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## The evolution of the CTO-PCI landscape in Belgium and Luxembourg: a four-year appraisal

Ward Eertmans<sup>a,b,\*</sup> , Peter Kayaert<sup>c,\*</sup>, Johan Bennett<sup>d</sup>, Claudiu Ungureanu<sup>e</sup>, Yoann Bataille<sup>f,g</sup>, Georges Saad<sup>f</sup>, Steven Haine<sup>h,i</sup> , Patrick Coussement<sup>j</sup>, Bruno Pereira<sup>k</sup>, Pierfrancesco Agostoni<sup>l</sup>, Luc Janssens<sup>m</sup>, Bert Vandeloos<sup>n</sup>, Patrick Maréchal<sup>o</sup>, Kristoff Cornelis<sup>p</sup> , Quentin de Hemptinne<sup>q</sup>, Adel Aminian<sup>r</sup>, Francis Stammen<sup>s</sup>, Stéphane Carlier<sup>t</sup>, Patrick Timmermans<sup>u</sup>, Steven Vercauteren<sup>v</sup>, Jeroen Sonck<sup>n,w</sup>, Frédéric De Vroey<sup>x</sup>, Benny Drieghe<sup>b</sup>, Keir McCutcheon<sup>c</sup>, Benjamin Scott<sup>l</sup> , Laurent Davin<sup>o</sup>, Chadi Gafari<sup>t</sup>, and Jo Dens<sup>a,b</sup>, On behalf of the BWGCTO Investigators

<sup>a</sup>Department of Medicine and Life Sciences, Hasselt University, Diepenbeek, Belgium; <sup>b</sup>Department of Cardiology, Ziekenhuis Oost-Limburg, Genk, Belgium; <sup>c</sup>Department of Cardiology, UZ Gent, Gent, Belgium; <sup>d</sup>Department of Cardiovascular Medicine, UZ Leuven, Leuven, Belgium; <sup>e</sup>Department of Cardiology, Hôpital de Jolimont, La Louvière, Belgium; <sup>f</sup>Department of Cardiology, CHR de la Citadelle, Liège, Belgium; <sup>g</sup>Department of Cardiology, Jessa Ziekenhuis, Hasselt, Belgium; <sup>h</sup>Department of Cardiology, Antwerp University Hospital, Edegem, Belgium; <sup>i</sup>Department of Cardiovascular Diseases, University of Antwerp, Wilrijk, Belgium; <sup>j</sup>Department of Cardiology, AZ Sint-Jan Brugge, Brugge, Belgium; <sup>k</sup>Department of Cardiology, INCCI Haerz Center, Luxembourg, Luxembourg; <sup>l</sup>HartCentrum, Ziekenhuis Netwerk Antwerpen (ZNA), Middelheim Hospital, Antwerp, Belgium; <sup>m</sup>Department of Cardiology, Imelda Ziekenhuis, Bonheiden, Belgium; <sup>n</sup>Department of Cardiology, Centrum voor Hart- en Vaatziekten, UZ Brussel, Jette, Belgium; <sup>o</sup>Department of Cardiology, CHU Liège, Liège, Belgium; <sup>p</sup>Department of Cardiology, AZ Maria Middelaers, Gent, Belgium; <sup>q</sup>Department of Cardiology, CHU Saint-Pierre Université Libre de Bruxelles, Brussel, Belgium; <sup>r</sup>Department of Cardiology, CHU Charleroi, Charleroi, Belgium; <sup>s</sup>Department of Cardiology, AZ Delta, Roeselare, Belgium; <sup>t</sup>Department of Cardiology, CHU Ambroise Paré, Mons, Belgium; <sup>u</sup>Department of Cardiology, Clinique Saint-Luc Bouge, Namur, Belgium; <sup>v</sup>Department of Cardiology, Kliniek Sint-Jan, Brussel, Belgium; <sup>w</sup>Department of Cardiology, Onze Lieve Vrouw Ziekenhuis, Aalst, Belgium; <sup>x</sup>Department of Cardiology, Grand Hôpital de Charleroi, Charleroi, Belgium

### ABSTRACT

**Background:** To chart the evolution of the CTO-PCI landscape in Belgium and Luxembourg, the Belgian Working Group on Chronic Total Occlusions (BWGCTO) was established in 2016.

**Methods:** Between May 2016 and December 2019, patients undergoing a CTO-PCI treatment were prospectively and consecutively enrolled. Twenty-one centres in Belgium and one in Luxembourg participated. Individual operators had mixed levels of expertise in treating CTO lesions. Demographic, angiographic, procedural parameters and incidence of major adverse cardiac and cerebrovascular events (MACCE) were systematically registered.

**Results:** Over a four-year enrolment period, 1832 procedures were performed in 1733 patients achieving technical success in 1474 cases (80%), with an in-hospital MACCE rate of 2.3%. Fifty-nine (3%) cases were re-attempt procedures of which 41 (69%) were successful. High-volume centres treated more complex lesions (mean J-CTO score:  $2.15 \pm 1.21$ ) as compared to intermediate (mean J-CTO score:  $1.72 \pm 1.23$ ;  $p < 0.001$ ) and low-volume centres (mean J-CTO score:  $0.99 \pm 1.21$ ;  $p = 0.002$ ). Despite this, success rates did not differ between centres ( $p = 0.461$ ). Overall success rates did not differ over time ( $p = 0.810$ ). High-volume centres progressively tackled more complex CTOs while keeping success rates stable. In all centres, the most applied strategy was antegrade wire escalation (83%). High-volume centres more often successfully applied antegrade dissection and re-entry and retrograde techniques in lesions with higher complexity.

