

Percutaneous coronary intervention of chronic total occlusion: A 5-year monocentric experience

Angioplastie coronaire des occlusions totales chroniques : Une expérience monocentrique de 5 ans

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ABSTRACT

Background: Chronic total occlusions (CTO) occur in 15-30% of coronary angiogram, yet this challenging lesion subset represents less than 10% of percutaneous coronary interventions (PCI). Tunisian data are lacking. This study analyses a real-life Tunisian CTO-PCI immediate and long-term results.

Methods: Single-center, observational retro-prospective study, between 2018 and 2023. Primary endpoint was to assess technical success, major procedural complications, and target lesion failure (TLF) at 12-months. Secondary endpoint was to identify factors associated to technical failure.

Results: 115 patients, 122 CTOs lesions, 133 CTO-PCIs. Mean age 62 ± 14.4 years. Gender-Ratio=6. Mean J-CTO score was 1.47 ± 1.12 . Dual injection (43.6%) and microcatheters (50.4%) were underused. Number of guidewires per procedure was 2.35 ± 1.12 . Anterograde, retrograde and hybrid approaches were noted in 85%, 9% and 6%, respectively. Technical success was 69.2% (of 133 procedures) and procedural success was 73.0% (of 115 patients). Major complication rate stood at 3%. At 12 months, cardiovascular mortality was 7.0%, without difference according to procedural success. TLF was 9.4% among successful CTO-PCIs. Associated factors to technical failure were bifurcation involvement (OR=5.83 [1.7–20.1]; $p=0.005$), use of more than 4 guidewires per-procedure (OR=6.83 [1.6–28.7]; $p=0.009$), de-novo CTO (HR=8.43 [1.9–36.6]; $p=0.004$), previous attempts (OR=8.87 [1.8–43.6]; $p=0.007$), and no microcatheter use (OR=11.4 [3.5–36.8]; $p=0.001$).

Conclusion: This real-life study fills a gap in Tunisian data on CTO-PCI outcomes with technical success, complications and TLF rates comparable to those reported in literature. 12-month survival rates were similar between successful and failed procedure groups.

Key words: Chronic total occlusion, Prognosis, Percutaneous coronary intervention, Technical success.

RÉSUMÉ

Introduction : Les occlusions totales chroniques (CTO) sont fréquentes (15-30%) mais leur désocclusion ne présente que 10% des interventions coronaires percutanées (ICP). Les données tunisiennes sont rares. Cette étude vise à combler cette lacune en analysant les résultats à court et long terme.

Méthodes : Étude rétrospective monocentrique, entre 2018 et 2023. Le critère principal de jugement était le succès technique, les complications et les échecs de la lésion cible à 12 mois. Le critère secondaire était d'identifier les facteurs associés à l'échec technique.

Résultats : 115 patients, 122 lésions CTO, 133 procédures. Age moyen $62 \pm 14,4$ ans. Genre-Ratio=6. Le J-CTO score était $1,47 \pm 1,12$. L'injection controlatérale (43,6%) et l'utilisation de microcathéters (50,4%) étaient sous-utilisées. Le nombre du guide était de $2,35 \pm 1,1$ par procédure. L'approche antérograde, rétrograde et hybride étaient de 85%, 9,0% et 6,0%, respectivement. Le taux de succès technique était de 69,2% (133 procédures) et procédural de 73,0% (115 patients). Le taux de complications majeures était à 3%. À 12 mois, la mortalité cardiovasculaire était de 7,0% non influencée par le résultat procédural. L'échec de la lésion cible était de 9,4%. Les facteurs associés à l'échec technique étaient l'implication de bifurcations (OR=5,83 [1,69–20,10]; $p=0,005$), l'utilisation de plus de 4 guides (OR=6,83 [1,63–28,65]; $p=0,009$), les CTO de-novo (OR=8,43 [1,94–36,55]; $p=0,004$), les tentatives précédentes (OR=8,87 [1,82–43,62]; $p=0,007$), et la non-utilisation de microcathéter (OR=11,39 [3,53–36,77]; $p=0,001$).

Conclusion : Ce registre confirme des résultats immédiats satisfaisants de l'ICP de CTO. La survie à 12 mois était indépendante du résultat procédural.

Mots clés : Occlusion chronique totale, Intervention coronaire percutanée, Pronostic, Succès technique.

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INTRODUCTION

Chronic total occlusions (CTOs) are encountered in 15% to 30% of patients with coronary artery disease undergoing angiography (1-3), while CTO percutaneous coronary intervention (PCI) accounts for less than 10% of all PCI performed in experienced centers (4).

CTO-PCI began in the mid-1980s with Japanese interventionalists (5), and technological advancements helped it spread globally. However, it remains a major challenge due to long procedure times, procedural failures, life-threatening complications and high costs (6,7), making coronary bypass or medical treatment often more favourable options.

2021 guidelines from the American College of Cardiology/American Heart Association downgraded CTO treatment class from IIA to IIB due to two randomized trials showing no improvement in left ventricle function and neutral effects on hard outcomes (8). In contrast, 2018 European guidelines maintained a class IIA recommendation (9). Despite some controversies, recent studies, including observational and randomized trials, suggest that CTO-PCI may offer benefits in terms of quality of life, left ventricular function, and long-term survival (10–14). 2024 ESC guidelines on chronic coronary syndrome also highlighted that CTO is an anatomical predictor of incomplete revascularization and sustained that even if CTO-PCI improved symptoms and left ventricular function in randomized trials, it did not reduce myocardial infarction or mortality incidence (15).

