = Multicenter CTO Registry in Japan; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; LMT = left main trunk; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; RCA = right coronary artery; SB = side branch.

urgent repeated revascularization (re-PCI or surgery), or pericardiocentesis. Procedural myocardial infarction was defined according to the European Society of Cardiology guidelines on myocardial revascularization.[12] MACCE included in this study occurred either periprocedurally or in the hospital during the index hospital stay. Bifurcations were defined by the presence of a side branch of diameter >2 mm within 5 mm of the proximal or distal cap of the CTO lesion.[15]

Consistent with previous studies, CTO calcifications, assessed semiquantitatively using angiography, were classified as mild (spots), moderate (radiopaque densities noted during the cardiac cycle involving only 1 side of the vascular wall), or severe (radiopaque densities noted without cardiac motion before contrast injection, generally involving both sides of the arterial wall).[11,16,17]

STATISTICAL ANALYSIS. Continuous variables are expressed as either mean ± SD or median (Q1-Q3),

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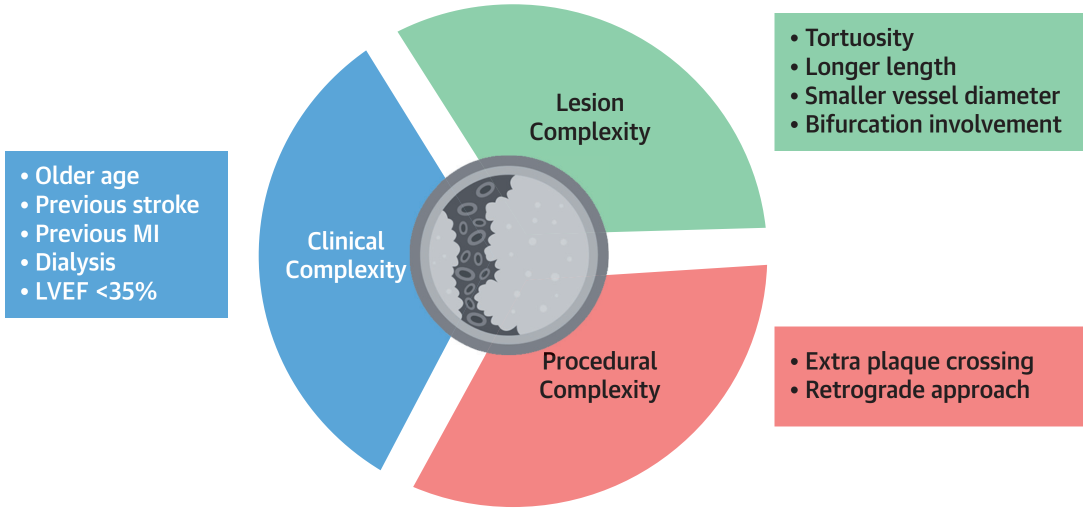
CENTRAL ILLUSTRATION Advanced Calcific Plaque Modification Devices (ACPMDs) for PCI of Severely Calcified CTO Lesions: Procedural Setting and Outcomes

ERCTO Registry in 2021-2023, N = 15,329

		Lesion Complexity	Procedural Time	Contrast Volume	IVUS	Technical Success	RS >30%	MACCE	Overall Perforations
Nonsevere calcium (n = 12,289)		↓	↓	↑	=	↑	↑	↓	↓
Severe Calcium (n = 3,040)	Non-ACPMD (n = 2,253)	↑↑	↑↑	↑↑	=	↓	↑↑	↑↑	↑↑
	ACPMD (n = 787)	↑	↑	↓	↑	↑↑	↓	↑	↑

Severely Calcified CTO at Coronary Angiography: Implications



ACPMD usage patterns	Lesion Complexity	Ostial Lesion	CTO Diameter	In-Stent CTO	Technical Success	RS >30%	MACCE	Overall Perforations
Atherectomy (n = 583)	=	↓	↓	↓	=	↑	=	=
IVL (n = 204)	=	↑	↑	↑	=	↓	=	=

- The presence of severe calcium within the CTO lesion is a marker of clinical, anatomical, and procedural complexity.
- ACPMD strategy showed higher technical success and lower MACE rate compared to non-ACPMD but was applied in less complex lesions.
- The use of ACPMD has increased; in recent years, atherectomy is the more common ACPMD strategy adopted.
- Atherectomy and IVL have similar technical success and MACCE rates, each used more often in specific anatomical and procedural settings.

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ACPMD = advanced calcific plaque modification device; CTO = chronic total occlusion; ERCTO = European Registry of Chronic Total Occlusions; IVL = intravascular lithotripsy; IVUS = intravascular ultrasound; LVEF = left ventricular ejection fraction; MACCE = major adverse cardiac and cerebrovascular event(s); MI = myocardial infarction; RS = residual stenosis.

depending on the data distribution. Categorical variables are expressed as counts and percentages. To evaluate statistical significance between groups, the chi-square test was used for categorical data, or Fisher exact test as appropriate. The Shapiro-Wilk test was used to assess the normality of continuous data, guiding the choice of statistical tests: 1-way analysis of variance for normally distributed data and nonparametric tests such as the Kruskal-Wallis test for non-normally distributed data. Pairwise comparisons were further examined using either Tukey's honestly significant difference test or Dunn post hoc test.

To investigate the relationship between procedural complications and various clinical or procedural factors, a logistic regression model was used, adjusting for relevant clinical, lesion, and procedural characteristics. Variables found to be significant in the univariable analysis were included in the multivariable model, with results expressed as adjusted ORs and corresponding 95% CIs. Statistical significance was determined using a 2-sided P value of <0.05. All analyses were performed using R version 4.4.1 (R Foundation for Statistical Computing).

RESULTS

PATIENT SELECTION AND STRATIFICATION. The study flowchart is depicted in Figure 1. A total of 15,329 patients undergoing CTO PCI between January 2021 and December 2023 were included. A total of 559 patients were excluded for missing data, and 11 patients were excluded because more than 1 ACPMD was used in combination.

