

Clinical Research

Prevalence and Outcomes of Percutaneous Coronary Interventions for Ostial Chronic Total Occlusions: Insights From a Multicenter Chronic Total Occlusion Registry

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See editorial by Azzalini, pages 1240–1243 of this issue.

ABSTRACT

Background: Ostial chronic total occlusions (CTOs) can be challenging to recanalize.

Methods: We sought to examine the prevalence, angiographic presentation, and procedural outcomes of ostial (side-branch ostial and aorto-ostial) CTOs among 1000 CTO percutaneous coronary interventions (PCIs) performed in 971 patients between 2015 and 2017 at 14 centres in the US, Europe, and Russia.

Results: Ostial CTOs represented 16.9% of all CTO PCIs: 9.6% were aorto-ostial, and 7.3% were side-branch ostial occlusions. Compared with nonostial CTOs, ostial CTOs were longer (44 ± 33 vs 29 ± 19 mm,

RÉSUMÉ

Contexte : Il peut être difficile de recanaliser les occlusions totales chroniques (OTC) ostiales.

Méthodologie : Nous avons cherché à examiner la prévalence, la présentation à l'angiographie et les résultats du traitement des OTC ostiales (aorto-ostiales et ostiales des branches latérales) chez 971 patients qui avaient subi au total 1000 interventions coronariennes percutanées (ICP) visant à traiter des OTC entre 2015 et 2017 dans 14 centres aux États-Unis, en Europe et en Russie.

Résultats : Au total, 16,9 % de toutes les ICP visant à traiter une OTC ont été réalisées chez des patients présentant une OTC ostiale : dans

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See page 1273 for disclosure information.

Ostial lesions can be challenging to treat owing to difficulties with vessel engagement (for aorto-ostial lesions), proximal cap ambiguity with flush/stumpless occlusions, and tedious equipment delivery due to poor guide catheter support. Adequate coverage of the vessel ostium and re-engaging the vessel after stenting can also be challenging.¹⁻³ Similar

$P < 0.001$) and more likely to have proximal-cap ambiguity (55% vs 33%, $P < 0.001$), moderate/severe calcification (67% vs 45%, $P < 0.001$), a diffusely diseased distal vessel (41% vs 26%, $P < 0.001$), interventional collaterals (64% vs 53%, $P = 0.012$), and previous coronary artery bypass graft surgery (CABG) (51% vs 27%, $P < 0.001$). The retrograde approach was used more often in ostial CTOs (54% vs 29%, $P < 0.001$) and was more often the final successful crossing strategy (30% vs 18%, $P = 0.003$). Technical (81% vs 84%, $P = 0.280$), and procedural (77% vs 83%, $P = 0.112$) success rates and the incidence of in-hospital major complication were similar (4.8% vs 2.2%, $P = 0.108$), yet in-hospital mortality (3.0% vs 0.5%, $P = 0.010$) and stroke (1.2% vs 0.0%, $P = 0.030$) were higher in the ostial CTO PCI group. In multivariable analysis, ostial CTO location was not independently associated with higher risk for in-hospital major complications (adjusted odds ratio 1.27, 95% confidence intervals 0.37 to 4.51, $P = 0.694$).

Conclusions: Ostial CTOs can be recanalized with similar rates of success as nonostial CTOs but are more complex, more likely to require retrograde crossing and may be associated with numerically higher risk for major in-hospital complications.

problems can be encountered in the treatment of ostial chronic total occlusions (CTOs), with ostial occlusion being included in some CTO percutaneous coronary intervention (PCI) planning scores.^{4,5} Some aorto-ostial CTOs, such as flush occlusions, may only be approachable using retrograde crossing (Fig. 1), and they often require creative selection of equipment, techniques⁶⁻¹³ and imaging.¹⁴⁻¹⁷ We examined a contemporary multicentre CTO PCI registry to determine the clinical and angiographic characteristics and procedural outcomes of ostial CTO PCI.

Material and Methods

We analyzed the clinical, angiographic, and procedural characteristics of 1000 consecutive CTO PCIs performed in 971 patients enrolled in the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention [NCT02061436]) registry between 2015 and 2017 at 14 centres in the US, Europe, and Russia. Some centres only enrolled patients during part of the study period due to participation in other studies. The study was approved by the institutional review board of each centre.

Definitions

Coronary CTOs were defined as coronary lesions with thrombolysis in myocardial infarction (TIMI) grade 0 flow of at least 3 months' duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina, history of MI in the target vessel territory, or comparison with a previous

angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving $\leq 50\%$ of the reference lesion diameter), or severe (involving $> 50\%$ of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends $> 70^\circ$ or 1 bend $> 90^\circ$ and severe tortuosity as 2 bends $> 90^\circ$ or 1 bend $> 120^\circ$ in the CTO vessel. Blunt or no stump was defined as lack of tapering or lack of a funnel shape at the proximal cap. Interventional collaterals were defined as collaterals considered amenable to crossing by a guidewire and a microcatheter by the operator. CTO was defined as ostial lesion if the location of the proximal cap was within 5 mm of the aortocoronary ostium (aorto-ostial) or a side branch occlusion cap was within 5 mm of the main branch ostium (side branch-ostial). A procedure was defined as "retrograde" if an attempt was made to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; if not, the procedure was classified as "antegrade-only." Antegrade dissection/re-entry was defined as antegrade PCI during which a guidewire was intentionally introduced into the subintimal space proximal to the lesion or re-entry into the distal true lumen was attempted following intentional or inadvertent subintimal guidewire crossing.

Technical success was defined as successful CTO revascularization with achievement of $< 30\%$ residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Procedural success was defined as the achievement of technical success without any in-hospital complications. In-hospital major adverse cardiac events

9,6 % des cas, l'occlusion était aorto-ostiale, et dans 7,3 % des cas, il s'agissait d'une occlusion ostiale des branches latérales. Comparativement aux OTC non ostiales, les OTC ostiales étaient plus longues (44 ± 33 mm vs 29 ± 19 mm, $p < 0,001$) et plus susceptibles d'être associées à une chape proximale mal définie (55 % vs 33 %, $p < 0,001$), à une calcification modérée ou sévère (67 % vs 45 %, $p < 0,001$), à une atteinte diffuse du vaisseau distal (41 % vs 26 %, $p < 0,001$), à des collatérales accessibles pendant l'intervention (64 % vs 53 %, $p = 0,012$), et à des antécédents de pontage aortocoronarien (51 % vs 27 %, $p < 0,001$). La voie rétrograde était empruntée plus fréquemment dans les cas d'OTC ostiales (54 % vs 29 %, $p < 0,001$) et se révélait plus souvent la stratégie de pénétration la plus fructueuse (30 % vs 18 %, $p = 0,003$). Les taux de réussite de la technique (81 % vs 84 %, $p = 0,280$) et de l'intervention (77 % vs 83 %, $p = 0,112$), et l'incidence de complications majeures à l'hôpital (4,8 % vs 2,2 %, $p = 0,108$) ont été similaires dans les deux groupes, mais le taux de mortalité à l'hôpital (3,0 % vs 0,5 %, $p = 0,010$) et le taux d'accidents vasculaires cérébraux (1,2 % vs 0,0 %, $p = 0,030$) ont été plus élevés dans le groupe de patients ayant subi une ICP pour traiter une OTC ostiale. Dans le cadre de l'analyse multivariable, le siège de l'OTC ostiale n'était pas associé de façon indépendante à un risque accru de complications majeures à l'hôpital (rapport de cotes ajusté = 1,27; intervalle de confiance à 95 % : 0,37 à 4,51; $p = 0,694$).