**Conclusion:** With variable experience levels, operators treated CTOs with high success and relatively few complications. Although AWE remains the most used technique, it is paramount for operators to be skilled in all contemporary techniques in order to be successful in more complex CTOs.

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Coronary total occlusion; percutaneous coronary intervention; in-hospital outcomes

### Introduction

With global incidences ranging from 15 to 25%, coronary chronic total occlusions (CTO) are common findings in patients suffering from coronary artery disease

[1–4]. Both observational and randomised data have shown that successful treatment of CTO lesions can improve overall clinical outcome measures and quality-of-life [5–7].

CTOs have long been considered as the final frontier of percutaneous coronary intervention (PCI), is technically challenging and associated with higher complication rates. Traditionally, only a minority of CTOs, therefore, got revascularised. However, the global landscape of CTO-PCI changed dramatically with the ongoing development of CTO-dedicated materials and techniques and the implementation of the (teachable) hybrid algorithm [8]. Numerous registries demonstrate that CTOs can nowadays be treated with a high guarantee of success (above 80%) and acceptably low complication rates (around 3%), even by operators with lower levels of expertise [9–12].

In 2016, a group of interventional cardiologists from Belgium and Luxembourg (BeLux) with different levels of expertise established the Belgian Working Group on Chronic Total Occlusions (BWGCTO). The aim was to develop a network of operators and centres that were committed to developing a dedicated CTO PCI programme. In this way, patients suffering from a CTO and with an indication for percutaneous revascularisation, would no longer be treated conservatively but would receive a proper CTO-PCI attempt. Here, the evolution of the CTO-PCI landscape in the BeLux region, and its impact on outcome and safety is reported.

## Materials and methods

Between May 2016 and December 2019, patients who underwent a CTO-PCI treatment were prospectively and consecutively enrolled in the BWGCTO registry. In Belgium, 21 PCI centres participated, and in Luxembourg, the only PCI-enabled centre was involved. The level of expertise in opening CTOs was heterogeneous between operators. Where some operators were only familiar with the use of antegrade wire escalation (AWE), others were full hybrid operators with several years of experience. The study protocol was approved by all local ethics committees, and written informed consent was obtained from all patients.

CTO lesions were defined as native coronary artery lesions exhibiting an antegrade 'thrombolysis in myocardial infarction' (TIMI) flow of 0 for at least 3 months. The complexity of the CTO target lesion was assessed by the Japanese CTO (J-CTO) score and categorised as easy (J-CTO score = 0), intermediate (J-CTO score = 1), difficult (J-CTO score = 2) and very difficult (J-CTO score  $\geq 3$ ) [13]. Technical success was defined as the ability to restore TIMI 3 antegrade flow in all major branches of the treated vessel and any residual

stenosis of  $>30\%$  was absent. CTO-PCI procedures was performed according to local institutional guidelines, and the choice of techniques, materials and devices was left to the operator.

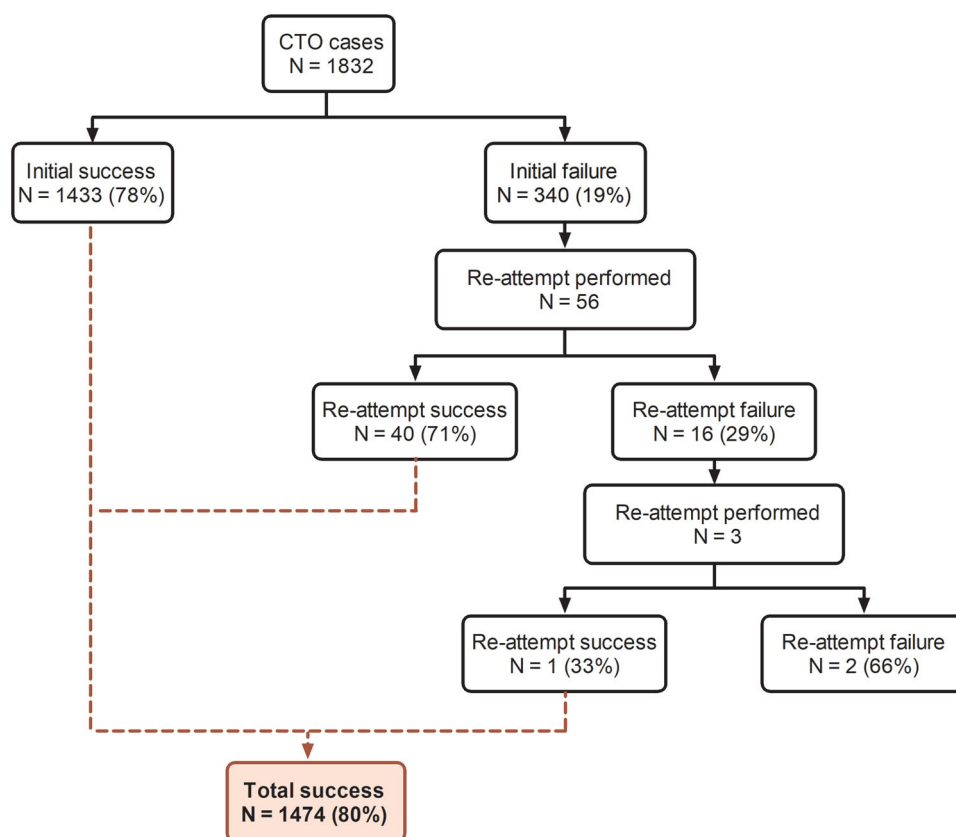
Per protocol defined in-hospital events and complications have been described previously [14]. To summarise, in-hospital major adverse cardiac and cerebrovascular events (MACCE) included death, periprocedural myocardial infarction (MI) [i.e. (non-)ST segment elevated MI], stroke (cerebrovascular accident or transient ischaemic attack), target vessel failure (i.e. vessel re-occlusion, with or without re-intervention, during the index hospitalisation), and target vessel revascularisation by PCI or coronary artery bypass graft surgery (CABG), and were counted as mutually exclusive. An MI was defined as ongoing chest pain, electrocardiogram changes and positive cardiac enzymes, although per protocol, collection of cardiac enzymes was not obligatory. Complications included life-threatening and major bleeding (Bleeding Academic Research Consortium criteria [15]), major vascular complications, acute cardiogenic shock, and renal failure requiring prolonged hospitalisation.