Advances in technology and techniques, such as the retrograde approach and hybrid algorithm, have led to improved success rates and reduced major cardiovascular events. Successful CTO revascularization relies on rational patient selection, guided by clinical symptoms, advanced imaging techniques, and a multidisciplinary approach (16).

In front of the persisting lack in Tunisian data on CTO-PCI, this study aimed to explore immediate and long-term outcomes and identify factors related to technical failure.

METHODS

This was a descriptive, monocentric study, longitudinal and retro-prospective led between June 2018 and June 2023.

Study population

All patients undergoing CTO-PCI were included. CTO was defined as a coronary occlusion without antegrade flow (TIMI 0 flow) through the lesion with no thrombus, no staining at the proximal cap and presence of mature collaterals with a presumed or documented duration of ≥ 3 months (17,18).

Non-inclusion criteria were PCI of coronary occlusion of less than 3 months, and PCI of functional CTO defined as severely stenotic, yet less than 100% occlusion of the coronary artery with TIMI 1 flow for a duration greater than or equal to 3 months based on angiographic

evidence (19,20).

Patients whose data were incomplete and those who were unable or unwilling to give their consent were excluded from our study.

Data collection

Study population was selected from Cath-lab database, specifically using the "CardioReport" software. Two experienced operators reviewed all coronary angiograms and PCIs. A detailed datasheet was created for each patient, capturing demographic data, clinical details, angiographic findings, therapeutic approaches, and clinical outcomes. J-CTO score, CASTLE score and PROGRESS CTO score were calculated for all patients. Data were collected during hospitalization and included long-term follow-up assessments.

Lesion crossing strategies and nomenclature

Crossing strategies can be divided mainly into the antegrade and the retrograde approaches.

Antegrade approach refers to the technique of advancing guidewire and other catheter equipment in the forward direction, following natural flow of blood through coronary arteries, towards site of the occlusion. divided into 2 groups: (I) antegrade wire escalation/de-escalation and (II) antegrade dissection and re-entry (21).

Retrograde approach involves navigating guidewires and catheters through collateral vessels or pathways that bypass the occluded segment in the coronary artery, moving in a reverse direction from the distal (far) to the proximal (near) part of the occlusion. This includes retrograde wiring and retrograde dissection and reentry (18,21).

Hybrid approach is a flexible approach combining antegrade and retrograde techniques, luminal and subintimal lesion crossing techniques, it is used to optimize success rates in difficult CTO cases (22,23).

Follow-up

Follow-up was carried out either at our outpatient clinic or via the corresponding physician or, failing that, by telephone contact with the patient or his family in purpose to identify Major Cardiac Adverse Events (MACE). Minimal targeted follow-up was of 3 months after the last inclusion, with a Kaplan Meier further estimation of time to first studied events.

Angiographic controls were guided by clinically suspected ischemia or non-invasive test results performed at the discretion of the treating cardiologist. No systematic control was scheduled during the follow-up.

Study endpoints

Primary endpoint was to describe the immediate and long-term results of CTO-PCI regarding:

- **Technical success** was defined by successful CTO revascularization with achievement of $<30\%$ residual diameter stenosis within the treated segment and

restoration of TIMI grade 3 antegrade flow (5,17,24).

- **Procedural success** was defined as the achievement of technical success with no in-hospital MACE (5,17,24).

- **Major procedural complications** were noticed (death, coronary perforation ...).

- **Target Lesion Failure (TLF) at 12 months.** This was defined as a composite of cardiac death, target vessel-related myocardial infarction (TVMI), and target lesion revascularization (TLR), when the myocardial infarction or revascularization were driven by ischemia in the stented region. The secondary endpoint was to identify associated factors with technical failure.

Statistical analysis

Data were analysed using SPSS software version 26. Survival analysis was conducted with Kaplan-Meier curves, and multivariate logistic regression was used to identify predictors of technical failure. Variables with a significance level of <0.2 in univariate analysis were included in multivariate model, with a significance threshold set at <0.05.

Ethical considerations

This study was performed in accordance with the Declaration of Helsinki and good clinical practice.

RESULTS

Study flow chart is illustrated in figure 1.

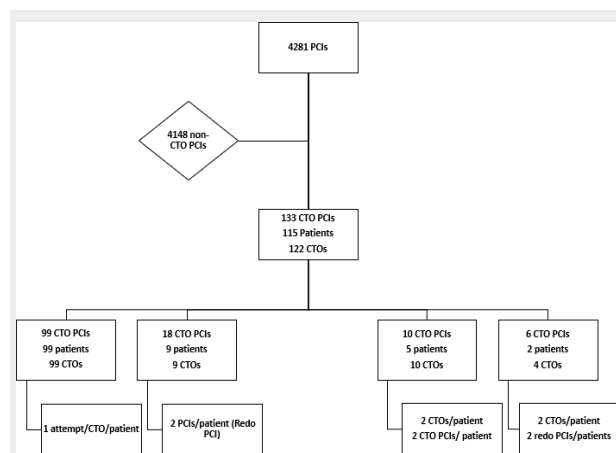


Figure 1. Study flowchart.

CTO: Chronic Total Occlusion, PCI: Percutaneous Coronary Intervention.