Conclusions : Il est possible de recanaliser les OTC ostiales en conservant un taux de réussite similaire à celui des recanalizations d'OTC non ostiales; toutefois, la recanalisation d'une OTC ostiale est plus complexe et plus susceptible d'exiger une pénétration de l'occlusion par voie rétrograde, et pourrait être associée à un risque de complications majeures à l'hôpital numériquement supérieur à celui de la recanalisation d'une OTC non ostiale.

angio-gram. Calcification was assessed by angiography as mild (spots), moderate (involving $\leq 50\%$ of the reference lesion diameter), or severe (involving $> 50\%$ of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends $> 70^\circ$ or 1 bend $> 90^\circ$ and severe tortuosity as 2 bends $> 90^\circ$ or 1 bend $> 120^\circ$ in the CTO vessel. Blunt or no stump was defined as lack of tapering or lack of a funnel shape at the proximal cap. Interventional collaterals were defined as collaterals considered amenable to crossing by a guidewire and a microcatheter by the operator. CTO was defined as ostial lesion if the location of the proximal cap was within 5 mm of the aortocoronary ostium (aorto-ostial) or a side branch occlusion cap was within 5 mm of the main branch ostium (side branch-ostial). A procedure was defined as "retrograde" if an attempt was made to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; if not, the procedure was classified as "antegrade-only." Antegrade dissection/re-entry was defined as antegrade PCI during which a guidewire was intentionally introduced into the subintimal space proximal to the lesion or re-entry into the distal true lumen was attempted following intentional or inadvertent subintimal guidewire crossing.

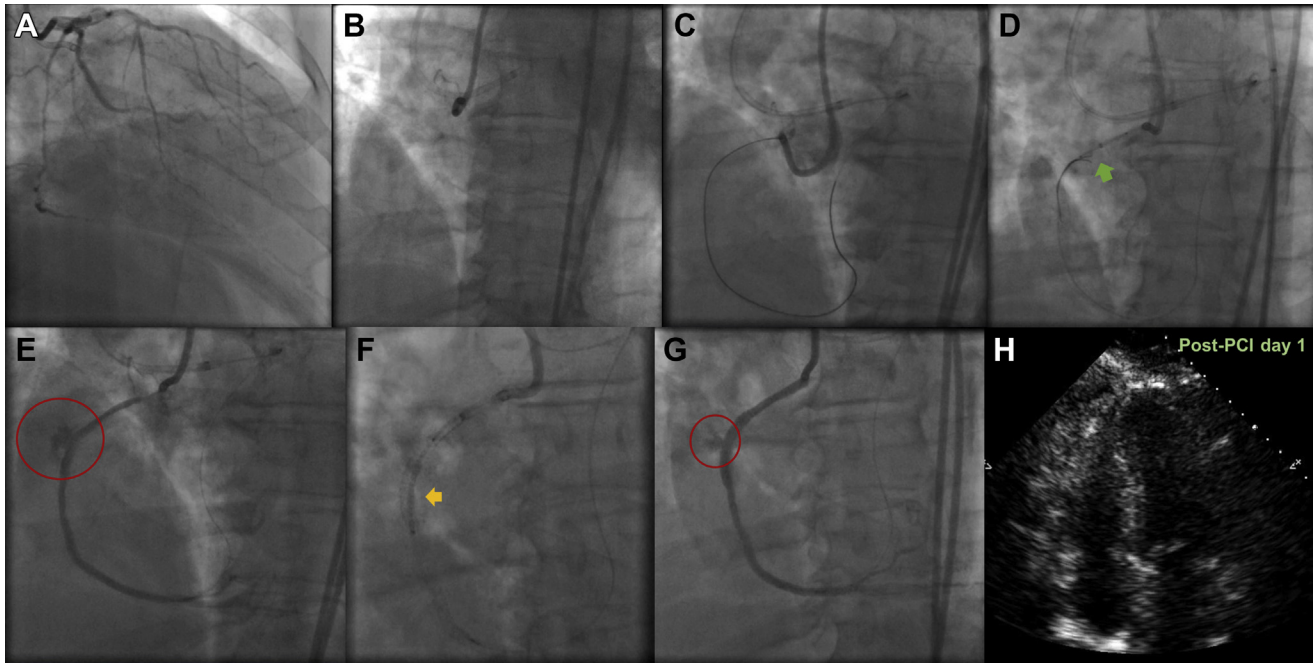


Figure 1. Challenging retrograde recanalization of an aorto-ostial right coronary artery chronic total occlusion via a septal collateral using the GuideLiner reverse-controlled antegrade and retrograde subintimal tracking (reverse CART) technique. (A, B) Ostial RCA CTO PCI with amenable collaterals (septal and epicardial) for the retrograde approach. (C, D) Successful wire crossing with initial retrograde approach using septal collateral, wire re-entry facilitated by the GuideLiner reverse CART technique (green arrow). (E) Ellis 2 extravasation after balloon rupture in balloon undilatable CTO. (F) Prolonged balloon inflation and multiple GuideLiner assisted covered stent deployment (yellow arrow) were performed. (G) Continued contrast extravasation was observed on coronary angiography, but the patient did not have any electrocardiographic and hemodynamics instability and no pericardial effusion on echocardiography. (H) Postprocedural (Day 1) echocardiography showed no pericardial effusion. The patient was discharged on post-PCI Day 2 in stable condition. CART, controlled antegrade and retrograde subintimal tracking; CTO, chronic total occlusion; PCI, percutaneous coronary intervention; RCA, right coronary artery.