Severe coronary calcification was present in 19.8% (n = 3,040). ACPMDs were applied in 25.9% of severely calcified CTOs (n = 787), of which intracoronary atherectomy was more likely used compared with IVL (74% [n = 583] vs 26% [n = 204]). The atherectomy group included 562 cases performed using rotational atherectomy and 21 using orbital atherectomy.

PATIENT AND LESION CHARACTERISTICS. Baseline characteristics are shown in Table 1. Patients with severe calcification were older (71.4 ± 9.2 years [ACPMD] vs 68.9 ± 9.4 years [non-ACPMD] vs 64.6 ± 10.4 years [nonsevere calcification]; P < 0.001); had higher rates of cardiovascular risk factors including arterial hypertension, dyslipidemia, and diabetes; were more likely to have experienced prior stroke; and had a higher rate of previous coronary artery bypass grafting (23.8% [ACPMD] vs 21.3% [non-ACPMD] vs 10.1% [nonsevere calcification]; P < 0.001).

In contrast, patients without severe calcification were less likely to be on dialysis (1.2% [nonsevere calcification] vs 2.7% [non-ACPMD] vs 2.3% [ACPMD]; P < 0.001) and to have left ventricular ejection fraction <35% at baseline (7.1% [nonsevere calcification] vs 10% [ACPMD] vs 9.4% [non-ACPMD]; P < 0.001).

Furthermore, they showed lower lesion complexity as assessed by J-CTO (Multicenter CTO Registry in Japan) score (2.05 ± 1.2 [nonsevere calcification] vs 3.19 ± 1 [non-ACPMD] vs 2.68 ± 1 [ACPMD]; P < 0.001) and EURO CTO score (1.98 ± 1.1 [nonsevere calcium] vs 3.23 ± 1 [non-ACPMD] vs 2.94 ± 1 [ACPMD]; P < 0.001).

TABLE 2 Procedural Characteristics

	Overall Population (N = 15,329)			
		Severe Calcification (n = 3,040)		
	Nonsevere Calcification (n = 12,289)	Non-ACPMD (n = 2,253)	ACPMD (n = 787)	*P* Value
Technical success	11,467 (93.3)	1,782 (79.1)	768 (97.6)	**<0.001**
Residual stenosis >30%	762 (6.2)	457 (20.3)	17 (2.2)	**<0.001**
Procedural metrics				
Fluoroscopic time, min	30 (18-46)	38.6 (29-61.4)	35 (25-56)	**<0.001**
Contrast volume, mL	200 (130-280)	205 (150-300)	180 (120-250)	**<0.001**
Procedural time, min	80 (52-120)	120 (75-171)	112 (70-160)	**<0.001**
Bifurcation stenting	3,187 (25.9)	541 (24)	244 (31)	**<0.001**
Two-stent technique	556 (4.5)	106 (4.7)	53 (6.7)	**0.045**
Implanted stents	2 (1-3)	2 (1-3)	2 (1-3)	0.536
Maximum stent diameter proximal, mm	3.25 (2.75-3.5)	3 (2.75-4)	3.5 (3-4)	**<0.001**
Total stent length, mm	55 (32-81)	58 (38-92)	62 (38-92)	**<0.001**
IVUS-assisted procedure	2,785 (22.7)	484 (21.5)	211 (26.8)	**0.008**
ACPMD				
NC/OPN[a] balloon	(29)	1,895 (84.1)	616 (78.3)	**0.001**
Scoring balloon	(12)	434 (19.3)	107 (13.6)	**0.031**
Mechanical support				
ECMO	4 (0)	–	–	**<0.001**
IABP	10 (0.1)	5 (0.2)	2 (0.3)	
Impella[b]	49 (0.4)	14 (0.6)	18 (2.3)	
Final crossing strategy				
AW-O	8,784 (71.5)	1,108 (49.2)	613 (77.9)	**<0.001**
AW-R	629 (5.1)	211 (9.4)	34 (4.3)	
ADR-O	416 (3.4)	135 (6)	17 (2.2)	
ADR-R	131 (1.1)	60 (2.7)	5 (0.6)	
RW	926 (7.5)	252 (11.2)	46 (5.8)	
RDR	1,403 (11.4)	487 (21.6)	72 (9.1)	

Values are n (%) or median (Q1-Q3). *P* values refer to 3-group comparison; *P* values in **bold** denote statistical significance. [a]SIS Medical. [b]Abiomed.

ACPMD = advanced calcific plaque modification device; ADR-O = antegrade dissection and re-entry without retrograde contribution; ADR-R = antegrade dissection and re-entry with retrograde contribution; AW-O = antegrade wiring without retrograde contribution; AW-R = antegrade wiring with retrograde contribution; ECMO = extracorporeal membrane oxygenation; IABP = intra-aortic balloon pump; IVUS = intravascular ultrasound; NC = noncompliant; RDR = retrograde dissection and re-entry; RW = retrograde wiring.

