
FIRST DES
CE INDICATED
FOR 1-MO
DAPT
IN HBR
PATIENTS
Based on Onyx
ONE Global
Study results
SEE THE DATA
CE
2797
UC202015073a ML ©2020 Medtronic.
All rights reserved. 10/2020
Medtronic

Received: 5 September 2017 | Revised: 14 November 2017 | Accepted: 26 November 2017
DOI: 10.1002/ccd.27472

ORIGINAL STUDIES

WILEY

Subadventitial stenting around occluded stents: A bailout technique to recanalize in-stent chronic total occlusions

Lorenzo Azzalini, MD PhD MSc[1] | Aris Karatasakis, MD[2] | James C. Spratt, BSc MD[3] | Péter Tajti, MD[4] | Robert F. Riley, MD[5] | Luiz F. Ybarra, MD[6] | Stefan P. Schumacher, MD[7] | Susanna Benincasa, MD[1] | Barbara Bellini, MD[1] | Luciano Candilio, MD (Res)[1] | Satoru Mitomo, MD[1] | Peter Henriksen, BSc, MB, ChB, PhD[3] | Francisco Hidalgo, MD[8] | Leo Timmers, MD, PhD[9] | Adriaan O. Kraaijeveld, MD, PhD[9] | Pierfrancesco Agostoni, MD, PhD[10] | James Roy, MB, BCh[11] | David R. Ramsay, MBBS[11] | James C. Weaver, MBBS, PhD[11] | Paul Knaapen, MD, PhD[7] | Alexander Nap, MD, PhD[7] | Boris Starcevic, MD, PhD[12] | Soledad Ojeda, MD, PhD[8] | Manuel Pan, MD, PhD[8] | Khaldoon Alaswad, MD[13] | William L. Lombardi, MD[14] | Mauro Carlino, MD[1] | Emmanouil S. Brilakis, MD, PhD[2,4] | Antonio Colombo, MD[1] | Stéphane Rinfret, MD, SM[6] | Kambis Mashayekhi, MD[15]

[1]Interventional Cardiology Unit, Cardio-Thoracic-Vascular Department, San Raffaele Scientific Institute, Milan, Italy

[2]Interventional Cardiology Unit, North Texas Healthcare System and University of Texas Southwestern Medical Center at Dallas, Dallas, Texas

[3]Department of Cardiology, New Royal Infirmary of Edinburgh, Edinburgh, Scotland, United Kingdom

[4]Minneapolis Heart Institute, Minneapolis, Minnesota

[5]The Christ Hospital Heart & Vascular Center and the Lindner Center for Research and Education, Cincinnati, Ohio

[6]Interventional Cardiology, McGill University Health Centre, Montreal, Quebec

[7]Department of Cardiology, VU University Medical Center, Amsterdam, the Netherlands

[8]Division of Interventional Cardiology, Reina Sofia Hospital, University of Córdoba, Maimonides Institute for Research in Biomedicine of Córdoba (IMIBIC), Córdoba, Spain

[9]Department of Cardiology, University Medical Centre Utrecht, Utrecht, the Netherlands

[10]Department of Cardiology, St. Antonius Hospital, Nieuwegein, the Netherlands

[11]Department of Cardiology, St. George Hospital, Sydney, Australia

[12]Department of Cardiology, Clinical Hospital Dubrava, Zagreb, Croatia

[13]Interventional Cardiology Unit, Edith and Benson Ford Heart and Vascular Institute, Henry Ford Hospital, Detroit, Michigan

[14]Division of Cardiology, Department of Medicine, University of Washington Medical Center, Seattle, Washington

[15]Division of Cardiology and Angiology II, University Heart Center Freiburg Bad Krozingen, Bad Krozingen, Germany

Correspondence
Lorenzo Azzalini, MD, PhD, MSc, Division of Interventional Cardiology, Cardio-Thoracic-Vascular Department, San Raffaele Scientific Institute, Via Olgettina 60, 20132 Milan, Italy.
Email: azzalini.lorenzo@hsr.it

Abstract

Objectives: To evaluate the outcomes of subadventitial stenting (SS) around occluded stents for recanalizing in-stent chronic total occlusions (IS-CTOs).

Funding information
None.

Background: There is little evidence on the outcomes of SS for IS-CTO.

Methods: We examined the outcomes of SS for IS-CTO PCI at 14 centers between July 2011 and June 2017, and compared them to historical controls recanalized using within-stent stenting (WSS). Target-vessel failure (TVF) on follow-up was the endpoint of this study, and was defined as a composite of cardiac death, target-vessel myocardial infarction, and target-vessel revascularization.

Results: During study period, 422 IS-CTO PCIs were performed, of which 32 (7.6%) were recanalized with SS, usually when conventional approaches failed. The most frequent CTO vessel was the right coronary artery (72%). Mean J-CTO score was 3.1 ± 0.9. SS was antegrade in 53%, and retrograde in 47%. Part of the occluded stent was crushed in 37%, while the whole stent was crushed in 63%. Intravascular imaging was used in 59%. One patient (3.1%) suffered tamponade. Angiographic follow-up was performed in 10/32 patients: stents were patent in six cases, one had mild neointimal hyperplasia, and three had severe restenosis at the SS site. Clinical follow-up was available for 29/32 patients for a mean of 388 ± 303 days. The 24-month incidence of TVF was 13.8%, which was similar to historical controls treated with WSS (19.5%, $P = 0.49$).

Conclusions: SS is rarely performed, usually as last resort, to recanalize complex IS-CTOs. It is associated with favorable acute and mid-term outcomes, but given the small sample size of our study additional research is warranted.

KEYWORDS
chronic total occlusion, crushing, in-stent restenosis, percutaneous coronary intervention, subadventitial, subintimal

1 | INTRODUCTION

In-stent chronic total occlusions (IS-CTO) constitute 11%–12% of CTO percutaneous coronary interventions (PCI) [1,2] and represent a particularly challenging lesion subset, due to the resistance created by stent struts, as well as the difficulty maintaining a within-stent course throughout the occluded segment. Although occluded stents are usually crossed in a within-stent fashion, this is sometimes impossible to achieve, and the only feasible approach is represented by subadventitial (i.e., external) stent crossing, with subsequent stenting around the occluded stent. However, the outcomes of this technique are poorly characterized, and available evidence comes from case reports [3–6]. Our aim was to study the outcomes of IS-CTOs recanalized with subadventitial stenting (SS) around the occluded stent(s), and to compare them with those of historical controls treated with conventional within-stent stenting (WSS).

