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Original article

Interventions in chronic total occlusions with bifurcation lesions: incidence, treatment, and in-hospital outcome

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ABSTRACT

Introduction and objectives: Coronary chronic total occlusions (CTO) involving bifurcation lesions are a challenging lesion subset that is understudied in the literature. This study analyzed the incidence, procedural strategy, in-hospital outcomes and complications of percutaneous coronary interventions (PCI) for bifurcation-CTO (BIF-CTO).
Methods: We assessed data from 607 consecutive CTO patients treated at the *Institut Cardiovasculaire Paris Sud* (ICPS), Massy, France between January 2015 and February 2020. Procedural strategy, in-hospital outcomes and complication rates were compared between 2 patient subgroups: BIF-CTO (n = 245 = and non–BIF-CTO (n = 362).
Results: The mean patient age was 63.2 ± 10.6 years; 79.6% were men. Bifurcation lesions were involved in 40.4% of the procedures. Overall lesion complexity was high (mean J-CTO score 2.30 ± 1.16, mean PROGRESS-CTO score 1.37 ± 0.94). The preferred bifurcation treatment strategy was a provisional approach (93.5%). BIF-CTO patients presented with higher lesion complexity, as assessed by J-CTO score (2.42 ± 1.02 vs 2.21 ± 1.23 in the non–BIF-CTO patients, *P* = .025) and PROGRESS-CTO score (1.60 ± 0.95 vs 1.22 ± 0.90 in the non–BIF-CTO patients, *P* < .001). Procedural success was 78.9% and was not affected by the presence of bifurcation lesions (80.4% in the BIF-CTO group, 77.8% in the non–BIF-CTO-CTO group, *P* = .447) or the bifurcation site (proximal BIF-CTO 76.9%, mid–BIF-CTO 83.8%, distal BIF-CTO 85%, *P* = .204). Complication rates were similar in BIF-CTO and non–BIF-CTO**.**
Conclusions: The incidence of bifurcation lesions is high in contemporary CTO PCI. Patients with BIF-CTO present with higher lesion complexity, with no impact on procedural success or complication rates when the predominant strategy is provisional stenting.

Intervención de lesiones en bifurcación relacionadas con oclusión coronaria crónica total: incidencia, tratamiento y resultados hospitalarios

Palabras clave:
Oclusión crónica total
Bifurcación
Intervención coronaria percutánea
Stent condicional
OCT en bifurcación

RESUMEN

Introducción y objetivos: Las oclusiones coronarias crónicas totales (OCT) que afectan a lesiones en bifurcación representan un subconjunto de lesiones difíciles de tratar y poco estudiadas en la literatura. Este estudio analiza la incidencia, la estrategia de tratamiento, los resultados hospitalarios y las complicaciones de la intervención coronaria percutánea (ICP) de las OCT en bifurcación (OCT-BIF).
Métodos: Se evaluaron los datos de 607 pacientes consecutivos con OCT tratados en el *Institut Cardiovasculaire Paris Sud* (ICPS), Massy, Francia, entre enero de 2015 y febrero de 2020. Se compararon 2 subgrupos de pacientes (OCT-BIF, n = 245; OCT-no BIF, n = 362) en cuanto a estrategia de procedimiento, resultado hospitalario y tasa de complicaciones.
Resultados: La media de edad de los pacientes fue 63,2 ± 10,6 años; el 79,6% eran varones. Las lesiones en bifurcación estuvieron implicadas en el 40,4% de los procedimientos. La complejidad general de la lesión fue alta (valores medios de las puntuaciones J-CTO, 2,30 ± 1,16, y PROGRESS CTO, 1,37 ± 0,94). El *stent* condicional fue la estrategia preferida para el tratamiento de las lesiones en bifurcación (93,5%). Los pacientes OCT-BIF presentaban una mayor complejidad de la lesión según la puntuación J-CTO (2,42 ± 1,02 frente a 2,21 ± 1,23 de los pacientes OCT-no BIF; p = 0,025) y la puntuación PROGRESS CTO (1,60 ± 0,95

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frente a 1,22 ± 0,90 de los pacientes OCT-no BIF; p < 0,001). El éxito de la intervención fue del 78,9% y no se vio afectado por la presencia de bifurcación (el 80,4% en el grupo de OCT-BIF y el 77,8% en el grupo de OCT-no BIF; p = 0,447) ni por el lugar de la bifurcación (OCT-BIF en segmento proximal, el 76,9%; OCT-no BIF en segmento medio, el 83,8%; OCT-BIF en segmento distal, el 85%; p = 0,204). Las tasas de complicaciones fueron similares en ambos grupos.

Conclusiones: La incidencia de lesiones en bifurcación es alta en las ICP de OCT contemporáneas. Los pacientes con BIF-OCT presentan una mayor complejidad de las lesiones, sin que ello repercuta en la tasa de éxito de la intervención ni en la tasa de complicaciones siempre y cuando se aplique predominantemente una estrategia de implante de *stent* condicional.

Abbreviations

BIF-CTO: chronic total occlusion involving bifurcation lesion
CTO: chronic total occlusion
PCI: percutaneous coronary intervention

INTRODUCTION

Coronary chronic total occlusions (CTO) are identified in 18% to 20% of patients with coronary artery disease in contemporary series and their incidence increases with age.[1,2] The prevalence of CTO exceeds 40% in patient with diabetes and heart failure.[3,4] Most patients are managed medically or are referred for coronary artery bypass grafting (CABG), with less than 10% being treated with percutaneous techniques.[5]

Coronary bifurcations are by nature prone to the development of atherosclerotic lesions and account for 15% to 20% of all percutaneous coronary interventions (PCI)[6] and have lower success rates and higher complication rates than nonbifurcation lesions.[7,8] In the context of a CTO, bifurcation lesions often pose an additional challenge, as side branch (SB) wiring and protection can be more difficult. Moreover, contemporary CTO PCI can involve dissection re-entry techniques that cause SB compromise. Conversely, the presence of a SB can be beneficial in selected cases. For example, a proximal SB might offer the possibility of intravascular ultrasound (IVUS)-guided puncture; equally, a SB within the CTO body can be considered as an island and aid access to the CTO by splitting it in 2 parts.