During the study period, a total 4.281 PCIs were performed. Among these procedures, 133 CTO-PCIs were performed on 115 patients with 122 CTO arteries. These represented 3.1% of the overall conducted PCIs.

Baseline characteristics

Mean age was 62±14.4 years. A male predominance (86.1% males) was noted.

Smoking emerged as the most prevalent cardiovascular risk factor (80.9%) as either current or former smokers.

ACS accounted for most revealing clinical presentations (54.8%), distributed as follows: 42.6% with either non-ST or ST segment elevation myocardial infarction, and 12.2% with unstable angina. A chronic coronary syndrome was observed in 45.2% of cases. Mean LVEF was 46.9±13.9%. Detailed clinical characteristics of the population are displayed in table 1.

Table 1. Baseline characteristics of the population.

	All patients (n=115)	CTO Success (n=85)	CTO Failure (n=30)	P value
Demographics				
Age (years)	62±14.4	61±9.6	61±12.4	0.902
Male gender	99 (86.1)	73 (85.9)	26 (86.7)	1
CVRF				
Current and former smoker	93 (80.9)	69 (81.2)	24 (80)	0.888
Current smoker	57 (49.6)	43 (50.6)	14 (46.7)	0.933
Diabetes	51 (44.3)	39 (45.9)	12 (40)	0.577
Hypertension	63 (54.8)	46 (51.4)	17 (56.7)	0.809
Dyslipidemia	57 (49.6)	42 (49.7)	15 (50)	0.956
BMI	26 [24-28.4]	26.1 [24-29.2]	25.9 [23.8-0.658 27.8]	
Medical history				
Previous PCI	50 (43.5)	37 (43.5)	13 (43.3)	1
Previous CABG	2 (1.7)	1 (1.2)	1 (3.3)	0.455
Cerebrovascular disease	4 (3.5)	3 (3.5)	1 (3.3)	1
Peripheral artery disease	6 (5.2)	3 (3.5)	3 (10)	0.182
Chronic obstructive pulmonary disease	2 (1.7)	1 (1.2)	1 (3.3)	0.455
Dialysis	6 (5.2)	6 (7.1)	0	0.337
Atrial fibrillation	3 (2.6)	1 (1.2)	2 (6.7)	0.166
Clinical revealing presentation				
Acute coronary syndrome	63 (54.8)	49 (57.6)	14 (46.7)	0.299
STEMI / NSTEMI	49 (42.6)	39 (45.9)	10 (33.3)	0.232
Unstable angina	14 (12.2)	10 (11.8)	4 (13.3)	0.757
Chronic coronary syndrome	52 (45.2)	36 (42.4)	16 (53.3)	0.299
Biology				
Hb	13±1.9	12.86±1.97	13.43±1.7	0.137
Platelet x1000	232±65	235±64	223±68	0.438
Creatinin	77 [70-97]	77 [68.5-94]	77.5 [70-103.5]	0.515
LVEF	46.9±3.9	47.6±13.5	44.8±14.8	0.374
LVEF ≥ 50%	57 (49.6)	43 (50.6)	14 (46.7)	0.712
40% ≤ LVEF < 50%	23 (20)	17 (20)	6 (20)	1
LVEF < 40%	35 (30.4)	25 (29.4)	10 (28.6)	0.818
Coronary status				
Single Vessel	21 (18.3)	12 (18.8)	5 (16.7)	0.793
Double Vessel	47 (40.9)	35 (41.2)	12 (40)	0.910
Triple Vessel	47 (40.9)	34 (40)	13 (43.3)	0.750
>1 CTO	28 (24.3)	17 (20)	11 (36.7)	0.067
Target vessel				0.918
LMCA	1 (0.8)	1 (0.8)	0	1
LAD	52 (39.1)	35 (38)	17 (41.5)	0.709
LCX	22 (16.5)	15 (16.3)	7 (17.1)	0.912

Table 1. Baseline characteristics of the population.

	All patients (n=115)	CTO Success (n=85)	CTO Failure (n=30)	P value
RCA	58 (43.6)	41 (44.6)	18 (42.9)	0.739
CTO location				
Ostial	15 (11.3)	9 (9.8)	6 (14.6)	0.553
Proximal	55 (41.4)	38 (41.3)	17 (41.5)	0.986
Mid	56 (42.1)	41 (44.6)	15 (36.6)	0.389
Distal	7 (5.3)	4 (4.3)	3 (7.3)	0.676

Values are mean±SD or n (%); BMI: Body Mass Index; CABG: Coronary Artery Bypass graft surgery; CVRF: Cardiovascular Risk Factors; CTO: Chronic Total Occlusion; Hb: hemoglobin; LAD: Left Anterior Descending artery; LCX: Left Circumflex artery; LMCA: Left Main Coronary Artery; LVEF: Left Ventricle Ejection Fraction; NSTEMI: Non-ST Elevation Myocardial Infarction; PCI: Percutaneous Coronary Intervention; RCA: Right Coronary Artery; STEMI: ST Elevation Myocardial Infarction.

Of the 122 target CTO arteries assessed, a majority (69.7%) supplied an underlying hypokinetic myocardium. Additional cardiac imaging tools were employed for further evaluation as mentioned in figure 2.

Angiographic and procedural data

Ninety-four patients (81.8%) had multi-vessel disease.