(MACE) included any of the following adverse events prior to hospital discharge: death, myocardial infarction, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft surgery (CABG), tamponade requiring either pericardiocentesis or surgery, and stroke. MI was defined using the Third Universal Definition of Myocardial Infarction (type 4a MI).¹⁸ Major bleeding was defined as bleeding causing reduction in hemoglobin > 3 g/dL or bleeding requiring transfusion or surgical intervention. The Japanese CTO (J-CTO) score was calculated as described by Morino et al.,¹⁹ the PROGRESS CTO score as described by Christopoulos et al.,²⁰ and the PROGRESS CTO Complications score as described by Danek et al.²¹

Statistical analysis

Categorical variables were expressed as percentages and were compared using Pearson's χ^2 test or Fisher's exact test. Continuous variables were presented as mean \pm standard deviation or median (interquartile range [IQR]) unless otherwise specified and were compared using the Student's *t*-test and 1-way analysis of variance (ANOVA) for normally distributed variables and the Wilcoxon rank-sum test, or the Kruskal-Wallis test for nonparametric continuous variables, as appropriate. Multivariable logistic regression with stepwise backward elimination was used to examine the association between ostial CTO location and procedural outcomes (procedural success and in-hospital MACE). Variables with

significant univariable association ($P < 0.1$) were entered into the models. All statistical analyses were performed with JMP 13.0 (SAS Institute, Cary, North Carolina). A 2-sided P value of 0.05 was considered statistically significant.

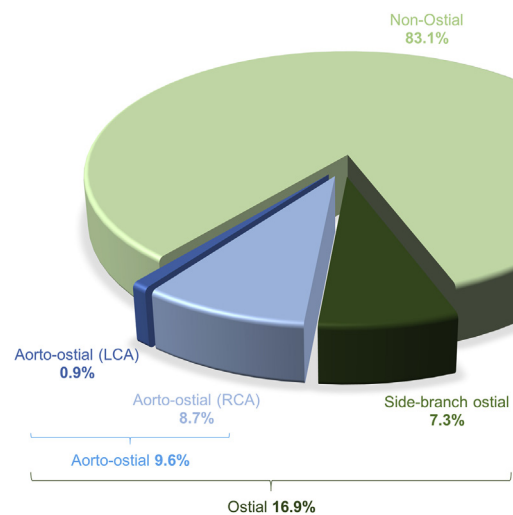


Figure 2. Distribution of aorto-ostial, side-branch ostial, and nonostial CTO lesions. CTO, chronic total occlusion; LCA, left coronary artery; RCA, right coronary artery.

Table 1. Clinical characteristics of the study patients, classified according to ostial location of the chronic total occlusion

Clinical characteristics	Ostial CTOs (n = 168)	Nonostial CTOs (n = 803)	P value
Age (years)*	65.6 ± 9.5	63.5 ± 9.7	0.010
Men	86.1% (142)	85.1% (677)	0.739
BMI (kg/m ²)*	30.2 ± 6.2	30.8 ± 6.0	0.303
Smoking (current)	22.5% (36)	25.5% (199)	0.432
Diabetes	52.7% (87)	37.9% (300)	< 0.001
Dyslipidemia	97.6% (161)	87.3% (691)	< 0.001
Hypertension	93.3% (154)	90.3% (715)	0.217
Family history of CAD	43.3% (55)	34.0% (234)	0.043
CAD presentation			< 0.001
• Stable angina	58.1% (93)	68.7% (527)	
• ACS	37.5% (60)	23.1% (177)	
• Other	4.4% (7)	8.2% (63)	
Previous MI	57.5% (92)	48.9% (375)	0.048
Previous congestive heart failure	32.1% (50)	35.1% (272)	0.466
Previous valve surgery or procedure	4.4% (7)	2.1% (16)	0.082
Previous CABG	50.9% (82)	27.4% (214)	< 0.001
Previous PCI	71.9% (115)	59.7% (472)	0.004
Baseline creatinine (mg/dL) [†]	1.1 (0.9, 1.3)	1.0 (0.9, 1.2)	0.542
Cerebrovascular disease	12.4% (20)	12.6% (99)	0.943
Peripheral artery disease	17.4% (28)	12.3% (96)	0.083
Anemia [‡]	36.2% (42)	21.9% (121)	0.001
Chronic lung disease	17.5% (28)	14.4% (113)	0.318
Left ventricular EF (%) [†]	49 (40, 58)	52 (43, 60)	0.008
Medications			
Long-acting nitrates	49.7% (78)	37.2% (282)	0.003
β-Blockers	92.0% (150)	85.7% (667)	0.031
Calcium channel blockers	23.9% (38)	25.2% (189)	0.731
Ranolazine	26.0% (40)	15.2% (113)	0.001
Antianginal therapy at maximal tolerated dose	80.2% (89)	49.6% (271)	< 0.001

Other includes asymptomatic patients, and patients with atypical angina symptoms. Bold indicates significant values.

BMI, body mass index; CABG, coronary artery bypass graft; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; CVD, cerebrovascular disease; EF, ejection fraction; MI, myocardial infarction; PCI, percutaneous coronary intervention; PAD, peripheral arterial disease.

* Mean ± standard deviation.

[†] median (interquartile range).

[‡] Preprocedural hematocrit <39% for men and <36% for women.

Results

Of the 1000 CTO PCIs attempted in 971 patients, 169 lesions (16.9%) in 168 patients were ostial CTOs (16.9% of total patients): 9.6% (n = 96) were aorto-ostial CTOs, and 7.3% (n = 72) were side-branch ostial CTOs (Fig. 2). One patient underwent PCI for 2 ostial CTOs during the same procedure (both side-branch ostial CTOs), and 9 patients underwent PCI attempt of 1 ostial CTO (7 side-branch ostial, 2 aorto-ostial) and 1 nonostial CTO during the same PCI.

Clinical characteristics

Compared with patients without ostial CTOs, patients who had at least 1 ostial CTO were older, had more coronary disease risk factors (diabetes mellitus, dyslipidemia, family history of coronary artery disease [CAD]), and were more likely to have history of previous MI, CABG, PCI, anemia, and lower left ventricular ejection fraction (LVEF) (Table 1). Patients with ostial CTOs presented more often with an acute coronary syndrome (ACS) (37.5% vs 23.1%, *P* < 0.001).