Events, success and the J-CTO scores were adjudicated by operators themselves. There was no independent clinical event committee and/or core lab analysis.

All data were collected in a web-based case report form (OpenClinica Community<sup>TM</sup>, LCC, Waltham, MA). Re-attempt procedures and secondary CTO lesions, treated during the index procedure or treated at a later stage, were considered as separate procedures. All statistical analyses were performed with SPSS, version 25.0 (SPSS Inc, Chicago, IL). Normality was tested using the Kolmogorov-Smirnov test. Categorical variables are expressed as numbers with percentages. Continuous data are shown as mean  $\pm$  standard deviation when normally distributed, or as median with first and third quartile (interquartile range) when non-normally distributed. Categorical data were compared using a Fisher exact, a Chi-Square or a Kendalls-Tau test, as appropriate. Continuous data between groups were compared with the independent Student's *t*-test, Mann-Whitney U test, One-Way Analysis of Variance or the Kruskal-Wallis Test, as appropriate. *p*-Values  $<0.05$  were considered as statistically significant.

## Results

Between May 2016 and December 2019, 1832 CTO-PCI procedures were performed in 1733 patients across 22 centres in Belgium and one in Luxembourg (Figure 1).



**Figure 1.** Flow chart depicting the case-wise technical success.

Forty patients had two CTOs, which were both treated and considered as separate interventions. Technical success was achieved in 1474 out of 1832 procedures (80%). In total, 59 (3%) cases were re-attempt procedures of which 41 (69%) were successful (Figure 1). Patient-wise technical success was achieved in 1435 out of 1733 patients (83%). With success rates of 95, 92, 85 and 65%, respectively, for easy (J-CTO = 0), intermediate (J-CTO = 1), difficult (J-CTO = 2) and very difficult CTO lesions (J-CTO  $\geq$  3), CTO-PCI in more complex lesions was significantly less successful ( $p < 0.001$ ). Table 1 illustrates the inclusion rates per centre divided per overall volume across centres. Out of the 23 participating centres, 9 (39%) enrolled more than 25 CTO-PCIs per year, and only three (13%) centres included more than 50 CTO-PCI procedures per year (Table 1).

### Patient demographics and angiographic characteristics

Patient demographics are listed in Table 2. The majority of patients were male (83%) with a median age of 65 (57–73) years. Compared to patients in whom the index CTO procedure was successful, patients in whom it failed ( $n = 331$ ) had a larger atherosclerotic

**Table 1.** Overview of procedural success according to centre and volume.

Centre	Cases	J-CTO score	Technical success rate
High volume (>100)	1421	2.15 $\pm$ 1.21	1153 (81)
Centre 1	261	1.82 $\pm$ 1.25	217 (83)
Centre 2	195	2.42 $\pm$ 1.38	160 (82)
Centre 3	195	2.03 $\pm$ 1.13	159 (82)
Centre 4	154	2.42 $\pm$ 1.16	131 (85)
Centre 5	135	2.52 $\pm$ 1.12	106 (79)
Centre 6*	127	2.39 $\pm$ 1.16	88 (69)
Centre 7	119	1.68 $\pm$ 1.07	94 (79)
Centre 8	118	2.06 $\pm$ 1.16	97 (82)
Centre 9	117	2.21 $\pm$ 0.95	101 (86)
Intermediate volume (50–100)	186	1.72 $\pm$ 1.23	147 (79)
Centre 10	71	1.80 $\pm$ 1.25	55 (77)
Centre 11	58	1.52 $\pm$ 1.26	49 (84)
Centre 12	57	1.82 $\pm$ 1.18	43 (75)
Low volume (<50)	222	1.86 $\pm$ 1.21	173 (78)
Centre 13	32	2.06 $\pm$ 1.29	27 (84)
Centre 14	31	1.10 $\pm$ 0.91	23 (74)
Centre 15	29	2.28 $\pm$ 1.33	23 (79)
Centre 16	28	1.68 $\pm$ 1.16	23 (82)
Centre 17	21	2.33 $\pm$ 1.35	14 (67)
Centre 18	21	2.29 $\pm$ 0.90	15 (71)
Centre 19	20	1.60 $\pm$ 0.49	13 (65)
Centre 20	17	1.76 $\pm$ 0.97	15 (88)
Centre 21	13	2.46 $\pm$ 0.88	11 (85)
Centre 22	10	0.80 $\pm$ 0.92	9 (90)
Total	1829*	2.07 $\pm$ 1.22	1473 (81)

Values are expressed as mean  $\pm$  SD,  $n$  and  $n$  (%).