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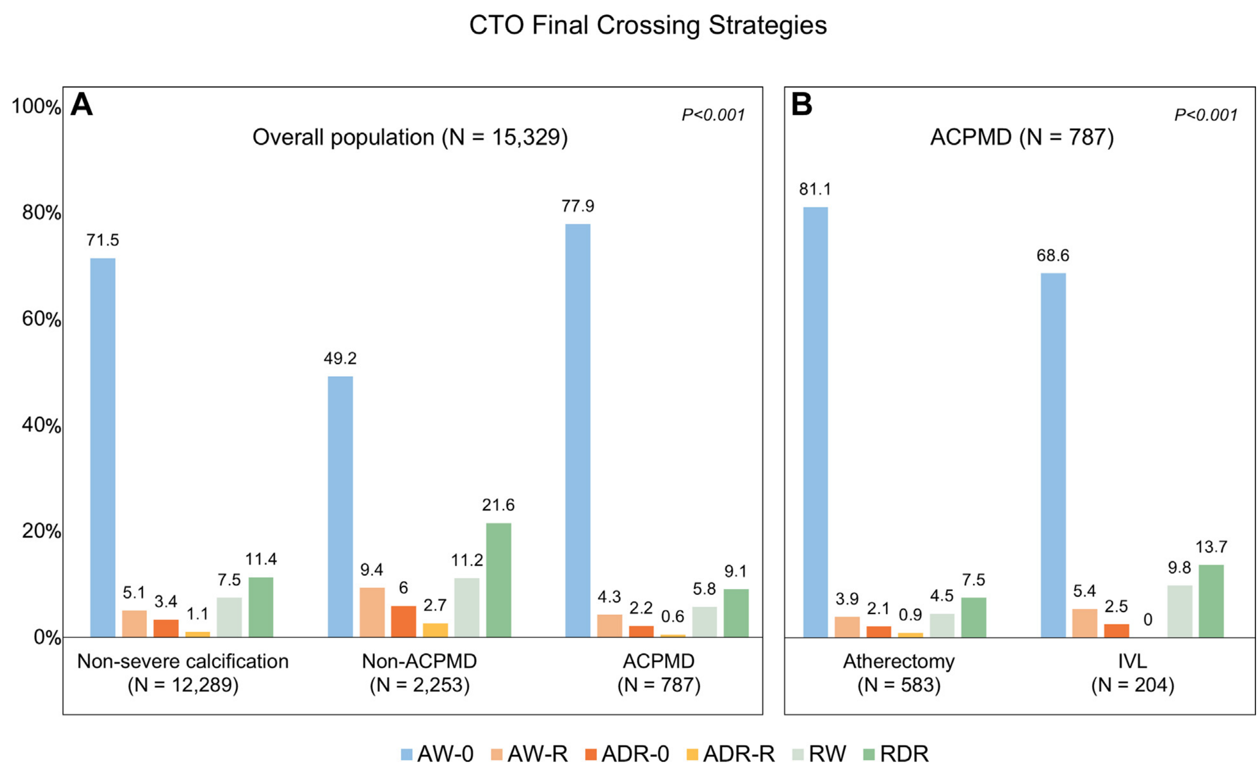
FIGURE 2 CTO Final Crossing Strategies



(A) Distribution of crossing strategies among the 3 study groups. (B) Distribution of crossing strategies in the atherectomy and IVL group. ADR-0 = antegrade dissection and re-entry without retrograde contribution; ADR-R = antegrade dissection re-entry with retrograde contribution; AW-0 = antegrade wiring without retrograde contribution; AW-R = antegrade wiring with retrograde contribution; CTO = chronic total occlusion; RDR = retrograde dissection and re-entry; RW = retrograde wiring; other abbreviations as in Figure 1.

The ACPMD group had higher CTO length (32.7 ± 19.7 mm [ACPMD] vs 27 ± 16 mm [non-ACPMD] vs 25.8 ± 15.6 mm [nonsevere calcium]; $P < 0.001$) and larger vessel diameters within the CTO (3.11 ± 0.6 mm [ACPMD] vs 3.03 ± 0.9 mm [non-ACPMD] vs 2.99 ± 0.7 mm [nonsevere calcification], respectively; $P < 0.001$) (Central Illustration).

Procedural characteristics. Procedural details are reported in Table 2. The ACPMD group had the highest technical success rates (97.6% [ACPMD] vs 93.3% [nonsevere calcification] vs 79.1% [non-ACPMD]; $P < 0.001$) and the lowest rates of residual stenosis >30% (2.2% [ACPMD] vs 6.2% [nonsevere calcification] vs 20.3% [non-ACPMD]; $P < 0.001$) despite a longer totally implanted stent length (62 mm [Q1-Q3: 38-92 mm] [ACPMD] vs 58 mm [Q1-Q3: 38-92 mm] [non-ACPMD] vs 55 mm [Q1-Q3: 32-81 mm] [nonsevere calcification]; $P < 0.001$) and higher rate of overall bifurcation stenting (31% [ACPMD] vs 25.9% [nonsevere calcification] vs 24% [non-ACPMD]; $P < 0.001$). Furthermore, intravascular ultrasound (IVUS) and left ventricular assist devices were used more frequently in the ACPMD group (IVUS: 26.8% [ACPMD] vs 22.7% [nonsevere calcification] vs 21.5% [non-ACPMD] [$P = 0.008$]; left ventricular assist devices: 2.6% [ACPMD] vs 0.8% [non-ACPMD] vs 0.5% [nonsevere calcification] [$P < 0.001$]).

Finally, focusing on the final crossing strategy, ACPMD showed a higher proportion of antegrade wiring without retrograde contribution (AW-0) (77.9% [ACPMD] vs 71.5% [nonsevere calcification] vs 49.2% [non-ACPMD]; $P < 0.001$) and a lower proportion of retrograde crossing (retrograde wiring: 5.8% [ACPMD] vs 7.5% [nonsevere calcification] vs 11.2% [non-ACPMD]; retrograde dissection and re-entry [RDR]: 9.1% [ACPMD] vs 11.4% [nonsevere calcification] vs 21.6% [non-ACPMD]; $P < 0.001$), and alternative antegrade crossing (antegrade dissection and re-entry without retrograde contribution: 2.2% [ACPMD] vs 3.4% [nonsevere calcification] vs 6% [non-ACPMD]; antegrade dissection and re-entry with retrograde contribution [ADR-R]: 0.6% [nonsevere calcification] vs 1.1 [ACPMD] vs 2.7% [non-ACPMD]; antegrade wiring with retrograde contribution: 4.3% [ACPMD] vs 5.1% [nonsevere calcification] vs 9.4% [non-ACPMD]; $P < 0.001$) (Figure 2).

PERIPROCEDURAL AND IN-HOSPITAL COMPLICATIONS. Table 3 depicts periprocedural and in-hospital adverse events. The non-ACPMD group showed the highest rate of MACCE (4.1% [non-ACPMD] vs 2.2% [ACPMD] vs 1.8% [nonsevere calcification]; $P < 0.001$) (Figure 3).