Table 2. Angiographic characteristics of the study lesions classified according to CTO location

Angiographic characteristics	Ostial CTOs (n = 169)	Nonostial CTOs (n = 831)	P value
Target vessel			< 0.001
• RCA	59.9% (100)	53.6% (442)	
• LAD	13.8% (23)	24.2% (200)	
• LCX	19.2% (32)	21.3% (174)	
• LM	3.6% (6)	0.0% (0)	
• Other*	3.6% (6)	1.0% (12)	
Bypassed target vessel	36.5% (57)	18.6% (146)	< 0.001
CTO length (mm) [†]	43.7 ± 33.4	28.7 ± 19.2	< 0.001
Vessel diameter (mm) [†]	3.0 ± 0.5	2.9 ± 0.5	< 0.001
Occlusion duration (months) [‡]	14.0 (5.3, 44.5)	12.5 (6.0, 38.8)	0.848
Proximal cap ambiguity	54.7% (87)	33.0% (263)	< 0.001
Side branch at proximal cap	54.4% (87)	53.0% (424)	0.750
Blunt stump/no stump	73.9% (119)	50.6% (411)	< 0.001
Interventional collaterals	64.2% (102)	53.3% (423)	0.012
Collateral filling			0.030
• Contralateral	59.3% (96)	46.9% (381)	
• Ipsilateral	16.1% (26)	23.0% (187)	
• Contralateral and ipsilateral	21.6% (35)	27.3% (222)	
• None	3.1% (5)	2.7% (22)	
Retrop 2 ≤ filling grade	76.8% (53)	84.4% (372)	0.118
Adequate distal landing zone	58.8% (94)	73.9% (598)	< 0.001
Moderate/severe calcification	67.1% (106)	44.8% (355)	< 0.001
Moderate/severe tortuosity	49.4% (79)	31.2% (245)	< 0.001
In-stent restenosis	22.2% (35)	16.1% (128)	0.064
Previously failed CTO PCI	25.9% (42)	20.8% (169)	0.151
J-CTO score [†]	3.2 ± 1.1	2.3 ± 1.4	< 0.001
PROGRESS CTO score [†]	1.6 ± 1.2	1.3 ± 1.0	0.004
PROGRESS CTO complication score [‡]	3.7 ± 1.8	2.7 ± 1.9	< 0.001

Bold indicates significant values.

CTO, chronic total occlusion; J, Japan; LAD, left anterior descending artery; LCX, left circumflex artery; LM, left main segment; PCI, percutaneous coronary intervention; PROGRESS, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA, right coronary artery.

* Other includes diagonal and ramus branches.

[†] Mean ± standard deviation.

[‡] Median (interquartile range).

Angiographic characteristics

The distribution of target vessel in ostial and nonostial CTOs is presented in Table 2. Ostial lesions were longer, larger in diameter, more frequently had an ambiguous proximal cap, were more often previously bypassed, were more likely to have interventional collaterals (mostly contralateral), and were less likely to have good-quality distal landing zone. Ostial CTOs had higher J-CTO and PROGRESS CTO scores.

Technical characteristics and the hybrid approach

The technical characteristics and application of the hybrid approach are shown in Table 3. Bilateral injection was used more often in the ostial group (75.0% vs 66.5%, *P* = 0.036), as was use of femoral access (86.4% vs 73.4%, *P* < 0.001) and use of at least 2 femoral access sites (52.7%, vs 33.5%, *P* < 0.001), whereas the frequency of radial access was similar in the 2 groups (45.0% vs 53.0%, *P* = 0.059).

Table 3. Technical characteristics of the study procedures classified according to CTO location

Technical characteristics	Ostial CTOs (n = 169)	Nonostial CTOs (n = 831)	P value
Dual injection	75.0% (120)	66.5% (506)	0.036
Crossing strategies used			
• AWE	76.9% (130)	88.6% (736)	< 0.001
• ADR	32.0% (54)	29.2% (243)	0.482
• Retrograde	54.4% (92)	28.5% (237)	< 0.001
First crossing strategy			< 0.001
• AWE	68.6% (116)	84.4% (700)	
• ADR	3.6% (6)	6.4% (53)	
• Retrograde	27.8% (47)	9.2% (76)	
Final crossing strategy			0.003
• AWE	38.3% (64)	51.2% (424)	
• ADR	15.0% (25)	16.9% (140)	
• Retrograde	29.9% (50)	18.0% (149)	
• None	16.8% (28)	14.0% (116)	
Balloon uncrossable	17.7% (25)	10.3% (72)	0.012
Balloon undilatable	18.5% (19)	9.5% (54)	0.007
IVUS use	49.0% (72)	31.0% (231)	< 0.001
• Proximal cap ambiguity (IVUS- guided antegrade puncture)	5.9% (10)	2.5% (21)	0.020
• Guidewiring	8.3% (14)	5.8% (48)	0.218
• Stent sizing	25.4% (43)	14.1% (117)	< 0.001
• Stent optimization	21.3% (36)	14.8% (123)	0.035
• IVUS-guided reverse CART	1.2% (2)	1.1% (9)	0.909
• Other*	5.9% (10)	2.5% (21)	0.020
Access site			
• Femoral access	86.4% (146)	73.4% (610)	< 0.001
• Bifemoral access	52.7% (89)	33.5% (278)	< 0.001
• Radial access	45.0% (76)	53.0% (440)	0.059
• Biradial access	16.0% (27)	16.4% (136)	0.900

Bold indicates significant values.

ADR, antegrade dissection re-entry; AWE, antegrade wire escalation; CART, controlled antegrade and retrograde subintimal tracking; IVUS, intravascular ultrasound; OCT, optical coherence tomography.

* Other includes: guide wiring (n = 14); ostial stent coverage (n = 6); evaluate extension of subintimal tracking (n = 4); in-stent CTO occlusion (n = 4); distal cap ambiguity (n = 2); assessment of dissection (n = 2); reduce contrast volume (n = 1).

Antegrade wire escalation was the most commonly used technique (86.6%); however, the retrograde approach was more frequently used in ostial CTOs (54.4% vs 28.5%, $P < 0.001$), while the frequency of antegrade dissection re-entry technique was similar (32.0% vs 29.2%, $P = 0.482$). The retrograde technique was more commonly selected as the initial approach in the ostial CTO group (27.8% vs 9.2%, $P < 0.001$), while antegrade dissection re-entry was rarely the initial approach in both ostial (3.6%) and nonostial (6.4%) CTO lesions. Retrograde techniques were used more commonly in ostial CTOs (Fig. 3), although antegrade wire escalation was overall the most common successful crossing strategy (38.3% in ostial CTOs vs 51.2% for nonostial CTOs, $P < 0.001$). Initial CTO crossing success was significantly lower in the ostial group (46.8% vs 56.2%, $P = 0.025$). In 4.7%, the procedure was stopped after failure of the first attempt, whereas in the remaining 48.5% of the cases with ostial CTO lesions, successful recanalization was achieved in 70.7%, resulting in 81.0% overall technical success. Antegrade wire escalation was the most frequent successful crossing strategy overall (47.1%). Retrograde crossing, however, was more frequently the successful approach in the ostial PCI group (29.9% vs 18.0%, $P = 0.003$). Dual lumen microcatheters were used in 16 cases in the current cohort: 14 (1.8%) in nonostial lesions, 1 (1.0%) in an aorto-ostial lesion, and 1 (1.4%) in a side-branch ostial lesion ($P = 0.839$).