\*In total, the J-CTO score was not reported in three cases of Centre 6.

burden, reflected by higher rates of prior CABG (24 vs. 12%;  $p < 0.001$ ), prior CABG on target vessel

**Table 2.** Patient demographics.

	Overall (n = 1733)	Success (n = 1402)	Failure (n = 331)	p-Value
Age, in years	65 (57–73)	65 (57–72)	67 (59–75)	<b>0.003</b>
BMI, in kg/m <sup>2</sup>	27.8 (25.3–30.8)	27.8 (25.2–30.7)	28.1 (25.5–30.9)	0.397
Male	1437 (83)	1165 (83)	272 (82)	0.689
Current smoker	510 (29)	414 (30)	96 (29)	0.857
Hypertension	1257 (73)	1004 (72)	253 (76)	0.077
Dyslipidemia	1508 (87)	1215 (87)	293 (89)	0.366
Diabetes mellitus	490 (28)	382 (27)	108 (33)	0.051
OSAS	121 (7)	98 (7)	23 (7)	0.987
Heart failure	211 (12)	177 (13)	34 (10)	0.234
Previous MI	670 (39)	520 (37)	150 (45)	<b>0.006</b>
Previous CABG	249 (14)	169 (12)	80 (24)	<b>&lt;0.001</b>
Previous CABG on TV	188 (11)	122 (9)	66 (20)	<b>&lt;0.001</b>
Previous PCI	858 (49)	669 (48)	189 (57)	<b>0.002</b>
Previous stroke	126 (7)	98 (7)	28 (8)	0.410
Peripheral vascular disease	290 (17)	214 (15)	76 (23)	<b>0.001</b>
CKI	234 (14)	186 (13)	48 (14)	0.567

Abbreviations. OSAS: Obstructive Sleep Apnoea Syndrome; CABG: coronary artery bypass graft surgery; PCI: percutaneous coronary intervention; CKI: chronic kidney insufficiency (defined as eGFR < 60ml/min/m<sup>2</sup>); TV: target vessel; BMI: body mass index. *p*-values < 0.05 are considered as significant and are indicated in bold.

**Table 3.** Angiographic characteristics.

	Overall (n = 1832)	Success (n = 1474)	Failure (n = 358)	p-Value
Preserved LVEF (≥51%)	1272 (69)	1037 (70)	235 (66)	0.897
LVEF ≤ 30%	88 (5)	76 (5)	12 (3)	0.261
CTO target vessel				0.253
LAD	466 (25)	390 (26)	76 (21)	
Cx	264 (14)	212 (14)	52 (15)	
RCA	1093 (60)	867 (59)	226 (63)	
LMCA	4 (<1)	3 (<1)	1 (<1)	
Ostial lesion	218 (12)	149 (10)	69 (19)	<b>&lt;0.001</b>
In-stent occlusion	181 (10)	138 (9)	43 (12)	0.118
Lesion length ≥ 20mm	1075 (59)	805 (55)	270 (75)	<b>&lt;0.001</b>
Blunt stump	853 (47)	616 (42)	237 (66)	<b>&lt;0.001</b>
Calcification	932 (51)	684 (46)	248 (69)	<b>&lt;0.001</b>
Tortuosity ≥ 45°	598 (33)	429 (29)	169 (47)	<b>&lt;0.001</b>
Re-attempt	333 (18)	259 (18)	74 (21)	0.151
J-CTO score	2.07 ± 1.22	1.90 ± 1.19	2.80 ± 1.09	<b>&lt;0.001</b>
Proximal cap side branch	784 (43)	612 (42)	172 (48)	<b>0.020</b>
Proximal cap ambiguity	805 (44)	560 (38)	245 (68)	<b>&lt;0.001</b>
Lack of interventional collaterals	717 (39)	591 (40)	126 (35)	0.109
Diseased distal landing zone	687 (38)	504 (34)	183 (51)	<b>&lt;0.001</b>
Distal cap at bifurcation	486 (27)	359 (24)	127 (35)	<b>&lt;0.001</b>

*p*-values < 0.05 are considered as significant and are indicated in bold.

(20 vs. 9%; *p* < 0.001), previous PCI treatment (57 vs. 48%; *p* = 0.002), prior MI (45 vs. 37%; *p* = 0.006), peripheral vascular disease (23 vs. 15%; *p* < 0.001) and diabetes (33 vs. 27%), though not statistically significant (*p* = 0.051).

Fifty-seven percent (989/1733) of the patients presented with stable angina and nearly half of them (47%; 815/1733) suffered from effort dyspnoea. The majority of patients had a preserved left ventricular ejection fraction (i.e. ≥51%) (Table 3). Ischaemia and viability assessments were carried out in 72% (*n* = 1338/1832) and 80% (*n* = 1467/1832) of cases, with the presence of ischaemia and viability in respectively 95% and 98% of cases. CTO target lesions involved: right coronary artery (60%), circumflex (14%),

left anterior descending artery (25%) and left main coronary artery (<1%).

According to the J-CTO score, 188 CTOs (10%) were classified as easy (J-CTO = 0), 431 (24%) as intermediate (J-CTO = 1), 541 (30%) as difficult (J-CTO = 2) and 669 (36%) as very difficult lesions (J-CTO ≥ 3). The J-CTO score was not reported in three cases. Angiographic characteristics, known to be associated with negative prognostic outcomes (i.e. a blunt or an ambiguous (proximal) cap, tortuosity ≥ 45%, severe calcification, lesion length ≥ 20 mm, lack of interventional collaterals, proximal cap side branch ≥ 2 mm, distal cap at the bifurcation and a diseased landing zone) were frequently observed (Table 3). As compared to successful cases, all aforementioned negative angiographic

