EuroIntervention

Title: **Contemporary Outcomes of the Retrograde Approach to Chronic Total Occlusion Interventions: Insights from an International CTO Registry.**

Authors: Peter Tajti, M.D; Iosif Xenogiannis, M.D; Fotis Gargoulas, M.D; Dimitri Karmpaliotis, M.D, PhD; Khaldoon Alaswad, M.D; Farouc A. Jaffer, M.D, PhD; Mitul Patel, M.D; M. Nicholas Burke, M.D; Santiago Garcia, M.D; Oleg Krestyaninov, M.D; Michalis Koutouzis, M.D; Wissam Jaber, M.D; Emmanouil S. Brilakis, M.D, PhD

DOI: 10.4244/EIJ-D-19-00441

Citation: Tajti P, Xenogiannis I, Gargoulas F, Karmpaliotis D, Alaswad K, Jaffer FA, Patel M, Burke MN, Garcia S, Krestyaninov O, Koutouzis M, Jaber W, Brilakis ES. Contemporary Outcomes of the Retrograde Approach to Chronic Total Occlusion Interventions: Insights from an International CTO Registry. *EuroIntervention* 2019; Jaa-666 2019, doi: 10.4244/EIJ-D-19-00441

Manuscript submission date: 01 May 2019

Revisions received: 06 September 2019, 03 October 2019, 05 October 2019

Accepted date: 16 October 2019

Online publication date: 22 October 2019

Contemporary Outcomes of the Retrograde Approach to Chronic Total Occlusion Interventions: Insights from an International CTO Registry.

Peter Tajti [1,2], MD, Iosif Xenogiannis [1], MD, Fotis Gargoulas [3], MD, Dimitri Karmpaliotis [3], MD, PhD, Khaldoon Alaswad [4], MD, Farouc A. Jaffer [5], MD, PhD, Mitul Patel [6], MD, M. Nicholas Burke [1], MD, Santiago Garcia [1], MD, Oleg Krestyaninov [7], MD, Michalis Koutouzis [8], MD, Wissam Jaber [9], MD, Emmanouil S. Brilakis [1], MD, PhD

[1]Minneapolis Heart Institute, Abbott Northwestern Hospital, Minneapolis, USA; [2]University of Szeged, Division of Invasive Cardiology, Second Department of Internal Medicine and Cardiology Center, Szeged, Hungary; [3]Columbia University, New York, USA; [4]Henry Ford Hospital, Detroit, USA; [5]Massachusetts General Hospital, Boston, USA; [6]VA San Diego Healthcare System and University of California San Diego, La Jolla, USA; [7]Meshalkin Siberian Federal Biomedical Research Center, Novosibirsk, Russian Federation; [8]Korgialeneio-Benakeio Hellenic Red Cross Hospital of Athens, Athens, Greece; [9]Emory University, Atlanta, USA.

Short title: Contemporary Retrograde CTO PCI

A list of study collaborators can be found in the appendix

Running title: Contemporary Retrograde CTO PCI

Corresponding author:

Emmanouil S. Brilakis, MD, PhD

Minneapolis Heart Institute, 920 E 28th Street #300, Minneapolis, Minnesota 55407

E-mail: esbrilakis@gmail.com.

Conflict of interest statement

Dimitri Karmpaliotis: Speaker honoraria: Abbott Vascular, Boston Scientific, Medtronic, Vascular Solutions. **Khaldoon Alaswad:** Consulting fees: Terumo, Boston Scientific; consultant: Abbott Laboratories. **Farouc A. Jaffer:** Consultant: Abbott Vascular, Boston Scientific, Siemens, Philips. Research grant: Canon, Siemens, National Institutes of Health. **Robert W. Yeh:** Career Development Award (1K23HL118138) from National Heart, Lung, and Blood Institute. **Mitul Patel:** Speakers' bureau: Astra Zeneca. **Ehtisham Mahmud:** Consulting fees: Medtronic, Corindus; speaker's fees: Medtronic, Corindus, Abbott Vascular; educational program fees: Abbott Vascular; clinical events committee fees: St. Jude. **M. Nicholas Burke:** Consulting/speaking honoraria: Abbott Vascular, Boston Scientific. **R. Michael Wyman:** Honoraria/consulting/speaking fees: Boston Scientific, Abbott Vascular, Asahi. **David Kandzari:** Research grant/consulting honoraria: Boston Scientific, Medtronic Cardiovascular; and research grant: Abbott. **Santiago Garcia:** Consulting fee: Medtronic. **Jaikirshan Khatri:** Research grant: Asahi Intecc; consultant/speaker honoraria: Abbott Vascular, Philips, Abiomed. **Jeffrey Moses:** Consultant: Boston Scientific, Abiomed. **Nicholas Lembo:** Speaker bureau: Medtronic; advisory board: Abbott Vascular,Medtronic. **Manish Parikh:** Speaker bureau: Abbot Vascular, Medtronic, CSI, BSC, Trireme; advisory boards: Medtronic, Abbott Vascular, Philips. **Ajay Kirtane:** Research grants: Boston Scientific, Medtronic, Abbott Vascular, Abiomed, St. Jude Medical, Vascular Dynamics, Glaxo SmithKline, Eli Lilly. **Ziad Ali:** Consultant fees/honoraria: St. Jude Medical, AstraZeneca Pharmaceuticals; ownership interest/partnership/principal: Shockwave Medical, VitaBx Inc; research grant: Medtronic, St. Jude Medical. **Bavana Rangan:** Research grants: InfraReDx, Inc., The Spectranetics Corporation. **Subhash Banerjee:** Research grants: Gilead, Medicines Company; consultant/speaker honoraria: Covidien, Medtronic; ownership: MDCARE Global (spouse); intellectual property: HygeiaTel. **Emmanouil S. Brilakis:** consulting/speaker honoraria: Abbott Vascular, American Heart Association (associate editor Circulation), Boston Scientific, Cardiovascular Innovations Foundation (Board of Directors), CSI, Elsevier, GE Healthcare, InfraRedx, Medtronic; research support: Regeneron, Siemens. Shareholder: MHI Ventures. Board of Trustees: Society of Cardiovascular Angiography and Interventions.

Abstract

Aims: The retrograde approach is critical for achieving high success rates in chronic total occlusion (CTO) percutaneous coronary intervention (PCI), but has been associated with higher risk of complications.

Methods and results: We compared the technical and procedural outcomes of retrograde (n=1,515) and antegrade-only CTO PCIs (n=2,686) in a contemporary multicenter CTO registry. The mean age of patients undergoing retrograde PCI was 65±10 years and 86% were men, with high prevalence of prior myocardial infarction (51%), prior PCI (71%), and coronary artery bypass graft surgery (45%). The mean J-CTO (3±1 vs 2±1 p<0.001) was higher in retrograde PCIs. The most commonly used collateral channels were septals (65%), epicardials (32%), saphenous venous grafts (14%) and left internal mammary artery grafts (2%). Overall technical (79% vs 91%, p<0.001) and procedural (75% vs 90%, p<0.001) success rates were lower with the retrograde approach, and patients had higher in-hospital major complications rate than antegrade-only PCIs (5.1% vs 0.8%, p<0.001), due to higher mortality (1.1% vs. 0.1%, p<0.001), acute myocardial infarction (1.9% vs 0.2%, p<0.001), repeat-PCI (0.7% vs 0.1%, p=0.001), and pericardiocentesis (1.7% vs 0.3%, p<0.001).

Conclusions: In summary, retrograde approach to CTO PCI is performed in higher complexity lesions and is associated with lower success and higher major complications rates.

Clinical Trial Registration: NCT02061436, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS CTO)

Classifications: chronic coronary total occlusion, stable angina, other techniques

Condensed abstract

The retrograde approach has become an essential tool for chronic total occlusion (CTO) percutaneous coronary intervention (PCI) improving overall success to ~85-90%. We compared the technical and procedural outcomes of the retrograde approach (n=1,515) with antegrade-only CTO PCIs (n=2,686) in a contemporary CTO registry. Lesion were more complex in the retrograde group (J-CTO [3±1 vs. 2±1 p<0.001]), whereas overall technical (79% vs. 91%, p<0.001) and procedural (75% vs. 90%, p<0.001) success rates were lower. Patients with retrograde approach had higher in-hospital major complications rate compared to antegrade-only PCIs (5.1% vs. 0.8%, p<0.001).

Abbreviations

CABG – Coronary Artery Bypass Graft

CTO – Chronic Total Occlusion

J-CTO – Japan Chronic Total Occlusion

MACE – Major Adverse Cardiac Events

MI – Myocardial Infraction

PCI – Percutaneous Coronary Intervention

PROGRESS CTO - Prospective Global Registry of Chronic Total Occlusion Interventions

Introduction

Since its introduction more than a decade ago (1,2), the retrograde approach has become an essential tool for chronic total occlusion (CTO) percutaneous coronary intervention (PCI), and has been instrumental in improving technical success to ~85-90% from ~80% achieved with antegrade-only interventions (3,4). The retrograde approach usually requires two guide catheters and has four key technical steps including: (a) advancement of a guidewire and microcatheter through a collateral vessel or a bypass graft distal to the occlusion, (b) crossing the occlusion, (c) wire externalization and (d) balloon angioplasty with stent implantation (5). The hybrid approach (6) recommends upfront retrograde crossing in CTOs with proximal cap ambiguity and/or poor distal target as well as after failure of antegrade crossing, if there are interventional collaterals. We examined the contemporary outcomes of the retrograde approach to CTO PCI aiming to identify areas in need of improvement.

Material and methods

We analyzed the clinical, angiographic, and procedural characteristics of 4,201 CTO PCIs performed in 4,108 patients enrolled in the PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention, NCT02061436) registry between May 2012 and November 2018 at 21 US, one European, and one Russian centers. Some centers only enrolled patients during part of the study period due to participation in other studies. The study was approved by the institutional review board of each center.