CTO PCI was performed on the right coronary artery (RCA) in 58 procedures (43.6%) followed by the left anterior descending coronary artery (LAD) in 52 cases (39.1%), left circumflex coronary artery (LCX) in 22 (16.5%), and on the left main in one case (0.8%). Mean CTO complexity scores were J-CTO score of 1.47 ± 0.86 ; CASTLE score of 1.19 ± 0.8 and PROGRESS CTO score of 0.62 ± 0.71 .

Mean CTO length was 25.74 ± 9.1 mm with 81 (60.9%) lesion length exceeding 20mm.

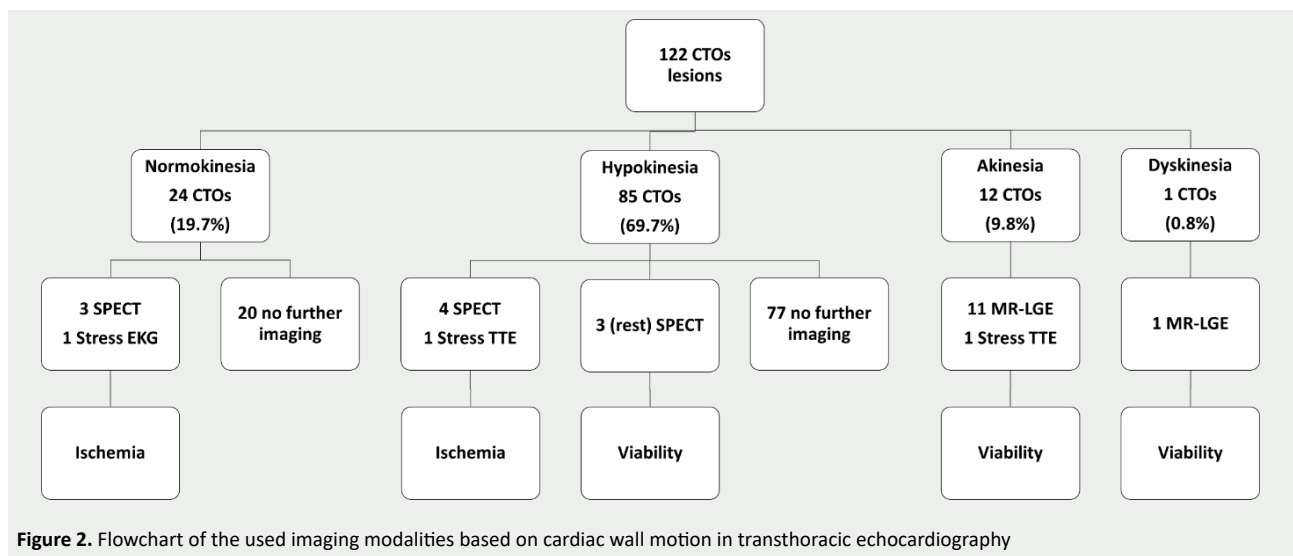
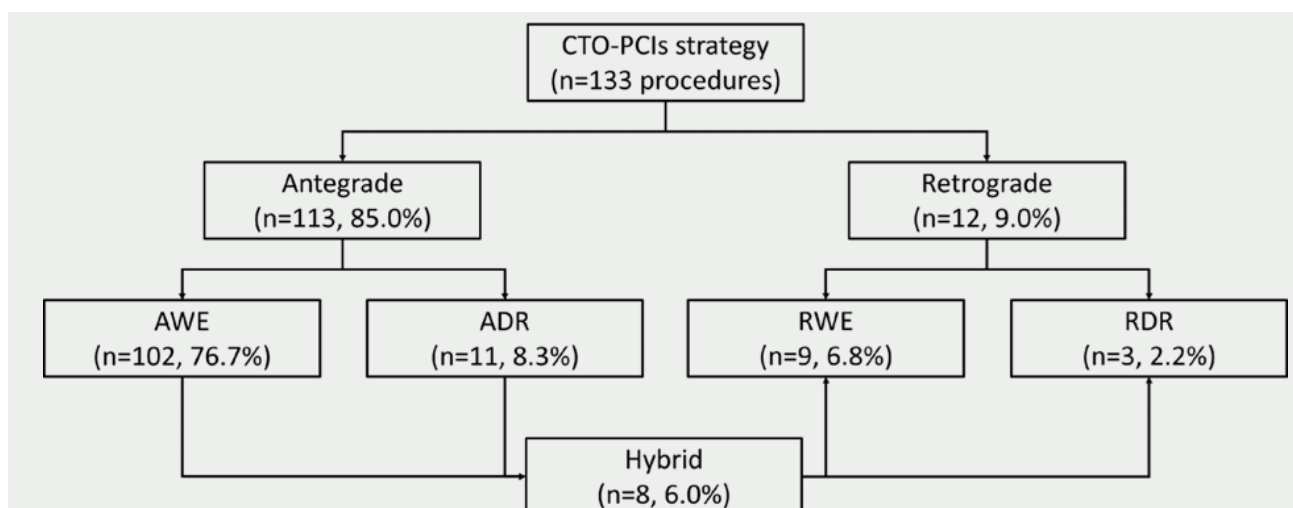
Dual arterial access sites for contralateral injections were used in 58 procedures (43.6%).

Average number of guidewires per lesion was 2.35 ± 1.12 .

Microcatheter was employed in 50.4% of procedures and over the wire (OTW) balloon was used in 1.5% of cases.