**Table 4.** Procedural characteristics.

	Overall (n = 1832)	Success (n = 1474)	Failure (n = 358)	p-Value
Dual catheter injection (%)	1379 (75)	1089 (74)	290 (81)	<b>0.003</b>
Bifemoral access (%)	350 (25)	269 (25)	81 (28)	0.412
Biradial access (%)	226 (16)	184 (17)	42 (14)	
Femoral/radial access (%)	802 (58)	635 (58)	167 (58)	
Procedure time (min)	87 (59–123)	80 (56–120)	120 (87–150)	<b>&lt;0.001</b>
Fluoroscopy time (min)	32 (20–53)	30 (19–50)	54 (39–73)	<b>&lt;0.001</b>
Air Kerma dose (Gray)	1.4 (0.8–2.5)	1.4 (0.8–2.4)	2.2 (1.3–3.4)	<b>&lt;0.001</b>
Contrast volume (mL)	240 (180–310)	230 (179–300)	270 (200–350)	<b>&lt;0.001</b>
Guidewires (n)	4 (3–7)	4 (2–6)	6 (4–8)	<b>&lt;0.001</b>
Balloons (n)	3 (2–4)	3 (2–4)	2 (0–3)	<b>&lt;0.001</b>
Stents (n)	2 (1–3)	2 (1–3)	0 (0–0)	<b>&lt;0.001</b>
Stent length (mm)	66 (40–91)	64 (40–90)	56 (30–88)	0.316
Microcatheters (n)	1 (1–2)	1 (1–2)	2 (1–2)	<b>&lt;0.001</b>

p-values < 0.05 are considered as significant and are indicated in bold.

characteristics, with the exception of the lack of interventional collaterals, were more common in the failed cases, with significantly higher J-CTO scores (mean J-CTO:  $2.80 \pm 1.19$  vs.  $1.90 \pm 1.19$ ;  $p < 0.001$ ; Table 3).

Success rates did not differ between high, intermediate and low volume centres ( $p = 0.461$ ), but high volume centres treated more complex lesions (mean J-CTO score:  $2.15 \pm 1.21$ ) as compared to intermediate (mean J-CTO score:  $1.72 \pm 1.23$ ;  $p < 0.001$ ) and low volume centres (mean J-CTO score:  $1.86 \pm 1.21$ ;  $p = 0.002$ ) (Table 1).

### Technical approach and hybrid algorithm

The procedural parameters are summarised in Table 4. Dual catheter access with bilateral injection was performed in 1379 out of 1832 (75%) cases, of which a femoral-radial approach was applied most commonly (59%), followed by bifemoral (25%) and biradial (16%) access. Dual catheter injection was avoided in cases with adequate antegrade visualisation by bridging or ipsilateral collaterals, or in cases where interventional collaterals were absent. In unsuccessful procedures, more guidewires, balloons and microcatheters were used ( $p < 0.001$  for all), and radiation doses, contrast volumes, fluoroscopy time and procedural duration were all higher ( $p < 0.001$  for all), as compared to the successful ones (Table 4).

The most frequent applied strategy was AWE (83%), followed by retrograde wire escalation (RWE) (17%). Retrograde dissection and re-entry (RDR) and antegrade dissection and re-entry (ADR) were both used in 16% of cases (Table 5). Independent of the complexity of the CTO lesion and the operator/centre, AWE was the final successful technique in 70%, ADR in 11% and a retrograde technique in 19% of the successful cases (Figure 2). Complex CTO lesions were more often (successfully) targeted by ADR or retrograde techniques, as compared to easy or intermediate lesions (Figures 2

and 3). As compared to low volume centres, high-volume centres more often successfully applied ADR and retrograde strategies (Table 5).

### Evolution of applied techniques over time and impact on technical success

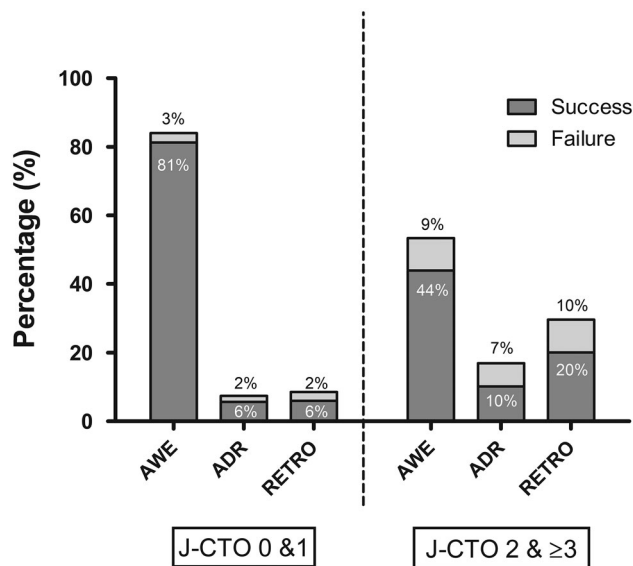
Overall success rates did not significantly change over time (2016: 198/252 (79%); 2017: 431/527 (82%); 2018: 403/497 (81%); 2019: 442/556 (80%);  $p = 0.810$ ). Although statistically not significant, success rates in high volume centres slightly increased over the years (2016–2017: 80% vs 2018–2019: 82%;  $p = 0.274$ ). In contrast, a trend towards lower success rates was visible over time in intermediate volume centres (2016–2017: 86% vs 2018–2019: 76%;  $p = 0.112$ ), and in low volume centres, success rates even declined significantly (2016–2017: 84% vs 2018–2019: 71%;  $p = 0.047$ ). Interestingly, complexity, determined by the J-CTO score, remained similar over time in high (2016–2017:  $2.19 \pm 1.25$  vs. 2018–2019:  $2.12 \pm 1.25$ ;  $p = 0.327$ ), an intermediate (2016–2017:  $1.82 \pm 1.27$  vs. 2018–2019:  $1.68 \pm 1.22$ ;  $p = 0.419$ ) and in low-volume centres (2016–2017:  $1.82 \pm 1.25$  vs.  $1.90 \pm 1.16$ ;  $p = 0.757$ ). Figure 4 shows the spectrum of applied strategies over time for high, intermediate and low volume centres, and the impact on success percentage. Between 2016–2017 and 2018–2019, there were no changes in the percentages of applied techniques in the high-volume centres ( $p > 0.05$ ). Already in 2016–2017, these centres frequently applied complex strategies such as ADR and the retrograde techniques (ADR: 15% and retrograde: 29%) and this slightly differed in 2018–2019 (ADR: 18% and retrograde: 31%). In contrast, intermediate volume centres tended to apply ADR numerically more frequently in 2018–2019 (19%) than in 2016–2017 (14%;  $p = 0.532$ ), and the low volume centres applied a retrograde strategy more often in 2018–2019 (39%) as compared to 2016–2017 (22%;  $p = 0.008$ ).