Coronary CTO was defined as a coronary lesion with Thrombolysis In Myocardial Infarction (TIMI) grade 0 flow of at least 3 months duration. Estimation of the duration of occlusion was clinical, based on the first onset of angina, prior history of myocardial infarction in the target vessel territory, or comparison with a prior angiogram. Calcification was assessed by angiography as mild (spots), moderate (involving ≤50% of the reference lesion diameter) and severe (involving >50% of the reference lesion diameter). Moderate proximal vessel tortuosity was defined as the presence of at least 2 bends >70° or 1 bend >90° and severe tortuosity as 2 bends >90° or 1 bend >120° in the CTO vessel. Blunt or no stump was defined as lack of tapering or lack of a funnel shape at the proximal cap. Interventional collaterals were defined as collaterals considered amenable to crossing by a guidewire and a microcatheter by the operator. Werner classification was used for collateral channel assessment (7).

A procedure was defined as "retrograde" if an attempt was made to cross the lesion through a collateral vessel or bypass graft supplying the target vessel distal to the lesion; if not, the procedure was classified as "antegrade-only". Antegrade dissection/re-entry was defined as antegrade PCI during which a guidewire was intentionally introduced into the subintimal space proximal to the lesion, or re-entry into the distal true lumen was attempted following intentional or inadvertent subintimal guidewire crossing.

Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI grade 3 antegrade flow. Procedural success was defined as the achievement of technical success without any in-hospital complications. In-hospital major adverse cardiac events (MACE) included any of the following adverse events prior to hospital discharge: death, myocardial infarction, recurrent symptoms requiring urgent repeat target vessel revascularization with PCI or coronary artery bypass graft surgery (CABG), tamponade requiring either pericardiocentesis or surgery, and stroke. Myocardial infarction (MI) was defined using the Third Universal Definition of Myocardial Infarction (type 4a MI). Major bleeding was defined as bleeding causing reduction in hemoglobin >3 g/dl or bleeding requiring transfusion or surgical intervention. The J-CTO score was calculated as described by Morino et al (8), the CASTLE score as described by Szijgyarto et al (9), the PROGRESS CTO score as described by Christopoulos et al (10), and the PROGRESS CTO Complications score as described by Danek et al (11).

Categorical variables were expressed as percentages and were compared using Pearson's chi-square test or Fisher's exact test. Continuous variables were presented as mean ± standard deviation or median [interquartile range, IQR] unless otherwise specified and were compared using the t-test and 1-way analysis of variance (ANOVA) for normally distributed variables; the Wilcoxon rank-sum test, and the Kruskal-Wallis test were applied for non-parametric continuous variables, as appropriate. Multivariable logistic regression was used to examine the association between use of the retrograde approach and in-hospital MACE, as well as to identify predictors for retrograde technical failure. Variables with significant univariable association ($p<0.1$) were entered into the models. All statistical analyses were performed with JMP 13.0 (SAS Institute, Cary, North Carolina). A two-sided p value of 0.05 was considered statistically significant.

Results

Retrograde CTO PCI was attempted in 1,505 patients (36.7%) undergoing 1,515 interventions which were compared to 2,686 antegrade-only CTO PCIs performed in 2,603 patients (63.3%).

Patients undergoing retrograde CTO PCI were older and had higher prevalence of coronary risk factors, prior myocardial infarction, history of prior PCI and coronary artery bypass graft surgery (CABG) **(Table 1)**.

In the retrograde group, lesions were significantly more complex **(Table 2)**. Retrograde cases had better developed collaterals (Werner Class 1: 58.1% vs. 49.0%; Werner Class 2: 31.8% vs. 20.7%, both p<0.001).

The main technical characteristics are summarized in **Table 3**. In primary retrograde cases the main indications for selection of the retrograde approach were the followings: long occlusion length (36.6%), ostial occlusions (27.5%), side-branch at proximal cap (25.6%), poor distal target vessel (24.6%), bifurcation at distal cap (22.1%), proximal cap ambiguity (15.8%), and tortuosity (14.2%). The retrograde approach was more successfully applied as crossing strategy in more complex lesions (**Figure 1**).

Overall technical and procedural success in the retrograde group was 79.2% and 75.4% respectively, and was significantly lower compared with antegrade-only cases (90.5% and 90.0%, both p<0.001). In cases with successful retrograde CTO crossing technical success was 98.4%, whereas in CTOs with retrograde wire crossing failure successful CTO revascularization was achieved in 49.4% (**Supplementary Table 1**). The following collateral pathways were used: septal collaterals (62.0%), contralateral epicardial collaterals (29.9%), and saphenous vein grafts (13.5%) (**Figure 2 Panel A**). Successful collateral channel crossing was achieved in 75.3% (**Figure 2 Panel B**). Epicardial collaterals were more likely to be attempted as a second or third collateral, and low profile microcatheters were used more frequently (**Figure 3**). The most commonly used crossing techniques are summarized in **Figure 2 Panel C**. In lesions with successful retrograde attempt, the most commonly used crossing technique was the reverse controlled antegrade and retrograde tracking (CART) (53.2%) (**Figure 2 Panel D**). In 8 cases retrograde wire crossing was achieved with various retrograde techniques (marker wire technique [n=4]; CART [n=2]; true-to-true wiring [n=1]; reverse CART [n=1]), however externalization failed leading to technical failure. The predictors of retrograde technical failure are summarized in **Supplementary Table 2**. Retrograde cases required longer procedure and fluoroscopy time, higher volume of contrast and air kerma radiation dose compared with antegrade-only procedures (**Figure 4**).

The overall in-hospital major adverse cardiac event (MACE) rate of retrograde CTO PCI was 5.1%, and any procedure related complication occurred in 18.9% (**Figure 5 Panel A** and **B**, **Table 4**). The incidence of coronary perforation was significantly higher in retrograde cases (8.6% vs. 2.2%, p<0.001), and perforations were more severe (Ellis Class III or Class III-cavity spilling 41.3% vs. 22.9%, p=0.133). The incidence of tamponade requiring pericardiocentesis, however, was caused similarly by antegrade wiring (n=12, 46.2%) and retrograde wiring (n=14, 53.8%) attempts during retrograde interventions, and it occurred more frequently if retrograde approach was the successful crossing technique (66.7% vs. 33.3%, p=0.225). Covered stents were used in 10.0% (n=10) of all perforations during the retrograde approach (n=140), and in 11.5% (n=3) of all cases when pericardiocentesis was required (n=26). On multivariable logistic regression (**Supplementary Table 3**), the retrograde approach was independently associated with increased risk for in-hospital MACE (OR 3.94, CI 95% 2.01-8.20, $p<0.001$). In-hospital MACE and periprocedural complication rates were similar in cases with retrograde success compared with retrograde attempt failure (**Figure 6 and 7**).

The temporal trends of retrograde CTO PCI outcomes are presented in **Supplementary Table 4**. Additional procedural and patient characteristics are given in **Supplementary Table 5**.

Discussion and limitations

Our study is one the largest published to date examining the technical outcomes of retrograde CTO PCI. The major findings are as follows: (a) retrograde CTO PCI remains essential for CTO PCI, especially in complex lesions; (b) retrograde interventions are associated with higher in-hospital and periprocedural complications compared to antegrade-only interventions; (c) collateral crossing is successful in three quarters of cases limiting retrograde CTO crossing success, (d) approximately half of the perforations requiring pericardiocentesis during retrograde CTO PCI were due to antegrade wiring attempts.

Antegrade wire escalation remains the most frequently used, and most often successful CTO crossing strategy. The retrograde approach, however, remains essential for CTO PCI success especially in complex occlusions when the antegrade approach fails or is not feasible (3). The decreasing use of the retrograde approach in recent years may reflect improvements in antegrade wiring techniques and devices (especially novel, highly torquable guidewires).

In our study the overall success rate of retrograde interventions was 79.2% with procedural success of 75.4%, which is similar to those of the European CTO Registry [n=1582 CTO PCI, clinical success of 75.3% (4)]. The slight decrease over time in technical and procedural success is likely explained by increasing CTO complexity (**Supplementary Table 4**) and high prevalence of prior coronary artery bypass graft surgery.

Septal surfing and contrast guided techniques (also known as distal tip injection technique) are currently used for collateral crossing (12). Dautov et al. showed that septal collateral surfing was successful in 81% in 240 CTO PCIs even if collaterals are invisible (Werner Class CC 0) (13). Septal surfing was the most common collateral crossing strategy in cases with retrograde success (75.5%) in our study, whereas microcatheter tip injection guidance was used in 24.5%. Overall collateral channel crossing (by guidewire and microcatheter) success was 75.3%.

Once the guidewire and microcatheter cross the collateral channel, CTO crossing can also be challenging and is usually achieved using the reverse CART technique (1). In our cohort reverse CART was the most commonly attempted and most commonly successful crossing strategy..

Retrograde CTO PCI has been reported to have higher risk of complications in numerous cohorts compared with antegrade approaches (both antegrade wiring and/or antegrade dissection re-entry techniques).

Similarly, in our study in-hospital MACE was 5.1% in the retrograde group (overall procedural complications 18.9%), and was significantly higher than antegrade-only interventions. However, approximately half of the complications (46.2%) were caused by antegrade wiring (46.2%), suggesting that a significant portion of the higher retrograde CTO PCI risk is related to the complexity of the treated lesions. Furthermore, although coronary perforations were observed in 8.6% of the procedures treated with the retrograde approach, only 1.7% required pericardiocentesis with the majority being treated conservatively.

Performing retrograde CTO PCI over the years has undergone significant changes with decreasing use of radiation and contrast despite increased lesion complexity as reflected in the increasing J-CTO scores (**Supplementary Table 4**). Such improvements could be attributed to optimized imaging, use of contrast saving equipment and techniques (such as the DyeVert system [Osprey Medical Inc., Minnetonka, MN, USA], use of IVUS) and continuous education. Although the retrograde approach carries increased risk for complications, our study shows that some of the complications attributed to the retrograde approach were actually due to antegrade crossing attempts during the same procedure and were likely related to high lesion complexity.

