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# In-Stent CTO Percutaneous Coronary Intervention

## Individual Patient Data Pooled Analysis of 4 Multicenter Registries

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### ABSTRACT

**OBJECTIVES** The authors sought to examine the outcomes of percutaneous coronary intervention (PCI) for in-stent restenosis (ISR) chronic total occlusions (CTOs).

**BACKGROUND** The outcomes of PCI for ISR CTOs have received limited study.

**METHODS** The authors examined the clinical and angiographic characteristics and procedural outcomes of 11,961 CTO PCIs performed in 11,728 patients at 107 centers in Europe, North America, Latin America, and Asia between 2012 and 2020, pooling patient-level data from 4 multicenter registries. In-hospital major adverse cardiovascular events (MACE) included death, myocardial infarction, stroke, and tamponade. Long-term MACE were defined as the composite of all-cause death, myocardial infarction, and target vessel revascularization.

**RESULTS** ISR represented 15% of the CTOs (n = 1,755). Patients with ISR CTOs had higher prevalence of diabetes (44% vs. 38%; p < 0.0001) and prior coronary artery bypass graft surgery (27% vs. 24%; p = 0.03). Mean J-CTO (Multicenter CTO Registry in Japan) score was 2.32 ± 1.27 in the ISR group and 2.22 ± 1.27 in the de novo group (p = 0.01). Technical (85% vs. 85%; p = 0.75) and procedural (84% vs. 84%; p = 0.82) success was similar for ISR and de novo CTOs, as was the incidence of in-hospital MACE (1.7% vs. 2.2%; p = 0.25). Antegrade wiring was the most common successful strategy, in 70% of ISR and 60% of de novo CTOs, followed by retrograde crossing (16% vs. 23%) and antegrade dissection and re-entry (15% vs. 16%; p < 0.0001). At 12 months, patients with ISR CTOs had a higher incidence of MACE (hazard ratio: 1.31; 95% confidence intervals: 1.01 to 1.70; p = 0.04).

**CONCLUSIONS** ISR CTOs represent 15% of all CTO PCIs and can be recanalized with similar success and in-hospital MACE as de novo CTOs. (J Am Coll Cardiol Intv 2021; ■:■-■) © 2021 by the American College of Cardiology Foundation.

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**ABBREVIATIONS  
AND ACRONYMS****CTO** = chronic total occlusion**IQR** = interquartile range**ISR** = in-stent restenosis**MACE** = major adverse  
cardiovascular event(s)**MI** = myocardial infarction**PCI** = percutaneous coronary  
intervention

Percutaneous coronary intervention (PCI) of in-stent restenosis (ISR) chronic total occlusions (CTOs) represents 5% to 25% of all CTO PCIs and has been associated with lower success rates in some (1) but not all (2-7) studies. Challenges specific to ISR CTO PCI include inability to maintain an intrastent track through the stented segment and difficulty re-entering in case of substent wire advancement, poor runoff associated with long stented lengths, and high rates of repeat restenosis (4,8). We examined the outcomes and different practices of ISR CTO PCI at a global level, by combining individual patient-level data from 4 large international multicenter registries.

**METHODS**

**STUDY POPULATION.** We analyzed the clinical, angiographic, and procedural characteristics of 11,961 CTO PCIs performed in 11,728 patients enrolled in 4 multicenter registries, the PROGRESS-CTO (Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; [NCT02061436](#); n = 6,683 procedures performed between 2012 and 2020 at 34 U.S. and international centers), the LATAM (Latin American) registry (n = 1,700 procedures performed between 2008 and 2020 at 48 centers in 9 Latin American countries), RECHARGE (Registry of Cross-Boss and Hybrid Procedures in France, the Netherlands, Belgium, and United Kingdom; [NCT02075372](#); n = 1,308 procedures performed between 2013 and 2015 at 18 centers in 4 European countries), and a multicenter registry that included 2,270 cases performed between 2009 and 2017 at 7 participating centers in Italy, Belgium, Japan, Spain, Canada, and the United States. The study was approved by the Institutional Review Board of each site. Patients were divided into 2 groups: in-stent CTOs and de novo CTOs.