**Table 5.** Overview of applied strategies and success rates according to centre and volume.

Centre	AWE applied	AWE success	ADR applied	ADR success	RWE applied	RWE success	RDR applied	RDR success
High volume (>100)	1160 (82)	970 (83)	235 (17)	154 (66)	247 (17)	182 (74)	239 (17)	158 (66)
Centre 1 (n = 261)	204 (77)	178 (87)	52 (20)	33 (63)	59 (23)	48 (81)	66 (25)	40 (61)
Centre 2 (n = 195)	188 (96)	154 (82)	24 (12)	21 (88)	10 (5)	3 (30)	5 (3)	2 (40)
Centre 3 (n = 195)	149 (76)	125 (84)	39 (20)	17 (44)	36 (18)	30 (83)	18 (9)	12 (67)
Centre 4 (n = 154)	114 (74)	100 (88)	29 (18)	23 (79)	19 (12)	14 (74)	31 (20)	24 (77)
Centre 5 (n = 135)	88 (65)	74 (84)	39 (29)	27 (69)	34 (25)	24 (71)	45 (33)	27 (60)
Centre 6* (n = 126)	97 (76)	72 (74)	11 (9)	7 (64)	28 (22)	14 (50)	20 (16)	11 (55)
Centre 7 (n = 119)	112 (94)	88 (79)	21 (18)	11 (52)	13 (11)	7 (54)	10 (8)	6 (60)
Centre 8 (n = 118)	111 (94)	92 (83)	5 (4)	4 (80)	23 (19)	17 (74)	7 (6)	6 (86)
Centre 9 (n = 117)	97 (83)	87 (90)	15 (13)	11 (73)	25 (21)	25 (100)	37 (32)	30 (81)
Intermediate volume (50-100)	169 (91)	135 (80)	33 (18)	18 (55)	31 (17)	12 (39)	15 (8)	10 (67)
Centre 10 (n = 71)	68 (96)	52 (76)	7 (10)	3 (43)	10 (14)	4 (40)	5 (7)	3 (60)
Centre 11 (n = 58)	47 (81)	41 (87)	10 (17)	6 (60)	11 (19)	6 (55)	5 (9)	4 (780)
Centre 12 (n = 57)	54 (95)	42 (78)	16 (28)	9 (56)	10 (18)	2 (20)	5 (9)	3 (60)
Low volume (<50)	183 (82)	151 (83)	28 (13)	14 (50)	38 (17)	20 (53)	32 (14)	19 (59)
Centre 13 (n = 32)	27 (84)	24 (88)	5 (16)	2 (40)	3 (9)	2 (66)	4 (13)	3 (75)
Centre 14 (n = 31)	28 (90)	22 (79)	6 (19)	1 (17)	5 (16)	3 (60)	7 (23)	1 (14)
Centre 15 (n = 29)	16 (55)	16 (100)	7 (24)	5 (71)	5 (17)	4 (80)	10 (34)	5 (50)
Centre 16 (n = 28)	25 (89)	20 (80)	2 (7)	1 (50)	9 (32)	7 (78)	4 (14)	3 (75)
Centre 17 (n = 21)	18 (86)	13 (72)	1 (5)	1 (100)	5 (24)	1 (20)	3 (14)	3 (100)
Centre 18 (n = 21)	20 (95)	15 (75)	0 (0)	0 (0)	2 (10)	0 (0)	0 (0)	0 (0)
Centre 19 (n = 20)	11 (55)	7 (64)	4 (20)	3 (75)	7 (35)	3 (43)	3 (15)	3 (100)
Centre 20 (n = 17)	15 (88)	14 (93)	1 (6)	1 (100)	2 (12)	0 (0)	1 (6)	1 (100)
Centre 21 (n = 13)	13 (100)	11 (85)	2 (15)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Centre 22 (n = 10)	10 (100)	9 (90)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	1512 (83)	1256 (83)	296 (16)	186 (63)	316 (17)	207 (66)	286 (16)	187 (65)

Values are expressed as n (%).

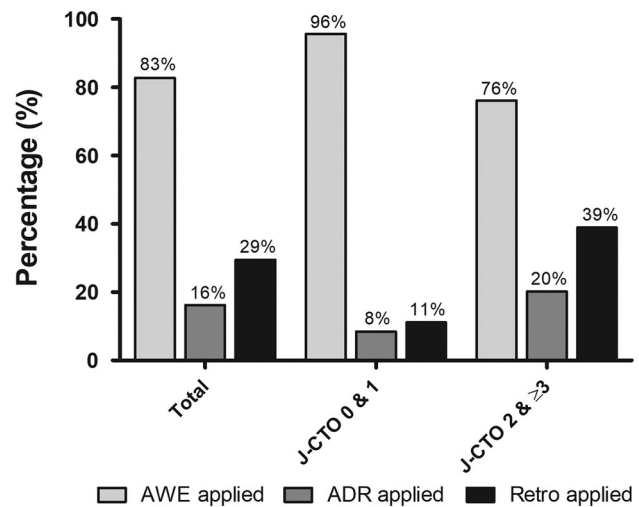
\*In total, the applied strategy was not reported in four cases of centre 6.