Guiding extension was used in 7 procedures (5.3%) while rotational atherectomy was employed in only one case (0.8%).

Anterograde approach was predominantly used in 85% of procedures followed by retrograde approach in 9% of cases. Hybrid approach was employed in 6% of procedures (Figure 3).

**Figure 2.** Flowchart of the used imaging modalities based on cardiac wall motion in transthoracic echocardiography**Figure 3.** Chronic total occlusion percutaneous coronary interventions strategies according to the hybrid algorithm (n=133).

ADR: Anterograde Dissection Re-entry; AWE: Anterograde Wire Escalation; CTO: Chronic Total Occlusion; PCI: Percutaneous coronary Intervention; RDR: Retrograde Dissection Re-entry; RWE: Anterograde Wire Escalation.

Technical and procedural success

Among 133 procedures, angiographic (technical) success was achieved in 92 procedures (69.2%) and a procedural success in 85 patients (73%).

No fatal complications were reported.

Procedural complications were noticed in four patients (3%): 1 coronary perforation, 1 dissection of the donor artery, 1 aorto-ostial dissection with tamponade and 1 right femoral artery dissection.

Angiographic and procedural data are summarized displayed in table 2. 159

Table 2. Angiographic and procedural data.

	All patients (n=115)	CTO Success (n=85)	CTO Failure (n=30)	P value
CTO occlusion duration				
Likely	77 (57.9)	56 (60.9)	21 (51.2)	0.298
Certain	50 (37.6)	33 (35.9)	17 (41.5)	0.539
Undetermined	6 (4.5)	3 (3.3)	3 (7.3)	0.372
In stent CTO	27 (20.3)	23 (25)	4 (9.8)	0.044
More than one segment	50 (37.6)	31 (33.7)	19 (46.3)	0.164
Bifurcation involvement	92 (69.2)	57 (62)	35 (85.4)	0.007
Moderate / severe tortuosity	2 (1.5)	1 (1.1)	1 (2.4)	0.523
Moderate / severe calcification	29 (21.8)	19 (20.7)	10 (24.4)	0.630
No or blunt stump	25 (18.8)	15 (16.3)	10 (24.4)	0.270
In CTO bend	10 (7.5)	4 (4.3)	6 (14.6)	0.068
Visual estimation of CTO length	25.89±9.67	24.64±9.21	28.68±10.20	0.033
CTO length >20mm	81 (60.9)	55 (59.8)	26 (63.4)	0.692
CTO scores				
J CTO score	1.47±0.86	1.30±0.83	1.83±0.83	0.001
CASTLE score	1.19±0.80	1.03±0.79	1.54±0.74	0.001
PROGRESS CTO score	0.62±0.71	0.62±0.72	0.63±0.69	0.913
Vascular access for CTO artery				
Radial	77 (57.9)	54 (58.7)	23 (56.1)	0.779
Femoral	56 (42.1)	38 (41.3)	18 (43.9)	
Catheter size				
6F	122 (91.7)	85 (92.4)	37 (90.2)	0.456
7F	11 (8.3)	7 (7.6)	4 (9.8)	
Contralateral injection	58 (43.6)	37 (40.2)	21 (51.2)	0.237
Microcatheter	67 (50.4)	53 (57.6)	14 (34.1)	0.012
OTW balloons	2 (1.5)	1 (1.1)	1 (2.4)	0.523
Total number of guidewires used per lesion	2.35±1.12	2.16±1.04	2.76±1.2	0.008
Hydrophilic coating wire	127 (95.5)	88 (96.7)	39 (95.1)	0.495
Polymer jacketed wire	79 (59.4)	47 (51.1)	32 (78)	0.004
Tapered tip wire	75 (56.4)	52 (56.5)	23 (56.1)	0.964
Guiding extension	7 (5.3)	6 (6.5)	1 (2.4)	0.305
Rotational Atherectomy	1 (0.8)	1 (1.1)	0	0.692
Approach				
Anterograde	113 (85)	82 (89.1)	31 (75.6)	0.044
Retrograde	12 (9)	6 (6.5)	6 (14.6)	0.121
Hybrid	8 (6)	4 (4.3)	4 (9.8)	0.203
Previous attempt	14 (10.6)	5 (5.4)	9 (21.9)	0.011
DES implantation	-	91 (98.9)	-	
POBA	-	1 (1.1%)	-	
Number of stents implanted per lesion	-	1.98±0.99	-	
Total stent length per lesion	-	62.14±25.82	-	
Average diameter of DES	-	2.97±0.50	-	
Procedural time (min)	43.5 [32.33-62.99]	43.75 [29.8-57.23]	42.41 [35.92-73.75]	0.209
Time of fluoroscopy (min)	30.67 [21.95-7.74]	31.75 [20.63-45.11]	30.31 [25.42-59.41]	0.257
Total of volume contrast administered (ml)	198.1±81.5	199.8±81.4	194.2±82.6	0.715
DAP (cGy/cm ²)	21983 [14967-33027]	21603 [14760-33129]	22377 [15338-32212]	0.954
Complete revascularization		61(71.8)		

Values are: mean ± SD or n (%); CTO: Chronic Total Occlusion; DAP: Dose Area Product; DES: Drug Eluting Stent; POBA: Plain Optimal Balloon Angioplasty; OTW: Over The Wire balloon.