Limitations of our study include the lack of core laboratory assessment of the study angiograms, lack of independent clinical event adjudication; limited availability of follow-up for the study patients. Furthermore, the procedures were performed in dedicated, high volume CTO centers by experienced operators, limiting the extrapolation to less experienced operators and lower volume centers. The selection of crossing strategy was made by each operator, likely reflecting local expertise and operator/patient preferences.

The novel classification of the reverse CART techniques were not used in our current study, however it was only introduced recently limiting the data revision retrospectively (14). Procedure related myocardial infarction events are site reported without systematic post-procedural biomarker assessment, hence the rate of such complications may be underestimated.

Conclusions

The retrograde approach remains critical for the success of CTO PCI, especially in more complex occlusions. The retrograde approach should be performed by experienced operators and centers given its association with higher risk for complications.

Impact on daily practice

The retrograde approach is an important technique for crossing coronary chronic total occlusions, especially for more complex lesions. However, the retrograde approach carries increased risk for complications, especially perforation, even though some of the complications are related to antegrade crossing attempts during the same procedure. As a result, appropriate case selection, early recognition – and if necessary – timely treatment of coronary perforation is critical for reducing the rate of complications during retrograde chronic total occlusion interventions.

Acknowledgements

Study data were collected and managed using Research Electronic Data Capture (REDCap) electronic data capture tools hosted at the Minneapolis Heart Institute Foundation, Minneapolis, MN, USA. REDCap is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

Funding Sources

The PROGRESS CTO registry has received support from the Abbott Northwestern Hospital Foundation, Minneapolis, MN, USA.

Appendix

Robert W. Yeh [1], Hector Tamez [1], MD, Ehtisham Mahmud [2], MD, James W. Choi [3], MD, Dmitrii Khelimskii [4], MD, Jaikirshan J. Khatri [5], MD, Ioannis Tsiafoutis [6], MD, Anthony H. Doing [7], MD, Phil Dattilo [7], MD, Catalin Toma [8], MD, Barry F. Uretsky [9], MD, Habib Samady [10], MD, Brian Jefferson [11], MD, Taral Patel [11], MD, Srinivasa Potluri, MD [12], David Kandzari [13], MD, R. Michael Wyman [14], MD, Shuaib Abdullah [15], MD, Jeffrey Moses [16], MD, Nicholas Lembo [16], MD, Manish Parikh [16], MD, Ajay Kirtane [16], MD, Ziad A. Ali [16], MD, Juan J. Russo [16], MD, Emad Hakemi [16], MD, Bavana Rangan [17], BDS, MPH, Imre Ungi [18], MD, PhD, Subhash Banerjee [15], MD

[1]Beth Israel Deaconess Medical Center, Boston, MA, USA; [2]VA San Diego Healthcare System and University of California San Diego, La Jolla, USA; [3]Baylor Heart and Vascular Hospital,

Dallas, USA; [4]Meshalkin Siberian Federal Biomedical Research Center, Ministry of Health of Russian Federation, Novosibirsk, Russian Federation; [5]Cleveland Clinic, Cleveland, USA; [6]Korgialeneio-Benakeio Hellenic Red Cross General Hospital of Athens, Athens, Greece; [7]Medical Center of the Rockies, Loveland, USA; [8]University of Pittsburgh Medical Center, Pittsburgh, USA; [9]VA Central Arkansas Healthcare System, Little Rock, USA; [10]Emory University, Atlanta, USA; [11]Tristar Centennial Medical Center, Nashville, USA; [12]The Heart Hospital Baylor Plano, Plano, USA; [13]Piedmont Heart Institute, Atlanta, USA; [14]Torrance Memorial Medical Center, Torrance, USA; [15]VA North Texas Health Care System and University of Texas Southwestern Medical Center. Dallas, USA; [16]Columbia University, New York, USA; [17]Minneapolis Heart Institute, Abbott Northwestern Hospital, Minneapolis, USA; [18]University of Szeged, Division of Invasive Cardiology, Second Department of Internal Medicine and Cardiology Center, Szeged, Hungary.

References

1. Saito S. Different strategies of retrograde approach in coronary angioplasty for chronic total occlusion. Catheter Cardiovasc Interv 2008;71:8-19.

2. Tsuchikane E, Katoh O, Kimura M, Nasu K, Kinoshita Y, Suzuki T. The first clinical experience with a novel catheter for collateral channel tracking in retrograde approach for chronic coronary total occlusions. JACC Cardiovasc Interv 2010;3:165-71.

3. Karmpaliotis D, Karatasakis A, Alaswad K, Jaffer FA, Yeh RW, Wyman RM, Lombardi WL, Grantham JA, Kandzari DE, Lembo NJ, Doing A, Patel M, Bahadorani JN, Moses JW, Kirtane AJ, Parikh M, Ali ZA, Kalra S, Nguyen-Trong PK, Danek BA, Karacsonyi J, Rangan BV, Roesle MK, Thompson CA, Banerjee S, Brilakis ES. Outcomes With the Use of the Retrograde Approach for Coronary Chronic Total Occlusion Interventions in a Contemporary Multicenter US Registry. Circ Cardiovasc Interv 2016;9.

4. Galassi AR, Sianos G, Werner GS, Escaned J, Tomasello SD, Boukhris M, Castaing M, Buttner JH, Bufe A, Kalnins A, Spratt JC, Garbo R, Hildick-Smith D, Elhadad S, Gagnor A, Lauer B, Bryniarski L, Christiansen EH, Thuesen L, Meyer-Gessner M, Goktekin O, Carlino M, Louvard Y, Lefevre T, Lismanis A, Gelev VL, Serra A, Marza F, Di Mario C, Reifart N, Euro CTOC. Retrograde Recanalization of Chronic Total Occlusions in Europe: Procedural, In-Hospital, and Long-Term Outcomes From the Multicenter ERCTO Registry. J Am Coll Cardiol 2015;65:2388-400.

5. Brilakis ES, Grantham JA, Thompson CA, DeMartini TJ, Prasad A, Sandhu GS, Banerjee S, Lombardi WL. The retrograde approach to coronary artery chronic total occlusions: a practical approach. Catheter Cardiovasc Interv 2012;79:3-19.

6. Brilakis ES, Grantham JA, Rinfret S, Wyman RM, Burke MN, Karmpaliotis D, Lembo N, Pershad A, Kandzari DE, Buller CE, DeMartini T, Lombardi WL, Thompson CA. A percutaneous treatment algorithm for crossing coronary chronic total occlusions. JACC Cardiovasc Interv 2012;5:367-79.

7. Werner GS, Ferrari M, Heinke S, Kuethe F, Surber R, Richartz BM, Figulla HR. Angiographic assessment of collateral connections in comparison with invasively determined collateral function in chronic coronary occlusions. Circulation 2003;107:1972-7.

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, Investigators JCR. 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;4:213-21.

9. Szijgyarto Z, Rampat R, Werner GS, Ho C, Reifart N, Lefevre T, Louvard Y, Avran A, Kambis M, Buettner HJ, Di Mario C, Gershlick A, Escaned J, Sianos G, Galassi A, Garbo R, Goktekin O, Meyer-Gessner M, Lauer B, Elhadad S, Bufe A, Boudou N, Sievert H, Martin-Yuste V, Thuesen L, Erglis A, Christiansen E, Spratt J, Bryniarski L, Clayton T, Hildick-Smith D. Derivation and Validation of a Chronic Total Coronary Occlusion Intervention Procedural Success Score From the 20,000-Patient EuroCTO Registry: The EuroCTO (CASTLE) Score. JACC Cardiovasc Interv 2019;12:335-342.

10. Christopoulos G, Kandzari DE, Yeh RW, Jaffer FA, Karmpaliotis D, Wyman MR, Alaswad K, Lombardi W, Grantham JA, Moses J, Christakopoulos G, Tarar MN,

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: The PROGRESS CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention) Score. JACC Cardiovasc Interv 2016;9:1-9.

11. Danek BA, Karatasakis A, Karmpaliotis D, Alaswad K, Yeh RW, Jaffer FA, Patel MP, Mahmud E, Lombardi WL, Wyman MR, Grantham JA, Doing A, Kandzari DE, Lembo NJ, Garcia S, Toma C, Moses JW, Kirtane AJ, Parikh MA, Ali ZA, Karacsonyi J, Rangan BV, Thompson CA, Banerjee S, Brilakis ES. Development and Validation of a Scoring System for Predicting Periprocedural Complications During Percutaneous Coronary Interventions of Chronic Total Occlusions: The Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS CTO) Complications Score. J Am Heart Assoc 2016;5.

12. Galassi AR, Werner GS, Boukhris M, Azzalini L, Mashayekhi K, Carlino M, Avran A, Konstantinidis NV, Grancini L, Bryniarski L, Garbo R, Bozinovic N, Gershlick AH, Rathore S, Di Mario C, Louvard Y, Reifart N, Sianos G. Percutaneous recanalisation of chronic total occlusions: 2019 consensus document from the EuroCTO Club. EuroIntervention 2019;15:198-208.

13. Dautov R, Urena M, Nguyen CM, Gibrat C, Rinfret S. Safety and Effectiveness of the Surfing Technique to Cross Septal Collateral Channels during Retrograde Chronic Total Occlusion Percutaneous Coronary Intervention. EuroIntervention 2016.

14. Matsuno S, Tsuchikane E, Harding SA, Wu EB, Kao HL, Brilakis ES, Mashayekhi K, Werner GS. Overview and proposed terminology for the reverse controlled antegrade and retrograde tracking (reverse CART) techniques. EuroIntervention 2018;14:94-101.

Figure legends

Figure 1. Technical success of CTO interventions with retrograde approach (n=1,515) compared to antegrade-only interventions (n=2,686) stratified by the J-CTO score.