The aim of this study was to determine the incidence, procedural strategy, in-hospital outcomes and complications of CTO PCI involving bifurcation lesions and compare 2 patient cohorts (BIF-CTO and non–BIF-CTO) treated in a high-volume European center in France.

METHODS

We retrospectively assessed data from 607 consecutive patients undergoing CTO PCI between January 2015 and February 2020 at the *Institut Cardiovasculaire Paris Sud* (ICPS), Massy, France. Of these, 245 patients (40.4%) had a SB ≥ 2 mm located within 5 mm of the proximal or distal cap or within the occluded segment. Procedural strategy, in-hospital outcomes and complication rates were compared between the 2 patient cohorts (BIF-CTO and non–BIF-CTO). The treatment indication was symptomatic myocardial ischemia and/or evidence of reversible myocardial ischemia on perfusion imaging or stress testing, as proposed in the EuroCTO Club position paper.[9] Patients were requested to provide informed consent before the procedure. The study was performed in accordance with the Declaration of Helsinki. Systematic troponin evaluation was performed on day 1 to evaluate myocardial injury.

Definitions

A coronary CTO is defined as a total occlusion in a coronary artery with noncollateral thrombolysis in myocardial infarction (TIMI) flow grade 0 for at least 3 months.[9] Patients were considered to have undergone retrograde CTO PCI if a guidewire was introduced into a collateral channel supplying the target vessel. A procedure was defined as an antegrade wire escalation if no guidewire was introduced into a collateral channel, as previously defined. A procedure was defined as antegrade dissection re-entry (ADR) if wire or device-based vessel dissection was adopted as part of the CTO recanalization strategy, either primarily or as bailout.

A bifurcation lesion is defined as a coronary artery narrowing occurring adjacent to, and/or involving, the origin of a significant SB.[10] Provisional stenting refers to the reconstruction of bifurcation anatomy with a single stent, implanted from the proximal to the distal segment of the main vessel (MV) across the ostium of the SB and followed by the systematic proximal optimization technique.[10,11] Two-stent techniques use a second stent implantation in the SB, either upfront or as bailout.[10] Specific techniques have been extensively studied in the literature and described in detail by dedicated groups of experts.[10,11] Anatomical criteria and the risk of SB occlusion/reaccess are key determinants of the treatment strategy, which is based either on MV stenting first (T/TAP-T/T and Protrusion-technique, culotte stenting) or SB stenting first (mini crush, inverted T/TAP, inverted culotte, DK-crush).[10,11]

The baseline bifurcation anatomy was assessed using the Medina classification.[12] The pattern of bifurcation disease was further classified into ‘true’ bifurcation lesions, in which the stenosis diameters in both the main branch and the SB were > 50% and ‘false’ bifurcation lesions, in which only the MV or the SB showed significant narrowing. Bifurcation lesions were divided into 3 types according to the SB take-off from the MV; bifurcation lesions within the occluded segment and those located within 5 mm of the proximal or distal CTO cap (figure 1). Lesions were further classified into 5 types to agree with relevant published literature.[13] The strategy for CTO revascularization and bifurcation treatment was left to the operator’s discretion.

Technical success was defined as angiographic success (final residual stenosis < 30% on visual estimation and TIMI flow grade 3 after CTO recanalization). Technical success was defined as residual stenosis of < 30% in the MV and a final TIMI flow grade 3 in both branches. Procedural success was defined as angiographic success without the occurrence of in-hospital major adverse cardiac events (MACE).

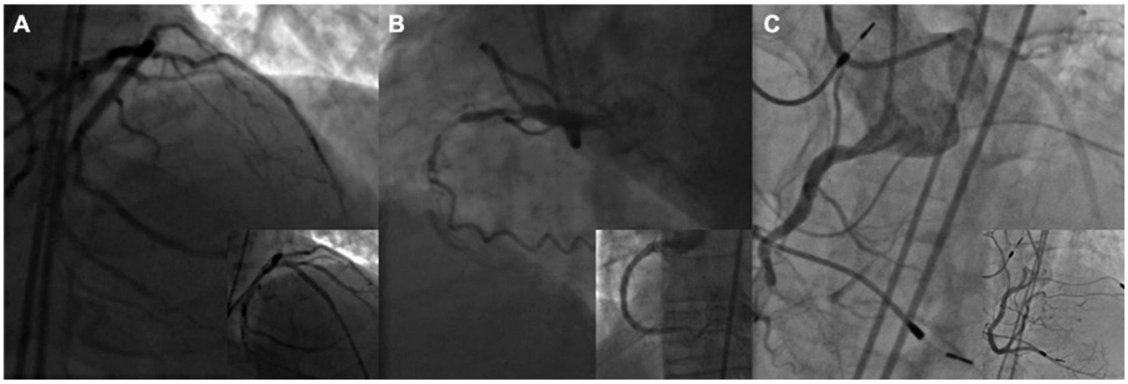

Figure 1. CTO bifurcation lesions divided according to side branch (SB) take-off from the main vessel. A: bifurcation lesion located within 5 mm proximal to CTO cap. B: bifurcation lesion arising within the CTO body. C: bifurcation lesion located within 5 mm distal to CTO cap. The final post-PCI angiographic result can be seen at the inserts. CTO, chronic total occlusion; PCI, percutaneous coronary intervention; SB, side branch.

