# Prevalence of Collateral Typology in Coronary Chronic Total Occlusion and Its Impact on Percutaneous Intervention Performance

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**The presence of collateral channels providing distal blood supply is a distinctive characteristic of chronic total occlusion (CTO) lesions. However, data about the distinct baseline and procedural characteristics of each collateral subset are scarce. Accordingly, we sought to explore the procedural aspects specific for each collateral typology (ipsilateral collaterals [ICs], contralateral collaterals [CCs] or mixed) in CTO-percutaneous coronary intervention (PCI). A retrospective analysis of our CTO-PCI registry was performed to investigate the prevalence, procedural characteristics, and outcomes specific for each CTO-PCI subset, defined according to the inter-arterial connection anatomy. A total of 209 cases were included. Of the included cases, 45 (22%) and 92 (44%) patients displayed solely IC or CC, respectively, whereas in 72 (34%) both IC and CC were present (mixed). The procedural success rate was high (91.1%) and comparable among the different groups, despite greater lesion complexity in the CC group. The most frequent target vessel was the left circumflex in the IC group (51% of cases) and the right coronary artery in the CC (63%) and mixed (57%) groups. Among the IC cases, 42% showed a poor collateral connection function (2% and 10% for the CC and mixed group, respectively), and 46% showed a suboptimal collateral recipient artery filling (21% and 20% for the CC and mixed group, respectively). Most of the IC cases were performed using a single access (96%). In conclusion, the success and complication rates were comparable among the collateral typology groups, irrespective of the differences in the baseline and procedural characteristics. Phenotyping CTO as hereby proposed might be helpful for targeted procedural considerations.**  **(Am J Cardiol 2024;210:153−162)**

**Keywords:** chronic total occlusion, collateral channels, percutaneous coronary intervention

Coronary chronic total occlusions (CTOs) are traditionally defined as "coronary occlusions without anterograde flow through the lesion (TIMI [thrombolysis in myocardial infarction] grade 0 flow) with a presumed or documented duration of more than 3 months."[1] A distinctive characteristic of CTO lesions is the presence of collateral channels providing blood flow to the vascular territory of the obstructed vessel. According to the anatomy of the inter-arterial connection, collateral vessels are categorized as ipsilateral collaterals (ICs) or contralateral collaterals (CCs), or in the case of patients who previously underwent coronary artery bypass graft (CABG) surgery, these collaterals may also originate from a vascular graft. The type of collateral channels is associated with unique challenges and raises specific procedural considerations.[2] For instance, CTO with predominant IC, despite being encountered in <1/3 of CTO lesions,[3,4] represents a particularly challenging subset especially in case of retrograde approach through ICs.[5,6] However, the available literature provides limited data on the distinct baseline and procedural characteristics of each CTO subset. To the best of our knowledge, an accurate distinction between CTO lesions displaying both IC and CC channels (mixed collateral channels origin), and those with solely IC or CC has never been performed. The aims of the present study were thus to investigate the procedural characteristics and outcomes specific for each CTO-percutaneous coronary intervention (PCI) subset, defined according to the kind of collateral vessel supply (i.e., IC, CC or mixed), and to provide useful insights for targeted procedural considerations.

## Methods

All the patients who underwent attempted CTO-PCI at our institution between February 2019 and March 2023 were analyzed. All the procedures were performed electively and indicated according to the presence of angina or angina equivalents and/or ischemia. Baseline data, procedural

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characteristics, and short-term outcomes were manually extracted from institutional electronic medical records and prospectively entered into a dedicated, anonymized database. The CTO revascularization strategy in our study followed the minimalistic hybrid approach (MHA) algorithm. Briefly, the MHA algorithm follows the reasoning and involves the use of the crossing techniques of the "classical" hybrid algorithm,[7] but with a focus on minimizing procedural invasiveness by limiting the routine upfront use of dual injection, large bore catheters, and femoral approach. Namely, there are 5 possible scenarios based on the CTO crossing technique chosen as first intention (anterograde wire escalation [AWE], anterograde dissection re-entry [ADR], retrograde wire escalation [RWE] or retrograde dissection re-entry [RDR]) and the presence of IC or CC channels as main collaterals for the CTO. For each scenario, a stepwise strategy approach is defined.[2] The present study is a retrospective analysis of prospectively collected data.

All patients gave written informed consent for being part of the prospective national Belgian Working Group of Chronic Total Occlusion (BWGCTO) registry,[8] allowing the investigators to use the anonymized data of the patients for scientific research purposes. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Most of the procedures (up to November 2022) have been published as short movies in LinkedIn (http://www.linkedin.com) under the hashtag MinimalisticHybridApproach.

CTO was defined as a 100% stenosis with TIMI flow grade 0 for >3 months.[9] Coronary dominance was determined by the artery supplying the posterior descending artery (i.e., right or left dominance). The J-CTO (Multicenter CTO Registry in Japan),[10] the EuroCTO (CASTLE, Multicenter CTO EuroCTO Registry)[11] and the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention)[12] scores were calculated for each lesion to appraise case complexity. To grade the collateral channel function and the filling pattern of the occluded artery segment, the Werner[13] and Rentrop[14] classifications were utilized, respectively (for details, see the Supplementary Materials).

For the purpose of this subanalysis, the study patients were classified into the following 3 categories according to the kind of collateral vessel supply: (1) IC channel group, in case of the presence of collateral channels from an ipsilateral donor artery; (2) CC channel group, in case of the presence of collateral channels from a contralateral donor artery; and (3) mixed group, when both IC and CC were present. In case of post-CABG patients, if the aortocoronary bypass graft per se allowed direct distal visualization of the target occluded segment, they were considered as CC and grouped accordingly.