Figure 4 depicts coronary perforations. The non-ACPMD group showed the highest rates of overall perforations (8.3% [non-ACPMD] vs 5% [ACPMD] vs 3.5% [nonsevere calcification], respectively; $P < 0.001$) and perforations at the site of the target vessel (5.9% [non-ACPMD] vs 3.9% [ACPMD] vs 2.3% [nonsevere calcification]; $P < 0.001$). Finally, perforations responsible for cardiac tamponade were less likely observed in the nonsevere calcification group, whereas they were equal in the ACPMD and non-ACMPD groups (0.6% vs 1.3% vs 1.3%, respectively; $P < 0.001$).

Furthermore, the non-ACPMD group showed higher rates of other relevant complications, including side branch occlusion (1.8% [non-ACPMD] vs 1.3% [ACPMD] vs 0.8% [nonsevere calcification]; $P < 0.001$), major vascular complications (1% [non-ACPMD] vs 0.36% [ACPMD] vs 0% [nonsevere calcification]; $P < 0.001$), and contrast-induced-nephropathy (1.4% [non-ACPMD] vs 0.7% [ACPMD] vs 0.6% [nonsevere calcification]; $P = 0.003$) (Supplemental Table 1).

RISK PREDICTION MODELS TO PREDICT MACCE AND TECHNICAL FAILURE. As illustrated in Figure 5, within a logistic regression model, body mass index <25 kg/m^2, previous stroke or myocardial infarction, technical failure, and extraplaque crossing by antegrade dissection and re-entry without retrograde contribution, ADR-R, or RDR were independently associated with MACCE, whereas the presence of severe coronary calcification within the CTO was not (OR: 0.88; 95% CI: 0.58-1.35; $P = 0.50$, Supplemental Table 2).

Finally, as shown in Figure 6, several clinical, anatomical, and procedural factors were associated with technical failure. Among these, severe coronary calcification within the CTO was one of the most substantial factors independently associated with technical failure (OR: 3.13; 95% CI: 2.43-4.09; $P < 0.001$), whereas applied ACPMD was independently associated with technical success (OR: 0.17; 95% CI: 0.09-0.29; $P < 0.001$, Supplemental Table 3).

TABLE 3 Procedural and In-Hospital Complications

	Overall Population (N = 15,329)			
		Severe Calcification (n = 3,040)		
	Nonsevere Calcification (n = 12,289)	Non-ACPMD (n = 2,253)	ACPMD (n = 787)	*P* Value
MACCE	222 (1.8)	93 (4.1)	18 (2.2)	**<0.001**
Death	30 (0.2)	12 (0.5)	5 (0.6)	**0.017**
Overall MI	64 (0.5)	29 (1.3)	2 (0.3)	**<0.001**
Urgent revascularization	44 (0.4)	20 (0.9)	1 (0.1)	**<0.001**
Perforations with tamponade	74 (0.6)	30 (1.3)	10 (1.3)	**<0.001**
Stroke	10 (0.1)	2 (0.1)	0 (0)	0.718
Other complications				
Side branch occlusion	159 (1.3)	40 (1.8)	6 (0.8)	**<0.001**
Stent thrombosis	32 (0.3)	9 (0.4)	1 (0.1)	0.367
Dissection of donor artery	46 (0.4)	16 (0.7)	1 (0.1)	**0.032**
Major vascular complications	77 (0.6)	22 (1)	5 (0.6)	**<0.001**
Contrast-induced nephropathy	81 (0.7)	32 (1.4)	5 (0.6)	**0.003**
Perforations				
Overall	431 (3.5)	186 (8.3)	39 (5)	**<0.001**
Without tamponade	357 (2.9)	156 (6.9)	29 (3.7)	**<0.001**
Target vessel site	283 (2.3)	132 (5.9)	31 (3.9)	**<0.001**
Collateral channel site	148 (1.2)	54 (2.4)	8 (1)	**<0.001**
Minor perforation	110 (0.9)	51 (2.3)	4 (0.5)	**<0.001**
Perforation treatment				
Coiling of perforation	26 (0.2)	10 (0.4)	5 (0.6)	**<0.001**
Covered stent	57 (0.5)	38 (1.7)	12 (1.5)	
Pericardiocentesis	70 (0.6)	29 (1.3)	9 (1.1)	
Surgical intervention	4 (0)	1 (0)	1 (0.1)	

Values are n (%). *P* values refer to 3-group comparison; *P* values in **bold** denote statistical significance.
MACCE = major adverse cardiac and cerebrovascular event(s); other abbreviations as in Table 1.

TRENDS AND OUTCOMES OF THE 2 ACPMD STRATEGIES. Trends of ACPMD strategies in CTO PCI in 2021, 2022, and 2023 are outlined in Supplemntal Table 4. Overall, ACPMDs have been increasingly applied, with intracoronary atherectomy being the most frequently used compared with IVL (74% vs 26%; $P < 0.001$).

The Central Illustration and Supplemental Tables 4 and 5 summarize the main characteristics of the 2 ACPMD strategies. Atherectomy and IVL showed similar CTO lesion complexity (EURO CTO score 2.92 ± 1 vs 2.99 ± 1.1 [$P = 0.402$], J-CTO score 2.66 ± 1 vs 2.75 ± 1.1 [$P = 0.278$]) and similar rates of technical success (97.6% vs 97.5%; $P = 1.00$) and MACCE (2.2% vs 2.5%; $P = 0.771$).