Figure 2. Technical outcomes of all the retrograde CTO interventions in terms of collateral crossing (**Panel A and B**) and wire crossing techniques (**Panel C and D***).

** 8 cases included with successful wire crossing, but retrograde failure due to failed wire externalization.*

Figure 3. Technical characteristics of collateral channel crossing attempts during the retrograde approach in terms of used collaterals, successfully crossed guidewires and microcatheters.

Figure 4. Procedural characteristics compared between retrograde CTO PCI versus antegrade-only interventions.

Figure 5. Distribution of periprocedural complications (**Panel A**) and in-hospital major complications (**Panel B**) of successful and failed retrograde CTO PCIs.

Figure 6. In-hospital major adverse cardiac events in failed and successful retrograde CTO PCIs.

Figure 7. Periprocedural complications of failed and successful retrograde CTO PCIs.

Table 1. Baseline characteristics of patients undergoing retrograde and antegrade-only CTO PCI.

Variable	Overall (n=4108)	Retrograde (n=1505)	Antegrade-only (n=2603)	P value
Age (years) [a]	64.5 ± 10.1	65.0 ± 10.2	64.2 ± 10.0	0.028
Male gender	84.2%	85.7%	83.4%	0.066
Coronary artery disease presentation				0.277
• Stabile angina	65.0%	66.3%	64.4%	
• Acute coronary syndrome	25.0%	24.8%	25.1%	
• Other	9.9%	8.9%	10.5%	
Diabetes mellitus	42.1%	42.3%	42.0%	0.874
Dyslipidemia	89.4%	92.6%	87.6%	***<0.001***
Hypertension	90.6%	90.4%	90.7%	0.798
Prior myocardial infarction	47.6%	50.8%	45.8%	***0.004***
Congestive heart failure	30.7%	31.7%	30.2%	0.356
Prior percutaneous coronary intervention	64.3%	71.2%	60.4%	***<0.001***
Prior coronary artery bypass graft surgery	31.9%	44.8%	24.6%	***<0.001***
Estimated glomerular filtration rate (ml/min/1.73 m^2) [a]	72.7 ± 21.7	71.7 ± 21.7	73.3 ± 21.8	0.065
Peripheral artery disease	14.0%	16.6%	12.6%	***<0.001***
Left ventricular ejection fraction (%) [b]	54 (42, 60)	54 (40, 60)	54 (43, 60)	0.246

[a] mean ± standard deviation; [b] median (interquartile range)

CTO, chronic total occlusion; PCI, percutaneous coronary intervention.

Table 2. Angiographic characteristics of chronic total occlusions undergoing retrograde and antegrade-only PCI.

Variable	Overall (n=4201)	Retrograde (n=1515)	Antegrade-only (n=2686)	P value
Target vessel				**<0.001**
• Right coronary artery	54.8%	67.0%	47.8%	
• Left anterior descending artery	24.5%	16.3%	29.2%	
• Circumflex artery	19.4%	15.7%	21.5%	
• Other	1.3%	1.0%	1.5%	
Occlusion length (mm)	32.7 ± 23.0	41.8 ± 26.6	28.0 ± 19.3	**<0.001**
Proximal cap ambiguity	36.2%	55.6%	25.9%	**<0.001**
Interventional collaterals	57.0%	79.4%	45.1%	**<0.001**
Werner collateral classification				**<0.001**
• Class 0	24.6%	10.1%	30.3%	
• Class 1	51.6%	58.1%	49.0%	
• Class 2	23.8%	31.8%	20.7%	
Moderate/severe calcification	52.9%	68.3%	43.6%	**<0.001**
Moderate/severe tortuosity	34.2%	46.6%	26.7%	**<0.001**
In-stent restenosis	16.6%	13.6%	18.3%	**<0.001**
Previously failed attempt	20.9%	26.3%	17.8%	**<0.001**
J-CTO Score [a]	2.4 ± 1.3	3.2 ± 1.1	2.0 ± 1.2	**<0.001**

PROGRESS CTO Score [a]	1.3 ± 1.0	1.4 ± 1.0	1.3 ± 1.1	**0.020**
CASTLE Score [a]	**2.1 ± 1.3**	**2.8 ± 1.3**	**1.7 ± 1.2**	**<0.001**
PROGRESS CTO Complication Score [a]	3.0 ± 1.9	4.0 ± 1.7	2.4 ± 1.8	**<0.001**

[a] mean ± standard deviation

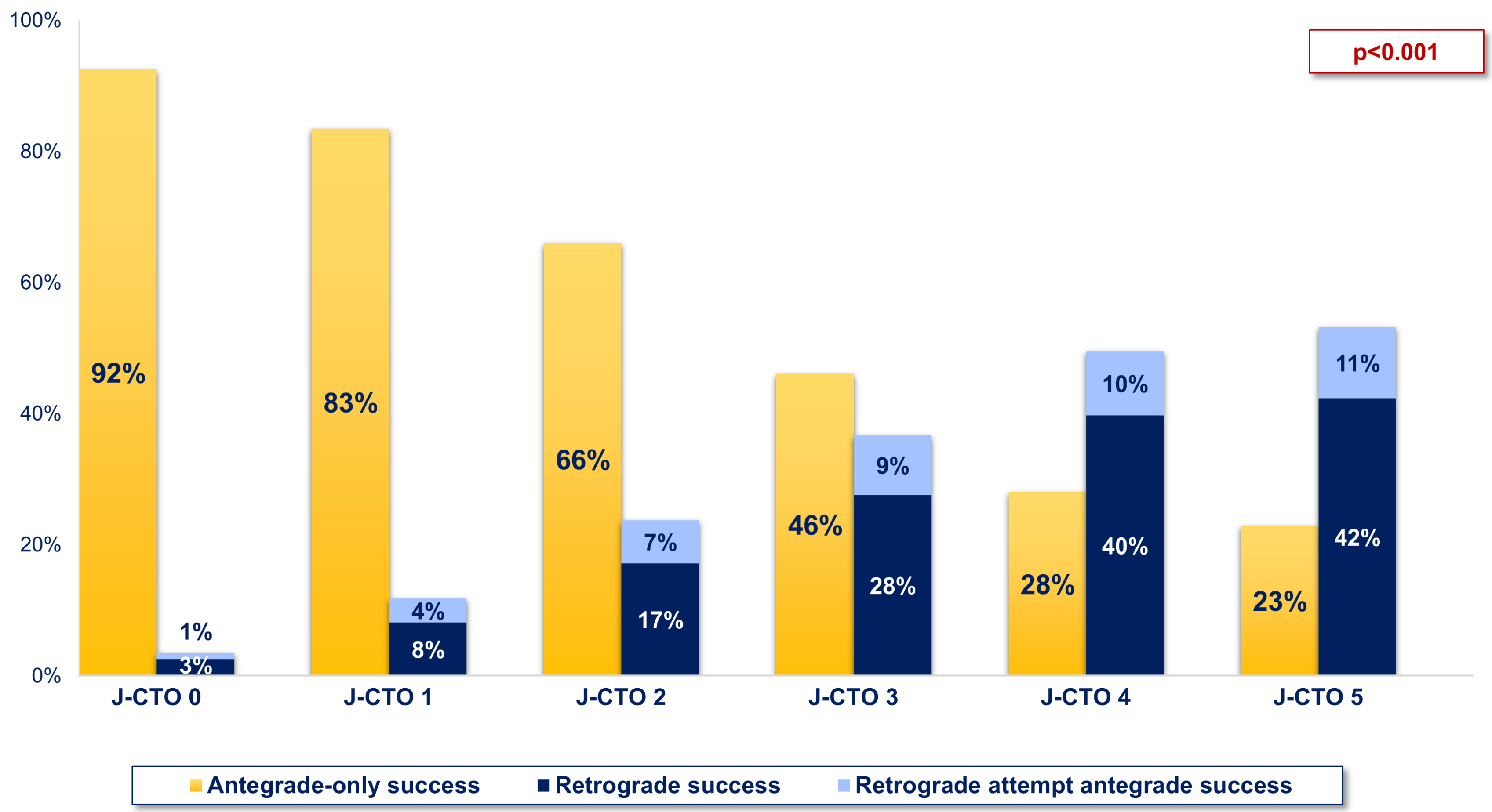
Table 3. Technical characteristics of CTO interventions in cases with the retrograde and antegrade only approaches.