An independent operator reviewed all baseline angiograms to assess the collateralization typology.

With regard to the study end points, technical success was defined as the successful deployment of the stent at the target CTO lesion, and the achievement of CTO revascularization with residual stenosis <30% and anterograde TIMI flow grade 3 in the CTO target vessel[9]; procedural success was defined as technical success plus the absence of in-hospital major adverse cardiac and cerebral events (MACCEs) (i.e., all-cause death, periprocedural type 4a myocardial infarction,[15] repeat target vessel revascularization, cardiac tamponade requiring pericardiocentesis, and stroke). Procedural complications and periprocedural adverse events included procedure-related death or stroke, stent thrombosis, major bleeding (causing a hemoglobin decrease >3 g/100 ml and/or requiring transfusion, vasopressors, percutaneous or surgical intervention), vascular complications (with the occurrence of local hematoma >5 cm, or pseudoaneurysm or dissection), clinically relevant coronary perforation requiring intervention (i.e., coil or fat embolization, covered stent implantation, pericardiocentesis, or surgery), and donor vessel damage.

Continuous variables are reported as mean ± SD or median and interquartile range [quartile 1 to quartile 3], according to normal versus non-normal distribution, respectively, whereas categorical variables are described as proportions and percentages. Kruskal-Wallis one-way analysis of variance and chi-square or Fisher's exact tests were carried out to investigate differences among groups, as appropriate. All p values were 2-tailed and considered statistically significant if <0.05. All statistical analyses were performed using SPSS version 28 (IBM, Armonk, New York).

## Results

A total of 209 cases were included. According to the kind of collateral vessel supply, 45 (22%) and 92 patients (44%) presented solely IC and CC, respectively, whereas in 72 cases (34%) both IC and CC were present (Figure 1).

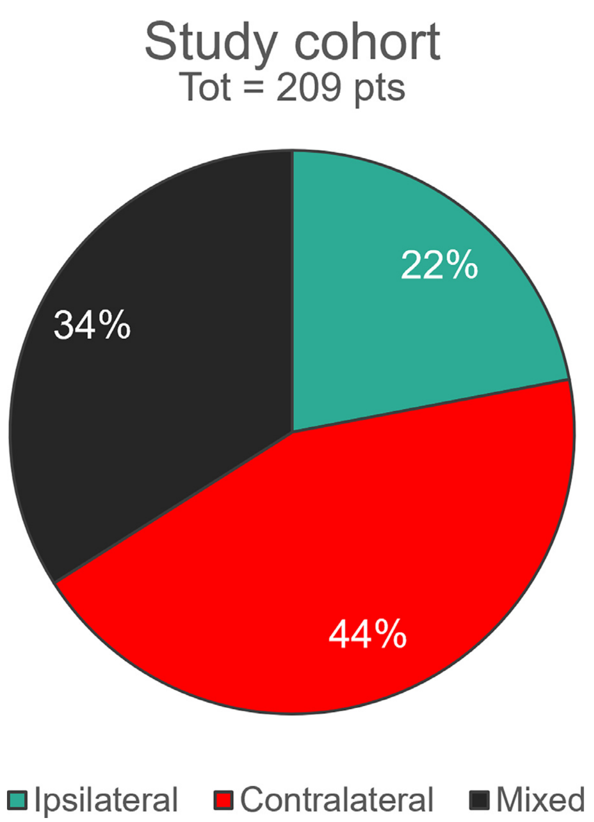


Figure 1. Distribution of the study cohort according to collateral typology. pts = patients; Tot = Total.

Table 1
Baseline clinical characteristics

| | Overall (n = 209) | Ipsilateral (n = 45) | Contralateral (n = 92) | Mixed (n = 72) | p-value |
|---|---|---|---|---|---|
| **Demographic and clinical features** | | | | | |
| Age (years) | 69.2 ± 11.5 | 71.3 ± 10.2 | 69.3 ± 11.9 | 67.7 ± 11.5 | 0.251 |
| Male gender, n (%) | 182 (87) | 36 (80) | 79 (86) | 67 (93) | 0.110 |
| BMI (kg/m$^2$) | 27.7 [24.9-31.0] | 26.8 [24.5-31.25] | 27.6 [24.9-32.2] | 28.4 [25.5-31.0] | 0.714 |
| Previous or current smoker, n (%) | 145 (69) | 29 (64) | 63 (68) | 53 (73) | 0.385 |
| eGFR (mL/min/1.73 m$^2$) | 78.4 [60.8-96.5] | 73.9 [50.6-87.2] | 77.0 [56.7-93.9] | 77.0 [67.6-96.6] | **0.014** |
| Left ventricular ejection fraction (%) | | | | | 0.418 |
| <35% | 9 (4) | 4 (9) | 2 (2) | 3 (4) | |
| 35-50% | 56 (27) | 12 (27) | 27 (29) | 17 (24) | |
| ≥50% | 144 (69) | 29 (64) | 63 (69) | 52 (72) | |
| CCS angina class ≥2 | 125 (60) | 25 (56) | 57 (62) | 43 (60) | 0.743 |
| NYHA class ≥2 | 85 (40) | 20 (44) | 38 (41) | 27 (37) | 0.789 |
| **Comorbidities, n (%)** | | | | | |
| Hypertension | 147 (73) | 32 (71) | 60 (65) | 55 (76) | 0.296 |
| Diabetes mellitus | 73 (35) | 18 (40) | 36 (39) | 19 (26) | 0.171 |
| Dyslipidemia | 188 (90) | 41 (91) | 83 (90) | 64 (89) | 0.921 |
| Prior myocardial infarction | 82 (39) | 14 (31) | 33 (36) | 35 (49) | 0.114 |
| Prior myocardial infarction in CTO territory* | 42/82 (51) | 7/14 (50) | 19/33 (58) | 16/35 (46) | 0.671 |
| Prior PCI | 139 (67) | 33 (73) | 58 (63) | 48 (67) | 0.487 |
| Prior PCI in CTO territory[†] | 37/139 (27) | 14/33 (42) | 12/58 (21) | 11/48 (23) | **0.027** |
| Prior CABG | 43 (21) | 5 (11) | 31 (34) | 7 (10) | **<0.001** |
| Prior CABG in CTO territory[‡] | 38/43 (88) | 5/5 (100) | 26/31 (84) | 7/7 (100) | **0.004** |
| Peripheral artery disease | 31 (15) | 6 (13) | 14 (15) | 11 (15) | 0.950 |
| Prior stroke | 19 (9) | 2 (4) | 11 (12) | 6 (8) | 0.343 |
| CKD (eGFR< 60 ml/min/1.73m$^2$) | 14 (7) | 4 (9) | 10 (11) | 0 (0) | **0.018** |
| COPD | 28 (13) | 6 (13) | 11 (12) | 11 (15) | 0.825 |