**DEFINITIONS.** Coronary CTOs were defined as 100% coronary stenosis with TIMI (Thrombolysis In Myocardial Infarction) flow grade 0 for at least 3 months. Estimation of the duration of occlusion was clinical, on the basis of the first onset of angina, history of myocardial infarction (MI) in the target vessel territory, or comparison with a prior angiogram. In-

stent CTOs were defined as occlusions at the stent site and/or at the stent site or within 5 mm proximal or distal to the stent. 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 and 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 after intentional or inadvertent subintimal guidewire crossing. Radial access was used to indicate cases with dual radial access or cases with a single access being radial. Technical success was defined as successful CTO revascularization with achievement of <30% residual diameter stenosis within the treated segment and restoration of TIMI flow grade 3 antegrade flow. Procedural success was defined as the achievement of technical success without any in-hospital major adverse cardiovascular events (MACE), which included any of the following adverse events prior to hospital discharge: death, MI, tamponade requiring either pericardiocentesis or surgery, and stroke. MI was defined using the third universal definition of MI (type 4a MI) (9). The J-CTO (Multicenter CTO Registry in Japan) score was calculated as described by Morino *et al.* (10) and the PROGRESS-CTO score as described by Christopoulos *et al.* (11).

One-year MACE was defined as the composite of all-cause death, MI, or target vessel revascularization at 12-month follow-up. Target vessel revascularization was defined as the performance of either PCI or coronary artery bypass surgery to revascularize the target vessel.

**STATISTICAL ANALYSIS.** Categorical variables are presented as percentages and were compared using the Pearson chi-square test or the Fisher exact test. Continuous variables are presented as mean  $\pm$  SD in case of normal distribution or as median (interquartile range [IQR]) in case of non-normal distribution and were compared using Student's *t*-test and one-way analysis of variance for normally distributed variables and using the Wilcoxon rank-sum test and the Kruskal-Wallis test for nonparametric continuous variables, as appropriate. Multivariable logistic regression was used to examine the

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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association between ISR versus de novo CTO and technical success, after adjusting for confounding variables selected on univariable association ( $p < 0.10$ ). A 2-sided  $p$  value  $< 0.05$  was considered to indicate statistical significance. The analysis was performed on a per patient basis for baseline characteristics and procedural outcomes and on a per procedure basis for angiographic parameters and technical aspects of the study procedures. The cumulative incidence of the composite endpoint at 1 year was calculated using Kaplan-Meier estimates and compared using the log-rank test. Although patients could experience more than 1 component of the composite endpoint, each patient was assessed until the occurrence of his or her first event and only once during the analysis for the composite endpoint. All statistical analyses except for the survival analysis were performed using JMP version 13.0 (SAS Institute, Cary, North Carolina). The survival analysis was performed with the survival, survminer, and finalfit R packages using jamovi version 1.2 (<https://www.jamovi.org>).

## RESULTS

**PATIENT CHARACTERISTICS.** A total of 1,755 ISR CTO PCIs (14.7% of total CTO PCIs) performed in 1,727 patients were included in the present analysis. The baseline characteristics of the study patients are summarized in **Table 1**. Patients in the ISR group had a higher prevalence of diabetes mellitus (43.5% vs. 37.8%;  $p < 0.001$ ), dyslipidemia, hypertension, and prior MI compared with patients who had de novo CTOs. They also had slightly higher body mass index and higher prevalence of prior coronary artery bypass graft surgery (26.5% vs. 24%;  $p = 0.028$ ) and peripheral artery disease (16.1% vs. 13.9%;  $p = 0.02$ ).

**ANGIOGRAPHIC CHARACTERISTICS.** The baseline angiographic characteristics of the study lesions are shown in **Table 2**. Radial access was used more often in the de novo group compared with the in-stent group (50% vs. 43%;  $p < 0.001$ ). Proximal cap ambiguity (26.8% vs. 36%;  $p < 0.001$ ) and moderate to severe calcification (35.6% vs. 48.3%;  $p < 0.001$ ) were more frequent in the de novo CTO group, while ostial occlusion location was more frequent in the ISR CTO group (17.1% vs. 12.0%;  $p < 0.001$ ). Mean J-CTO score was higher in the ISR CTO group ( $2.32 \pm 1.27$  vs.  $2.22 \pm 1.27$ ;  $p = 0.01$ ).