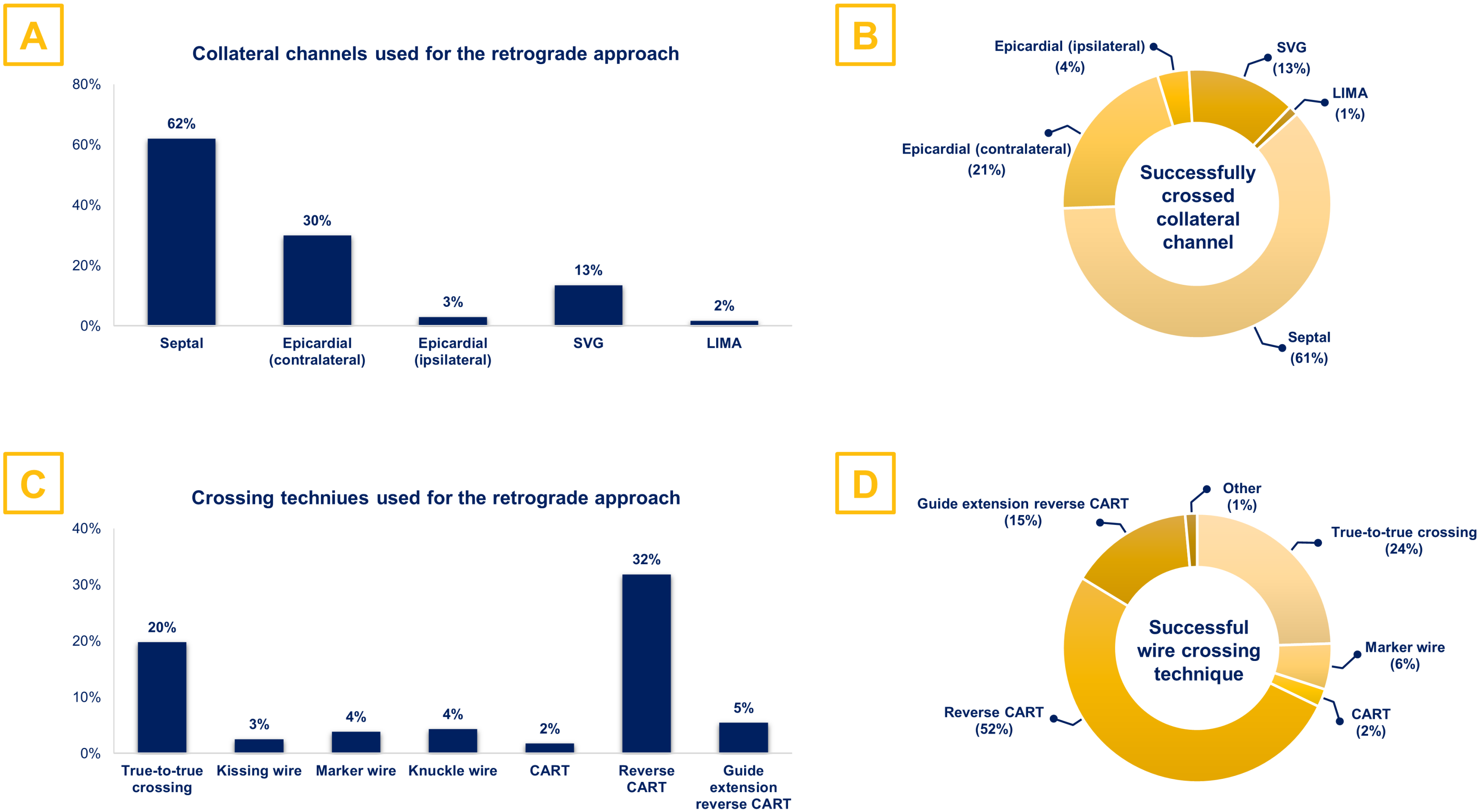
Variable	Overall (n=4201)	Retrograde (n=1515)	Antegrade-only (n=2686)	P value
Dual injection	68.9%	85.9%	59.3%	**<0.001**
Crossing strategies used				
• AWE	84.4%	68. 5%	93.5%	**<0.001**
• ADR	28.6%	36.1%	24.4%	**<0.001**
• Retrograde	36.1%	100.0%	0.0%	**<0.001**
First crossing strategy				**<0.001**
• AWE	78.9%	55.4%	92.2%	
• ADR	7.0%	5.5%	7.8%	
• Retrograde	14.1%	39.1%	0.0%	
Final crossing strategy				**<0.001**
• AWE	49.4%	7.9%	72.7%	
• ADR	17.2%	12.6%	19.8%	
• Retrograde	22.0%	61.0%	0.0%	
• None	11.5%	18.4%	7.6%	
Access site				
• Right femoral	75.0%	82.8%	70.7%	**<0.001**
• Left femoral	46.5%	61.1%	38.2%	**<0.001**
• Right radial	38.9%	39.2%	38.7%	0.737
• Left radial	19.8%	24.5%	17.2%	**<0.001**
Technical success	86.4%	79.21%	90.51%	**<0.001**
Number of stents [a]	2.4 ± 1.1	2.9 ± 1.1	2.1 ± 1.1	**<0.001**
Overall stent length (mm) [a]	70.4 ± 36.3	89.4 ± 36.5	61.5 ± 32.7	**<0.001**

[a] mean ± standard deviation
ADR, antegrade dissection and re-entry; AWE, antegrade wire escalation.

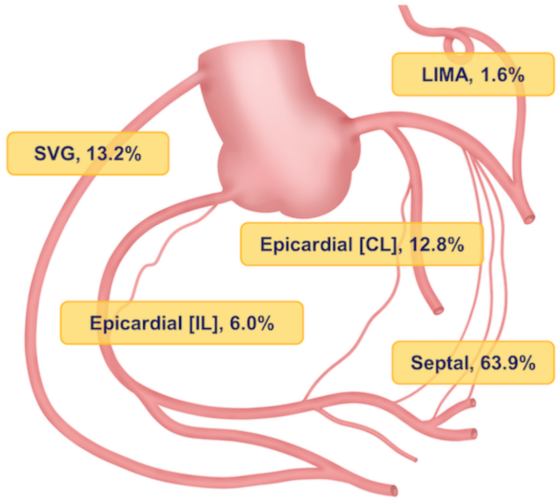
Table 4. Procedural outcomes of retrograde and antegrade-only CTO PCIs.

Variable	Overall (n=4108)	Retrograde (n=1505)	Antegrade-only (n=2603)	P value
Procedural success	84.8%	75.4%	90.0%	**<0.001**
In-hospital major adverse cardiac event	2.36%	5.05%	0.81%	**<0.001**
Death	0.46%	1.06%	0.12%	**<0.001**
Acute myocardial infarction	0.85%	1.93%	0.23%	**<0.001**
Stroke	0.22%	0.40%	0.12%	0.083
Emergency re-intervention	0.29%	0.66%	0.08%	**0.001**
Emergency surgery	0.12%	0.20%	0.08%	0.363
Pericardiocentesis	0.80%	1.66%	0.31%	**<0.001**
Procedural complications	10.6%	18.9%	5.9%	**<0.001**
Perforation	4.53%	8.57%	2.19%	**<0.001**
• Target vessel	1.83%	2.86%	1.23%	**<0.001**
• Collateral vessel	0.58%	1.53%	0.04%	**<0.001**
▪ Septal	0.34%	0.86%	0.04%	**<0.001**
▪ Epicardial	0.32%	0.86%	0.00%	**<0.001**
• Other	0.17%	0.07%	0.23%	0.434
Peroration type				0.133
• Ellis Class I	20.87%	17.50%	28.57%	
• Ellis Class II	43.48%	41.25%	48.57%	
• **Ellis Class III**	35.65%	41.25%	22.86%	


100%
80%
60%
40%
20%
0%
p<0.001
92%
1%
3%
83%
4%
8%
66%
7%
17%
46%
9%
28%
28%
10%
40%
23%
11%
42%
J-CTO 0
J-CTO 1
J-CTO 2
J-CTO 3
J-CTO 4
J-CTO 5
Antegrade-only success
Retrograde success
Retrograde attempt antegrade success


A
Collateral channels used for the retrograde approach
80%
60%
40%
20%
0%
62%
30%
3%
13%
2%
Septal
Epicardial (contralateral)
Epicardial (ipsilateral)
SVG
LIMA
B
Epicardial (ipsilateral) (4%)
SVG (13%)
LIMA (1%)
Epicardial (contralateral) (21%)
Successfully crossed collateral channel
Septal (61%)
C
Crossing techniues used for the retrograde approach
40%
30%
20%
10%
0%
20%
3%
4%
4%
2%
32%
5%
True-to-true crossing
Kissing wire
Marker wire
Knuckle wire
CART
Reverse CART
Guide extension reverse CART
D
Guide extension reverse CART (15%)
Other (1%)
True-to-true crossing (24%)
Successful wire crossing technique
Marker wire (6%)
Reverse CART (52%)
CART (2%)