2 | METHODS

2.1 | Patient population

This retrospective multicenter registry included consecutive patients who underwent successful IS-CTO PCI involving SS around the occluded stent(s) at the 14 participating centers, between July 2011 and June 2017. Centers were requested to provide the number of IS-CTO PCI cases performed during the study period. However, patient-level data was provided only for cases involving SS. These patients were then compared with patient-level data from a cohort of historical controls with IS-CTO successfully recanalized with WSS [2]. All procedures were indicated to treat angina, ischemia or both, and were performed electively (ad hoc PCI was discouraged) [7]. Baseline, procedural, and hospitalization data were recorded. Follow-up was performed by means of phone interview, review of hospital records, or outpatient visit. All patients signed an informed consent, approved by the local ethics committees, for procedural data collection and for the anonymous use of data for retrospective evaluation.

2.2 | Definitions

CTO was defined as a 100% stenosis with thrombolysis in myocardial infarction (TIMI) 0 flow for >3 months [1]. A CTO was considered to be in-stent if the occlusion was located within a previously deployed stent or within the 5 mm proximal and distal to it [1,2]. The J-CTO score [8] and the PROGRESS-CTO score [9] were calculated for each lesion. Major procedural complications included: coronary perforation with or without need for intervention (pericardiocentesis, coiling, covered stent implantation, or surgery), tamponade, major bleeding (bleeding requiring transfusion, vasopressors, surgery, or percutaneous intervention), contrast-induced nephropathy (increase in serum creatinine >25% or >0.5 mg/dL at 48 hr post-procedure), periprocedural type 4a myocardial infarction (MI) [10], procedure-related stroke, and procedure-related death. Target-vessel failure (TVF) was a composite of cardiac death, target-vessel MI, and ischemia-driven target-vessel revascularization (TVR) on follow-up.

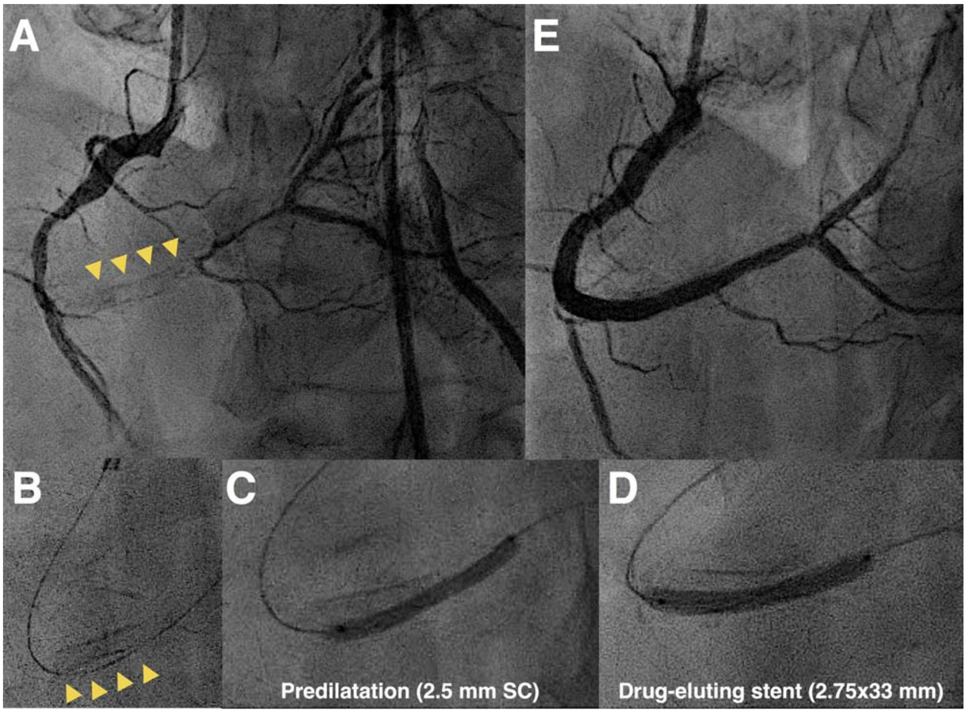


FIGURE 1 Subadventitial stenting around an occluded stent—Case 1. Index procedure. (A) In-stent CTO of the distal right coronary artery (arrowheads). After several attempts of antegrade within-stent crossing, the retrograde approach was undertaken. The wire crossed the occluded stent in a subadventitial fashion (arrowheads in B) and (C) crushing of the whole occluded stent was performed with a 2.5 mm semi-compliant (SC) balloon. (D) A 2.75 × 33 mm drug-eluting stent (DES) was implanted at the occluded stent site. (E) Optimal final result, after implantation of a total of 4 DES [Color figure can be viewed at wileyonlinelibrary.com]

2.3 | Subadventitial crossing and stenting

Subadventitial crossing was classified according to the approach used (antegrade vs. retrograde). The reason for failure to achieve a WSS was collected, when available. The specific technique by which the occluded stent was crossed was also registered [straight vs. knuckle wire, use of a microcatheter or the CrossBoss catheter (Boston Scientific, Marlborough, MA)]. Subadventitial crushing was classified according to its extent (i.e., whole vs. partial stent crushing). Data on balloons and stents used to perform crushing were recorded. Representative cases of SS of IS-CTO are presented in Figures 1–4.

2.4 | Statistical analysis

Continuous variables are presented as mean ± standard deviation and Student's *t* test was used for comparisons. Categorical variables are presented as frequency (percentages), and compared using chi-square test. Kaplan–Meier curves of TVF-free survival were plotted and compared with the log-rank test. For all tests, a $P < 0.05$ was considered significant. Statistical analysis was performed using SPSS 24 (IBM Corp., Armonk, NY).

3 | RESULTS

3.1 | Clinical characteristics

During study period, 422 IS-CTO PCIs were performed, of which 32 (7.6%) were recanalized with SS. These patients were compared with a cohort of 97 historical controls that were successfully recanalized with WSS. Table 1 shows the clinical characteristics of the study population. Mean age was 62.3 ± 10.2 years in SS and 64.4 ± 10.1 years in WSS ($P = 0.31$). The prevalence of cardiovascular risk factors and comorbidities was high, with no differences between groups, with the exception of chronic kidney disease, which was more frequent in SS (28% vs. 9%, $P = 0.006$). There were no significant differences in left ventricular ejection fraction, severity of symptoms, or indication of CTO PCI.