**TECHNICAL CHARACTERISTICS AND PROCEDURAL OUTCOMES.** The technical aspects of CTO PCI are summarized in **Table 3**. The retrograde approach (26.2% vs. 36%;  $p < 0.001$ ) and antegrade dissection

**TABLE 1** Baseline Characteristics of the Study Patients Classified According to Whether the Target CTO Was In-Stent or De Novo

	ISR CTOs (n = 1,727)	De Novo CTOs (n = 10,001)	p Value
Men	1,378 (82.8)	8,142 (83.5)	0.48
Age (yrs)	65 (58-71)	65 (58-72)	0.10
BMI (kg/m <sup>2</sup> )	29.4 (26.1-33.2)	28.7 (25.8-32.3)	<i>&lt;0.0001</i>
Diabetes	713 (43.5)	3,641 (37.8)	<i>&lt;0.0001</i>
Dyslipidemia	1,436 (87.3)	7,888 (81.6)	<i>&lt;0.0001</i>
Hypertension	1,456 (88.5)	8,037 (83.2)	<i>&lt;0.0001</i>
Prior MI	903 (57.1)	3,926 (42)	<i>&lt;0.0001</i>
Prior CABG	443 (26.5)	2,333 (24)	0.0275
LVEF >50%	888 (60.8)	5,402 (61.1)	0.80
Heart failure	319 (25.5)	1,721 (23.1)	0.07
Peripheral artery disease	250 (16.1)	1,262 (13.9)	0.0227
Cerebrovascular disease	123 (7.9)	779 (8.6)	0.38
Estimated GFR (ml/min/1.73 m <sup>2</sup> )	73 (59-87)	75 (60-90)	0.0059
CTO indication			<i>&lt;0.0001</i>
Symptom relief	1,025 (73.4)	5,166 (66.6)	
Ischemia reduction	157 (11.3)	1,058 (13.6)	
Reduced ejection fraction	54 (3.9)	346 (4.5)	
Other	64 (4.6)	473 (6.1)	

Values are n (%) or median (interquartile range). P values in italics indicate statistical significance.  
CABG = coronary artery bypass grafting; CTO = chronic total occlusion; GFR = glomerular filtration rate; ISR = in-stent restenosis; LVEF = left ventricular ejection fraction, MI = myocardial infarction.

**TABLE 2** Baseline Angiographic Characteristics, Classified According to Whether the Target CTO Was In-Stent or De Novo

	ISR CTOs (n = 1,755)	De Novo CTOs (n = 10,206)	p Value
Arterial access (radial)	746 (42.6)	5,065 (49.6)	<i>&lt;0.0001</i>
Target vessel			0.29
LAD	450 (26.4)	2,771 (27.8)	
RCA	881 (51.7)	5,197 (52.1)	
LCx	365 (21.5)	1,971 (19.8)	
Other	7 (0.4)	29 (0.3)	
Proximal cap ambiguity	429 (26.8)	3,379 (36.2)	<i>&lt;0.0001</i>
Moderate/severe calcification	555 (35.6)	4,219 (48.3)	<i>&lt;0.0001</i>
Moderate or severe proximal tortuosity	396 (25.6)	2,338 (26.9)	0.37
Ostial lesion	226 (17.1)	931 (12)	<i>&lt;0.0001</i>
Interventional collateral vessels	879 (55.9)	5,746 (62.2)	<i>&lt;0.0001</i>
Werner classification of collateral vessels			<i>&lt;0.0001</i>
CC 0	257 (22.4)	1,141 (17.6)	
CC 1	612 (53.3)	3,358 (51.8)	
CC 2	279 (24.3)	1,978 (30.5)	
J-CTO score	2.32 ± 1.26	2.22 ± 1.27	0.0111
J-CTO score ≥2	1,209 (72.7)	6,909 (69.2)	0.0048
PROGRESS-CTO score	1 (0-2)	1 (0-2)	0.74
PROGRESS-CTO ≥2	489 (34.7)	2,784 (34.2)	0.76

Values are n (%), mean ± SD, or median (interquartile range). P values in italics indicate statistical significance.  
CC = collateral connection; J-CTO = Multicenter CTO Registry in Japan; LAD = left anterior descending coronary artery; LCx = left circumflex coronary artery; PROGRESS-CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RCA = right coronary artery; other abbreviations as in **Table 1**.