In a logistic regression model, the following anatomical and procedural factors were independently associated with using IVL over atherectomy: ostial CTO lesion (OR: 2.16; 95% CI: 1.36-3.41; $P < 0.001$), vessel diameter ≥3 mm (OR: 2.45; 95% CI: 1.44-4.38; $P = 0.002$), in-stent CTO (OR: 6.32; 95% CI:

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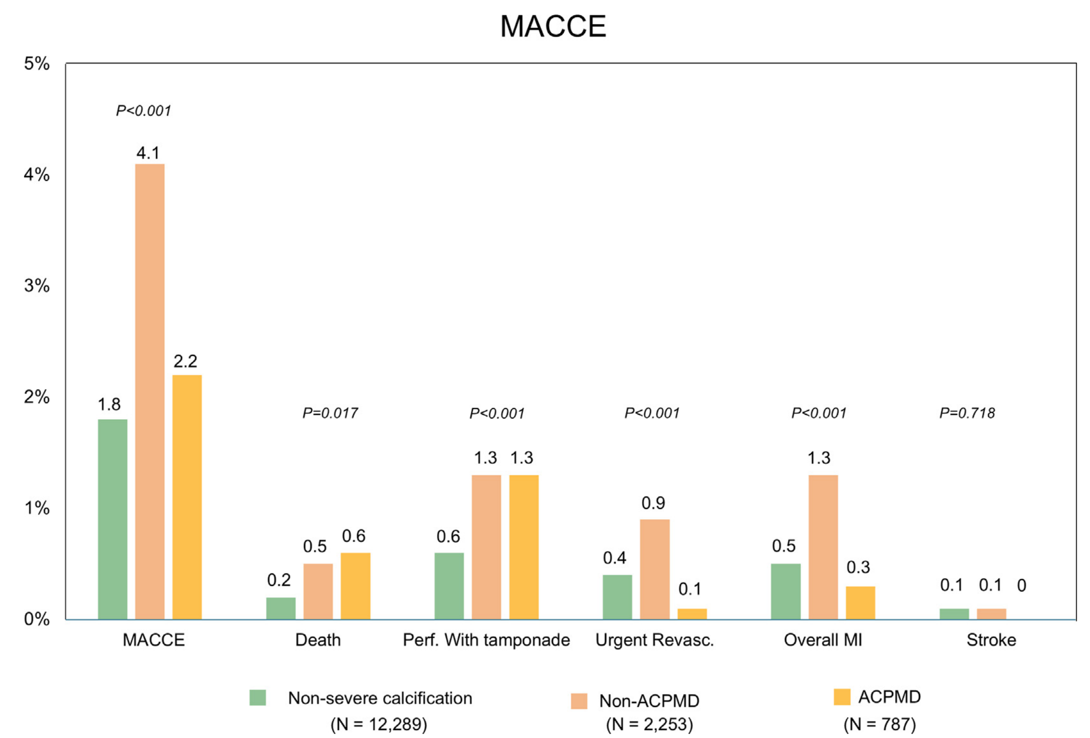
FIGURE 3 Distribution of MACCE Among the Study Groups



ACPMD = advanced calcific plaque modification device; MACCE = major adverse cardiac and cerebrovascular event(s); MI = myocardial infarction; Perf. = perforation; Revasc. = revascularization.

3.55-8.5; $P < 0.001$), and extraplaque crossing (OR: 1.88; 95% CI: 1.14-3.04; $P = 0.012$) (**Figure 7** and Supplemental Table 6).

Finally, compared with IVL, atherectomy had a higher rate of IVUS-assisted procedures (54.4% vs 17.2%; $P < 0.0001$).

DISCUSSION

The main findings of the present study can be summarized as follows: 1) patients with severely calcified CTOs had overall higher complexity compared with those without; 2) over the past few years, severely calcified CTOs have been increasingly treated using ACPMDs, predominantly using atherectomy followed by IVL; and 3) ACPMD strategies applied in severely calcified CTOs were associated with higher technical success and lower rates of MACCE and overall perforations but were applied overall in less complex lesions and were less likely in the case of alternative antegrade or retrograde crossing.

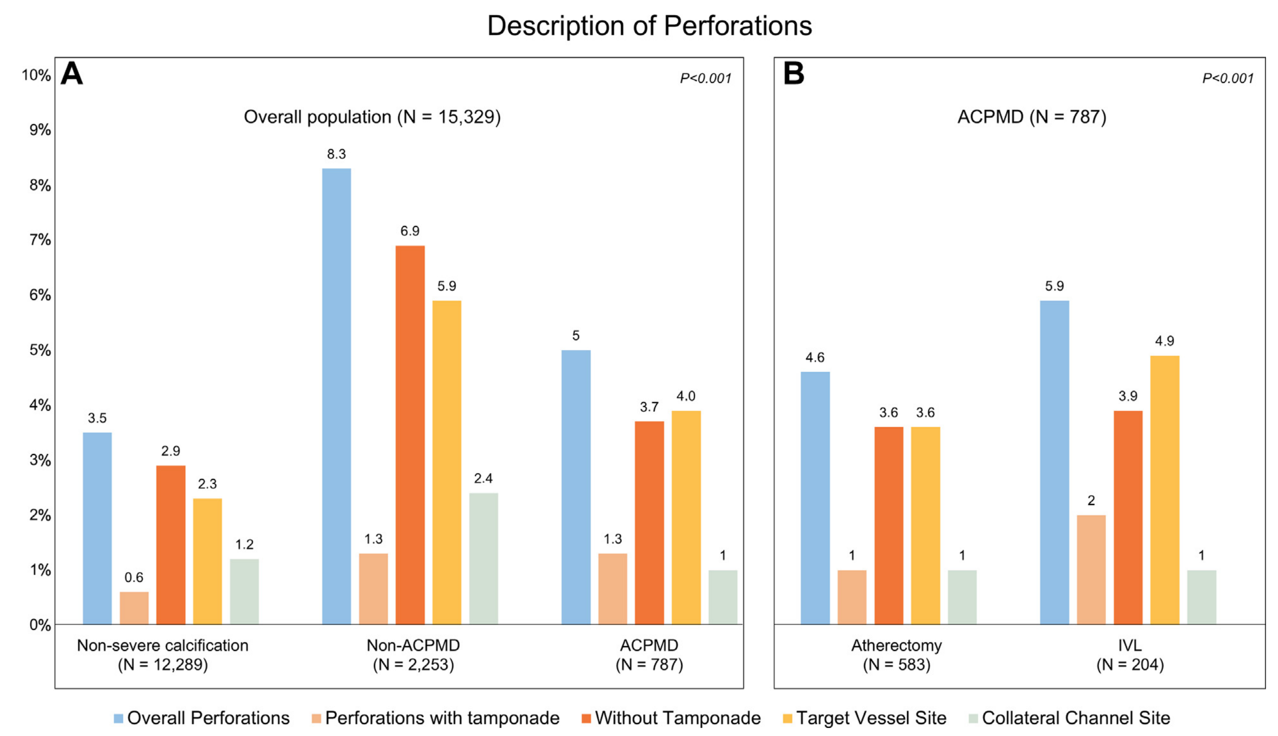
THE ROLE OF CALCIFICATIONS. The presence of severe calcification within a coronary CTO, as assessed on coronary angiography, represents an indicator of global complexity that encompasses the following 3 patterns of risk: 1) clinical, explained by higher rates of previous cardiovascular and cerebrovascular events; 2) anatomical, explained by higher lesion complexity assessed by increasing J-CTO and EURO CTO scores; and 3) procedural, exemplified by longer procedural time, higher x-ray doses and contrast volumes, and a higher rate of bailout strategies such as alternative antegrade or retrograde crossing.