**Figure 2.** Technical success of the applied techniques according to the J-CTO score. Outcomes are presented as the percentage of the percentage applied strategy.

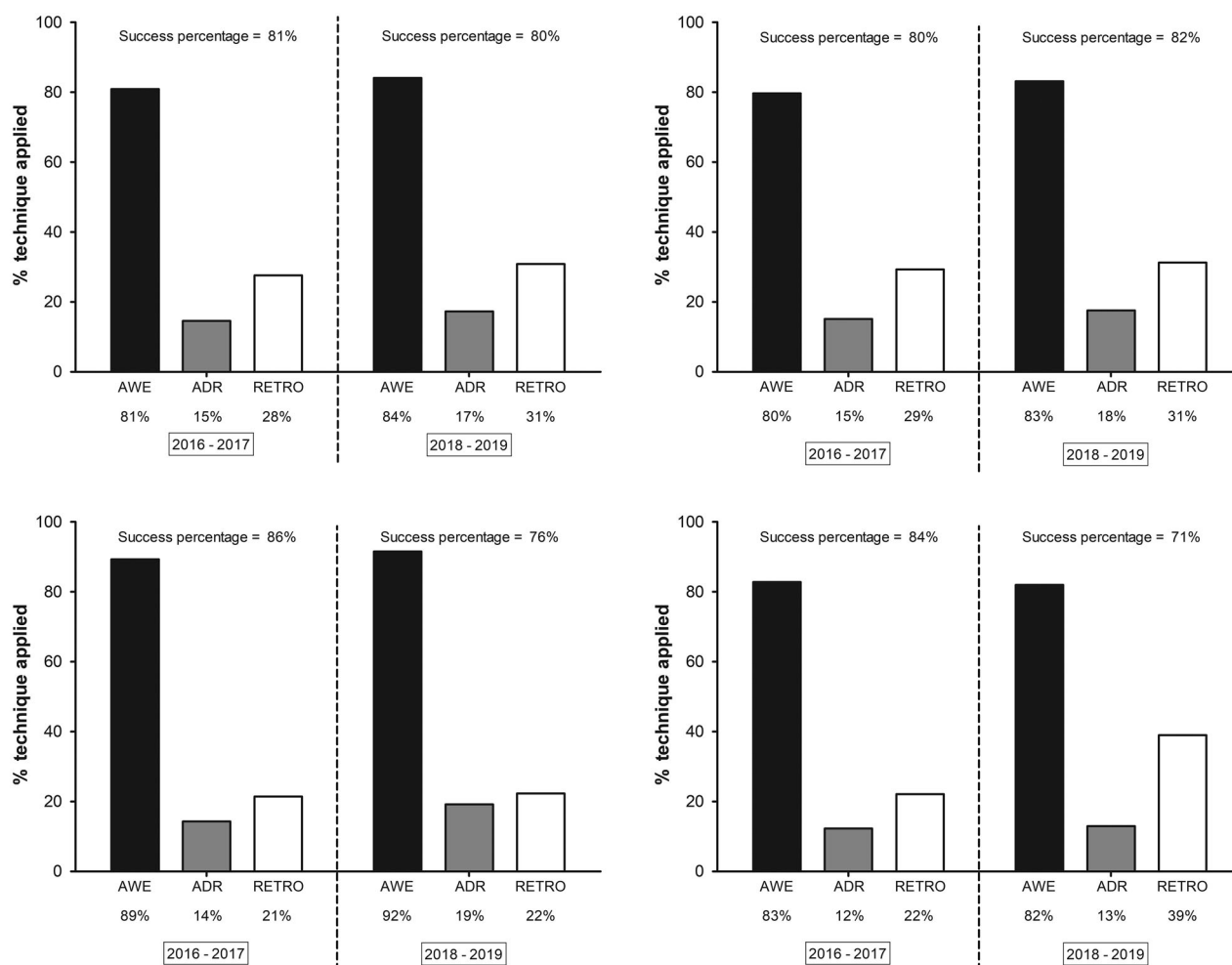
### In-hospital outcome

In-hospital MACCE occurred in 43 cases (2.3%). Five patients died: one patient due to worsening hypotension culminating in electromechanical dissociation, probably related to diffuse ischaemia, one patient due to coronary perforation with rapid cardiac arrest, one patient due to cardiogenic shock, one patient due to an unknown non-cardiovascular cause and one patient, admitted with an out-of-hospital cardiac arrest



**Figure 3.** Overview of the applied techniques according to the J-CTO score.

where the CTO lesion was successfully treated, died as the result of irreversible hypoxic brain injury. In total, 31 patients suffered an in-hospital MI: non ST-segment elevated MI (n = 24), a STEMI (n = 3) and a not further defined MI (n = 4). Four patients experienced a stroke. Three patients had target vessel revascularisation during index hospitalisation. A pericardial effusion occurred in 21 patients. In 15 out of these 21 patients, the management was not reported, but of the remaining six patients, one required urgent surgery, three had pericardiocentesis, and two patients did not require any treatment.



**Figure 4.** The spectrum of applied strategies over time depending on volume. The percentage of applied strategies is depicted for all procedures (top left) and categorised according to volume: high (top right), intermediate (bottom left) and low volume (bottom right) centres.