In-hospital MACE were defined as a composite of non-Q wave and Q wave myocardial infarction (MI), recurrent angina requiring urgent repeat revascularization with PCI or CABG, stroke, death, pericardiocentecis, or surgical drainage of pericardial hematoma. Periprocedural MI definition was derived from the recent Academic Research Consortium-2 consensus document.[14]

Statistical analysis

Continuous variables are expressed as the mean ± standard deviation and were compared with 1-way analysis of variance. Categorical variables are expressed as percentages and were compared with the chi-square test. IBM SPSS Statistics version 22 software package (IBM Corporation, United States) and R language were used for all analyses. Two-sided *P* values < .05 were considered as indicative of statistical significance.

RESULTS

During a period of approximately 5 years (January 2015 to February 2020), operators from the ICPS, Massy, France performed 607 consecutive CTO PCI procedures. Mean patient age was 63.2 ± 10.6 years (79.6% male). Overall, patients with bifurcation lesions (BIF-CTO, 40.4%) and without bifurcation lesions (non–BIF-CTO, 59.6%) had similar baseline clinical characteristics, with a high prevalence of cardiovascular risk factors (table 1).

The angiographic data are summarized in table 2. Bifurcation lesions were more frequently located in the CTO of the left anterior descending artery (42.4%), followed by the right coronary artery (27.3%). CTO not involving BIF were predominantly located in the right coronary artery (67%), followed by the left anterior descending artery (16.1%) and the left circumflex coronary artery (10.5%). A blunt stump or no stump was identified in 69% of BIF-CTO lesions compared with 51.1% of non–BIF-CTO lesions (*P* < .001). BIF-CTO lesions also had more developed ipsilateral collaterals (48.2% vs 25.8%, *P* < .001). The characteristics of the remaining lesions and collateral circulation were similar between the 2 groups. The bifurcation was located at the proximal CTO cap in 63.7% of patients, followed by the distal CTO cap (29.8%), and the body of the occluded segment (6.5%).

The procedural characteristics are summarized in table 3. Procedural success was 78.9% (BIF-CTO 80.4% vs non–BIF-CTO-CTO 77.8%; *P* = .447). The main reason for failure was unsuccessful wire crossing. The radial artery was used for primary arterial access in 86.2% of patients (*P* = .259 for the 2 cohorts) and for secondary arterial access in 75.6% of patients (*P* = .223 for the 2 cohorts). Bilateral injection was applied in 83.6% of patients. The predominant approach was antegrade wire escalation (66.6% in BIF-CTO vs 69.2% in non–BIF-CTO-CTO; *P* = .586). ADR was used in 8.2% of patients (6.9% wire-based ADR and 1.3% device-based ADR; *P* = .957). Retrograde techniques were applied in 21.7% of CTO involving a bifurcation and 18.7% of CTO without a bifurcation (*P* = .356). Septal collateral channels were used in 65.8% of retrograde cases, followed by epicardial channels (32.5%; *P* = .73 between the 2 arms). Hydrophilic wires were used in 74.5% of patients, with soft and intermediate stiffness wires (≤ 3 gr tip load) with success in 52.9% of CTOs (*P* = .58 between the 2 treatment arms). Dual lumen microcatheters were more frequently used in BIF-CTO (11.4% vs 5.3% of non–BIF-CTO; *P* = .005). IVUS use was higher in BIF-CTO (4.9% vs 1.9%, *P* = .040). Procedural duration, contrast media use and radiation dosage were also higher in patients with BIF-CTO.

The angiographic and procedural characteristics of the BIF-CTO cohort (n = 245) are summarized in table 4. A proximal optimization technique was applied in all treated bifurcation lesions. The SB diameter was 2.30 ± 0.23 mm. True bifurcations [Medina (1,1,1), (1,0,1), (0,1,1)] were observed in 26.5% of the lesions. Dissection of the SB ostium occurred in 6.5%. A single stent strategy was adopted in 93.4% of treated bifurcations, followed by 2-stent techniques in 6.5% (13 patients treated with T/TAP technique, 2 with mini crush, 1 with culotte). Of these, an upfront 2 stent strategy was adopted in 3 patients (1.2%). Kissing balloon dilatation was applied to 63.3% of patients. SB TIMI III flow was preserved in 92.2% of patients. SB compromise had no impact on procedural success (*P* = .081).

Baseline SB wiring was performed in all the bifurcations located proximal to the CTO, but in only 51.8% of the SB located within and distal to the CTO. Dual lumen microcatheters were used for SB wiring in 10.6% of the patients.

Procedural complexity was higher in BIF-CTO patients, as assessed by the Multicenter Chronic Total Occlusion Registry of Japan (J-CTO) (2.42 ± 1.02 vs 2.21 ± 1.23; *P* = .025) and Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO) (1.60 ± 0.95 vs 1.22 ± 0.90; *P* < .001) scores (figure 2). The PROGRESS-CTO complication score was similar in the 2 study cohorts (table 5). The complication rate was also similar between the 2 study cohorts (table 6). Periprocedural MI, as assessed by high sensitivity troponin T, was 2.4% overall and was higher for BIF-CTO patients, but without statistical significance (3.2% vs 1.9%; *P* = .325). The perforation rate was 3.1% and cardiac death was 0.3% overall. Prolonged stays in the intensive care unit, acute kidney injury and