Ostial CTOs were also more likely to be balloon uncrossable and undilatable (17.7% vs 10.3%, $P = 0.012$; and 18.5% vs 9.5%, $P = 0.007$, respectively). Intravascular ultrasound (IVUS) was more commonly used in ostial CTO PCIs (49.0% vs 31.0%, $P < 0.001$), for stent sizing (25.4%), stent optimization (21.3%), guidewiring (8.3%), and to overcome proximal-cap ambiguity (5.9%).

Procedural outcomes

The overall procedural outcomes are presented in Table 4 and Supplemental Figure S1. Technical and procedural

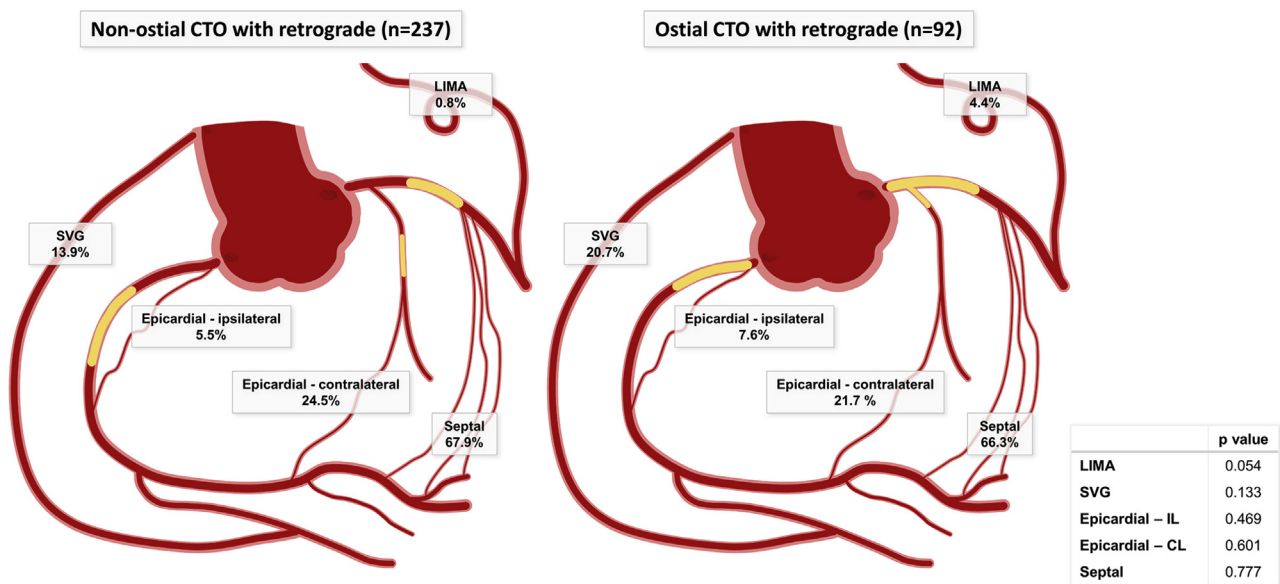


Figure 3. Distribution of collateral channel use during the retrograde approach in ostial and nonostial CTO lesions. CL, contralateral; CTO, chronic total occlusion; IL, ipsilateral; LIMA, left internal mammary artery; SVG, saphenous venous graft.

Table 4. Procedural characteristics of the study interventions classified according to the location of the target lesion

Procedural outcomes	Ostial CTOs (n = 168)	Nonostial CTOs (n = 803)	P value
Procedural success	77.4% (130)	82.6% (660)	0.112
Technical success*	80.5% (137)	83.9% (697)	0.280
LVAD use	15.4% (25)	5.3% (41)	< 0.001
• Prophylactic	11.3% (19)	4.1% (33)	< 0.001
• Urgent	3.6% (6)	0.9% (7)	0.015
LVAD device used			
• Intra-aortic balloon pump	1.8% (3)	0.5% (4)	0.104
• Impella 2.5	0.6% (1)	0.5% (4)	1.000
• Impella 5.0	0.0% (0)	0.0% (0)	-
• Impella CP	9.5% (16)	2.4% (19)	< 0.001
• Tandem Heart	1.8% (3)	1.4% (11)	0.720
• HeartMate PHP	0.0% (0)	0.0% (0)	-
• VA-ECMO	0.6% (1)	0.1% (1)	0.316
Procedure time (min) [†]	172 (110, 248)	115 (71, 180)	< 0.001
Contrast volume (mL) [†]	250 (199, 344)	255 (190, 340)	0.873
Patient AK dose (Gray) [†]	3.1 (2.2, 4.6)	2.8 (1.7, 4.0)	0.017
Fluoroscopy time (min) [†]	71.2 (37.8, 104.5)	40.5 (24.3, 67.5)	< 0.001
In-hospital MACE	4.8% (8)	2.2% (18)	0.108
• Death	3.0% (5)	0.5% (4)	0.010
• Acute MI	1.2% (2)	0.5% (4)	0.278
• Stroke	1.2% (2)	0.0% (0)	0.030
• Re-PCI	0.0% (0)	0.3% (2)	1.000
• Re-CABG	0.0% (0)	0.4% (3)	1.000
• Tamponade requiring pericardiocentesis	1.2% (2)	1.3% (10)	1.000
• Perforation	5.4% (9)	3.2% (26)	0.180
• Vascular access complication	2.4% (4)	0.9% (7)	0.106
• Acute kidney injury	0.0% (0)	0.4% (3)	1.000
• Bleeding	2.4% (4)	1.1% (9)	0.257
• Aortocoronary dissection	0.6% (1)	0.1% (1)	0.316
• Donor vessel dissection/thrombosis	1.8% (3)	1.1% (9)	0.460

Bold indicates significant values.

AK, air kerma; CABG, coronary artery bypass graft; CTO, chronic total occlusion; LVAD, left ventricular assist device; MACE, major adverse cardiac event; MI, myocardial infarction; PCI, percutaneous coronary intervention; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

* Technical success is calculated on a per lesion base.

[†] Median (interquartile range).

success rates were 80.5% and 77.4%, respectively, in patients with ostial lesions, and were not statistically different from patients who underwent PCI for nonostial CTOs (83.9% and 82.6%, $P = 0.280$ and $P = 0.112$). Ostial CTO PCIs required longer procedures (172 [IQR 110-248] min vs 115 [IQR 71-180] min, $P < 0.001$) and fluoroscopy (71.2 [IQR 37.8-104.5] min vs 40.5 [IQR 24.3-67.5] min, $P < 0.001$) time, higher air kerma radiation dose (3.1 [IQR 2.2-4.6] Gray vs 2.8 [IQR 1.7-4.0] Gray, $P = 0.017$), but similar contrast volume (250 [IQR 199-344] mL vs 255 [IQR 190-340] mL, $P = 0.873$) mL. Mechanical circulatory support (MCS) was more commonly used in ostial CTO PCIs (15.4% vs 5.3%, $P < 0.001$), either prophylactically (11.3% vs 4.1%, $P < 0.001$) or urgently (3.6% vs 0.9%, $P = 0.015$). The most commonly used MCS device was the Impella CP (Abiomed,

Inc., Danvers, Massachusetts) (6.1% overall) that was used in 9.5% of patients with ostial CTOs vs 2.4% of patients without ostial CTOs ($P < 0.001$).