BMI = body mass index; CABG = coronary artery by-pass graft; CCS = Canadian Cardiovascular Society; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; CTO = chronic total occlusion; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; TIA = transient ischemic attack.

Data are presented as n (%) or mean ± SD or median [IQR].

*Data are reported as ratio (%) between the number of prior myocardial infarction in CTO territory and the total number of prior myocardial infarction.

[†] Data are reported as ratio (%) between the number of prior PCI in CTO territory and the total number of prior PCI.

[‡] Data are reported as ratio (%) between the number of prior CABG in CTO territory and the total number of prior CABG.

The baseline clinical characteristics of the entire study cohort and the comparison among the 3 groups (IC, CC, and mixed groups) are illustrated in Table 1.

Overall, the mean age was 69.2 ± 11.5 years, and 87% of patients were male. Cardiovascular risk factors and comorbidities were highly prevalent and equally distributed among the study groups except for chronic kidney disease. A comparable proportion had experienced previous myocardial infarction (MI) (31% in the IC group, 36% in the CC group, and 49% in the mixed group); however, despite similar rates of previous PCI, almost half were performed in the CTO territory in the IC group (41% IC vs 21% CC vs 23% mixed, p = 0.027); besides, a higher proportion of patients in the CC group had previously undergone CABG (34% CC vs 11% IC vs 10% mixed, p <0.001).

The presence of angina or angina-equivalent symptoms was the main driver for revascularization in all the groups (significant symptom burden in 87%, 91%, and 90% in IC, CC, and mixed group, respectively, p = 0.694), and left ventricular ejection fraction was mostly preserved.

The target CTO vessel differed significantly among the groups, with the left circumflex coronary artery (LCx) being the most frequent in the IC group (i.e., in 51% of cases, compared with 11% and 15% in the CC and mixed group, respectively), followed by the left anterior descending (31%) and the right coronary artery (RCA) (7%) (left anterior descending 24% in CC and 28% in mixed; RCA: 63% in CC and 57% in mixed). In contrast, CTO location and in-stent restenosis CTO were uniformly distributed.

Importantly, CTO complexity was overall pronounced (mean J-CTO score in the entire population: 2.3 ± 1.1; EuroCTO score: 2.1 ± 1.3; PROGRESS-CTO score: 1.5 ± 0.9) but significantly different among the study groups with a trend toward a higher complexity in the CC group. In particular, the angiographic characteristics accounting for increased complexity were highly prevalent in our cohort and generally more frequent in the CC group: blunt stump in 35% of lesions (IC 27%, CC 42%, mixed 32%, p = 0.146), lesion length>20 mm in 48% (IC 38%, CC 60%, mixed 40%, p = 0.013), moderate or severe calcification in 58% (IC 47%, CC 67%, mixed 54%, p = 0.046), and intra-lesion bending >45° in 70% (IC 62%, CC 79%, mixed 64%, p = 0.040). In contrast, the higher proportion of LCx in the IC group as target CTO vessel likely accounted for the higher PROGRESS-CTO score observed in this subset.

Of note, the presence of a distal vessel of suboptimal quality tended to be more frequent in the IC group (poor distal opacification in 62% of cases, with a diseased distal landing zone and/or a distal luminal diameter <2 mm characterizing 38% of lesions, p <0.05 for both the triple-wise comparisons).

Regarding the characteristics of the collateral channels, the majority were classified as CC1 (73%), however almost half of the cases in the IC group presented poor collateral connection function (42% labeled as CC0 vs 2% and 10% in the CC and mixed group, respectively); likewise, collateral recipient artery filling was suboptimal (Rentrop grade 0 or 1) in 46% of the IC cases and 2 times the proportions observed in the other groups (Rentrop grade 0 or 1 : 21% CC and 20% mixed). In the mixed group, distal visualization of the CTO was mainly provided by IC, CC, or bypass grafts in 51%, 46% and 3% of the cases, respectively. The angiographic data are shown in Table 2.

Regarding the procedural setup, the majority of IC cases were performed using a single access approach (96% vs 35% in the CC and 74% in the mixed group, p <0.001); in line with the MHA specifications, 7Fr was the access size of choice in most of the IC cases (7Fr: 60%; 6Fr: 40%). On the contrary, a dual access approach was frequently necessary in the CC group (65% CC vs 4% IC and 26% mixed, p <0.001) (Figure 2). Overall, a single- or dual-forearm access was performed in 60% and 37% of the cases, respectively, whereas a single-femoral, dual-femoral, or forearm/femoral in approximately 1% each.