3.2 | Angiographic characteristics

Angiographic data are presented in Table 2. There was a trend toward higher number of diseased vessels in SS. The right coronary artery was the most frequent target CTO vessel in both groups. Features of occlusions complexity were highly prevalent, especially in the SS group. In particular, all SS patients had a lesion length >20 mm, and blunt stump was present in 81%. Mean J-CTO score was markedly higher in SS, compared to WSS (3.1 ± 0.9 vs. 1.9 ± 1.2, $P < 0.001$), with 75% vs. 30% of patients having a J-CTO score ≥3 ($P < 0.001$). The prevalence of distal cap at a bifurcation and of distal vessel of suboptimal quality was also higher in SS. The PROGRESS-CTO score was however similar between groups. Mean occlusion age in SS was 4.6 ± 4.0 years.

3.3 | Procedural data

Procedural data are shown in Table 3. Femoral access was used more frequently in SS than in WSS (97% vs. 69%, $P = 0.001$). In all but two

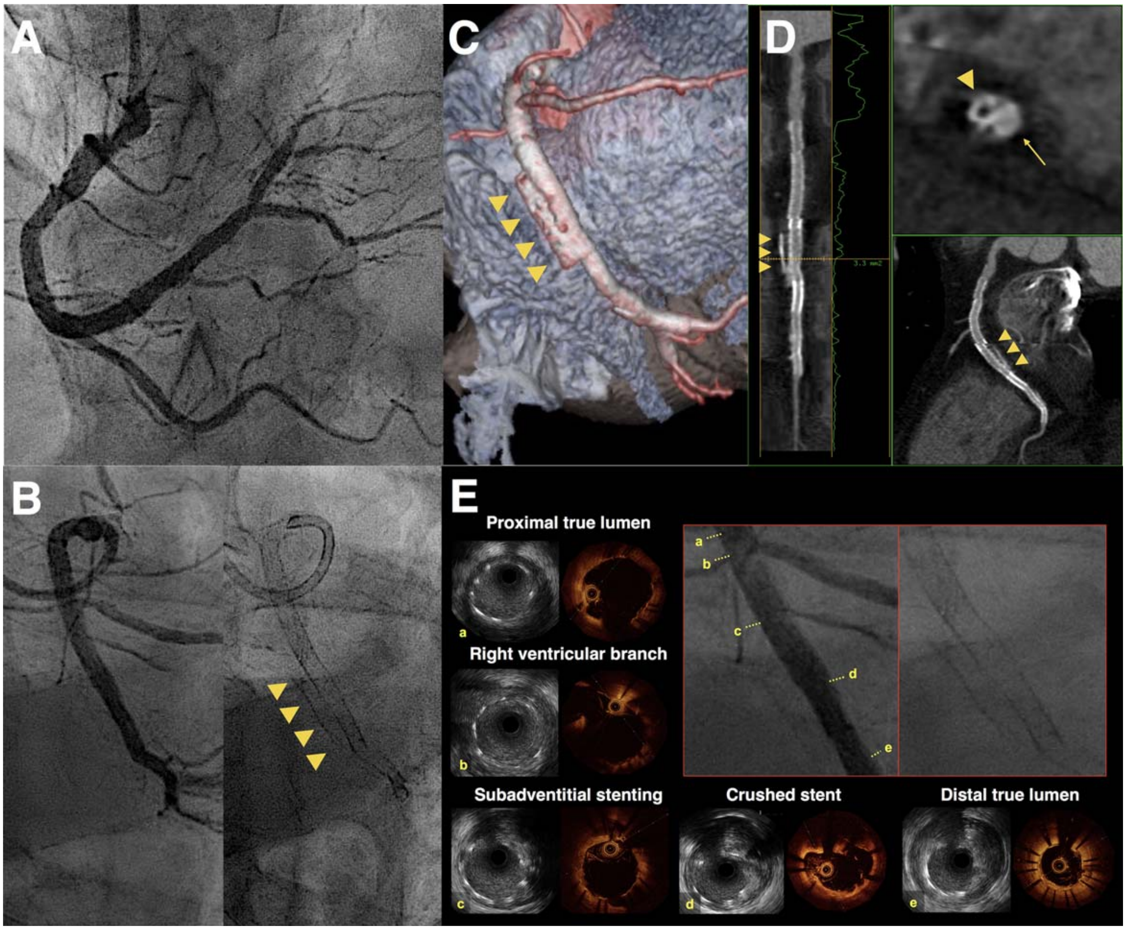


FIGURE 2 Two-month angiographic and imaging follow-up—Case 1. (A, B) A persistent optimal result was observed, with an evident double-contour image at the crushed stent site (arrowheads in B). (C, D) Multidetector computed tomography showed exclusion of the crushed stent (arrowheads) from coronary flow, with a patent newly implanted stent (arrow). (E) Intravascular ultrasound and optical coherence tomography imaging confirmed an optimal result [Color figure can be viewed at wileyonlinelibrary.com]

cases, alternative techniques were used prior to attempting SS. Reasons for failure to achieve a within-stent crossing were varied, and included stent undersizing or fracture, gap between stents, stent originally implanted in the subaventitial space, hard fibrocalcific tissue, uncrossable distal cap, and vessel tortuosity. However, in more than half of cases the reason for failure could not be identified. The CrossBoss catheter was used in about one-third of patients, with no differences between SS and WSS. In SS, the antegrade and retrograde approaches were equally represented (53% and 47%, respectively), while in WSS three quarters of cases were recanalized with antegrade techniques. Several techniques were utilized to achieve subadventitial crossing of the occluded stent(s): these included straight wires and knuckle wires, with or without microcatheter support, the use of CrossBoss, and even ElectroCautery-Assisted Re-enTry (E-CART) [11]. Subadventitial crushing involved part of the occluded stent in 37% and the whole stent in 63%. When partial crushing had to be performed ($n = 12$), this was due to a subintimal track beginning outside the occluded stent with subsequent re-entry into the stent ($n = 6$), or to an initial within-stent track with subsequent wire exit into the subadventitial space ($n = 6$).

Semi-compliant or non-compliant balloons were equally used for stent crushing. The use of mother-and-child catheters (to enhance support during lesion crossing and allow easier stent deployment) was more frequent in SS (41% vs. 16%, $P = 0.003$), reflecting higher procedural difficulty. Likewise, intravascular imaging was also more commonly performed in SS, compared with WSS (59% vs. 8%, $P < 0.001$). There were no differences between groups regarding the type of stents implanted: in particular, in SS drug-eluting stents were implanted in all but one case, where plain old balloon angioplasty was performed due to small vessel size. Post-dilatation in SS was performed in all but one case with non-compliant balloons, which were on average large (3.3 ± 0.5 mm) and inflated at high pressures (20.0 ± 5.4 atm). Total stent length was markedly longer in SS (106 ± 35 vs. 77 ± 50 mm, $P = 0.004$). Procedural metrics reflected the high complexity of these procedures and were worse in the SS group (with the exception of contrast volume).