Table 1
Baseline clinical characteristics

Variable	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
Age, y	62.87 ± 10.31	63.42 ± 10.91	63.19 ± 10.63	.201
Male sex	78.4	80.4	79.6	.545
BSA, m²	2.02 ± 0.23	1.99 ± 0.21	2.00 ± 0.22	.269
BMI, kg/m²	28.56 ± 5.22	28.39 ± 4.95	28.94 ± 12.86	.701
Hypertension	62.5	69.0	66.4	.106
Dyslipidemia	73.7	73.6	73.7	.982
Smoking	50.0	51.9	51.9	.592
Current smoker	28.0	31.9	30.3	
Previous smoker	22.0	20.0	20.8	
Diabetes mellitus	31.0	34.5	33.1	.630
Medical treatment	26.3	28.4	27.6	
Insulin dependent	4.7	6.1	5.5	
Family history of CAD	25.0	24.3	24.6	.858
Clinical presentation				.278
Stable angina	62.0	53.3	56.8	
Acute coronary syndrome	4.9	5.5	5.3	
Asymptomatic	27.8	35.6	32.5	
Cardiac arrest	0.8	0.6	0.7	
Heart failure	4.5	5.0	4.8	
Angina	60	52.8	56.7	.174
Class 1	1.6	0.8	1.2	
Class 2	42.4	41.4	41.8	
Class 3	15.5	9.9	12.2	
Class 4	0.4	0.6	0.5	
Killip class				.302
Class 1	98.8	98.3	98.5	
Class 2	0.0	1.1	0.7	
Class 3	0.8	0.3	0.5	
Class 4	0.4	0.3	0.3	
Provocation test prior to PCI	41.2	50.4	46.7	.016
Stress test	0.0	3.1	1.8	
Myocardial scintigraphy	2.4	2.8	2.7	
CMR	38	44.3	41.7	
ECHO stress	0.8	0.3	0.5	
Creatinine, μmol/L	92.65 ± 41.51	95.17 ± 55.54	94.15 ± 50.35	.883
Clearance, mL/min	92.62 ± 33.50	89.79 ± 32.41	90.93 ± 32.85	.321
Clearance > 90 mL/min	47.5	45.7	46.4	.146
Clearance 60-89 mL/min	34.3	38.6	36.9	
Clearance 45-59 mL/min	14.0	8.2	10.5	
Clearance 30-44 mL/min	3.4	5.4	4.6	
Clearance 15-29 mL/min	0.0	0.6	0.3	
Clearance < 15 mL/min	0.8	1.4	1.2	
History of MI	17.1	14.6	15.7	.405
History of CAD	25	24.3	24.6	.858
History of CABG	7.8	7.8	7.8	1
History of stroke	2.9	2.2	2.5	.614
History of peripheral artery disease	3.7	6.6	5.4	.115
History of heart failure	4.1	3.0	3.5	.490
NYHA class 1	18.0	16.6	17.1	.316
NYHA class 2	3.7	2.2	2.8	
NYHA class 3	1.2	0.3	0.7	
NYHA class 4	0.0	0.0	0.0	

BIF-CTO, chronic total occlusion involving bifurcation lesion; BMI, body mass index; BSA, body surface area; CABG, coronary artery bypass grafting; CAD, coronary artery disease; CTO, chronic total occlusion; ECHO, echocardiogram; PCI, percutaneous coronary intervention; CMR, cardiovascular magnetic resonance imaging; MI, myocardial infarction; NYHA; New York Heart Association classification of heart failure.
Values are expressed as percentages or as mean ± standard deviation.

Table 2
Angiographic characteristics

Variable	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
Diseased vessels, No.	1.85 ± 0.72	1.86 ± 0.73	1.86 ± 0.73	.907
CTO vessel				
LM	0.4	0.0	0.2	.224
LAD	42.4	16.1	26.7	< .001
RCA	27.3	67.0	51.0	< .001
LCX	14.3	10.5	12.0	.163
Intermediate branch	2.0	0.3	1.0	.031
Diagonal branch	1.6	0.3	0.8	.070
Marginal branch	8.6	3.6	5.6	.009
RCA branch	0.8	1.4	1.2	.539
CTO location				
Ostial	3.2	1.9	2.1	.134
Proximal	39.1	38.0	38.5	.115
Mid	49.1	51.0	50.5	.162
Distal	8.6	9.1	8.9	.821
CTO vessel diameter, mm	2.75 ± 0.26	2.76 ± 0.30	2.76 ± 0.28	.781
CTO length, mm	29.12 ± 20.15	27.03 ± 14.82	27.87 ± 17.19	.474
CTO blunt stump	69	51.1	58.3	< .001
Interventional collaterals	95.1	93.1	93.9	.306
Ipsilateral collateral circulation	48.2	25.8	34.8	< .001
Werner classification				.590
CC0	0.5	1.1	0.8	
CC1	22.4	15.3	18.2	
CC2	77.1	83.6	81.0	
CTO vessel calcification				.721
Mild	37.6	40.2	39.1	
Moderate	58	54.3	55.8	
Severe	4.5	5.6	5.1	
Proximal tortuosity				.907
Straight (< 70° 1 bend)	66.1	68.7	67.7	
Slight (> 70° 1 bend)	24.1	21.3	22.4	
Moderate (> 90° 1 bend, > 70° 2 bends)	0.4	0.3	0.3	
Severe (> 120° 1 bend, > 90° 2 bends)	6.9	7.8	7.4	
Non applicable	2.4	1.9	2.1	
Distal opacification				.131
Absent/cannot be identified	0.8	0.8	0.8	
Faint	43.7	35.6	38.8	
Good	55.0	63.6	60.3	
Distal vessel disease				.202
Absent	20.4	25.0	23.1	
Moderate	79.6	74.4	76.5	
Severe	0.0	0.6	0.3	

BIF-CTO, chronic total occlusion involving bifurcation lesion; CC, collateral channel classification according to Werner classification; CTO, chronic total occlusion; LAD, left anterior descending coronary artery; LCX, left circumflex coronary artery LM, left main coronary artery; RCA, right coronary artery.
Values are expressed as percentages or as mean ± standard deviation.

perforation rates were numerically higher in patients with BIF-CTO, but differences were nonsignificant.