Target lesion failure at 12 months

98.3% of patients have finished the minimal follow-up of 3 months. 73% of patients have successfully completed a follow-up period of 12 months. Median follow-up was about 22 [11-35] months.

All-cause and cardiovascular mortality were superimposed and were recorded in 8 patients (7.0%) at 12-month follow-up.

Notably one cardiac death (0.8%) resulted from a fatal myocardial infarction, while the second was linked to acute heart failure. Additionally, two deaths (1.7%) showed cardiac involvement alongside other factors

(bleeding, sepsis). Four patients passed away at home without an authenticated cause of death (Table 3).

Based on Kaplan-Meier estimation, survival rate (all-cause and cardiovascular mortality) was $92.0 \pm 2.7\%$ at 12 months. According to procedural success, there was not a significant difference between successful and failed CTO PCI groups at 12 months in terms of survival rates (all-cause and cardiovascular mortality), (91.7% vs 92.7% ; p Log Rank=0.933) (Figure 4).

It is of note that at 12 months, among successful group incidence of TLF was 9.4% (6 cardiac deaths, 2 TVMI/TLR in relation with 1 definite stent thrombosis and 1 in-stent restenosis) (Table 3).

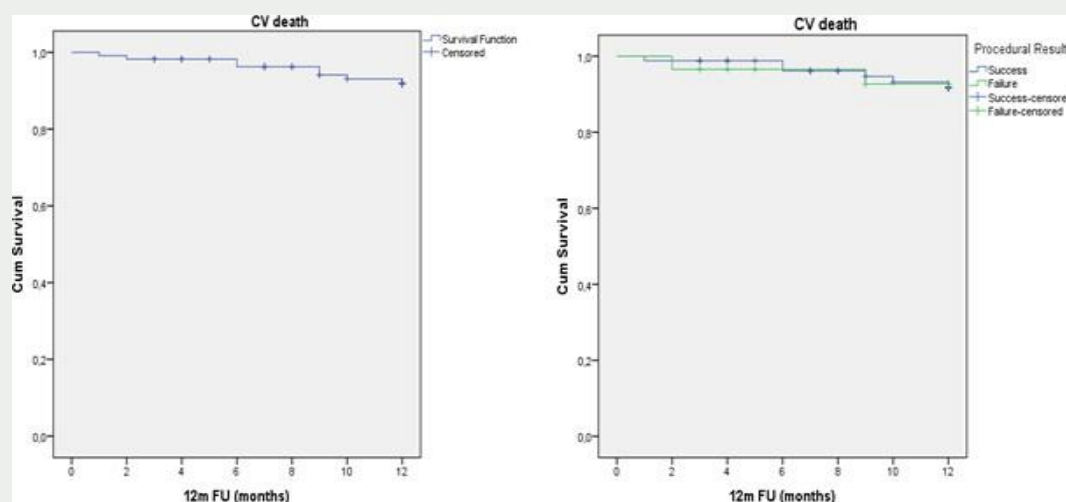


Figure 4. Overall and according to procedural result survival curves at 12 months (N=115 patients).

Table 3. Target lesion failure and its components at 12-month follow-up.

Case	Gender	Age (years)	LVEF (%)	CTO artery	CTO-PCI Result	CR	Event	Time to event	Details
1	M	84	35	Mid RCA	Success	No	Cardiovascular death	20 days	Cardiogenic shock Bleeding of non-determined aetiology
2	M	81	41	Mid LAD	Failure	No	Cardiovascular death	2 months	Cardiogenic shock Cardiorenal syndrome Sepsis
3	M	51	41	Proximal RCA	Success	Yes	Cardiovascular death	6 months	Acute heart failure
4	M	78	37	Ostial LAD	Success	Yes	Cardiovascular death	6 months	Fatal MI Probable ST DAPT cessation
5	F	70	55	Proximal RCA	Success	Yes	Undetermined death	9 months	—
6	F	71	30	Mid RCA	Failure	No	Undetermined death	9 months	—
7	F	62	25	Proximal LAD	Success	No	Undetermined death	10 months	—
8	M	53	60	Mid RCA	Success	No	Undetermined death	12 months	—
9	M	44	59	Proximal RCA	Success	Yes	Non-fatal TVMI TLR	13 days	Definite ST Stent length=48 mm
10	M	59	20	Distal RCA	Success	Yes	Non-fatal TVMI TLR	9 months	ISR Stent length=56mm Double stent layer

CR: Complete Revascularisation, CTO: Chronic Total Occlusion, DAPT: Dual Antiplatelet Therapy, F: Female, ISR: In-Stent Restenosis, LAD: Left Anterior Descending artery, LVEF: Left Ventricle Ejection Fraction, M: Male, MI: Myocardial Infarction, PCI: Percutaneous Coronary Intervention, RCA: Right Coronary Artery, ST: Stent Thrombosis, TLR: Target Lesion Revascularisation.

Secondary endpoint

Associated angiographic and procedural factors to technical failure in univariate analysis were in univariate analysis (Table 2):

- Angiographic factors: de-novo CTO, bifurcation

involvement, visual estimation of CTO length, J-CTO score and CASTLE score.

- Procedural factors: No use of microcatheter, number of guidewires ≥ 4 , polymer jacketed wire, non-antegrade approach, previous attempt.

Success rate according to J-CTO score is highlighted in figure 5.