Procedural complications in the SS group included one wire-induced perforation during subadventitial crossing of the occluded stent that was managed conservatively, and two cases of perforation with need for intervention: one was treated with covered stent

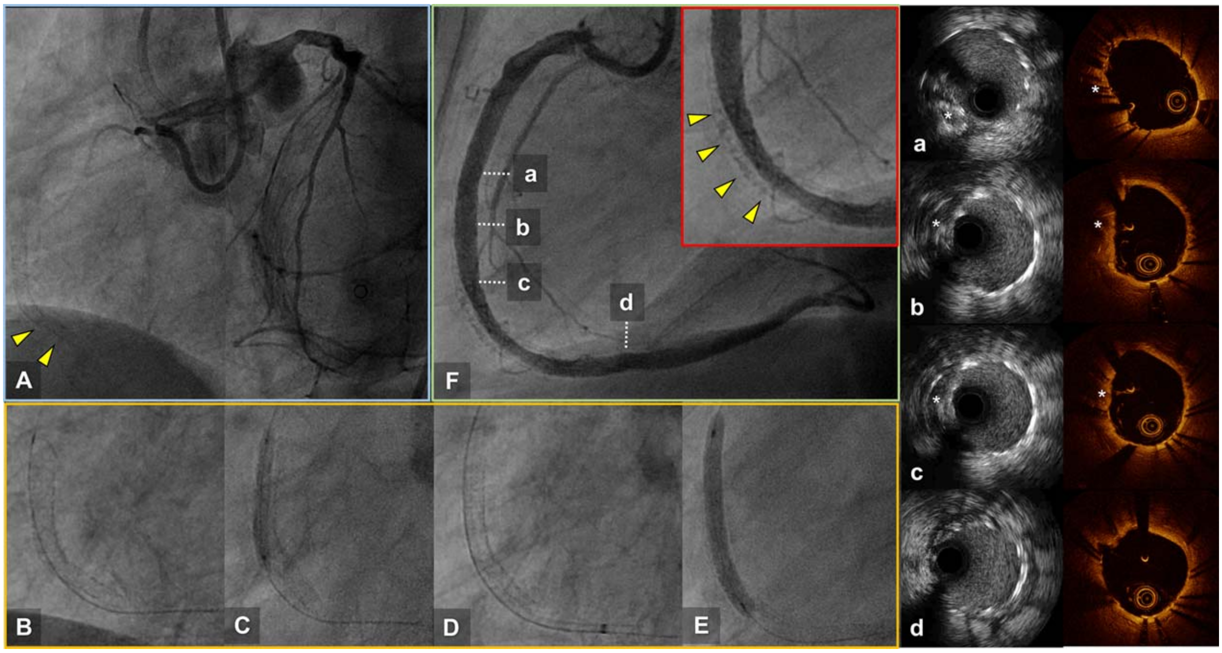


FIGURE 3 Subadventitial stenting around an occluded stent—Case 2. Index procedure. (A) In-stent CTO of the mid-to-distal right coronary artery, likely due to stent undersizing (arrowheads). After multiple within-stent crossing attempts, (B) the occluded stents were eventually crossed in a subadventitial fashion. (C) Predilatation followed. (D) Due to difficulties with stent delivery, a mother-and-child catheter was advanced in the subadventitial space, behind the crushed occluded stent, and (E) new drug-eluting stents were deployed. (F) A good final result was observed, with evident stent crushing (arrowheads). (a–d) Intravascular ultrasound and optical coherence tomography showed adequate crushing of the occluded stent (asterisks) and expansion of the newly deployed stents [Color figure can be viewed at wileyonlinelibrary.com]

implantation, and the other (a post-coronary artery bypass graft patient) underwent surgical removal of a loculated thrombus around the right ventricle (this latter patient also suffered tamponade and periprocedural MI). These two cases were due to predilatation in the subadventitial space with a super-high pressure balloon due to unsuccessful attempts with non-compliant balloons, and to wire exit during

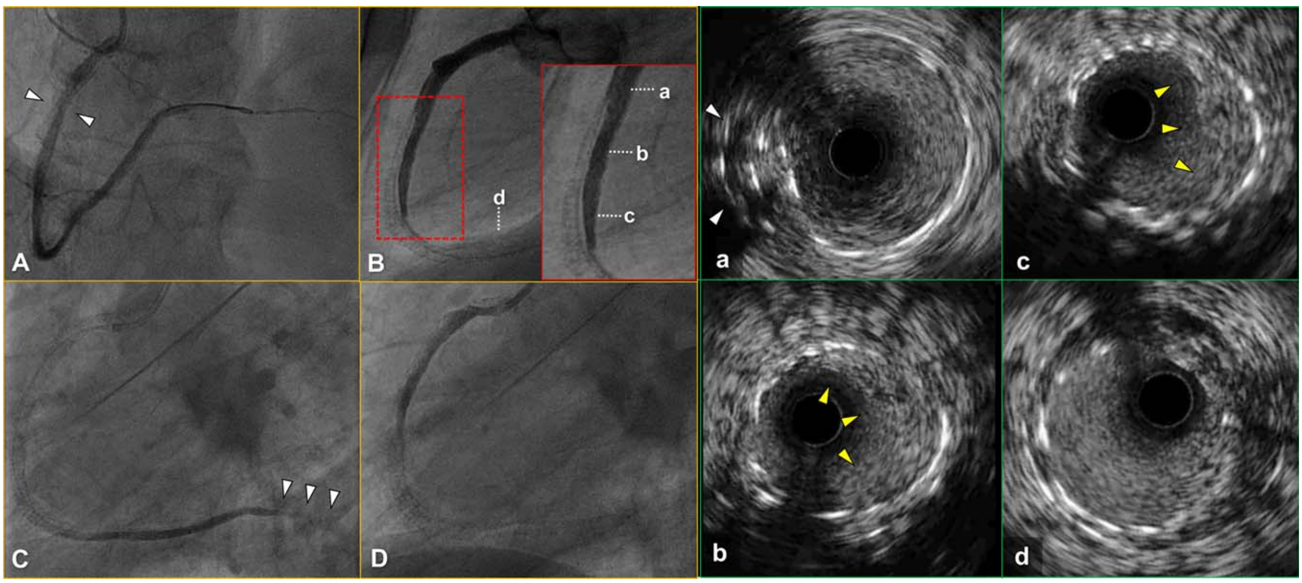


FIGURE 4 Three-month angiographic and imaging follow-up—Case 2. (A) A filling defect was observed in the proximal-to-mid segment (arrowheads). (B) Upon closer examination, a long longitudinal image consistent with a laminar thrombus was identified and predilatation was performed. (C) Intravascular ultrasound confirmed (yellow arrowheads in b–c) stent thrombosis at the (white arrowheads in a) stent crush site. (C) Following multiple balloon dilatations and thrombectomy passages, contrast injection through a microcatheter advanced into the distal vessel indicated a no-reflow phenomenon (arrowheads). (D) Final result, with TIMI 0 flow starting from the proximal right coronary artery [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 1 Baseline clinical characteristics