The incidence of in-hospital MACE was 2.7% overall (26 patients) and was numerically higher in patients with ostial CTOs (4.8% vs 2.2%, $P = 0.108$) (Table 4). PCI of ostial CTOs was associated with significantly higher in-hospital mortality (3.0% vs 0.5%, $P = 0.010$) and stroke (1.2% vs 0.0%, $P = 0.03$). In the ostial group (2 aorto-ostial, 3 side-branch ostial), 5 patients died during their hospital stays, and 2 patients had procedure-related strokes (both in the aorto-ostial group). Detailed descriptions of the hospital course of patients who died or had strokes are summarized in Table 5. There were no significant differences in the incidence of vascular access complications (2.4% vs 0.9%, $P = 0.106$), aortocoronary dissection (0.6% vs 0.1%, $P = 0.316$), or donor vessel dissection/thrombosis (1.8% vs 1.1%, $P = 0.460$). Two patients had aortocoronary dissection: 1 patient had ostial right coronary artery (RCA) CTO that had been crossed antegradely and stented without the need of further treatment; the other patient had failed retrograde mid-RCA PCI with aortocoronary dissection requiring no additional treatment.

On multivariable analysis (Fig. 4), ostial CTO location was not associated independently with higher in-hospital MACE (odds ratio [OR] 1.29, confidence interval [CI], 95% 0.37-4.51, $P = 0.694$) (Fig. 4A). In addition, ostial location was not an independent predictor of procedural success (OR 1.27, CI 95%, 0.59-2.75, $P = 0.694$), whereas proximal-cap ambiguity (OR 0.45, CI 95%, 0.25-0.80, $P = 0.007$), bifurcation at distal cap (OR 0.47, CI 95%, 0.26-0.85, $P = 0.012$), and interventional collaterals (OR 1.95, CI 95%, 1.09-3.49, $P = 0.025$) were independent predictors of procedural success (Fig. 4B).

The overall technical and procedural rates of success of ostial CTOs in which the retrograde approach was used (75.0% and 70.3%, respectively) were comparable with nonostial retrograde CTO PCIs (78.9% vs 75.3%, $P = 0.445$ and $P = 0.358$) with similar in-hospital MACE rates (5.5% vs 4.7%, $P = 0.0773$). Use of the retrograde approach was associated with higher incidence of in-hospital MACE compared with antegrade-only cases (4.9% vs 1.6%, $P = 0.002$) in the overall cohort. Comparing retrograde cases in the ostial (n = 92, 54.4%) and nonostial (n = 237, 28.5%) group, the distribution of collateral channel use are presented in Figure 3. There were no differences in use of crossing techniques and procedural outcomes between the 2 groups (Supplemental Table S1). However, PCI of ostial CTOs required longer fluoroscopy (93.0 [IQR 66.0-122.7] min vs 77.8 [IQR 60.4-100.8] min, $P = 0.007$) and procedural (227 [IQR 160-300] min vs 193 [IQR 143-253] min, $P = 0.012$) time.

The procedural outcomes in aorto-ostial and side-branch ostial CTO PCIs are summarized in Table 6. Use of the retrograde approach was more common in the aorto-ostial CTO group (66.7% vs 38.4% and 28.5%, $P < 0.001$) compared with side-branch ostial and nonostial CTOs, and was more commonly the final successful crossing strategy (41.1% vs 15.3% and 18.0%, $P < 0.001$). PCI of aorto-ostial CTOs was associated with similarly high technical (81.3% vs 79.5% and 83.9%, $P = 0.531$) and procedural success

Table 5. Procedure related in-hospital mortality and stroke in patients with and without ostial CTO lesion

Patient number	CAD presentation	Target vessel	Lesion type	Technical success	Crossing strategy	LVAD use	Comments
Death							
1	Stable angina	RCA	Aorto-ostial	Yes	Retrograde	Yes	CTO lesion crossed with reverse CART, but due to side branch loss (posterolateral branch) the patient developed acute right ventricular failure and progressive cardiogenic shock.
2	STEMI	LAD	Side-branch ostial	Yes	Retrograde	Yes	Retrograde LAD CTO PCI via SVG (reverse CART) with Ellis 2 coronary perforation without pericardial effusion. Patient developed cardiogenic shock.
3	NSTEMI	RCA	Nonostial	Yes	Retrograde	Yes	Successful retrograde CTO crossing (reverse CART) via an epicardial collateral, but patient had an Ellis 3 coronary perforation that led to cardiogenic shock despite LVAD escalation (Impella CP to Tandem Heart)
4	Unstable angina	RCA	Nonostial	Yes	Retrograde	Yes	Successful retrograde CTO crossing (reverse CART), but balloon uncrossable lesion that required laser atherectomy resulting in perforation and tamponade. The patient developed progressive cardiogenic shock that required left and right sided support, but eventually developed multi-organ failure (likely related to acute right ventricular failure).
5	Stable angina	LCX	Side-branch ostial	Yes	ADR	Yes	Patient had coronary perforation and subsequent tamponade requiring pericardiocentesis that progressed to cardiogenic shock.
6*	Unstable angina	LAD + RCA	Aorto-ostial (RCA)	Yes + Yes	ADR + retrograde	Yes	PCI of 2 target CTOs was attempted with prophylactic LVAD support (last remaining conduit). Both of them were recanalized and additional non-CTO PCI (left main and first diagonal branch) was performed, had hemorrhagic stroke and died.
7	Stable angina	LCX + RCA	Side-branch ostial (LCX)	No + No	ADR	Yes	Two target CTOs were attempted without success. Patient had coronary perforation and subsequent tamponade, complicated with left main thrombosis that led to cardiogenic shock.
8	NSTEMI	LAD	Nonostial	No	Retrograde	Yes	Patient with RCA CTO and left ventricular ejection fraction of 27%. He underwent rotational atherectomy of the proximal LAD to facilitate retrograde crossing via septal collaterals, but had hemodynamic collapse and ventricular fibrillation, requiring CPR and LVAD insertion.
9	Stable angina	RCA	Nonostial	Yes	AWE	No	Patient had a balloon undilatable CTO requiring rotational atherectomy that resulted in perforation (treated with covered stent), tamponade requiring pericardiocentesis with subsequent ventricular fibrillation and cardiogenic shock.
Stroke							
6*	Unstable angina	LAD + RCA	Aorto-ostial (RCA)	Yes + Yes	ADR + retrograde	Yes	Two CTOs were attempted with prophylactic LVAD support (due to last remaining conduit). Both of them were recanalized and additional non-CTO PCI was performed in the left main and first diagonal branch. The patient developed stroke (hemorrhagic) and died in hospital.
10	Stable angina	RCA	Aorto-ostial	Yes	Retrograde	Yes	Donor artery dissection (left main) occurred during retrograde CTO PCI and was treated with additional stenting, but due to progressive cardiogenic shock patient required LVAD support. He subsequently had ischemic stroke and bleeding.