Many of these findings are consistent with those reported in other large CTO registries and patient-level meta-analyses.[2,3,17,18]

However, whether the presence of severe coronary calcification within a CTO affects periprocedural and in-hospital complications has rarely been investigated in detail.

For instance, Kostantinis et al[17] showed that the presence of moderate to severe calcification within a CTO was independently associated with lower technical success (OR: 0.73; 95% CI: 0.63-0.84; $P < 0.001$) and more in-hospital major adverse cardiac events (OR: 2.33; 95% CI: 1.66-3.27; $P < 0.001$). In this regard,

FIGURE 4 Perforations



(A) Different types of perforations in the 3 study groups. (B) Different types of perforations in the atherectomy and IVL group. Abbreviations as in Figure 1.

our study reveals additional insights. For example, patients undergoing CTO PCI in severely calcified lesions in combination with ACPMDs had a similar MACCE rate (2.2% vs 1.8%; $P = 0.439$) and a higher technical success rate (97.6% vs 93.3%; $P < 0.001$) compared with those without severely calcified lesions (Supplemental Table 1). Conversely, patients undergoing CTO-PCI in severely calcified lesions without ACPMD showed the highest rates of MACCE and technical failure.

In addition, we demonstrated that the presence of severe CTO calcification was not independently associated with MACCE within a multivariable logistic regression model. This notable finding can be explained as follows: first, within the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) registry, moderate and severe calcifications were grouped together, whereas we separated severe calcification from lower degrees of calcification.[6,17] Therefore, this fundamentally different classification of patient subsets may have resulted in a biased distribution of MACCE among them.

From the perspective of the Euro-CTO expert operators, only severe coronary calcification can be reasonably assessed during coronary angiography. This estimation agrees with recent reports demonstrating that pure coronary angiography, compared with IVUS, revealed similar diagnostic accuracy for detecting severe coronary calcification but definitively lower accuracy for assessing mild or moderate coronary calcifications.[19,20]

Second, the PROGRESS-CTO study summarized as retrograde all those procedures with retrograde attempts, without differentiating the final crossing strategies (eg, retrograde wiring, RDR, ADR-R, and antegrade wiring with retrograde contribution) as recommended by the CTO-ARC classification.[6,13,17] Conversely, in the present Euro-CTO data set, the CTO-ARC classification of final crossing strategies was applied. This issue could have been responsible for a different attribution of complications among different crossing strategies, which in turn are differently distributed between the ACPMD (77.9% with AW-0 vs 22.1% with other crossing strategies) and non-ACPMD (49.2% with AW-0 vs 50.8% with

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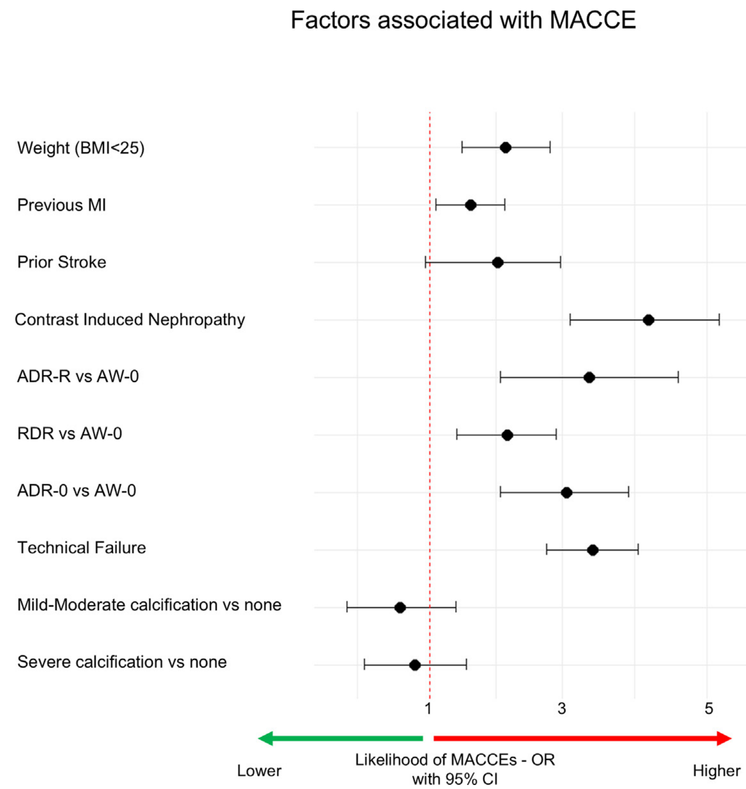
FIGURE 5 **Factors Associated With MACCE: Multivariable Logistic Regression Model**