Variable	SS (*n* = 32)	WSS (*n* = 97)	*P*
Age (years)	62.3 ± 10.2	64.4 ± 10.1	0.31
Male gender	29 (91%)	79 (81%)	0.22
Body mass index (kg/m^2)	30.7 ± 6.4	29.3 ± 5.2	0.25
Diabetes	12 (38%)	42 (44%)	0.51
Dyslipidemia	26 (81%)	79 (85%)	0.62
Hypertension	27 (84%)	73 (79%)	0.47
Current smoker	11 (34%)	20 (23%)	0.20
Prior myocardial infarction	25 (78%)	63 (67%)	0.24
Prior PCI	32 (100%)	97 (100%)	...
Prior coronary artery bypass graft	10 (31%)	21 (22%)	0.27
eGFR (mL/min/1.73 m^2)	70.9 ± 24.0	82.4 ± 26.5	0.03
eGFR <60 mL/min/1.73 m^2	9 (28%)	8 (9%)	0.006
LVEF (%)	52.0 ± 12.5	51.6 ± 11.4	0.87
LVEF <50%	12 (40%)	28 (31%)	0.37
CCS angina class			0.71
I	3 (10%)	4 (5%)	
II	10 (31%)	30 (38%)	
III	13 (41%)	33 (42%)	
IV	3 (9%)	12 (15%)	
Indication of CTO PCI			0.09
Symptoms	21 (66%)	58 (60%)	
Silent ischemia	6 (19%)	17 (18%)	
Low LVEF	4 (13%)	4 (4%)	
Acute coronary syndrome	1 (3%)	17 (18%)	

Abbreviations: CAD, coronary artery disease; eGFR, estimated glomerular filtration rate; LVEF, left ventricular ejection fraction; SS, subadventitial stenting; WSS, within-stent stenting.

CrossBoss redirection while performing subadventitial crossing, respectively.

Complications in the WSS group included five perforations that were managed conservatively; one patient who suffered a perforation with tamponade and major bleeding, and was treated with covered stent implantation; another case of major bleeding; one case of contrast-induced nephropathy; and one periprocedural MI.

3.4 | Follow-up

Table 4 shows angiographic and clinical follow-up of our population. Ten SS patients underwent angiographic follow-up after a mean of 148 ± 123 days. In half of the cases, intravascular imaging was performed, and one patient also underwent multidetector computed tomography (Figure 2). Six of these 10 patients showed persistent stent patency, one had mild in-stent neointimal hyperplasia, and the other three presented in-stent restenosis (ISR) at the SS location, which required treatment. One of these three patients (Figure 4) had also subclinical stent thrombosis at the SS site, which was diagnosed during angiographic follow-up (87 days after the index procedure). Balloon dilatation and thrombectomy were performed. However, final TIMI flow was 0 due to persistent no reflow phenomenon, despite the intracoronary administration of large amounts of sodium nitroprusside. The patient developed periprocedural MI, and subsequently recovered without further complications.

Clinical follow-up was available for 29 SS patients for a mean of 388 ± 303 days, and for 83 subjects in WSS for a mean of 545 ± 379 days. At 24 months, there were no differences in clinical outcomes between SS and WSS. In particular, TVF rates were 13.8% vs. 19.5%, respectively (P = 0.49), driven by TVR (13.8% vs. 15.7%, P = 0.81). Two-year Kaplan–Meier curves of TVF-free survival (Figure 5) showed no differences between groups (log-rank P = 0.92).

4 | DISCUSSION

Our multicenter registry provides novel data on SS for IS-CTO PCI. This technique was feasible when performed by experienced operators and was usually employed exceptionally, after alternative approaches had failed. A variety of techniques was utilized to achieve subadventitial crossing of the occluded stent(s), and crushing involved either the whole stent or just part of it. Invasive imaging was used in a significant proportion of cases, to assess adequate crushing of the occluded stent (s) and evaluate the final result. Procedural complications were low.

TABLE 2 Baseline angiographic characteristics

Variable	SS (*n* = 32)	WSS (*n* = 97)	*P*
Number of diseased vessels	2.0 ± 0.9	1.7 ± 0.8	0.06
Target CTO vessel			0.19
Left anterior descending	6 (19%)	28 (29%)	
Circumflex	3 (9%)	17 (18%)	
Right coronary artery	23 (72%)	52 (54%)	
Blunt stump	26 (81%)	47 (49%)	0.001
Moderate or severe calcifications	13 (41%)	19 (20%)	0.02
>45° bending	18 (56%)	33 (35%)	0.03
Lesion length >20 mm	32 (100%)	65 (69%)	<0.001
Retry	12 (38%)	23 (24%)	0.13
J-CTO score	3.1 ± 0.9	1.9 ± 1.2	<0.001
J-CTO score ≥3	24 (75%)	29 (30%)	<0.001
Proximal cap ambiguity	13 (41%)	32 (34%)	0.50
Absence of interventional collaterals	10 (31%)	20 (21%)	0.25
Moderate or severe tortuosity	9 (28%)	20 (21%)	0.41
PROGRESS-CTO score	1.1 ± 0.9	1.0 ± 0.8	0.38
Ostial CTO	11 (34%)	25 (26%)	0.35
Distal cap at bifurcation	15 (47%)	19 (20%)	0.004
Good distal landing zone	12 (38%)	62 (67%)	0.004
Age of stent occlusion (years)	4.6 ± 4.0	N/A	...

Abbreviations: SC + C, subadventitial stenting; WSS, within-stent stenting.