AWE, antegrade wire escalation, ADR, antegrade dissection and re-entry; CAD, coronary artery disease; CPR, cardiopulmonary resuscitation; LAD, left anterior descending artery; LCX, left circumflex artery; LVAD, left ventricular assist device; RCA, right coronary artery; VF, ventricular fibrillation.

*Patient had both in-hospital death and procedure related stroke (hemorrhagic).

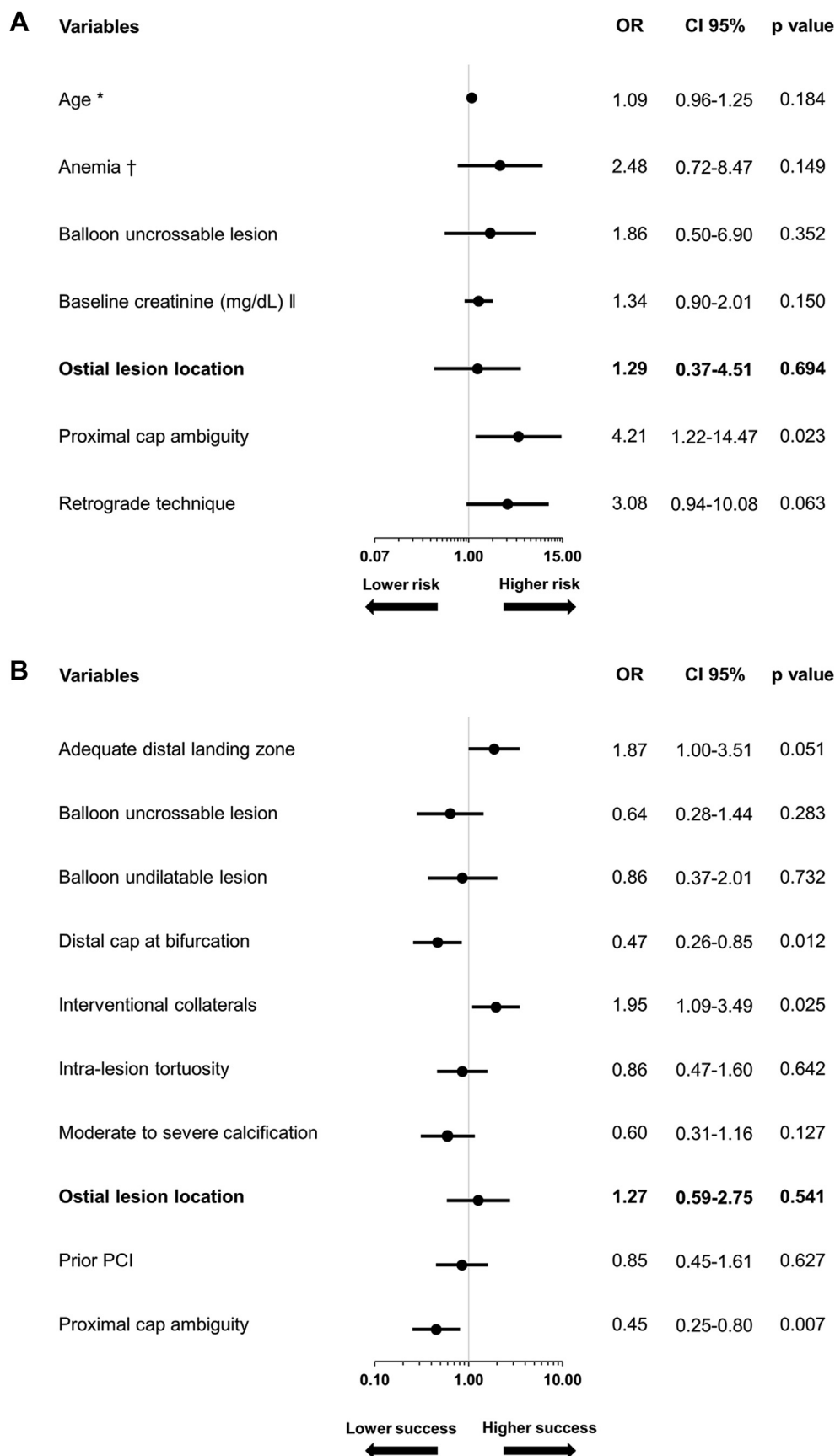


Figure 4. Multivariable logistic regression of baseline clinical and angiographic characteristics for in-hospital major adverse cardiovascular events (A) and for procedural success (B) in patients undergoing CTO PCI. *Per 5 unit (year) change in regressor. †Defined as preprocedural hematocrit < 39% for men and < 36% for women. ‡Per 1 unit (mg/dL) change in regressor.

Table 6. Technical and procedural outcomes of CTO PCI according to presence and type of ostial lesions

Technical outcomes	Aorto-ostial CTOs (n = 96)	Side-branch ostial CTOs (n = 73)	Nonostial CTOs (n = 831)	P value
Crossing strategy used				
• AWE	66.7% (64)	90.4% (66)	88.6% (736)	< 0.001
• ADR	33.3% (32)	30.1% (22)	29.2% (243)	0.706
• Retrograde	66.7% (64)	38.4% (28)	28.5% (237)	< 0.001
First crossing strategy				< 0.001
• AWE	58.3% (56)	82.2% (60)	84.4% (700)	
• ADR	5.2% (5)	1.4% (1)	6.4% (53)	
• Retrograde	36.5% (35)	16.4% (12)	9.2% (76)	
Final crossing strategy				< 0.001
• AWE	26.3% (25)	54.2% (39)	51.2% (424)	
• ADR	16.9% (16)	12.5% (3)	16.9% (140)	
• Retrograde	41.1% (39)	15.3% (11)	18.0% (116)	
• None	15.8% (15)	18.1% (13)	14.0% (149)	
Technical success	81.3% (58)	79.5% (58)	83.9% (697)	0.531
Procedural outcomes	Aorto-ostial CTOs (n = 96)	Side-branch ostial CTOs (n = 72)	Nonostial CTOs (n = 803)	P value
Procedural success	77.1% (74)	77.8% (56)	82.6% (660)	0.280
Procedure time (min)*	170 (109, 277)	184 (113, 237)	115 (71, 180)	< 0.001
Contrast volume (mL)*	260 (200, 363)	246 (184, 339)	255 (190, 340)	0.368
Patient AK dose (Gray)*	3.1 (2.0, 4.6)	3.3 (2.3, 4.7)	2.8 (1.7, 4.0)	0.054
Fluoroscopy time (min)*	71.9 (44.3, 108.3)	71.0 (33.7, 97.9)	40.5 (24.3, 67.5)	< 0.001
In-hospital MACE	5.2% (5)	4.2% (3)	2.2% (18)	0.169
• Death	2.1% (3)	4.2% (2)	0.5% (4)	0.004
• Acute MI	2.1% (2)	0.0% (0)	0.5% (4)	0.136
• Stroke	2.1% (2)	0.0% (0)	0.0% (0)	0.001
• Re-PCI	0.0% (0)	0.0% (0)	0.3% (2)	0.811
• Re-CABG	0.0% (0)	0.0% (0)	0.4% (3)	0.730
• Pericardiocentesis	1.0% (1)	1.3% (1)	1.4% (10)	0.978
• Perforation	6.3% (6)	4.2% (3)	3.2% (26)	0.315