1st collateral crossing attempt



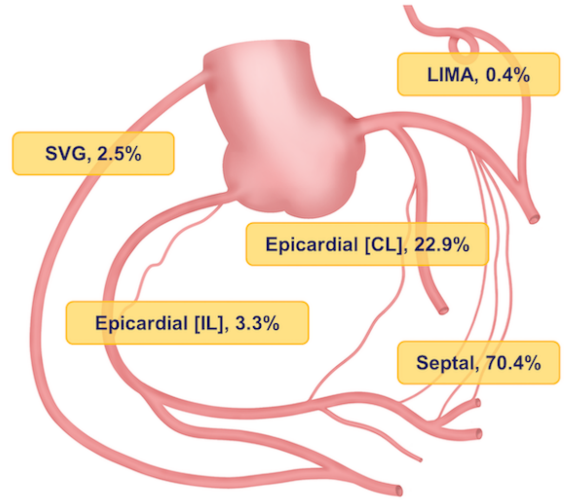
Guidewire crossed

1. Sion (43.7%)
2. Pilot 200 (14.8%)
3. Fielder FC (9.6%)

Microcatheter crossed

1. Corsair (55.9%)
2. TurnPike LP (12.7%)
3. Caravel (9.6%)

2nd collateral crossing attempt



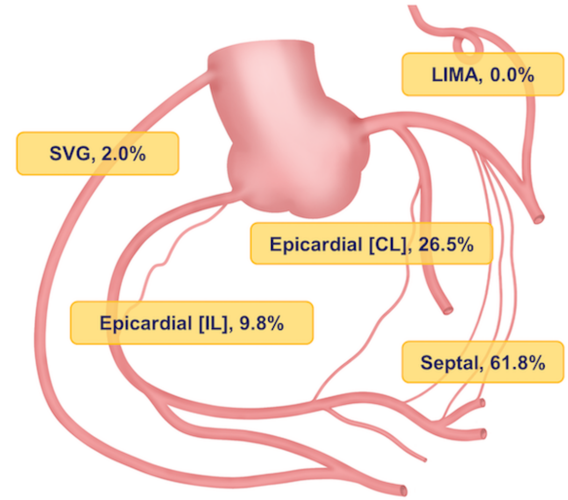
Guidewire crossed

1. Sion (48.2%)
2. Fielder FC (18.1%)
3. Whisper MS (12.1%)

Microcatheter crossed

1. Caravel (31.2%)
2. TurnPike LP (30.3%)
3. Corsair (15.8%)

3rd collateral crossing attempt

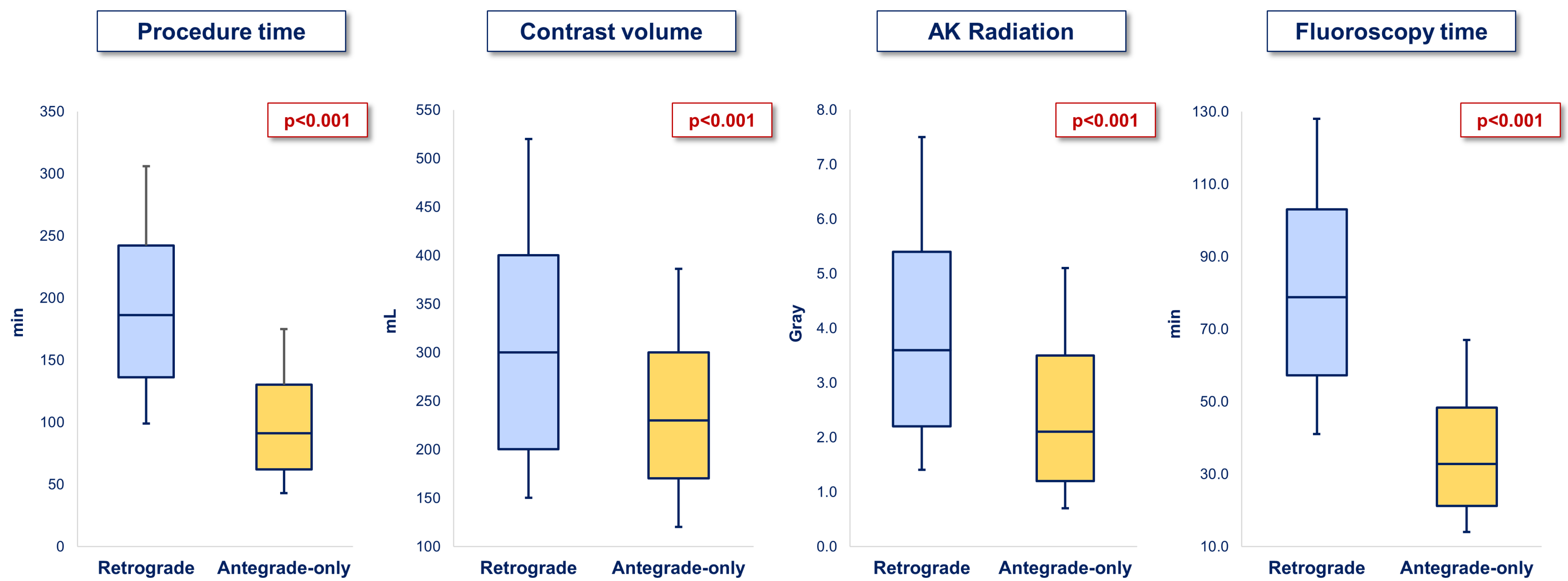


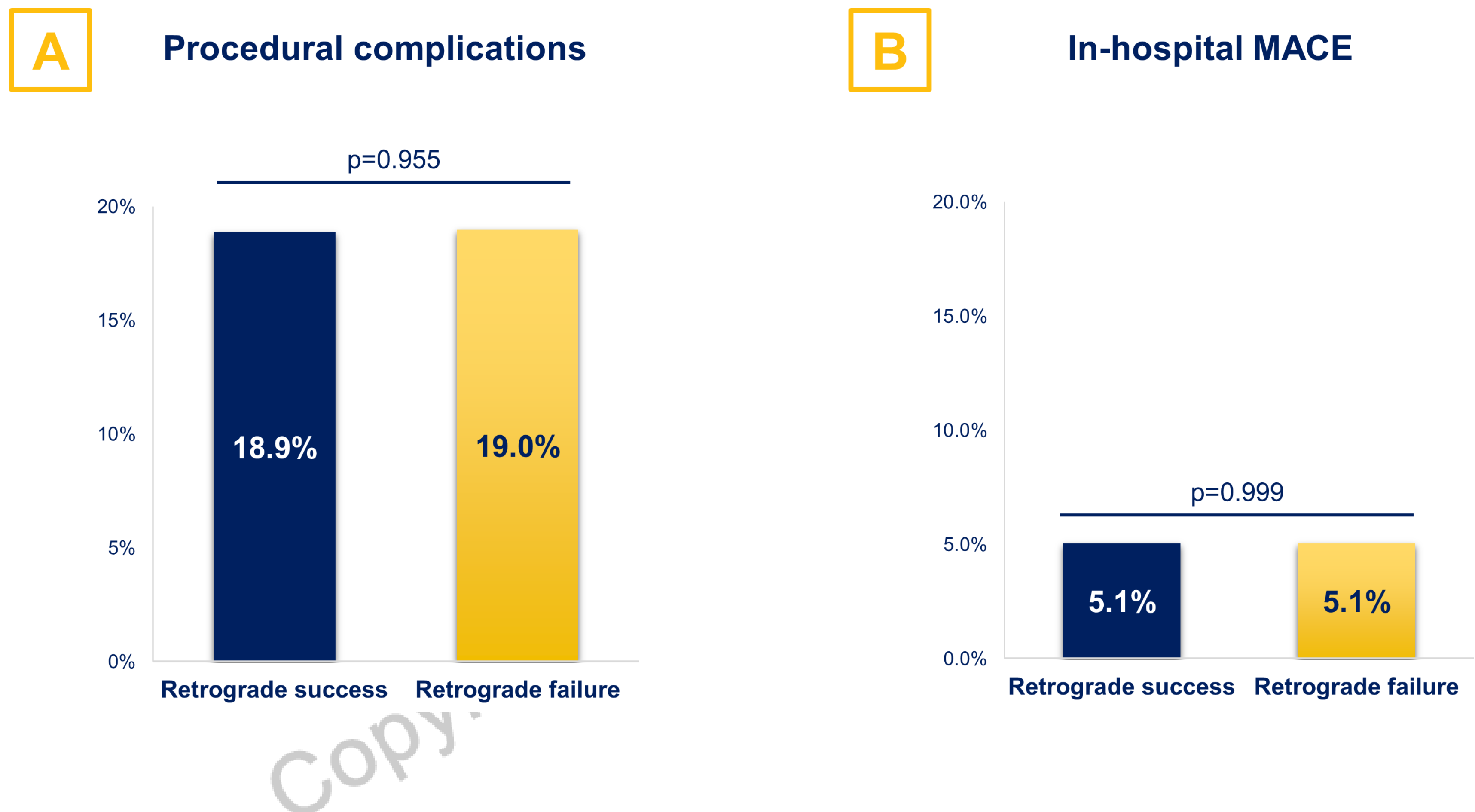
Guidewire crossed

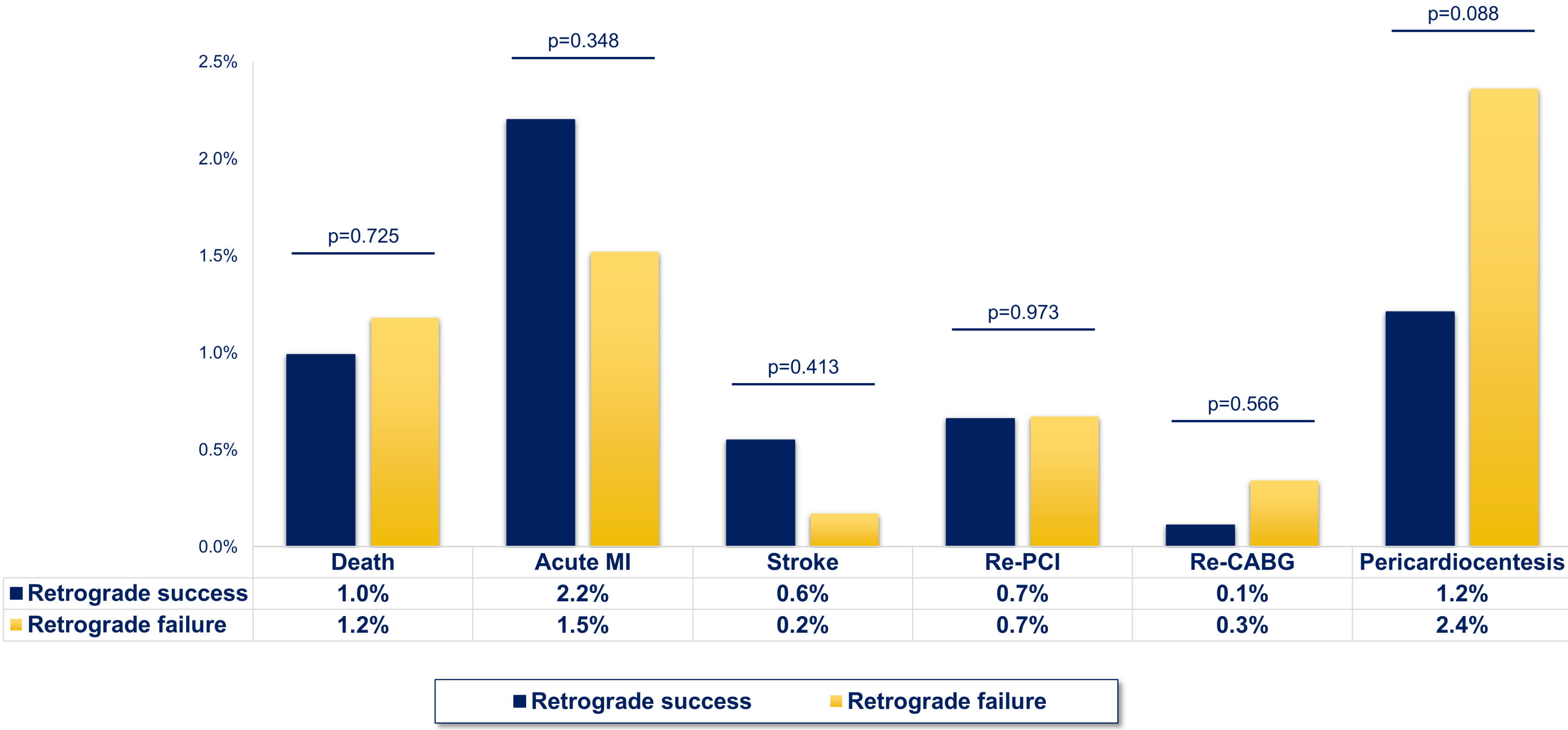
1. Sion (36.5%)
2. Whisper MS (19.2%)
3. Fielder FC (15.4%)