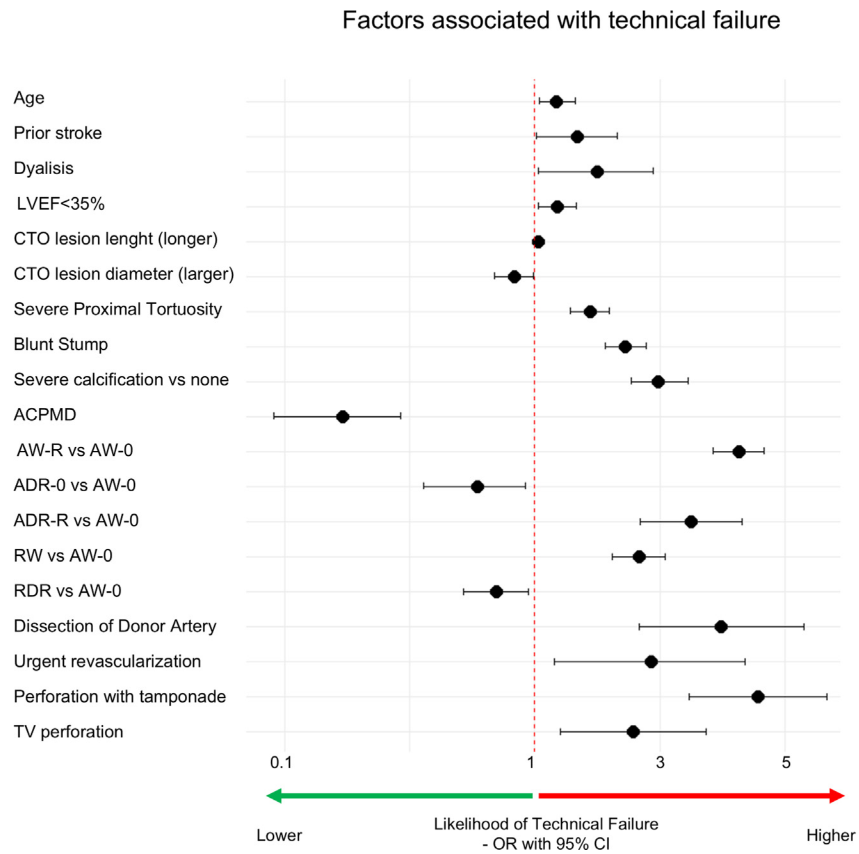
OR	95%CI	Pr(>|z|)
1.88	1.30, 2.72	<0.001
1.40	1.05, 1.86	0.022
1.75	0.96, 2.95	0.049
4.16	3.11, 5.21	<0.001
3.12	1.67, 4.11	0.049
1.90	1.25, 2.86	0.002
3.12	1.79, 5.20	<0.001
3.88	2.64, 5.66	<0.001
0.78	0.50, 1.24	0.3
0.88	0.58, 1.35	0.5

BMI = body mass index; other abbreviations as in Figures 2 and 3.

other crossing strategies) groups. Recently, the prognostic impact of differentiating alternative antegrade crossing strategies from pure antegrade and retrograde wiring as suggested in the CTO-ARC recommendations was proved.[14] In our study, ACPMD strategies were more likely used in the presence of intraplaque crossing, which somehow reflects the recommendation not to apply ACPMD in case of extraplaque crossing.[10] Indeed, rotational atherectomy applied in the subintimal or extraplaque space was recently demonstrated to increase the rate of relevant coronary perforation.[21] In addition, the pathophysiologic and therapeutic effect of IVL shockwaves sent out from the outside of the vessel structure and coronary calcification has never been proved.[22]

It may be argued whether the final crossing strategy or the burden of coronary calcification itself is the main contributing factor in the occurrence of complications. However, as the presence of coronary calcification within the CTO does often requires the adoption of extraplaque crossing techniques to overcome long calcified segments, it is difficult to separate them in this context. However, it is our opinion that the information provided by coronary angiography is not always able to predict whether the CTO might be crossed by a riskier extraplaque strategy, instead of a definitively safer true antegrade wiring. This aspect could be related to the fact that compared with intravascular imaging, coronary angiography alone does not provide accurate information about the exact location of the calcified spots within the vascular architecture (adventitial vs mediointimal), which in turn could be responsible for an intraplaque vs extraplaque CTO crossing. Potentially, a more extensive use of coronary computed tomographic angiography might allow a more accurate assessment of the burden and the distribution of coronary calcifications improving the safety of CTO-PCI in severely calcified segments.[23]

FIGURE 6 Factors Associated With Technical Failure: Multivariable Logistic Regression Model



	OR	95%CI	Pr(>|z|)
Age	1.22	1.04, 1.45	0.018
Prior stroke	1.48	1.01, 2.14	0.039
Dyalisis	1.78	1.03, 2.97	0.033
LVEF<35%	1.23	1.03, 1.46	0.025
CTO lesion lenght (longer)	1.03	1.03, 1.04	<0.001
CTO lesion diameter (larger)	0.83	0.69, 0.99	0.034
Severe Proximal Tortuosity	1.66	1.39, 1.99	<0.001
Blunt Stump	2.30	1.92, 2.78	<0.001
Severe calcification vs none	3.13	2.43, 3.49	<0.001
ACPMD	0.17	0.09, 0.29	<0.001
AW-R vs AW-0	4.15	3.44, 4.86	<0.001
ADR-0 vs AW-0	0.59	0.36, 0.92	0.026
ADR-R vs AW-0	3.24	2.65, 4.27	<0.001
RW vs AW-0	2.61	2.05, 3.32	<0.001
RDR vs AW-0	0.70	0.52, 0.94	0.018
Dissection of Donor Artery	4.18	2.91, 5.61	<0.001
Urgent revascularization	2.92	1.20, 6.96	0.016
Perforation with tamponade	4.84	3.36, 5.77	<0.001
TV perforation	2.48	1.26, 4.86	0.008

LVEF = left ventricular ejection fraction; TV = target vessel; other abbreviations as in Figure 2.

However, on the basis of the data analyzed and the methodology of the study, all these points should be interpreted as hypothesis generating; hopefully they will be explored in new dedicated prospective studies.