TABLE 3 Procedural characteristics

Variable	SS (*n* = 32)	WSS (*n* = 97)	*P*
Femoral[a]/radial access	31 (97%)/1 (3%)	67 (69%)/30 (31%)	0.001
Number of techniques used prior to subadventitial crossing	1.4 ± 0.8	...	...
Reasons for failure to achieve within-stent crossing	...	...	...
Stent undersizing	2 (6%)	...	...
Stent fracture	1 (3%)	...	...
Gap between stents	1 (3%)	...	...
Stent was originally implanted subadventitially	1 (3%)	...	...
Hard fibrocalcific tissue	5 (16%)	...	...
Uncrossable distal cap	1 (3%)	...	...
Vessel tortuosity	2 (6%)	...	...
Unknown reason for failure to maintain a within stent track	19 (59%)	...	...
Use of CrossBoss	12 (38%)	27 (28%)	0.30
Crossing technique	...	...	<0.001
Antegrade true-to-true	...	57 (59%)	
Antegrade dissection/re-entry	17 (53%)	16 (17%)	
Retrograde true-to-true	...	11 (11%)	
Retrograde dissection/re-entry	15 (47%)	13 (13%)	
Technique of subadventitial crossing	...	...	...
Wire alone (straight) crossed, then MC followed	5 (16%)	...	...
Wire alone (knuckle) crossed, then MC followed	4 (13%)	...	...
Wire (straight) crossed supported by MC	3 (9%)	...	...
Wire (knuckle) crossed supported by MC	14 (44%)	...	...
CrossBoss	4 (13%)	...	...
Wire + CrossBoss	1 (3%)	...	...
E-CART	1 (3%)	...	...
Subadventitial crushing	...	...	...
Part of stent	12 (37%)	...	...
Whole stent	20 (63%)	...	...
Balloon used for stent crushing	...	...	...
Semi-compliant	17 (53%)	...	...
Non-compliant	15 (47%)	...	...
Balloon diameter for stent crushing (mm)	2.7 ± 0.6	...	...
Diameter of stent implanted in the crushed segment (mm)	3.1 ± 0.4	...	...
Balloon used for post-dilatation	...	...	...
Semi-compliant	1 (3%)	...	...
Non-compliant	30 (97%)	...	...
Balloon diameter for post-dilatation (mm)	3.3 ± 0.5	...	...
Balloon pressure for post-dilatation (atm)	20.0 ± 5.4	...	...
Use of mother-and-child catheter	13 (41%)	15 (16%)	0.003
Imaging	...	...	<0.001
None	13 (41%)	89 (92%)	
IVUS	17 (53%)	8 (8%)	
IVUS and OCT	2 (6%)	0	
Number of guidewires used	8.9 ± 6.1	N/A	
Number of microcatheters used	2.0 ± 0.8	N/A	
Type of stents			
Drug-eluting stents	31 (97%)	93 (98%)	
Bioresorbable scaffolds	0	2 (2%)	0.16
Balloon angioplasty only	1 (3%)	0	...
Number of stents implanted	3.3 ± 1.3	N/A	...

(Continues)

TABLE 3 (Continued)

Variable	SS ($n = 32$)	WSS ($n = 97$)	P
Total stent length (mm)	106 ± 35	77 ± 50	0.004
Contrast volume (mL)	305 ± 144	307 ± 138	0.96
Fluoroscopy time (min)	79 ± 45	51 ± 38	0.002
Radiation dose (Gy·cm^2)	358 ± 256	218 ± 149	0.02
Total procedure time (min)	188 ± 94	121 ± 76	<0.001
Procedural complications			
Perforation managed conservatively	1 (3.1%)	5 (5.2%)	0.64
Perforation with need for intervention	2 (6.3%)	1 (1.0%)	0.09
Tamponade	1 (3.1%)	1 (1.0%)	0.41
Major bleeding	0	2 (1.0%)	0.41
Contrast-induced nephropathy	0	1 (1.0%)	0.56
Periprocedural myocardial infarction	1 (3.1%)	1 (1.0%)	0.41
Stroke	0	0	...
Death	0	0	...

Abbreviations: E-CART, electrocautery-assisted re-entry; IVUS, intravascular ultrasound; MC, microcatheter; OCT, optical coherence tomography; SS, subadventitial stenting; WSS, within-stent stenting.
[a]Indicates cases with at least one femoral access (single femoral, dual femoral, radial and femoral).

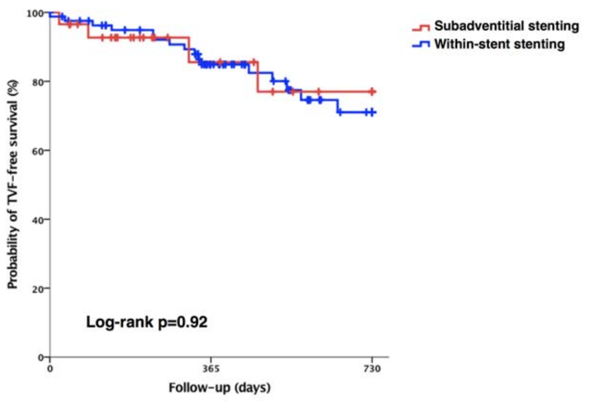
Two-year outcomes revealed an acceptable rate of TVF (13.8%). Importantly, when these data were compared with historical controls recanalized with conventional techniques, it was reassuring to observe no differences in clinical outcomes, despite the fact that lesions were markedly more challenging (higher J-CTO score) in the SS group.

Prior to the present study, evidence on SS for IS-CTO PCI relied on isolated case reports [3–6]. Those procedures were performed either antegradely [3,6] or retrogradely [4,5], both with wire-based dissection [3–5] and re-entry [4,5] or a CrossBoss- [6]/Stingray-based [3,6] approach. Crushing involved either the whole stent [3,4,6] or just part of it [5]. Intravascular ultrasound was performed during the index procedure in two reports [3,5], while no invasive imaging was performed in the other two studies [4,6]. Angiographic follow-up was reported at two [4], six [3], nine [5,6], and 60 [5] months, and showed a durable result in all cases. Compared with these reports, our study presents several strengths. First, it is a cohort study involving a much larger sample size. Second, it involved 14 centers from three continents, and it is therefore representative of a contemporary global experience with this challenging technique. Third, our larger sample size allowed us to identify, for the first time, adverse outcomes at the SS site: namely, three cases of significant ISR requiring treatment, likely secondary to stent recoil in the subadventitial space. Additionally, one

TABLE 4 Angiographic and clinical outcomes on follow-up

	SS	WSS	P
Angiographic follow-up	...	N/A	...
n	10	...	...
Imaging			
None	5 (50%)	...	...
IVUS	3 (30%)	...	...
OCT	1 (10%)	...	...
IVUS + OCT + MDCT	1 (10%)	...	...
Findings at stent crush site			
Persistent good result	6 (60%)	...	...
Mild in-stent neointimal hyperplasia	1 (10%)	...	...
In-stent restenosis requiring treatment[a]	3 (30%)	...	...
Clinical follow-up			
N	29	83	...
2-year outcomes			
Target-vessel failure	4 (13.8%)	16 (19.5%)	0.49
Cardiac death	0	3 (3.6%)	0.30
Target-vessel myocardial infarction	1 (3.4%)	3 (3.6%)	0.97
Target-vessel revascularization	4 (13.8%)	13 (15.7%)	0.81

Abbreviations: IVUS, intravascular ultrasound; MDCT, multidetector computed tomography; OCT, optical coherence tomography; SS, subadventitial stenting; WSS, within-stent stenting.
[a]One patient had also subclinical stent thrombosis proximal to the crush site.