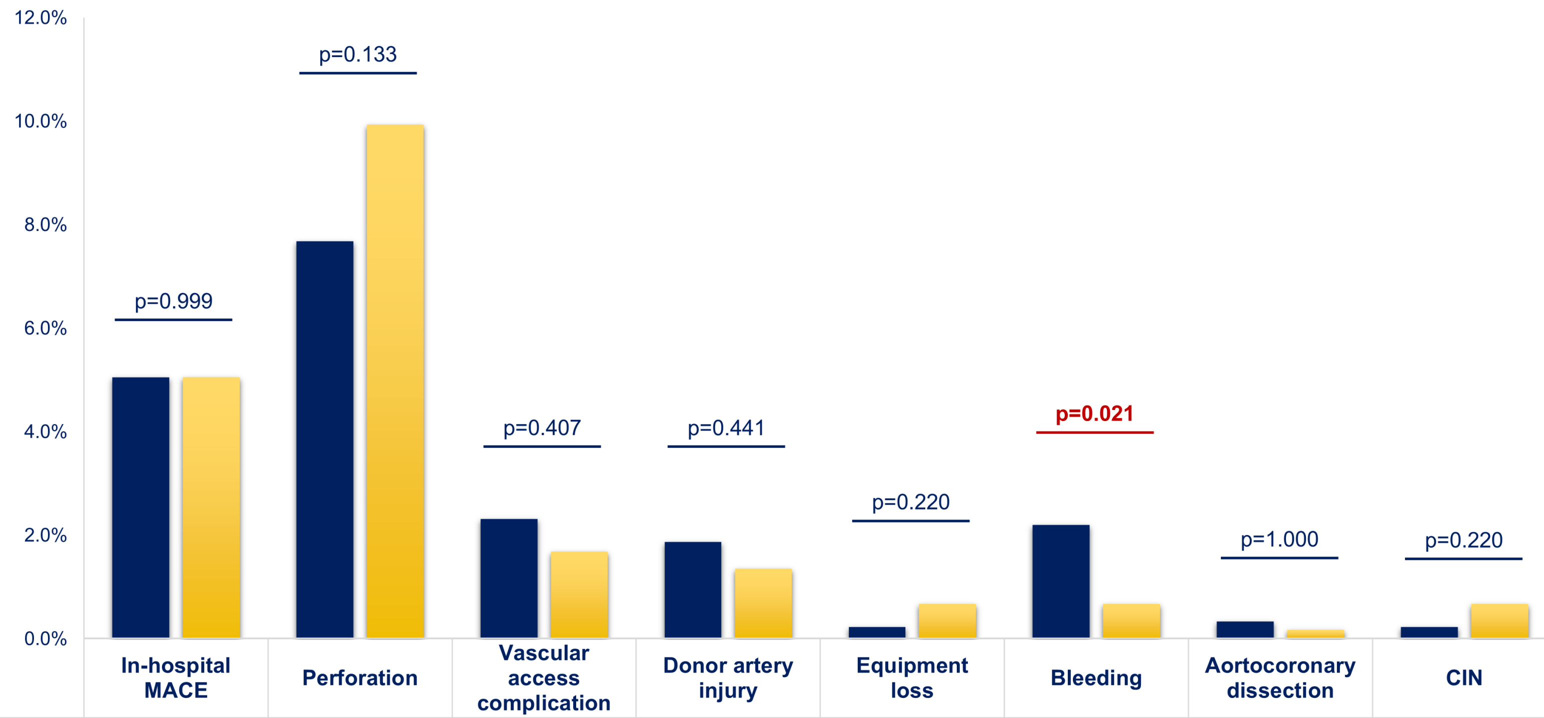
Microcatheter crossed

1. Caravel (36.4%)
2. Corsair (30.6%)
3. TurnPike LP (18.4%)


Procedure time
Contrast volume
AK Radiation
Fluoroscopy time
p<0.001
p<0.001
p<0.001
p<0.001
min
mL
Gray
min
350
300
250
200
150
100
50
0
550
500
450
400
350
300
250
200
150
100
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
Retrograde
Antegrade-only
Retrograde
Antegrade-only
Retrograde
Antegrade-only
Retrograde
Antegrade-only


A
Procedural complications
p=0.955
20%
15%
10%
5%
0%
18.9%
19.0%
Retrograde success
Retrograde failure
B
In-hospital MACE
20.0%
15.0%
10.0%
p=0.999
5.0%
0.0%
5.1%
5.1%
Retrograde success
Retrograde failure


p=0.725
p=0.348
p=0.413
p=0.973
p=0.566
p=0.088
2.5%
2.0%
1.5%
1.0%
0.5%
0.0%
Death
Acute MI
Stroke
Re-PCI
Re-CABG
Pericardiocentesis
Retrograde success
1.0%
2.2%
0.6%
0.7%
0.1%
1.2%
Retrograde failure
1.2%
1.5%
0.2%
0.7%
0.3%
2.4%
Retrograde success
Retrograde failure



	In-hospital MACE	Perforation	Vascular access complication	Donor artery injury	Equipment loss	Bleeding	Aortocoronary dissection	CIN
Retrograde success	5.1%	7.7%	2.3%	1.9%	0.2%	2.2%	0.3%	0.2%
Retrograde failure	5.1%	9.9%	1.7%	1.4%	0.7%	0.7%	0.2%	0.7%

Retrograde success   Retrograde failure

Supplementary Material

Centers participating in the current study

1. Appleton Cardiology, Appleton, WI, USA;

2. Baylor Heart and Vascular Hospital, Dallas, TX, USA;

3. Beth Israel Deaconess Medical Center, Boston, MA, USA;

4. Central Arkansas Veterans Health System, Little Rock, AR, USA;

5. Cleveland Clinic, Cleveland, OH, USA;

6. Columbia University, New York, NY, USA;

7. Emory University, Atlanta, GA, USA;

8. Henry Ford Hospital, Detroit, MI, USA;

9. Korgialeneio-Benakeio Hellenic Red Cross General Hospital of Athens, Athens, Greece;

10. Massachusetts General Hospital, Boston, MA, USA;

11. Medical Center of the Rockies, Loveland, CO, USA;

12. Meshalkin Siberian Federal Biomedical Research Center, Ministry of Health of Russian Federation, Novosibirsk, Russian Federation;

13. Minneapolis Heart Institute, Minneapolis, MN, USA;

14. Minneapolis VA Medical Center, Minneapolis, MN, USA;

15. Piedmont Heart Institute, Atlanta, GA, USA;

16. PeaceHealth St. Joseph Medical Center, Bellingham, WA, USA;

17. St. Luke's Health System's Mid-America Heart Institute, Kansas City, MO, USA;

18. The Heart Hospital Baylor Plano, Plano, TX, USA;

19. Torrance Memorial Center, Torrance, CA, USA;

20. Tristar Centennial Medical Center, Nashville, TN, USA;

21. VA North Texas Health Care System, Dallas, TX, USA;

22. UC San Diego / VA San Diego Healthcare System, San Diego, CA, USA;

23. UPMC Presbyterian, Pittsburgh, PA, USA.

Definitions (Supplement)

Adequate distal landing zone was defined as a distal vessel segment with a diameter of larger than 2.0 mm, and without diffuse disease. Angiographic assessment of collateral channels were performed as described by Werner (CC0 grade: no continuous connection; CC1 grade: threadlike continuous connection; CC2: side branch-like continuous connection).

Reverse controlled antegrade and retrograde subintimal tracking and dissection (reverse CART) was defined as retrograde wire crossing facilitated by antegrade balloon inflation thus allowing retrograde wire re-entry to proximal true lumen, whereas the CART technique was defined as retrograde balloon advancement and inflation to facilitate antegrade wire re-entry. Guide extension reverse CART was defined as antegrade insertion of a guide catheter extension to serve as target for the advancement of the retrograde guidewire. True-to-true retrograde wiring was defined as intraluminal wire crossing from the distal to proximal cap of the occlusion, and marker wire technique was defined as advancement of a retrograde guidewire to facilitate antegrade wire escalation (AWE) or antegrade dissection re-entry (ADR).

Procedural complications are the composite of in-hospital MACE, perforation, pericardial tamponade, vascular access complications, bleeding, contrast nephropathy, donor vessel dissection/thrombosis, aortocoronary dissection, equipment loss.

Supplementary Table 1. Collateral channel crossing techniques during successful and failed retrograde CTO PCIs.