## Discussion

This prospective, multicentre registry aimed to assess the evolution of the CTO-PCI landscape in Belgium and Luxembourg. Over a four-year period, 1832 CTO-PCI procedures were captured. There are three main findings from an analysis of the BWGCTO registry. First, CTO lesions were treated with high success rates (80%) and acceptably low complication rates (2.3%) and this despite different levels of expertise. Also, two-thirds of the re-attempts were successful, although the number of re-attempts was low. Second, high volume centres treated more complex CTO lesions without compromising success rate. Third, the overall success percentage did not change over time, but in low-volume centres, the success rate declined significantly over time.

Due to the promising results of global CTO registries and the randomised studies, patients are being

increasingly and correctly referred for CTO-PCI [6,7]. To attain the highest possible success in CTO-PCI, operators need to become experienced with the hybrid algorithm, the dedicated devices and the specific techniques [5,16]. In 2016, the Belgian Working Group on CTOs was established involving centres with a heterogeneous level of expertise. This Belgian-Luxembourgish initiative has led to a representative and valuable registry with results comparable to existing global registries [14]. The BWGCTO registry also enabled us to investigate whether time and experience influence success rates.

Although it is commonly known that dedicated CTO programmes and networks are key to success in the CTO-PCI field, overall success was unexpectedly high given the heterogeneity in expertise and volume of the participating centres. Our reported success percentage of 80% was comparable with registries where operators were considered experts in the field



[10,12,17]. International registries involving operators with a mixed expertise level reported success percentages that were substantially lower (range: 58.5–72.5%) [18,19]. Not unimportantly, our high success rate was achieved with relatively few complications (in-hospital MACCE: 2.3%), and especially if compared to other registries, the mortality rate is reassuring [9,12,20,21]. Correct lesion selection most probably played a pivotal role here.

Success rates were high and remained stable over time. It is very unlikely that the level of expertise in Belgium and Luxembourg was already on a plateau in all centres when the registry started. Therefore, the stable success rate over time is probably related to patient selection. Over the four-year period of enrolment, 9 high-volume centres were responsible for the enrolment of 78% of patients. It is likely that these centres predominantly drove the overall success rate of the registry. As high-volume centres already had built up some experience before the registry started, they already achieved high success rates in the beginning. The fact that their success rates remained stable over time, while simultaneously tackling an increasing number of CTOs, many of which with high complexity, suggests that high-volume centres broadened their patient selection and became better at CTO-PCI. Intermediate and low-volume centres progressively enrolled fewer patients or sometimes even no patients in the second half of the registry. Because their first inclusions were highly successful, which is probably related to a careful patient selection (which is evident from the lower J-CTO scores of CTOs treated in these centres), this may have contributed to the high success rate at the beginning of the registry. These observations add further weight to existing data that high volumes and a dedicated programme are paramount in obtaining the best possible results in all patients being referred for CTO revascularisation.

In line with others, the preferred (primary) strategy was AWE across all centres, and the application of more complex techniques varied among centres depending on volume and expertise [10,12,22]. To attain a high level of success, high volume centres applied – already in 2016 – more frequently complex techniques such as ADR, RWE, and/or RDR. Moreover, they treated more complex CTO lesions without negatively impacting success (2016–2017: 80% and 2018–2019: 82%). Low volume centres initially limited themselves to the treatment of less complex CTOs with a high revascularisation probability and mainly used AWE as a single strategy. During the last two years of enrolment, more complex strategies were applied by

low volume centres, though with lower success rates. In this regard, it should be possible to provide high procedural success to all CTO patients, as long as centres invest in a dedicated CTO programme and proper risk management. Once again, patient and strategy selection remains crucial for success. In such a context, CTO-PCI can also be performed safely in low-volume centres, as long as referral to a more experienced centre or operator is timely considered if the CTO is complex or a first attempt fails. Of notice, the number of re-attempts was surprisingly low, suggesting that there is still room for re-attempts by or referrals to more experienced operators or centres. The concept of establishing a dedicated workgroup plays an important role here and has shown to have a beneficial impact on the overall outcome in the BeLux region.

The study results derived from this registry are subjected to certain limitations. First, the success level of less experienced centres almost equalled the success of centres with years of expertise, a potential indication of a different patient selection. There was also no monitoring to ensure consecutive enrolment through which the risk of selection bias cannot be fully excluded. Second, the reporting of angiographic lesion characteristics and J-CTO score might have been prone to bias due to the lack of an independent core lab analysis. Third, underreporting of peri-procedural MI is likely in this registry as a collection of cardiac enzymes was not mandatory. Due to potential underreporting of these kinds of complications, it was decided to report on technical, rather than on procedural success. From this perspective, the absence of an independent event adjudication committee can be considered as an additional limitation. Fourth, the only in-hospital outcome was reported and no one-year follow-up data is available so far. Finally, operators were left free in the choice of techniques and devices to treat CTO lesions, and hence, the clear impact of this choice on outcome could not be studied.

## Conclusions

The results of the BWGCTO registry demonstrate that a strong (inter)national network can beneficially impact the overall outcome of CTO-PCI. Given the mixed level of expertise, technical success was high and complication rates were acceptably low. Although AWE remains the preferred wiring strategy, our results show once again that CTO-operators should master all contemporary techniques to successfully open more complex CTOs.

## Disclosure statement

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## ORCID

Ward Eertmans  <http://orcid.org/0000-0002-0052-7684>

Steven Haine  <http://orcid.org/0000-0003-3065-3443>

Kristoff Cornelis  <http://orcid.org/0000-0001-6704-8410>

Benjamin Scott  <http://orcid.org/0000-0003-2917-3872>  
and

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