Patients at risk	Baseline	1 year	2 years
Subadventitial stenting	29	12	6
Within-stent stenting	83	48	18

FIGURE 5 Kaplan–Meier curves of two-year target-vessel failure (TVF)-free survival in patients with subadventitial vs. within-stent stenting [Color figure can be viewed at wileyonlinelibrary.com]

of these patients also presented subclinical stent thrombosis at the SS site, which highlights the fact that CTOs might suffer asymptomatic reocclusion due to stent thrombosis, a finding already reported by others [2,12,13]. Finally, our analysis could rely on a contemporary control group of IS-CTOs recanalized with WSS, allowing a comparison between SS and a conventional approach.

The present study provides practical recommendations on how to perform SS to recanalise IS-CTO. Several points deserve discussion. First, given the limited availability of data on the procedural and long-term outcomes of SS, the default approach to recanalise IS-CTO should involve maintaining a within-stent track throughout the occlusion. However, our data suggest that SS is a feasible alternative approach, which was attempted in very challenging IS-CTOs after conventional techniques had failed, and had similar mid-term outcomes compared with historical controls recanalized with WSS.

Second, a variety of devices and techniques are available to achieve subadventitial crossing, including both the antegrade and retrograde approach, using straight or knuckle wires, with or without the assistance of a microcatheter, and even the CrossBoss catheter. In particular, the CrossBoss is often preferred in case of IS-CTOs, since the presence of stent struts is thought to prevent device exit to the subadventitial space, and the CrossBoss blunt tip can easily carve a channel through the occluded stent to the distal true lumen [2,14]. However, Ntatsios and Smith had previously reported that the CrossBoss catheter can actually track through stent struts into the subadventitial space [15]. Additionally, in our experience, a subadventitial track started proximal to the occluded stent with the CrossBoss is also associated with subadventitial crossing.

Third, we have previously reported on the great tensile strength of the adventitia, which can be effectively and safely manipulated to recanalize challenging CTOs, as long as advancement of wires and other devices takes place through a plane that is longitudinal to the vessel main axis [16,17]. The data presented herein extend these findings, suggesting that occluded stents (and their in-stent restenotic tissue) can be crushed from the subadventitial space, and new stents can be deployed and post-dilated, even with large non-compliant balloons. However, it should also be noted that, when dilatation with a non-compliant balloon sized 1:1 with the estimated vessel diameter is unsuccessful (i.e., incomplete expansion is observed), it might be prudent to refrain from performing more aggressive maneuvers (such as using super-high pressure balloons), as shown by one of the cases of perforation in our series.

The use of invasive imaging in the setting of SS can help evaluating reference vessel diameter proximal and distal to the occluded stent(s) (hence choosing the correct balloon size for stent crushing), achieving optimal expansion of the newly implanted stent(s), and confirming exclusion of the occluded stent(s) from coronary flow. Indeed, we believe that invasive imaging should be performed in any case of IS-CTO PCI (tackled with both SS or WSS), in order to ascertain the mechanism leading to stent occlusion, guide stent sizing, and optimize the procedural result, thus minimizing the probability of recurrent restenosis.

Additionally, the use of mother-and-child catheters was highly prevalent in our experience, driven by the difficulty advancing stents and balloons through long subadventitial tracks in close proximity with crushed stents.

Furthermore, mid-term follow-up of our cohort revealed an acceptable rate of TVF (13.8%, driven by TVR), which was similar to conventional WSS (19.5%). In a seminal study in the bare-metal stent era, Mehran et al. indicated that up to a half of IS-CTO cases had suffered a prior episode of ISR, and that IS-CTO was an independent predictor of target-lesion revascularization after recanalization [18]. In this setting, we believe that the benefit of being able to recanalize the occluded stent still outweighs the moderate risk of restenosis.

Our study has several limitations. First, it is an observational study, and is thus susceptible to the effect of unidentified confounders. Second, sample size was small, which might influence exact event rate estimation. Third, only successful cases of SS were included, since identification of procedures in which SS was attempted but failed was not feasible, due to the retrospective nature of our study. Fourth, angiographic follow-up was not available for all patients. Fifth, comparison with WSS was performed using a group of historical controls. Finally, this is a multicenter registry with several experienced operators involved, and our study findings might therefore not be extrapolated to other institutions.

5 | CONCLUSIONS

Our study reports, for the first time, the feasibility and outcomes of IS-CTO recanalized with SS. This technique appears to be feasible and safe, and was associated with acceptable outcomes on mid-term follow-up. Given the small sample size, our findings should be taken with caution, and SS shall currently be used as a last resort to recanalize chronically occluded stents, after failure of conventional within-stent approaches.

CONFLICT OF INTEREST

Dr. Azzalini received honoraria from Guerbet and research support from ACIST Medical Systems. Dr. Riley received honoraria from Spectranetics. Dr. Agostoni received honoraria from Aquilant, Meril, Neovasc, Genae, and Angiodynamics. Dr. Brilakis received consulting/speaker honoraria from Abbott Vascular, Amgen, Asahi, Cardinal Health, Elsevier, GE Healthcare, and Medicure; research support from Osprey and Boston Scientific; spouse is employee of Medtronic. Dr. Rinfret received consulting fees from Boston Scientific. Dr. Mashayekhi has received consulting fees from Asahi Intecc; and has received honoraria from Vascular Solutions. The other authors have no disclosures.