Table 2
Angiographic characteristics

| | Overall (n = 209) | Ipsilateral (n = 45) | Contralateral (n = 92) | Mixed (n = 72) | p-value |
|---|---|---|---|---|---|
| Target CTO vessel | | | | | **<0.001** |
| LM | 2 (1) | 0 (0) | 2 (2) | 0 (0) | |
| LAD | 56 (27) | 14 (31) | 22 (24) | 20 (28) | |
| LCx | 44 (21) | 23 (51) | 10 (11) | 11 (15) | |
| RCA | 102 (49) | 3 (7) | 58 (63) | 41 (57) | |
| Others | 5 (2) | 5 (11) | 0 (0) | 0 (0) | |
| CTO location | | | | | 0.279 |
| Proximal | 49 (23) | 7 (16) | 22 (24) | 20 (28) | |
| Mid-segment | 116 (56) | 28 (62) | 46 (50) | 42 (58) | |
| Distal | 23 (11) | 7 (16) | 11 (12) | 5 (7) | |
| Ostial | 21 (10) | 3 (6) | 13 (14) | 5 (7) | |
| Dominance | | | | | **0.005** |
| Right | 197 (94) | 38 (84) | 90 (98) | 69 (96) | |
| Left | 12 (6) | 7 (16) | 2 (2) | 3 (4) | |
| In-stent CTO | 24 (12) | 8 (18) | 9 (10) | 7 (10) | 0.327 |
| CTO vessel diameter by visual estimation (mm) | 3 [3.0-3.5] | 3 [2.5-3.0] | 3 [3.0-3.5] | 3 [3.0-3.5] | **<0.001** |
| Lesion length by visual estimation (mm) | 18 [10-30] | 16 [10-30] | 30 [15-40] | 17 [10-30] | **0.003** |
| Lesion length >20mm | 101 (48) | 17 (38) | 55 (60) | 29 (40) | **0.013** |
| Blunt stump | 74 (35) | 12 (27) | 39 (42) | 23 (32) | 0.146 |
| Moderate or severe calcification | 122 (58) | 21 (47) | 62 (67) | 39 (54) | **0.046** |
| Intra-lesion bending >45° | 147 (70) | 28 (62) | 73 (79) | 46 (64) | **0.040** |
| Retry | 33 (16) | 9 (20) | 9 (10) | 15 (21) | 0.207 |
| J-CTO score | 2.3 ± 1.1 | 1.9 ± 1.2 | 2.6 ± 1.2 | 2.1 ± 0.9 | **0.002** |
| EuroCTO score | 2.1 ± 1.3 | 1.8 ± 1.3 | 2.5 ± 1.4 | 1.74 ± 1.1 | **<0.001** |
| PROGRESS-CTO score | 1.5 ± 0.9 | 2.0 ± 0.9 | 1.3 ± 0.8 | 1.4 ± 0.9 | **<0.001** |
| Good distal opacification | 101 (48) | 17 (38) | 55 (60) | 29 (40) | **0.013** |
| Diseased distal landing zone and/or a distal lumen diameter <2 mm | 61 (29) | 17 (38) | 26 (28) | 18 (25) | **0.016** |
| Collateral function (Werner) | | | | | **<0.001** |
| CC0 | 28 (14) | 19 (42) | 2 (2) | 7 (10) | |
| CC1 | 152 (73) | 14 (53) | 68 (74) | 60 (85) | |
| CC2 | 28 (14) | 2 (4) | 22 (24) | 4 (6) | |
| Collateral recipient artery filling (Rentrop) | | | | | **0.002** |
| grade 0 | 9 (4) | 6 (13) | 1 (1) | 2 (3) | |
| grade 1 | 45 (22) | 15 (33) | 18 (20) | 12 (17) | |
| grade 2 | 32 (15) | 7 (16) | 17 (19) | 8 (11) | |
| grade 3 | 122 (59) | 17 (38) | 56 (61) | 49 (69) | |
| Collateral channels providing distal visualization | | | | | **<0.001** |
| Ipsilateral | 81 (39) | 45 (100) | 0 (0) | 37 (51) | |
| Contralateral | 117 (56) | 0 (0) | 84 (91) | 33 (46) | |
| via bypass | 11 (5) | 0 (0) | 8 (9) | 2 (3) | |

CC = collateral connection; CTO = chronic total occlusion; J-CTO = Japanese-CTO; LAD = left anterior descending artery; LCx = left circumflex artery; LM = left main coronary artery; PROGRESS = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA = right coronary artery.

Data are presented as n (%) or mean ± SD or median [IQR].

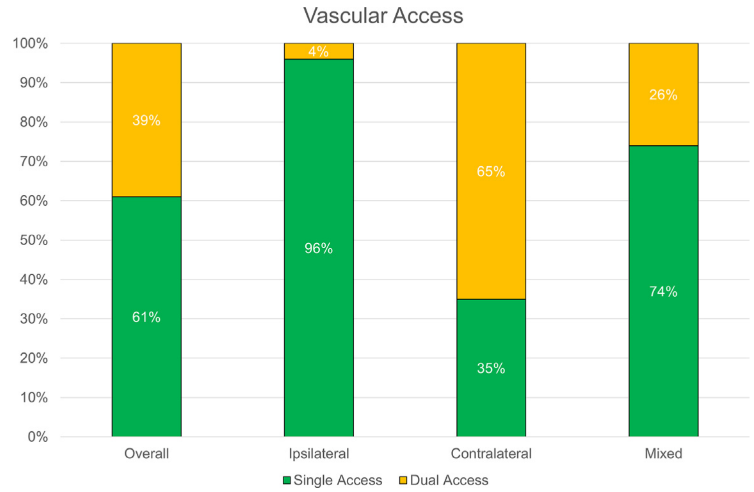


Figure 2. Proportions of single versus dual access in the entire study cohort and in the different collateral subgroups.