DISCUSSION

Our study evaluated the incidence, procedural strategy, in-hospital outcomes and complications of CTO PCI involving bifurcation lesions treated in a high-volume European center at Massy, France. The main findings of our study were the following: *a)* the incidence of bifurcation-CTO was high; *b)* procedural complexity, as assessed by J-CTO and PROGRESS-CTO scores, was higher in CTO involving bifurcation lesions; *c)* the success rate of CTO PCI was high overall and was not affected by the presence of bifurcations at CTO lesions; *d)* the complication rate was unchanged between the 2 study cohorts, as was the PROGRESS-

Table 3
Procedural data

Variable	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
Procedural success	80.4	77.8	78.9	.447
Reason of failure				.264
Wire did not cross	17.6	19.9	18.9	
Balloon did not cross	0.0	1.4	0.8	
Complication	1.6	0.6	1.0	
Primary arterial access				.259
Radial artery	84.5	87.3	86.2	
Femoral artery	15.5	12.2	13.5	
Other (branchial)	0.0	0.6	0.3	
Second arterial access				.223
Radial artery	72.2	77.8	75.6	
Femoral artery	27.8	22.2	24.4	
Other (branchial)	0.0	0.0	0.0	
Primary access sheath				.077
5 Fr	4.1	4.7	4.5	
6 Fr	79.2	74	76.1	
7 Fr	13.5	20.2	17.5	
8 Fr	3.3	1.1	2.0	
Second access sheath				.827
5 Fr	15.3	16.7	16.1	
6 Fr	65.3	68.4	67.1	
7 Fr	16.7	13.6	14.8	
8 Fr	2.7	1.3	2.0	
Bilateral injection	84.3	83.1	83.6	.390
Revascularization approach				
Antegrade approach	70.1	73.0	71.9	.586
AWE	66.6	69.2	68.2	
Parallel wire	3.1	3.8	3.5	
IVUS guided puncture	0.4	0.0	0.2	
ADR	8.2	8.3	8.2	.957
Wire-based ADR	6.5	7.2	6.9	
Device-based ADR	1.7	0.9	1.3	
Retrograde approach	21.7	18.7	19.9	.356
Primary retrograde	9.4	9.1	9.2	.551
Collaterals used				.733
Septal channels	69.8	62.7	65.8	
Epicardial channels	30.2	34.4	32.5	
Grafts	0.0	1.5	0.8	
PCI wires used	2.74 ± 1.55	2.49 ± 1.57	2.59 ± 1.56	.024
Successful wires characteristics				.524
Polymer wire	54.8	60.0	57.8	
Spring coil, nonpolymer	45.2	40.0	42.2	
Wire hydrophilic coating	73.9	74.9	74.5	.536
Tip load				
< 1 g soft	41.2	48.1	45.3	
< 3 g intermediate	7.8	7.5	7.6	
< 9 g moderate	25.3	18.8	21.4	
> 9 g hard	6.9	5.5	6.1	
No data available	18.8	19.9	19.4	
Tapered wire tip	73.5	68.5	70.5	.375
Balloon dilatation catheters used	1.01 ± 0.806	0.96 ± 0.697	0.98 ± 0.743	.566
Microcatheters (MC) used	1.18 ± 0.539	1.14 ± 0.540	1.16 ± 0.540	.222
Dual lumen MC	11.4	5.3	7.8	.005
Dual lumen reason of use				.007
Branch rewiring	10.6	3.9	6.6	

Table 3 *(Continued)*
Procedural data

Variable	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
Parallel wiring	0.8	1.4	1.2	
Wire externalization	68.0	68.7	68.3	.670
Guide extension use	13.1	16.1	14.9	.307
Anchoring	7.0	8.3	7.8	.564
Snaring	0.8	0.6	0.7	.696
Rotablator use	0.4	2.5	1.7	.048
Laser	0.8	2.8	2.0	.090
IVUS utilization	4.9	1.9	3.1	.040
Procedural duration (min)	106.85 ± 52.22	98.81 ± 51.72	102.05 ± 52.03	.030
Stent implantation (no)	1.70 ± 0.90	1.73 ± 0.84	1.74 ± 1.04	.988
Stented length	50.42 ± 31.24	55.10 ± 28.15	53.11 ± 29.52	.006
Minimal stent diamter	2.57 ± 0.34	2.74 ± 0.43	2.67 ± 0.40	< .001
Maximal stent diameter	2.79 ± 0.45	2.96 ± 0.47	2.89 ± 0.47	< .001
Fluoroscopy time, min	48.22 ± 36.08	43.48 ± 30.92	45.70 ± 33.15	.053
Contrast media	199.73 ± 159.69	175.57 ± 156.50	185.32 ± 158.11	.017
Radiation (air kerna)	2862.0 ± 2037.6	2510.2 ± 2098.1	2652.2 ± 2079.4	.004

ADR, antegrade dissection re-entry; AWE, antegrade wire escalation; BIF-CTO, chronic total occlusion involving bifurcation lesion; CTO, chronic total occlusion; FR, French size; IVUS, intravascular ultrasound; MC, microcatheter; PCI, percutaneous coronary intervention.
Values are expressed as percentages or as mean ± standard deviation.