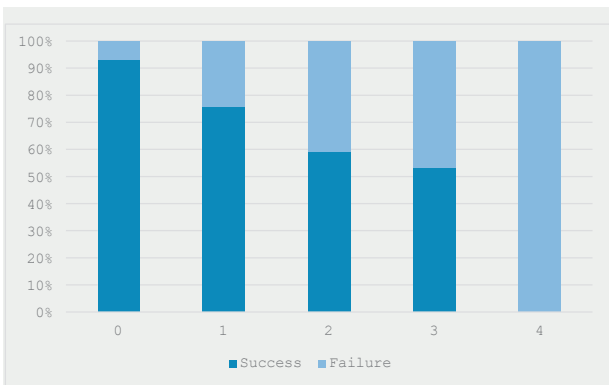


Figure 5. Success and failure rates according to J-CTO score categories.

Associated factors to technical failure on multivariate analysis were: bifurcation involvement (OR=5.83, IC95% [1.69 – 20.10], $p=0.005$), number of guidewires ≥ 4 (OR=6.83, IC95% [1.63 – 28.65], $p=0.009$), de-novo CTO (OR=8.43, IC95% [1.94 – 36.55], $p=0.004$), previous attempt (OR=8.87, IC95% [1.82 – 43.62], $p=0.007$) and no microcatheter use (OR=11.39, IC95% [3.53 – 36.77], $p<0.001$) (Figure 6).

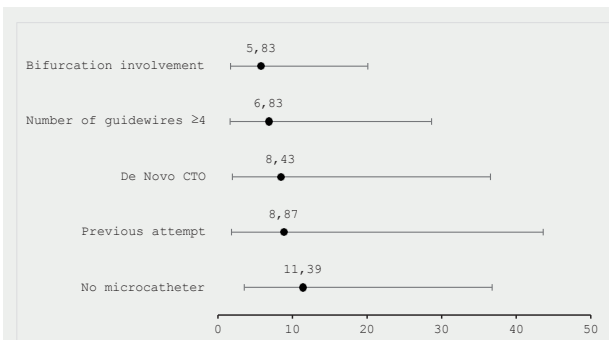


Figure 6. Forest plot representing associated factors to technical failure and their adjusted hazard ratios in multivariate analysis.

DISCUSSION

In this descriptive retro-prospective study, we gathered clinical, angiographic and procedural characteristics of 115 patients with 122 CTO lesions who underwent 133 PCI procedures between 2018 and 2023, being the largest Tunisian contemporary series.

The main findings of our study were:

- Mean J-CTO score was 1.47 ± 0.86 with a higher value observed in the failed PCI group versus successful PCI group (1.83 ± 0.83 vs. 1.30 ± 0.83 ; $p=0.001$). Attempted CTOs were easy or intermediate in 54.9% of cases whereas difficult (J-CTO=2) and very difficult (J-CTO ≥ 3) cases were noted in 45.1%.
- Microcatheters were underused in half of the procedures constituting 50.4%.
- Technical success was achieved in 69.2% of procedures and procedural success rate was 73% of patients.
- Major complications occurred in 3% of procedures

accounting tamponade, coronary perforation, donor artery dissection and dissection of femoral artery. All of them were successfully managed.

- At 12 months, all-cause and cardiovascular mortality were superimposed and were recorded in 8 patients (7.0%). According to procedural success, there was not a significant difference between the successful and the failed CTO PCI groups in terms of survival rates, (91.7% versus 92.7%; $p=0.934$).

- Determined associated factors to technical failure in CTO recanalization included bifurcation involvement, use of more than 4 guidewires per procedure, de-novo CTO, previous attempts and no use of microcatheter.

CTO-PCI represents a complex and high-risk procedure, with notable increased complications.

Hence, it is crucial to thoroughly assess indications and both immediate and long-term outcomes. Moreover, it is essential to interpret these outcomes in light of existing literature data for comprehensive understanding and context.

Comparison of baseline, angiographic and procedural characteristics with literature data:

In this study, mean age was 62 ± 14.4 years, consistent with other studies where the average age is between 60 and 70 years. Male predominance was observed across major CTO studies, including ours. Smoking and hypertension were the dominant cardiovascular risk factors, with diabetes mellitus ranking fifth at 44.3%, differing from international trends where dyslipidaemia is more prevalent. Our findings aligned with Tunisian studies, such as the FAST- MI and TAHINA registries (25,26). Prevalence of PCI history was consistent with other studies (16%-65%), while CABG history was underrepresented (1.7%). Clinical presentation showed more acute coronary syndrome (54.8%), similar to the OPEN CTO and DECISION CTO trials, although there were some variations in coronary syndrome types (27,28). Mean LVEF was 46.9% with 30.4% of patients having LVEF $<40\%$, which is lower compared to studies reporting preserved LVEF (DECISION CTO and PROGRESS CTO) (28,29). In summary, this registry had a high prevalence of smoking, more ACS cases, and lower LVEF.

In this study, most attempted CTO artery was RCA (43.6%), followed by LAD (39.1%) and LCX (16.5%), aligning with most studies except the EXPLORE CTO trial (30), which reported more LCX than LAD. LM CTO was rare in our study (0.8%), consistent with the OPEN CTO and ERCTO registries (27,31). In-stent CTO recanalization was higher in this registry (20.3%) compared to other trials (7.17%-10.7%). CTO length was shorter (25.89 ± 9.67 mm) than in other studies (around 30 mm), and 60.9% of lesions were ≥ 20 mm, lower than in the DECISION CTO trial (28). Calcification rates varied across studies, with current registry showing moderate to severe calcifications in 37.2%. Proximal cap characteristics also differed, with 18.8% having non-tapered caps in this study. CTO tortuosity was rare in study population (1.5%). J-CTO score was lower indicating less complex lesions. In

summary, population in this series had lower CTO complexity with higher in-stent CTO prevalence than major CTO registries.