The starting CTO crossing technique significantly differed among the groups: the anterograde approach (AWE or ADR) was chosen as the first intention in 92% of the IC PCI (vs 67% CC and 77% mixed), whereas the retrograde approach (RWE or RDR) in up to 33% of the CC procedures (vs 8% IC and 24% mixed). More than one technique was attempted in 27%, 44%, 24% of the IC, CC, and mixed cases, respectively (p = 0.016), and, finally, the most frequently successful crossing techniques were AWE (56%) and RDR (19%), although with different distribution among the groups, as displayed in Figure 3. As expected, the collaterals successfully crossed for RWE or RDR were mostly epicardial in the IC group (75%) and septal in the CC and mixed group (59% and 53%, respectively).

It is worth mentioning that in case of attempted retrograde procedure, a single-guiding approach was possible in the vast majority of the IC CTO-PCI (90%) compared with the CC and mixed groups (2% and 42%, respectively, p <0.001). Notably, the reported case of a single-guiding approach in the CC group refers to an attempted retrograde procedure that ultimately failed (started with a single retrograde guiding catheter) with discontinuation of further anterograde CTO crossing attempts.

When required, externalization was most commonly performed using the tip-in or rendez-vous techniques in the IC and mixed group, while in the CC group by the conventional externalization technique.

The procedural metrics (i.e., radiation dose, fluoroscopy, and procedural time) reflected the high procedural complexity, which appeared to be particularly pronounced for the CC CTOs. The procedural data are reported in Table 3.

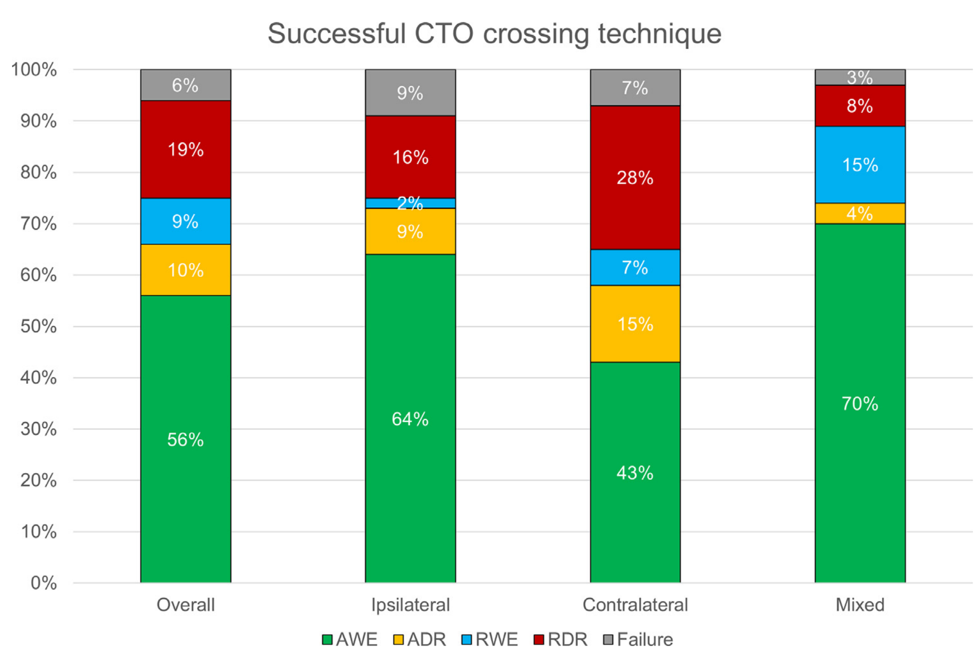


Figure 3. Proportions of successful CTO crossing technique in the entire study cohort and in the different collateral subgroups.