Table 4
BIF-CTO cohort

SB diameter	2.30 ± 0.23
True BIF	26.5
False BIF	73.5
Proximal CTO BIF	63.7
Type 1	10.6
Type 2	53.1
Within CTO BIF	6.5
Distal CTO BIF	29.8
Type 4	24.1
Type 5	5.7
SB protection in case non proximal BIF	51.8
BIF treatment strategy	
Single stent strategy	93.46
2 stent strategy	6.53
Other (DEB, etc.)	0.01
SB compromised	
No	92.2
Yes, TIMI 0	6.5
Yes, TIMI 1-2	1.2
Final kissing balloon	63.3
Final POT with no final kissing balloon	36.7
POT-side-POT	19.6
Final POT only	17.1

BIF, bifurcation; BIF-CTO, chronic total occlusion involving bifurcation lesion; CTO, chronic total occlusion; DEB, drug eluting balloon; FKB, final kissing balloon; POT, proximal optimization technique; SB, sidebranch; TIMI, thrombolysis in myocardial infarction.
Values are expressed as percentages or as mean ± standard deviation.

CTO complication score; *e)* the default bifurcation treatment strategy was a provisional approach, as is the case in nonocclusive coronary artery disease.

Incidence of bifurcation-coronary chronic total occlusions

Previous series on bifurcation-CTO lesions reported an incidence ranging from 26.5% to 67%.[13,15–18] In line with our study (40.4% incidence), Ojeda et al.[17] (30.3%), Galassi et al.[16] (26.5%) and Baystrukov et al.[13] (54.3%) reported single-center experiences and used the same definitions (proximal, within the CTO body, distal bifurcation). Chen et al.[18] reported proximal and distal SB arising from the CTO segment (47% incidence), whereas Nikolakopoulos et al.[15] reported only bifurcation-CTOs with SB arising within 5 mm of the proximal or distal cap (67% incidence).

Procedural success rate, revascularization strategy, predictive scores

Procedural success in our study was high, averaging 78.9%. Dedicated groups of experts worldwide have consistently reported success rates in the range of 90% in the last few years.[5,19–23] In our study, the procedural complexity of the treated patients was relatively high (J-CTO score 2.30 ± 1.16) compared with that reported in studies based on large scale European[24] and Japanese registries.[25] Of note, in 2018 the EuroCTO Club reported a mean J-CTO score of 2.37 ± 1.14 in failed cases vs 2.08 ± 1.15 in successful cases ($P < .001$; 17 626 procedures cohort).[24]

As per European practice,[24] the predominant revascularization strategy was the antegrade approach (71.9%), followed by retrograde (19.9%) and ADR (8.2%). CTO crossing was successful with soft and moderate stiffness wires in most cases, reflecting contemporary technique and wire technology development.[24]

The overall J-CTO score and PROGRESS-CTO score in our study were 2.30 ± 1.16 and 1.37 ± 0.94, respectively. Procedural complexity was higher in CTOs involving a bifurcation lesion than in non–BIF-CTO, as assessed by both J-CTO score (2.42 ± 1.01 vs 2.21 ± 1.23; $P = .025$) and PROGRESS-CTO score (1.60 ± 0.95 vs 1.22 ± 0.90; $P < .001$) (figure 2). Similar to our study, Nikolakopoulos et al.[15] reported a higher J-CTO score in BIF-CTO patients. All the other relevant studies reported data from relatively small cohorts and

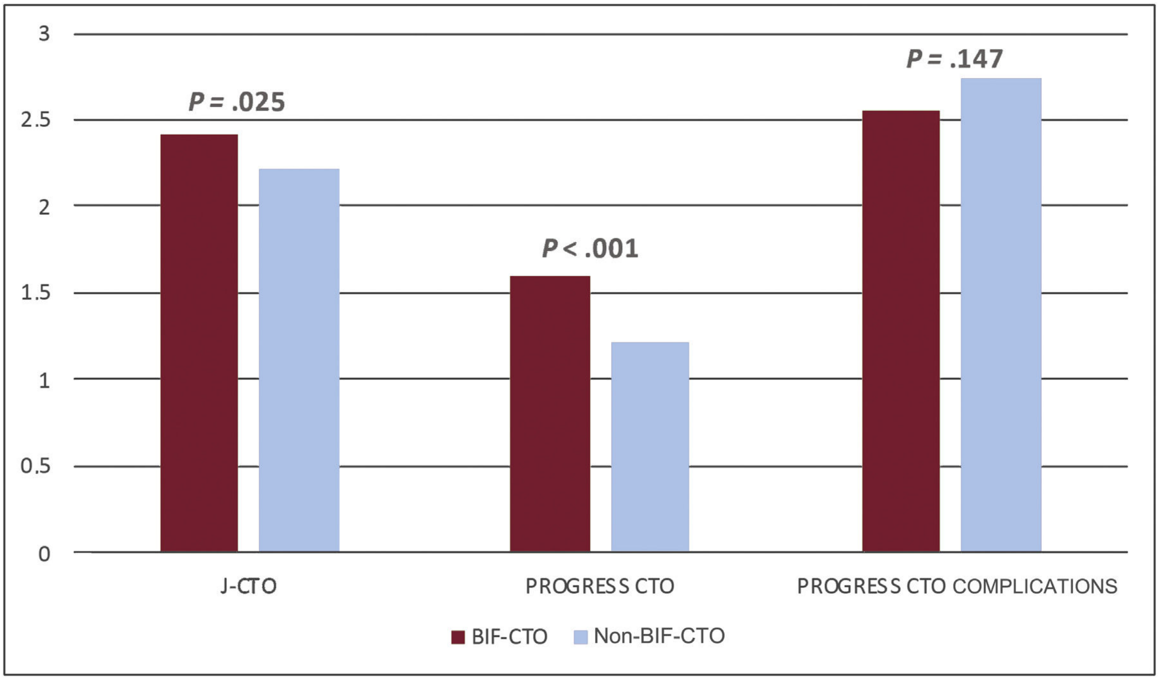

Figure 2. Central illustration. CTO PCI predictive scores in 2 treatment cohorts (BIF-CTO and non–BIF-CTO-CTO patients). BIF-CTO, chronic total occlusion involving bifurcation lesion; CTO, chronic total occlusion; J-CTO, Multicenter Chronic Total Occlusion Registry of Japan; PCI, percutaneous coronary intervention; PROGRESS-CTO, prospective global registry for the study of chronic total occlusion intervention.