ORCID

Lorenzo Azzalini MD PhD MSc http://orcid.org/0000-0001-9758-0360
Aris Karatasakis MD http://orcid.org/0000-0001-5468-3941
Péter Tajti MD http://orcid.org/0000-0002-3449-7604
Luciano Candilio MD (Res) http://orcid.org/0000-0002-1886-0119
Satoru Mitomo MD http://orcid.org/0000-0001-8972-4352
Emmanouil S. Brilakis MD, PhD http://orcid.org/0000-0001-9416-9701

REFERENCES

[1] Christopoulos G, Karmpaliotis D, Alaswad K, Lombardi WL, Grantham JA, Rangan BV, Kotsia AP, Lembo N, Kandzari DE, Lee J, Kalynych A, Carlson H, Garcia S, Banerjee S, Thompson CA, Brilakis ES. The efficacy of “hybrid” percutaneous coronary intervention in chronic total occlusions caused by in-stent restenosis: Insights from a US multicenter registry. Catheter Cardiovasc Interv 2014;84:646–651.

[2] Azzalini L, Dautov R, Ojeda S, Benincasa S, Bellini B, Giannini F, Chavarría J, Pan M, Carlino M, Colombo A, Rinfret S. Procedural and long-term outcomes of percutaneous coronary intervention for in-stent chronic total occlusion. JACC Cardiovasc Interv 2017;10:892–902.

[3] Roy J, Lucking A, Strange J, Spratt JC. The difference between success and failure: subintimal stenting around an occluded stent for treatment of a chronic total occlusion due to in-stent restenosis. J Invasive Cardiol 2016;28:E136–E138.

[4] Capretti G, Mitomo S, Giglio M, Carlino M, Colombo A, Azzalini L. Subintimal crush of an occluded stent to recanalize a chronic total occlusion due to in-stent restenosis: insights from a multimodality imaging approach. JACC Cardiovasc Interv 2017;10:e81–e83.

[5] Ohya H, Kyo E, Katoh O. Successful bypass restenting across the struts of an occluded subintimal stent in chronic total occlusion using a retrograde approach. Catheter Cardiovasc Interv 2013;82:678–683.

[6] Quevedo HC, Irimpen A, Abi Rafeh N. Succesful antegrade subintimal bypass restenting of in-stent chronic total occlusion. Catheter Cardiovasc Interv 2015;86:E268–E271.

[7] Azzalini L, Vo M, Dens J, Agostoni P. Myths to debunk to improve management, referral, and outcomes in patients with chronic total occlusion of an epicardial coronary artery. Am J Cardiol 2015;116:1774–1780.

[8] Morino Y, Abe M, Morimoto T, Kimura T, Hayashi Y, Muramatsu T, Ochiai M, Noguchi Y, Kato K, Shibata Y, Hiasa Y, Doi O, Yamashita T, Hinohara T, Tanaka H, Mitsudo K. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: The J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. JACC Cardiovasc Interv 2011;4:213–221.

[9] Christopoulos G, Kandzari DE, Yeh RW, Jaffer FA, Karmpaliotis D, Wyman MR, Alaswad K, Lombardi W, Grantham JA, Moses J, Christakopoulos G, Tarar MNJ, Rangan BV, Lembo N, Garcia S, Cipher D, Thompson CA, Banerjee S, Brilakis ES. Development and validation of a novel scoring system for predicting technical success of chronic total occlusion percutaneous coronary interventions. JACC Cardiovasc Interv 2016;9:1–9.

[10] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Thygesen K, Alpert JS, White HD, Jaffe AS, Katus HA, Apple FS, Lindahl B, Morrow DA, Chaitman BR, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Gabriel Steg P, Wijns W, Bassand J-P, Menasche P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon J-L, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S, Bax JJ, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Popescu BA, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Torbicki A, Vahanian A, Windecker S, Morais J, Aguiar C, Almahmeed W, Arnar DO, Barili F, Bloch KD, Bolger AF, Botker HE, Bozkurt B, Bugiardini R, Cannon C, de Lemos J, Eberli FR, Escobar E, Hlatky M, James S, Kern KB, Moliterno DJ, Mueller C, Neskovic AN, Pieske BM, Schulman SP, Storey RF, Taubert KA, Vranckx P, Wagner DR. Third universal definition of myocardial infarction. Eur Heart J 2012;33:2551–2567.

[11] Nicholson W, Harvey J, Dhawan R. E-CART (ElectroCautery-Assisted Re-enTry) of an aorto-ostial right coronary artery chronic total occlusion. JACC Cardiovasc Interv 2016;9:2356–2358.

[12] Ojeda S, Pan M, Romero M, Suárez De Lezo J, Mazuelos F, Segura J, Espejo S, Morenate C, Blanco M, Martín P, Medina A, Suárez De Lezo J. Outcomes and computed tomography scan follow-up of bioresorbable vascular scaffold for the percutaneous treatment of chronic total coronary artery occlusion. Am J Cardiol 2015;115:1487–1493.

[13] Cheneau E, Pichard AD, Stabile E, Waksman R. Asymptomatic late stent thrombosis after sirolimus stent implantation. Cardiovasc Radiat Med 2004;5:57–58.

[14] Wilson WM, Walsh S, Hanratty C, Strange J, Hill J, Sapontis J, Spratt JC. A novel approach to the management of occlusive in-stent restenosis (ISR). EuroIntervention 2014;9:1285–1293.

[15] Ntatsios A, Smith WHT. Exit of CrossBoss between stent struts within chronic total occlusion to subintimal space: Completion of case via retrograde approach with rendezvous in coronary. J Cardiol Cases 2014;9:183–186.

[16] Azzalini L, Carlino M, Brilakis ES, Vo M, Rinfret S, Uretsky BF, Karmpaliotis D, Colombo A. Subadventitial techniques for chronic total occlusion percutaneous coronary intervention: the concept of “vessel architecture.”. Catheter Cardiovasc Interv 2017;Mar 17. doi:10.1002/ccd.27025. [Epub ahead of print].

[17] Capretti G, Carlino M, Colombo A, Azzalini L. Rotational atherectomy in the subadventitial space to allow safe and successful chronic total occlusion recanalization: Pushing the limit further. Catheter Cardiovasc Interv 2017;Apr 18. doi:10.1002/ccd.27035. [Epub ahead of print].

[18] Mehran R, Dangas G, Abizaid AS, Mintz GS, Lansky AJ, Satler LF, Pichard AD, Kent KM, Stone GW, Leon MB. Angiographic patterns of in-stent restenosis: Classification and implications for long-term outcome. Circulation 1999;100:1872–1878.

How to cite this article: Azzalini L, Karatasakis A, Spratt JC, et al. Subadventitial stenting around occluded stents: A bailout technique to recanalize in-stent chronic total occlusions. *Catheter Cardiovasc Interv*. 2018;92: 466–476. https://doi.org/10.1002/ccd.27472