Table 3
Procedural data

| | Overall (n = 209) | Ipsilateral (n = 45) | Contralateral (n = 92) | Mixed (n = 72) | p-value |
|---|---|---|---|---|---|
| Single access | 128 (61) | 43 (96) | 32 (35) | 53 (74) | **<0.001** |
| Size of the antegrade guiding | | | | | **<0.001** |
| 6F | 144 (69) | 18 (40) | 75 (82) | 51 (71) | |
| 7F | 65 (31) | 27 (60) | 17 (18) | 21 (29) | |
| Size of the retrograde guiding* | | | | | 0.415 |
| 5F | 1/80 (1) | 0/2 (0) | 0/59 (0) | 1/19 (5) | |
| 6F | 77/80 (96) | 2/2 (100) | 57/59 (97) | 18/19 (95) | |
| 7F | 2/80 (2) | 0/2 (0) | 2/59 (3) | 0/19 (0) | |
| One guiding-only in attempted retrograde approach† | 20/82 (24) | 9/10 (90) | 1/48 (2) | 10/24 (42) | **<0.001** |
| Successful blind wiring‡ | 50/79 (63) | - | 31/54 (57) | 19/25 (76) | **0.137**§ |
| Dual-lumen microcatheter | 16 (8) | 4 (9) | 8 (9) | 4 (6) | 0.709 |
| Total number of guidewires used | 4 [3-7] | 4 [3-6] | 6 [4-8] | 4 [2-5] | **0.005** |
| Total number of microcatheters used | 1 [1-2] | 1 [1-2] | 1 [1-2] | 1 [1-1] | 0.286 |
| Guide-extension | 27 (13) | 5 (11) | 15 (16) | 7 (10) | 0.432 |
| Starting CTO crossing technique | | | | | **0.041** |
| AWE | 153 (73) | 41 (92) | 59 (64) | 53 (74) | |
| ADR | 5 (2) | 0 (0) | 3 (3) | 2 (3) | |
| RWE | 40 (19) | 2 (4) | 23 (25) | 15 (21) | |
| RDR | 11 (5) | 2 (4) | 7 (8) | 2 (3) | |
| More than 1 technique attempted | 69 (33) | 12 (27) | 40 (44) | 17 (24) | **0.016** |
| Successful CTO crossing technique | | | | | **<0.001** |
| AWE | 118 (56) | 29 (64) | 39 (43) | 50 (70) | |
| ADR | 21 (10) | 4 (9) | 14 (15) | 3 (4) | |
| RWE | 18 (9) | 1 (2) | 6 (7) | 11 (15) | |
| RDR | 39 (19) | 7 (16) | 26 (28) | 6 (8) | |
| Failure | 13 (6) | 4 (9) | 7 (7) | 2 (3) | |
| Anatomy of the collaterals successfully crossed for RWE or RDR‖ | | | | | 0.181 |
| Septal | 30/57 (53) | 2/8 (25) | 19/32 (59) | 9/17 (53) | |
| Epicardial | 21/57 (37) | 6/8 (75) | 9/32 (28) | 6/17 (35) | |
| Bypass | 6/57 (10) | 0/8 (0) | 4/32 (13) | 2/17 (12) | |
| Externalization technique in successful retrograde approach¶ | | | | | |
| Conventional externalization | 28/57 (49) | 1/8 (13) | 22/32 (69) | 5/17 (29) | **0.003** |
| Tip-in / rendez-vous maneuvers | 29/57 (51) | 7/8 (87) | 10/32 (31) | 12/17 (71) | **0.003** |
| Snaring | 2/57 (3) | 0/8 (0) | 2/32 (6) | 0/17 (0) | 0.445 |
| Total number of stents | 2 [1-2] | 2 [1-2] | 2 [1-3] | 2 [1-2] | 0.057 |
| Total stent length (mm) | 63 [40-96] | 48 [38-76] | 71 [38-111] | 63 [46-96] | 0.064 |
| Maximum stent diameter (mm) | 3.5 [3.0-3.5] | 3 [3.0-3.5] | 3.5 [3.0-3.5] | 3.5 [3.0-3.5] | 0.115 |
| Contrast volume (ml) | 250 [150-315] | 230 [140-350] | 280 [190-350] | 200 [150-280] | 0.134 |
| Radiation dose (mGy) | 1189 [651-2061] | 1040 [590-1975] | 1682 [876-2534] | 1050 [600-1580] | **0.043** |
| Fluoroscopy time (min) | 41 [22-70] | 28 [20-61] | 60 [35-83] | 29 [19-63] | **0.003** |
| Total procedural time (min) | 100 [60-160] | 90 [58-133] | 140 [100-178] | 70 [50-120] | **0.001** |

ADR = antegrade dissection re-entry; AWE = antegrade wire escalation; CTO = chronic total occlusion; RDR = retrograde dissection re-entry; RWE = retrograde wire escalation.

Data are presented as n (%) or mean ± SD or median [IQR].

* Data are reported as ratio (%) between the number of retrograde guiding catheters used for each size and the total number of retrograde guiding catheters.

† Data are reported as ratio (%) between the number of one guiding-only procedures and the total number of attempted retrograde approach procedures.

‡ Data are reported as ratio (%) between the number of successful blind wiring and the total number of attempted blind wiring.

§ Fisher's exact test.

‖ Data are reported as ratio (%) between the number of epicardial collaterals or septal collaterals or bypasses successfully crossed for retrograde approach and the total number of successful retrograde approaches.

¶ Data are reported as ratio (%) between the number of each specific externalization technique and the total number of successful retrograde approaches.

As outlined in Table 4, the technical and procedural success rates were high and comparable among the 3 groups (technical success: 93.8% overall, 91.1% IC, 92.4% CC, 97.2% mixed; procedural success: 91.9% overall, 88.9% IC, 89.1% CC, 97.2% mixed). Similarly, the occurrence of MACCE was low and did not significantly differ among the study groups. Namely, clinically relevant coronary perforation occurred in 4 patients: in 3 patients, a pericardiocentesis was performed because of impeding cardiac tamponade and in 2 of these patients, a covered stent implantation was needed to stop the bleeding source; in 1 case, the coronary perforation was tackled successfully by fat embolization. Of note, in none of the IC cases the coronary perforation was related to damage of the ICs themselves (for further details, see the Supplementary Materials).