Table 5
Predictive scores

Variable	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
J-CTO score	2.42 ± 1.02	2.21 ± 1.23	2.30 ± 1.16	.025
Lesion length > 20 mm	76.3	71.7	73.6	.202
Calcification	62.4	60.6	61.3	.639
Angulation	28.2	30.3	29.4	.575
CTO blunt stump	69	51.1	58.3	< .001
Previous attempt	6.1	7.8	7.1	.437
CASTLE score	2.67 ± 1.20	2.51 ± 1.30	2.58 ± 1.26	.114
Lesion length > 20 mm	76.3	71.7	73.6	.202
Calcification	62.4	60.6	61.3	.639
Angulation	28.2	30.3	29.4	.575
CTO stump blunt	69	51.1	58.3	< .001
Age > 70 y	24.5	31.0	28.4	.167
Previous CABG	7.8	7.8	7.8	1.0
PROGRESS-CTO score	1.60 ± 0.95	1.22 ± 0.90	1.37 ± 0.94	< .001
Proximal cap ambiguity	69	51.1	58.3	< .001
Absence of interventional collaterals	31.8	20.3	25.0	< .001
Tortuosity	35.1	36.1	35.7	.799
LCX lesion	24.5	14.2	18.3	< .001
PROGRESS complication score	2.55 ± 1.87	2.74 ± 1.83	2.66 ± 1.85	.147
Age > 65 y	42.0	51.8	47.9	.018
Lesion length > 23 mm	53.5	50.1	51.5	.421
Retrograde use	21.7	18.7	19.9	.356

CABG, coronary artery bypass grafting; CASTLE, coronary artery bypass graft history, age, stump anatomy, tortuosity, length of occlusion, calcification; CTO, chronic total occlusion; J-CTO, Multicenter Chronic Total Occlusion Registry of Japan; LCX, left circumflex coronary artery; PROGRESS-CTO, prospective global registry for the study of chronic total occlusion intervention.
Values are expressed as percentages or as mean ± standard deviation.

Table 6
Complications

	BIF-CTO (n = 245, 40.4%)	Non–BIF-CTO-CTO (n = 362, 59.6%)	All CTO patients (N = 607)	*P*
Periprocedural MI	3.2	1.9	2.4	.325
Prolonged ICU	6.2	4.0	4.9	.539
Acute kidney injury	1.8	1.1	1.3	.731
Hemoglobin drop > 3 g/dL	6.3	6.3	6.3	1.0
Cardiac death	0.0	0.6	0.3	.244
Perforation	3.3	3.0	3.1	.875
MACE	5.7	5.0	5.3	.688

BIF-CTO, chronic total occlusion involving bifurcation lesion; CTO, chronic total occlusion; ICU, intensive coronary unit; MACE, major adverse cardiac events; MI, myocardial infarction.
Values are expressed as percentages or as mean ± standard deviation.

identified no differences in procedural complexity.[13,16–18] The PROGRESS-CTO complication score was 2.66 ± 1.85 overall and was similar in both arms (*P* = .147).

Coronary chronic total occlusions and bifurcation approach

Procedural success was similar in the 2 treatment cohorts (80.4% for BIF-CTO patients, 77.8% for non–BIF-CTO patients; *P* = .447), even though procedural complexity was higher in patients with BIF-CTO, as assessed by J-CTO and PROGRESS-CTO scores (figure 2). All other relevant studies reported lower procedural success rates in CTO involving bifurcation lesions, with Galassi et al.[16] reporting a single operator experience and Nikolakopoulos et al.[15] reporting data from a global US registry. Compared with the above studies, in our cohort the provisional stenting strategy for bifurcation treatment was predominant (93.4%) and ADR techniques were infrequently adopted (8.2%).

Bifurcation treatment has greatly evolved over the years and has reached a period of standardization in terminology and practice.[10] Provisional stenting has been established as the preferred treatment modality, since complex coronary interventions with 2 stents have been associated with greater periprocedural MI, target lesion revascularization, and mortality.[26–28] In our study, the provisional strategy was the predominant approach and was applied in 93.46% of bifurcations, matching the results of other contemporary European cohorts.[17] The ADR approach, by definition responsible for controlled vessel dissection in contemporary CTO PCI, had low adoption in our center (8.2% in BIF-CTO patients), accounting, to a certain extent, for the low use of techniques requiring 2-stent implantation (6.5%).