This real-life study reported a lower technical success rate (69.2%) compared to literature, with the EXPLORE CTO study (77%) being the closest (30). The REVASC Trial (99%) had the highest success rate (32), followed by DECISION CTO (91%) (28) and EURO CTO (86.6%) (10,28). Variability in success rates across studies can be attributed to differing definitions of technical success, as there is no standardized criterion. In this study, technical success was defined according to the CTO-Academic Research Consortium consensus. While most studies agree on achieving <30% residual stenosis, other studies, like OPEN CTO and ERCTO (27,31), use more specific criteria such as guidewire positioning or TIMI flow grade. These differences highlight the variability in success definitions across trials, emphasizing the need to consider each study's context when evaluating outcomes.

This registry showed several unique aspects in CTO recanalization procedures. Anterograde approach was most common (85%), with radial access used in over 50% of cases, higher than in other studies. Contralateral injection was used in only 43% of cases, significantly lower than the EUROCTO and ERCTO registries (10,31). Mean number of used guidewires, microcatheter, extension catheter, rotational atherectomy use were lower compared to other studies. Intravascular imaging was not employed. DES implantation was the default strategy in successful cases, aligning with current guidelines. The lower procedural complexity in our study, reflected in lower J-CTO scores, may explain lower average procedure times, fluoroscopy times, and radiation exposure compared to other registries. In summary, key differences include high radial access use but limited contralateral injection, microcatheter and other advanced techniques use.

Comparison of clinical outcome with literature data

Data from this series were consistent with a higher cardiovascular mortality rate at 12 months (7%) compared to the DECISION CTO (1.9%) and EUROCTO (0.8%) trials. Complication rate was low at 3%, similar to the EUROCTO trial (2.9%) but higher than the DECISION CTO trial (0.7%). Incidence of myocardial infarction (1.7%) was comparable to DECISION CTO and EUROCTO. TLR was 1.7%, lower than in both the EUROCTO (2%) and DECISION CTO (7.9%) trials. In summary, CTO-PCI patients in this registry had higher mortality, low complications, and similar TLR rates compared to literature (10,28).

Comparison of associated factors to technical failure with literature data

Factors associated with technical failure in CTO PCI in our registry include de-novo CTO, bifurcation involvement, previous attempts, non-use of microcatheters, and the use of more than four guidewires. De-novo CTO cases, compared to in-stent CTO, present challenges in re-entry and restenosis, with antegrade approaches showing

higher success rates (69.5% vs. 60.8%) (33).

Hybrid approaches have shown comparable success in both de-novo and in-stent cases (34).

Bifurcations complicate procedures, requiring IVUS to enhance safety and success (35, 36).

The J-CTO score helps predict success but may not always correlate with technical failure in multivariate analysis (37, 38). The CASTLE score, incorporating factors like age and CABG history, is also a predictor of outcomes (39). Microcatheter use is linked to higher success rates, as shown in this registry (40, 41). Number of guidewires used, especially when more than four are necessary, correlates with failure (42). Polymer-jacketed wires, despite their widespread use, were also linked to failure in this registry, contradicting findings from the PROGRESS CTO registry that suggest better success with polymer wires (43). Retrograde approaches, often necessary after previous failed attempts, tend to have lower success rates but can still be successful with more sophisticated techniques (44, 45, 46).

Comparing predictors across different studies can be challenging due to the small sample size in this study, absence of elaborated angiographic and procedural characteristics of CTOs in some trials, and variations in the definitions used to detect angiographic features. Additionally, it's worth noting that advancements in materials and techniques have significantly transformed CTO PCI over the past five years. Therefore, in this monocentric study, being at the initial stage of CTO recanalization makes the comparison to recent trials challenging and unreliable.

Study limitations

This study is a single-center, retrospective observational analysis. The small sample size results in a limited number of cardiac events, which reduces the statistical power of the study.

Additionally, absence of a comparison group, such as non-CTO PCIs or patients receiving medical treatment, hinders a broader understanding of the results. Finally, due to differences in inclusion and exclusion criteria, follow-up protocols, as well as limited resources in terms of CTO dedicated devices, often expensive in a developing country, comparing our findings to those of major randomized trials and registries may not yield fully reliable or comparable conclusions.

CONCLUSION

This real-life study fills a gap in Tunisian data on CTO-PCI outcomes with technical success (69.2%), complications (3%) and TLF at 12 months (7%) rates comparable to literature. In multivariate analysis, associated factors to technical failure in CTO recanalization included previous attempts, de-novo CTO, bifurcation involvement, use of more than 4 guidewires per procedure, and no microcatheter use. If successful, CTO-PCI did not improve 12-month survival rates, which should be interpreted with caution due to the limited sample size and the

relatively short follow-up duration.

Abbreviations:

CTO: Chronic Total Occlusion

PCI: Percutaneous Coronary Intervention

TLF: Target Lesion Failure

TLR: Target Lesion Revascularisation

TVMI: Target Vessel Myocardial Infarction

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