Table 4
Procedural and periprocedural outcomes

| | Overall (n = 209) | Ipsilateral (n = 45) | Contralateral (n = 92) | Mixed (n = 72) | p-value |
|---|---|---|---|---|---|
| **Procedural outcomes** | | | | | |
| Technical success | 196 (93.8) | 41 (91.1) | 85 (92.4) | 70 (97.2) | 0.314 |
| Procedural success | 192 (91.9) | 40 (88.9) | 82 (89.1) | 70 (97.2) | 0.121 |
| **Procedural complications** | | | | | |
| Tamponade | 3 (1.4) | 2 (4.4) | 1 (1.1) | 0 (0) | 0.135 |
| Clinically relevant coronary perforation | 4 (1.9) | 2 (4.4) | 2 (2.2) | 0 (0) | 0.537 |
| Covered stents | 2 (0.9) | 2 (4.4) | 0 (0) | 0 (0) | |
| Pericardiocentesis | 3 (1.4) | 2 (4.4) | 1 (1.1) | 0 (0) | |
| Fat embolisation | 1 (0.5) | 0 | 1 (1.1) | 0 (0) | |
| Donor vessel damage | 1 (0.5) | 0 (0) | 1 (1.1) | 0 (0) | 0.528 |
| Vascular complication | 5 (2.5) | 0 (0) | 3 (3.3) | 2 (2.8) | 0.493 |
| Access site hematoma | 4 (1.9) | 0 (0) | 2 (2.2) | 2 (2.8) | |
| Pseudoaneurysm | 1 (0.5) | 0 (0) | 1 (1.1) | 0 (0) | |
| **Periprocedural adverse events** | | | | | |
| Myocardial infarction | 6 (2.9) | 1 (2.2) | 4 (4.3) | 1 (1.4) | 0.508 |

Data are presented as n (%).

Periprocedural type 4a MI was diagnosed in 6 patients overall (2.9%), although without need for urgent revascularization (for details, see the Supplementary Materials). No cases of periprocedural death, stroke, major bleeding, and stent thrombosis were reported.

Importantly, the vast majority of vascular complications reported in our cohort were represented by relatively minor hematomas, with no need for additional invasive intervention or blood transfusion, with just one case of pseudoaneurysm treated with thrombin injection.[16]

## Discussion

In the present study, we reported the baseline clinical and angiographic characteristics, and the procedural data and in-hospital outcomes of our single-center MHA CTO-PCI registry in patients stratified according to the collateral typology (solely IC or CC, vs mixed groups).

The main results of our analysis are as follows: (1) despite high lesion complexity, particularly pronounced in those cases with CC, the achieved technical and procedural success rates were uniformly high, with limited occurrence of procedural complications and in-hospital adverse events; (2) each group, as defined by the anatomy of the collateral channel connection, showed distinctive angiographic characteristics with regard to the target CTO vessel and the collateral channel size and function; (3) recanalization of CTOs with solely IC was largely possible through a single vascular access, preferentially adopting a large bore sheath (i.e., 7Fr); in contrast, dual access approach appeared to be necessary in the majority of CC-CTO cases but with a minimal need for femoral vascular puncture; (4) the CTOs with a mixed collateralization showed characteristics which were intermediate between the IC- and CC-CTO, possibly suggesting that the main source of collateralization (despite both being available) determined the technical features related to the CTO itself.

To the best of our knowledge, this is the first detailed description of the procedural characteristics and outcomes in CTO-PCI procedures grouped according to the kind of collateral vessel supply (i.e., IC, CC, or mixed).

The procedural success and complication rates observed in our study for the overall population and for each CTO subset are in line with those described in large recent registries of experienced centers[17]: the success and MACCE rates were reported to span between 81% and 90% and between 0.5% and 7%, respectively,[17−23] as illustrated in Figure 4 (keeping in mind the possibility of different definitions of these end points for each study). Importantly, although AWE generally represented the most commonly successful crossing technique,[22,24]—and this was consistent with our findings—the proportion of retrograde techniques and ADR use in our study was comparable with that of the above-mentioned registries,[20,22] and the grade of lesion complexity assessed by traditional dedicated CTO scores (e.g., mean J-CTO of 1.6 to 2.4). Nevertheless, none of these registries specifically investigate the characteristics of each CTO collateral-based phenotype.

According to our descriptive analysis, distinctive angiographic characteristics regarding the target CTO vessel and the collateral channel size and function emerged for each specific CTO subset. Namely, the most frequent target CTO vessel in the IC group was the LCx (51%), whereas the RCA was the most represented in the CC and mixed group (63% and 57%, respectively), and these frequencies are consistent with the scant data available to date.[3,5,6] In particular, as described by Mashayekhi et al,[4] it is extremely rare for a RCA CTO to have solely IC, as in 92% of cases with IC, accounting for 1/3 of the RCA CTOs, some CCs also coexist (a condition coherent with the definition of “mixed group” in our study). This might be explained by the very few branches proximal to the crux cordis, that could potentially give origin to IC channels.

Interestingly, almost half of the cases in the IC group presented poor collateral connection grade (42% Werner CC0), mainly epicardial, and, consistently, the collateral recipient artery filling was found to be suboptimal (Rentrop grade 0 or 1) in almost half of the cases, thus reducing the likelihood of feasible retrograde techniques. In contrast, the