In the context of CTO PCI, the presence of dissection affecting the SB origin has been identified as a predictor for the adoption of the 2-stent strategy,[17] leading to a 46% adoption of 2-stent techniques in a single operator cohort.[16] Larger studies reported the use of the 2-stent technique in the range of 8% to 8.9%.[17,29] Adachi et al.[29] reported that 2-stent techniques were more efficient in preserving SB patency for bifurcations located within the CTO body. Ojeda et al.[30] reported no differences in procedural and mid-term clinical outcomes between 1-stent and 2-stent techniques for the treatment of CTO bifurcation lesions. Interestingly, a single center randomized study comparing the mini crush technique and the provisional approach in CTOs involving bifurcation lesions revealed no differences in angiographic or clinical success but did reveal improved 1-year outcomes with the mini crush technique.[13]

Side branch patency

SB patency with TIMI III flow was achieved in 92.2% of the bifurcations treated. Baseline SB wiring, a well identified predictor of procedural success in non-CTO bifurcation PCI, [31] was achieved in all SBs located proximal to the CTO, but in only 51.8% of the SBs located within or distal to the CTO. A previous study reported unsuccessful baseline SB wiring in 25% of nonproximal BIF-CTO,[17] which can be largely attributed to dissections involving the carina during CTO crossing. A dual lumen microcatheter was used for SB wiring in 10.6% of the patients.

SB compromise is a well identified cause of periprocedural myocardial injury in coronary interventions.[32] In the context of CTO PCI, Adachi et al.[29] identified the presence of stenosis in the SB, bifurcations located within the occluded segment and subintimal tracking at the SB ostium as independent predictors of a suboptimal result in SB. In that study, a suboptimal SB result itself, had an impact on target lesion revascularization of the main branch for lesions located in the right coronary artery.[29] Another single-center CTO PCI study identified SB occlusion as the only parameter associated with troponin elevation during the procedure.[33] Elevation of cardiac biomarkers reflects myocardial necrosis and has been linked to an increased risk of future cardiac events.[33–35]

Complications

In this study, the presence of a bifurcation had no impact on the in-hospital complication rate following CTO revascularization. In our cohort, the key determinants for this result were operator expertise, a predominantly provisional stenting strategy for bifurcation treatment (93.4%), and low adoption of dissection re-entry techniques for CTO crossing (8.2%). Prior studies identified higher periprocedural MI[17] and more frequent coronary perforation and cardiac tamponade in CTOs with bifurcation lesions.[16] In the first study, ADR was applied in up to 31% of the cases and in the second study, 1-stent techniques for bifurcation treatment were applied in only 54% of the patients. In our cohort, periprocedural MI was documented in 2.4% of the patients overall. Of note, periprocedural MI in CTOs involving bifurcations seems to affect MACE-free survival and mortality at 12 months.[17,36]

Limitations

Our study has a number of limitations. First, all patients in our registry were treated by experienced operators, with varied experience in CTO treatment and extensive experience in the treatment of bifurcation lesions. The data presented in this study reflect their practice and might not be generalizable to centers with limited complex PCI experience. Second, this is an observational retrospective single center study, with all the inherent bias of this kind of design. Yet, no randomized data are available on this topic. Third, the angiographic data were estimated by visual assessment only; no quantitative coronary angiographic analysis or core laboratory adjudication was performed. Fourth, no follow-up was available in our study.

CONCLUSIONS

Coronary CTO and bifurcation lesions are both cornerstone anatomical entities in the field of complex PCI, which has evolved dramatically over the last decade due to technique standardization and technological advances. These entities coexist in 40.4% of contemporary CTO PCI, increasing the procedural complexity of treated patients. The presence of bifurcation has no impact on the procedural success rate, which remains high. The complication rate of CTO PCI is unaffected by the presence of bifurcation. A provisional approach provides excellent results and should be the preferred treatment strategy, as is in nonocclusive coronary artery disease. Further studies are required to investigate CTO PCI involving bifurcation lesions, focusing on procedural effectiveness, safety, and long-term outcomes.

WHAT IS KNOWN ABOUT THE TOPIC?

- The incidence of bifurcation lesions in CTO ranges from 26.5% to 67% in contemporary literature.
- Prior studies have shown that the procedural success rate of CTO PCI is lower in CTOs involving bifurcations than in CTOs without bifurcations.
- The complication rate of PCI for CTOs has been reported to be higher in CTOs involving bifurcations.

WHAT DOES THE STUDY ADD?

- The incidence of bifurcation lesions in CTO was 40.4%.
- BIF-CTO patients presented with higher lesion complexity, as assessed by the J-CTO score and PROGRESS-CTO score.
- In contemporary CTO PCI, the presence of a bifurcation in a CTO lesion had no impact on the procedural success rate or the complication rate when ADR adoption was low and a provisional stenting strategy was the predominant approach.

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AUTHORS' CONTRIBUTIONS

N.V. Konstantinidis: conceptualization, methodology, formal analysis, investigation, resources, writing original draft, reviewing, editing. B. Chevalier: methodology, investigation, resources, writing, reviewing and editing, validation, supervision. T. Hovasse: investigation, resources. P. Garot: investigation, resources. H. Benamer, T. Unterseeh, S. Champagne, F. Sanguineti, A. Neylon, A. Avran, Y. Louvard: investigation, resources. T. Moysiadis: formal analysis, data curation. T. Lefèvre : conceptualization, methodology, investigation, resources, writing, reviewing, editing, validation, supervision.

CONFLICTS OF INTEREST

P. Garot is a medical shareholder of CERC, a CRO dedicated to cardiovascular research. He has received speaker's fees from Abbott, Biosensors, Boston Scientific, Edwards, Terumo, and GE Healthcare outside the submitted work. F. Sanguineti has received support for attending the PCR London Valve and the EBC Main meeting. A. Neylon has received honoraria from Medtronic, Shockwave Medical, and Boston Scientific. She has received support for attending meetings from Medtronic. She is a medical shareholder of CERC, a CRO dedicated to cardiovascular research. T. Lefèvre has received speaker's fees from Terumo, Boston Scientifics, and Edwards. He has a leadership role in the European Society of Cardiology, Euro PCR, and London Valve. The remaining authors have no conflicts of interest to disclose.

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