Bold indicates significant values.

ADR, antegrade dissection and re-entry; AK, air kerma; AWE, antegrade wire escalation; CABG, coronary artery bypass graft; CTO, chronic total occlusion; LVAD, left ventricular assist device; MACE, major adverse cardiac event; MI, myocardial infarction; PCI, percutaneous coronary intervention.

*Median (interquartile range).

(77.1% vs 77.8% and 82.6%, $P = 0.280$), and with similar in-hospital major complication rates (5.2% vs 4.2% and 2.2%, $P = 0.169$). In-hospital mortality was significantly higher in the side-branch ostial CTO group compared with aorto-ostial and nonostial CTOs (4.2% vs 2.1% and 0.5%, $P = 0.004$), whereas procedure-related stroke only occurred after aorto-ostial CTO PCIs (2.1% vs 0.0% and 0.0%, $P = 0.001$).

Discussion

To the best of our knowledge, this is the first systematic study of ostial CTO PCI. The key findings were that, compared with nonostial CTOs, ostial CTOs are common, representing 16.9% of all CTO PCIs and are associated with high lesion complexity, are more likely to require retrograde crossing, have similar procedural success, yet carry higher risk for in-hospital major complications.

Ostial CTOs were the target lesions in approximately 1 out of 6 patients in our study population (16.9%), and these patients had a higher incidence of coronary disease risk factors (diabetes mellitus, dyslipidemia, and history of CAD). Patients with ostial CTOs had lower baseline ejection fraction, possibly as a consequence of the proximal vessel obstruction that may affect a larger myocardial mass²² and were more likely referred for PCI for ACS. Most patients with ostial CTOs received antianginal therapy at maximal tolerated dose (80.2%) and had higher rates of previous MI, CABG, and PCI, highlighting their increased baseline risk and more complex coronary anatomy. Ostial CTOs were more likely to

be located in previously bypassed vessels and to have proximal-cap ambiguity, tortuosity, and severe calcification. Ostial lesions were also more often associated with severely diseased distal vessels that could hinder application of antegrade dissection re-entry techniques. However, ostial CTOs often had interventional collaterals (mostly contralateral) that facilitated use of the retrograde approach. The most common CTO target vessel was the RCA (59.9%); left anterior descending (LAD) CTOs were less common, possibly because of patent left internal mammary grafts.

As anticipated, retrograde techniques were used more commonly in ostial CTO PCIs and were often used as the initial crossing strategy in very complex CTOs (mean J-CTO score: 3.7 ± 0.8). However, antegrade wire escalation remained the most common initial crossing strategy (68.6%), even in aorto-ostial lesions (58.3%). As presented in [Supplemental Table S1](#), the retrograde approach was similarly successful in ostial and nonostial lesions with similar risk for in-hospital MACE (5.5% vs 4.7%, $P = 0.773$). Use of retrograde techniques likely contributed to the high rates of success achieved in ostial CTO PCI but should be used with caution, as they are associated with increased risk for complications as compared with antegrade-only techniques.²³

Ostial CTO location has been associated with higher risk for procedural failure in 2 previous studies that developed CTO scoring systems^{4,5} (although neither provided a definition for ostial CTO). Galassi et al. created the ORA-score (Ostial Location of Proximal Cap, Rentrop < 2 Collateral Filling, Patient Age ≥ 75), based upon 1076 CTO PCIs performed by a single operator over a period of 10 years.⁴ The

prevalence of ostial CTOs was 14.1% overall and increased over time from 11.7% during 2005 to 2009 to 15.5% during 2010 to 2014 ($P = 0.203$). The Ellis scoring system includes ostial location as a predictor of procedure failure along with several other variables (proximal-cap ambiguity, operator experience, adequate distal target, lesion length > 10 mm, tortuosity, calcification, and collateral score²⁴).⁵ In a single-operator study, Fang et al. compared ostial LAD CTO PCIs ($n = 70$) with any other CTO PCI ($n = 551$) and showed similar procedural success rates (80.0% vs 81.9%, $P = 0.706$) but higher use of contrast material and longer procedure and fluoroscopy time in the ostial LAD group. This study, however, focused on identifying the clinical and angiographic predictors of successful ostial LAD CTO crossing and not on clinical outcomes of ostial CTO PCI.

Our study is in agreement with the aforementioned reports, showing similarly high rates of success with ostial and nonostial CTOs. The risk for major in-hospital complications was numerically higher in ostial CTOs (4.8% vs 2.2%, $P = 0.108$), but there was no significant association on multivariable analysis, suggesting that potentially increased risk may be related to more adverse baseline clinical characteristics and more frequent use of retrograde techniques. In the future, novel techniques, such as real-time computed tomography guidance²⁵ might improve the success and safety of the procedure.

Our study has limitations. First, we only included in-hospital outcomes without long-term follow-up. Second, there was no core laboratory assessment of the study angiograms or clinical event adjudication. Third, ostial lesions were defined as lesions located within 5 mm from the coronary orifice, which is different from the 3-mm cutoff used in the Syntax score.²⁶ Fourth, the procedures were performed in dedicated, high-volume CTO centres by experienced operators, limiting extrapolation to less experienced operators and lower-volume centres that may be less likely to attempt PCI of such lesions and opt for medical therapy or surgical revascularization instead.

Conclusions

In conclusion, as compared with nonostial CTOs, ostial CTOs are more challenging to recanalize and more often require use of the retrograde approach. However, high rates of success can be achieved with an acceptable—albeit numerically higher—risk of major complications.

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Supplementary Material

To access the supplementary material accompanying this article, visit the online version of *Canadian Journal of Cardiology* at www.onlinecjc.ca and at <https://doi.org/10.1016/j.cjca.2018.07.472>.