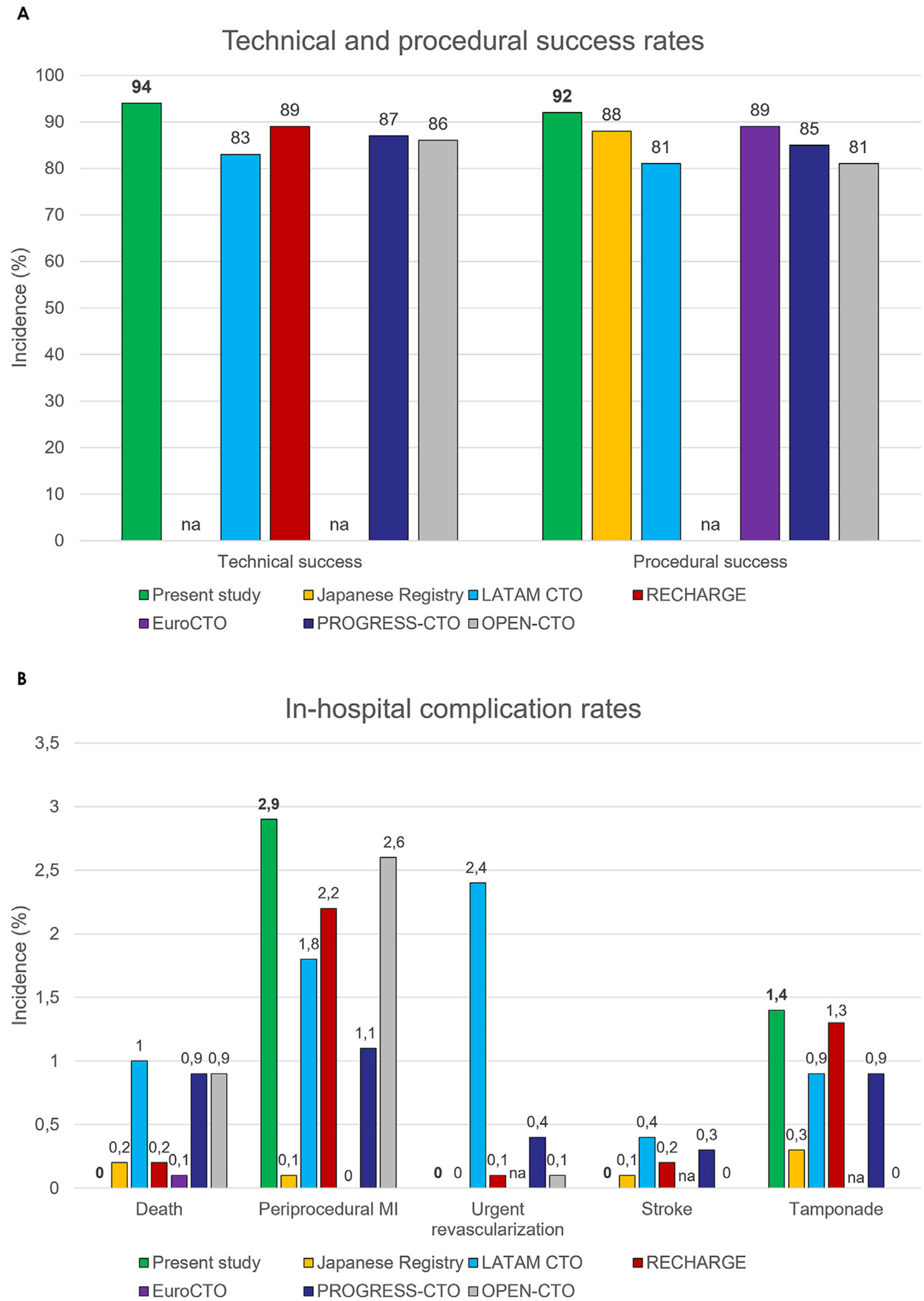


Figure 4. Success and complication rates in the present study and in large multicenter registries. (*A*) Technical and procedural success and (*B*) rates of complications and in-hospital adverse events in the present study and in large multicenter registries. Reproduced from data from referencess.[17–23]

frequently encountered poor distal target characterized by small or diseased vessels at the distal cap (38%) and poor distal angiographic visualization (62%) would have preferentially dictated an upfront retrograde approach[7] (and this was the case in only 4 patients, 8%), thus posing the need for carefully tailored considerations balancing advantages and drawbacks.

Importantly, even in the attempted retrograde IC cases, a single access 7Fr approach was the most frequent strategy of choice (90%), unlike previously available data.[6] This is likely to be referred to the different adopted treatment algorithm in the report by Azzalini et al: classic hybrid algorithm promotes the routine use of double access; in contrast, MHA limits the routine use of dual injection.[25]

The following aspects can be outlined for targeted procedural considerations. In case of CTO lesions with solely IC, likely involving the LCx with epicardial collaterals, advanced operator skills are required to tackle the frequently encountered poor collateral connection function and poor distal CTO target. Nevertheless, high level of procedural success can be achieved by a single access approach (favoring 7Fr bore sheath). On the contrary, a dual access approach is frequently required during CTO-PCI with solely CC, but femoral puncture is largely avoidable. In this typology, the main challenges are generally posed by the lesion complexity itself, in terms of length, presence of significant calcification, and in-segment tortuosity, whereas the quality of collateral channels is overall satisfying. Interestingly, the mixed phenotype appeared to be associated with a numerically higher procedural success, albeit not statistically significant; we can speculate that the presence of both IC and CC provides the operator with more interventional strategy options, ultimately leading to greater success with lower occurrence of clinically relevant complications.

The major limitations of the present study are the single-center and the retrospective design. Nevertheless, all procedures included in the study were all-comer consecutive patients treated with CTO-PCI after the MHA.

Besides, the CTO lesions were grouped according to the "angiographically visible" kind of collateral vessel supply, thus without taking into account the fact that several parallel collateral pathways may be "dormant" and "angiographically not visible." However, the purpose of this analysis was to provide useful practice-oriented insights for targeted procedural considerations starting from routinely available clinical and angiographic features.

Finally, it must be kept in mind that the MHA algorithm is meant for operators who are already proficient with all the classic hybrid techniques, and it should not be considered for interventionalists who want to start a CTO-PCI program.

Despite these limitations, the study provides valuable information on the distinctive baseline and procedural characteristics of specific CTO subsets, defined according to the anatomy of the collateral channels.

In conclusion, although differences in the baseline and procedural characteristics emerged according to collateral typology, the achieved technical and procedural success rates were uniformly high, with limited occurrence of procedural complications and in-hospital adverse events. Phenotyping CTO as hereby proposed might provide useful targeted procedural considerations.

## Declaration of Competing Interest

The authors have no competing interests to declare.

## Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.09.113.


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