TRENDS AND OUTCOMES OF CALCIFIC PLAQUE MODIFICATION DEVICES. The present study demonstrates a consistent increase in the use of ACPMDs to prepare severely calcified CTO from 2021 until 2023. Hence, the present study supports recommendations outlined within international expert consensus documents to improve technical success and outcomes after PCI of calcified CTO.[8,10,20]

We have demonstrated the safety of ACPMD strategies, including atherectomy and IVL, in which the MACCE rate was comparable with that of nonseverely calcified CTOs and lower than severely calcified CTOs treated without ACPMDs (Figure 3, Supplemental Table 1).

Furthermore, ACPMD strategy was associated with lower rates of overall perforations and of target vessel perforations (Figure 4). Of note, target vessel perforations, which are obtained by subtracting the collateral channel perforations from the total count of perforations, provide a more accurate indicator of the risk for perforation related to the actions taken at the level of CTO lesion (eg, intraplaque vs extraplaque crossing, lesion preparation or stenting). Conversely, the excluded collateral perforations, which are specifically related to collateral crossing attempts, often occur before any action is taken at the level of the CTO lesion, including the use of ACPMDs. In conclusion, the present study delivers an in-depth and far-reaching analysis of the impact of severe calcification on the outcomes of contemporary CTO-PCI and about trends of ACPMD application across Europe.

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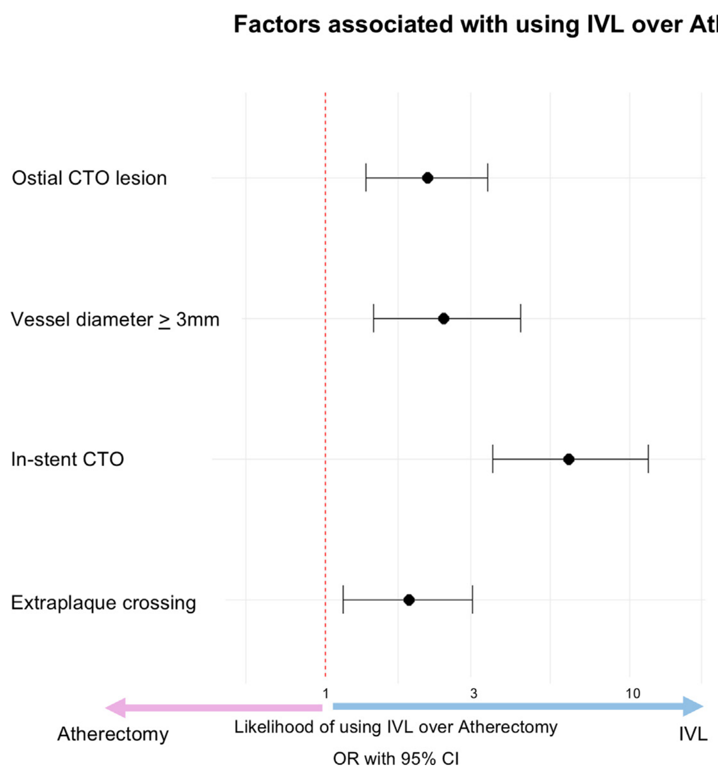
FIGURE 7 **Predictive Model for Using IVL Over Atherectomy**



OR	95%CI	Pr(>|z|)
2.16	1.36, 3.41	0.001
2.45	1.44, 4.38	0.002
6.32	3.55, 11.5	<0.001
1.88	1.14, 3.04	0.012

Abbreviations as in Figures 1 and 2.

STUDY LIMITATIONS. The ERCTO registry is a nonrandomized, all-comers, retrospective, but multicenter registry, and known limitations of this type of observational study must be kept in mind. Selection bias might be present, as the CTO PCI operators participating in ERCTO are proven expert operators with documented evidence of advanced practical experience in CTO-PCI. Therefore, the generalizability of our data might be limited. Because of the retrospective nature all ERCTO patients were treated depending on the individual operators' discretion, thereby intentionally reflecting current daily practice across Europe. Additionally, ERCTO does not provide a central core laboratory adjudication or a critical event committee to reassess results from coronary angiograms, CTO lesion characteristics, the final procedural approach, and further clinical events, which might have been responsible for an underestimation of adverse events. Taken together, the main advantage of ERCTO is to monitor and ensure the quality insurance and standard of care of CTO PCI in the experienced hands of expert operators in the European CTO club.

CONCLUSIONS

Patients undergoing PCI of severely calcified CTOs, which account for 20% of procedures in the contemporary ERCTO, showed the highest clinical, anatomical, and procedural complexity. The presence of severe coronary calcification within the CTO, as assessed USING coronary angiography, was an independent factor associated with technical failure but not with MACCE. The use of ACPMDS, consisting of coronary atherectomy more commonly than IVL, has significantly increased over the PAST few years. Compared with non-ACPMD, ACPMD strategies were associated with higher technical success and lower rates of MACCE but were applied in less complex lesion.

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PERSPECTIVES

WHAT IS KNOWN? The presence of relevant coronary calcification within a CTO increases the procedural complexity and the risk for complications. Advanced devices to modify calcific plaque, including intracoronary atherectomy or lithotripsy have been used to face this challenge, but the available data on their procedural impact are very limited.

WHAT IS NEW? Among PCI of severe calcified CTOs, the application of ACPMDs was associated with higher technical success and lower MACCE. Although the presence of severe coronary calcifications was not independently associated with MACCE, the use of alternative antegrade or retrograde crossing strategies, often necessary to cross calcified CTOs, was.

WHAT IS NEXT? To verify if a systematic preprocedural assessment of coronary calcifications beyond coronary angiography might facilitate a safer intraplaque CTO crossing, in which the use of ACPMDs is applicable rather than a riskier extraplaque crossing, in which the use of ACPMDs should be avoided.

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APPENDIX For contributions of each author to the study, supplemental tables, a figure, and a video of the interactive Central Illustration, please see the online version of this paper.