Variable	Overall (n=1515)	Retrograde success (n=922)	Retrograde failure (n=593)	P value
Technical success	79.2%	98.4%	49.4%	**0.0001**
Used collateral channel				
• Septal	62.0%	62.6%	61.1%	0.5478
• Epicardial – contralateral	29.9%	27.3%	33.9%	**0.0065**
• Epicardial – ipsilateral	3.0%	2.0%	4.6%	**0.0036**
• Saphenous vein graft	13.5%	14.0%	12.7%	0.4546
• Left internal mammary artery	1.7%	1.6%	1.9%	0.7387
Number of collaterals used [a]	1.5 ± 0.8	1.4 ± 0.7	1.8 ± 0.8	**0.0001**
Collateral crossing attempt #1				
Crossing technique				**0.0001**
• Surfing-only	58.4%	65.3%	47.2%	
• Contrast guided	41.6%	34.7%	52.8%	
Successful wire crossing	65.6%	87.3%	31.3%	**0.0001**
Successful microcatheter crossing	61.4%	84.8%	23.8%	**0.0001**
Collateral crossing attempt #2				
Crossing technique				0.1250
• Surfing-only	61.0%	66.4%	56.3%	
• Contrast guided	39.0%	33.7%	43.7%	
Successful wire crossing	35.1%	63.3%	12.5%	**0.0001**
Successful microcatheter crossing	32.5%	61.8%	8.3%	**0.0001**

Collateral crossing attempt #3				
Crossing technique				0.4460
• Surfing-only	55.1%	59.5%	51.8%	
• Contrast guided	44.9%	40.5%	48.2%	
Successful wire crossing	50.5%	90.9%	21.3%	**0.0001**
Successful microcatheter crossing	48.0%	90.9%	15.5%	**0.0001**
Successful collateral crossing	75.3%	100.0%	35.0%	**0.0001**
Final collateral crossing technique				**0.0482**
• Surfing-only	73.5%	75.5%	64.5%	
• Contrast guided	26.5%	24.5%	35.5%	
Finally crossed collateral channel				**0.0001**
• Septal	61.1%	63.1%	40.0%	
• Epicardial – contralateral	20.8%	18.3%	46.7%	
• Epicardial – ipsilateral	3.8%	4.2%	0.0%	
• Saphenous vein graft	13.1%	13.1%	13.3%	
• Left internal mammary artery	1.1%	1.3%	0.0%	

[a] mean ± standard deviation

Supplementary Table 2. Multivariable analysis for predicting technical failure of retrograde CTO PCI.

Variable	Odds Ratio	Lower CI 95%	Upper CI 95%	P value
CASTLE score [a] [per 1 unit increase]	*1.22*	*1.04*	*1.42*	*0.013*
eGFR *[per 1 unit increase]*	0.99	0.99	1.00	0.154
PROGRESS CTO score [b] [per 1 unit increase]	*1.28*	*1.05*	*1.56*	*0.017*
Prior PCI	1.29	0.85	2.00	0.237
Prior Failed CTO PCI Attempt	1.46	0.96	2.22	0.077
Dual Injection	0.59	0.35	1.00	0.050
Radial Access Used	*0.67*	*0.46*	*0.98*	*0.039*
Smoking	1.09	0.67	1.74	0.718
>2 CTO PCI During The Same Procedure	*3.28*	*1.33*	*8.02*	*0.010*
IVUS Use For Crossing	0.81	0.44	1.44	0.489

[a] Described bySzijgyarto et al. [b] Described by Christopoulos et al.

CI, confidence interval; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; IVUS, intravascular ultrasound; PCI, percutaneous coronary intervention.

Supplementary Table 3. Multivariable analysis for in-hospital major adverse cardiac events (MACE).

	Odds Ratio	Lower CI 95%	Upper CI 95%	P value
CASTLE score [a] [per 1 unit increase]	*1.30*	*1.05*	*1.61*	*0.015*
eGFR *[per 1 unit increase]*	0.99	0.98	1.00	0.054
>2 CTO Lesions Treated During The Same Procedure	*3.21*	*1.04*	*8.13*	*0.043*
Prophylactic LVAD Use	2.53	0.96	5.81	0.060
Female Gender	1.89	0.98	3.46	0.058
Retrograde Approach	*3.94*	*2.01*	*8.20*	*<0.001*
Peripheral Artery Disease	1.81	0.92	3.38	0.085
Prior MI	1.29	0.75	2.26	0.361
Interventional Collaterals	1.61	0.85	3.26	0.150
Prior Failed CTO PCI Attempt	1.47	0.79	2.66	0.218

[a] Described by Szijgyarto et al. CI, confidence interval; CTO, chronic total occlusion; eGFR, estimated glomerular filtration rate; LVAD, left ventricular assist device; MI, myocardial infarction; PCI, percutaneous coronary intervention.

Supplementary Table 4. Temporal trends of technical and procedural outcomes of CTO PCI with using the retrograde approach.

	2012	2013	2014	2015	2016	2017	2018	P value
Overall CTO PCI success rate (including antegrade-only cases)	**91.1%**	**88.1%**	**87.6%**	**84.6%**	**81.0%**	**82.7%**	**84.5%**	**<0.001**
Outcomes of the retrograde approach								
Prevalence *	39.3%	42.9%	36.8%	42.8%	40.2%	30.4%	29.9%	<0.001
J-CTO score * [a]	3.1 ± 0.9	3.2 ± 1.0	2.7 ± 1.1	3.3 ± 1.0	3.2 ± 1.1	3.0 ± 1.1	3.4 ± 1.1	<0.001
Final successful crossing strategy *								0.010
• **AWE**	5.1%	11.6%	8.6%	5.6%	9.0%	7.4%	7.7%	
• **ADR**	13.0%	15.2%	13.7%	18.8%	13.4%	7.1%	9.8%	
• **Retrograde**	68.8%	60.4%	61.9%	54.9%	58.2%	65.5%	61.1%	
• **None**	13.0%	12.8%	15.8%	20.7%	19.5%	20.0%	21.4%	
Technical success	86.7%	86.6%	82.0%	77.5%	75.4%	78.1%	76.1%	0.014
Procedural success	85.4%	83.1%	78.1%	73.0%	72.8%	73.4%	69.6%	0.004
In-hospital MACE	1.46%	3.75%	6.57%	7.58%	6.33%	4.93%	3.52%	0.132

Procedural time (min) [b]	156 (114, 191)	160 (110, 211)	200 (142, 268)	225 (174, 272)	197 (150, 264)	183 (129, 245)	179 (146, 230)	<0.001
Fluoroscopy time (min) [b]	64.8 (49.3, 90.5)	69.3 (46.5, 91.8)	82.4 (57.8, 107.2)	84.6 (66.7, 110.0)	77.8 (58.0, 103.0)	82.5 (62.4, 108.6)	82.1 (62.0, 99.8)	<0.001
Contrast volume (ml) [b]	350 (225, 480)	275 (210, 395)	300 (220, 400)	350 (249, 450)	300 (229, 425)	300 (200, 396)	210 (150, 293)	<0.001
Air Kerma radiation (Gray) [b]	5.7 (4.5, 8.2)	3.2 (2.2, 5.6)	4.1 (2.5, 5.8)	3.9 (2.5, 5.6)	2.9 (1.8, 4.3)	3.5 (2.0, 5.0)	3.2 (1.6, 4.9)	<0.001

* per lesion based

[a] mean ± standard deviation [b] median (interquartile range)

ADR, antegrade dissection re-entry; AWE, antegrade wire escalation; J, Japanese; MACE, major adverse cardiac event.

Supplementary Table 5. Baseline, angiographic, technical, and procedural characteristics of retrograde versus antegrade-only CTO PCI.

Variable	Overall (n=4108)	Retrograde (n=1505)	Antegrade-only (n=2603)	P value
Baseline clinical characteristics				
Body mass index (kg/m^2) [b]	30.6 ± 6.3	30.7 ± 6.1	30.5 ± 6.3	0.367
Smoking (current)	26.2%	24.9%	26.9%	0.205
CCS angina classification				0.297
• **CCS 2≤**	89.7%	90.5%	89.2%	
• **<CCS 2**	10.3%	9.5%	10.8%	
Family history of coronary artery disease	34.4%	37.6%	32.7%	**0.009**
Prior valve surgery or procedure	3.0%	3.7%	2.5%	0.050
Baseline creatinine (mg/dL) [c]	1.0 (0.9, 1.2)	1.1 (0.9, 1.2)	1.0 (0.9, 1.2)	0.090
Currently on dialysis	2.4%	2.5%	2.3%	0.694
Prior cerebrovascular disease	11.2%	11.7%	11.0%	0.478
Chronic pulmonary disease	14.1%	16.2%	12.9%	**0.007**
Angiographic characteristics [a]				
Vessel diameter (mm) [a]	2.9 ± 0.5	3.0 ± 0.5	2.8 ± 0.5	**<0.001**
Collateral filling [a]				**<0.001**
• **Contralateral [a]**	48.7%	64.0%	40.7%	
• **Ipsilateral [a]**	21.3%	12.5%	25.8%	
• **Contralateral & ipsilateral [a]**	27.4%	22.0%	30.2%	
• **None [a]**	2. 7%	1.5%	3.3%	

Rentrop collateral filling [a]				**0.022**
• **Rentrop 0 [a]**	3.5%	2.1%	4.1%	
• **Rentrop 1 [a]**	17.0%	20.4%	15.6%	
• **Rentrop 2 [a]**	43.4%	40.8%	44.4%	
• **Rentrop 3 [a]**	36.1%	36.7%	35.9%	
Side branch at proximal cap [a]	52.7%	60.5%	48.5%	**<0.001**
Blunt/no stump [a]	52.4%	73.1%	41.7%	**<0.001**
Distal cap at bifurcation [a]	33.9%	48.4%	26.4%	**<0.001**
Adequate distal landing zone [a]	67.7%	53.4%	75.1%	**<0.001**
Technical [a] and procedural characteristics				
Intravascular ultrasound use [a]	29.1%	36.0%	25.2%	**<0.001**
• **Facilitate wiring [a]**	9.7%	15.7%	6.25%	**<0.001**
• **Stent optimization [a]**	15.0%	16.8%	14.0%	0.012
• **Other [a]**	3.1%	3.3%	2.9%	0.473
Vascular access complication	1.46%	2.06%	1.11%	0.015
Equipment loss	0.22%	0.40%	0.12%	0.083
Donor artery dissection/thrombosis	0.97%	1.66%	0.58%	**<0.001**
Bleeding	0.97%	1.59%	0.61%	**0.002**
Aortocoronary dissection	0.17%	0.27%	0.12%	0.268
Contrast induced nephropathy	0.27%	0.40%	0.19%	0.226

[a] Per lesion-based percentages.

[b] mean ± standard deviation; [c] median (interquartile range)