**TABLE 3 Technical Characteristics and Outcomes in the Study Procedures, Classified According to Whether the Target CTO Was In-Stent or De Novo**

	ISR CTOs (n = 1,755)	De Novo CTOs (n = 10,206)	p Value
Crossing strategies used			
Antegrade wiring	1,480 (84.8)	8,187 (81)	<i>0.0002</i>
ADR	439 (25.3)	2,739 (26.4)	<i>0.0302</i>
Retrograde	455 (26.2)	3,619 (36)	<i>&lt;0.0001</i>
Retrograde wire escalation (% of retrograde)	172 (51.5)	1,284 (45.6)	<i>0.041</i>
Retrograde dissection/re-entry (% of retrograde)	138 (41.4)	1,402 (49.9)	<i>0.0036</i>
Successful crossing strategy			<i>&lt;0.0001</i>
Antegrade wiring	1,042 (69.5)	5,286 (60.8)	
ADR	218 (14.5)	1,402 (16.1)	
Retrograde	239 (15.9)	2,005 (23.1)	
IVUS and/or OCT used	628 (40.5)	2,795 (32.7)	<i>&lt;0.0001</i>
CrossBoss	19 (11.5)	832 (8.6)	<i>0.0001</i>
Stenting	1,391 (83.5)	8,490 (86.8)	<i>0.0003</i>
Number of stents	2 (1-3)	2 (1-3)	0.25
Stent type			0.17
Drug-eluting stent	1,167 (97.4)	6,788 (96.6)	
Bare-metal stent	10 (0.83)	106 (1.5)	
Bioresorbable vascular scaffold	21 (1.8)	136 (1.9)	
Total stent length	64 (38-94)	64 (38-94)	0.10
Technical success	1,489 (84.9)	8,686 (85.2)	0.75

Values are n (%) or median (interquartile range). P values in italics indicate statistical significance.  
ADR = antegrade dissection and re-entry; IVUS = intravascular ultrasound; OCT = optical coherence tomography; other abbreviations as in [Table 1](#).

or re-entry (25.3% vs. 26.4%;  $p < 0.001$ ) were used less often in ISR CTOs compared with de novo lesions, and intravascular imaging (intravascular ultrasound or optical coherence tomography) was used more often (40.5% vs. 32.7%;  $p < 0.001$ ). Stenting was used less often in the ISR CTO group (80.0% vs. 84.4%;  $p < 0.001$ ).

**TABLE 4 Procedural Outcomes of the Study Patients Classified According to Lesion Type**

	ISR CTOs (n = 1,727)	De Novo CTOs (n = 10,001)	p Value
Procedural success	1,446 (83.7)	8,413 (83.9)	0.82
In-hospital MACE	33 (1.9)	248 (2.5)	0.15
Death	3 (0.18)	51 (0.51)	<i>0.0565</i>
Myocardial infarction	14 (0.82)	90 (0.91)	0.72
Stroke	6 (0.35)	23 (0.23)	0.37
Tamponade	13 (0.75)	113 (1.13)	0.16
Fluoroscopy time (min)	40 (24-62)	41 (25-66)	0.07
Procedure time (min)	110 (69-159)	107 (69-159)	0.78
Contrast volume (ml)	215 (150-300)	250 (180-340)	<i>&lt;0.0001</i>
Bleeding	3 (0.3)	40 (0.7)	0.09

Values are n (%) or median (interquartile range). P values in italics indicate statistical significance.  
MACE = major adverse cardiovascular events; other abbreviations as in [Table 1](#).

Procedural outcomes are summarized in [Table 4](#). Technical (84.9% vs. 85.2%;  $p = 0.75$ ) and procedural (84% vs. 84%;  $p = 0.82$ ) success and in-hospital MACE rates (1.7% vs. 2.2%;  $p = 0.25$ ) were similar between ISR and de novo CTOs. Contrast volume was lower in the ISR CTO group (median 215 ml [IQR: 150 to 300 mL] vs. 250 ml [IQR: 180 to 340 ml];  $p < 0.001$ ). Technical success of ISR CTO PCI, number of ISR CTOs, in-hospital MACE rate, median J-CTO score, and contrast volume according to year of procedure are shown in [Figure 1](#).

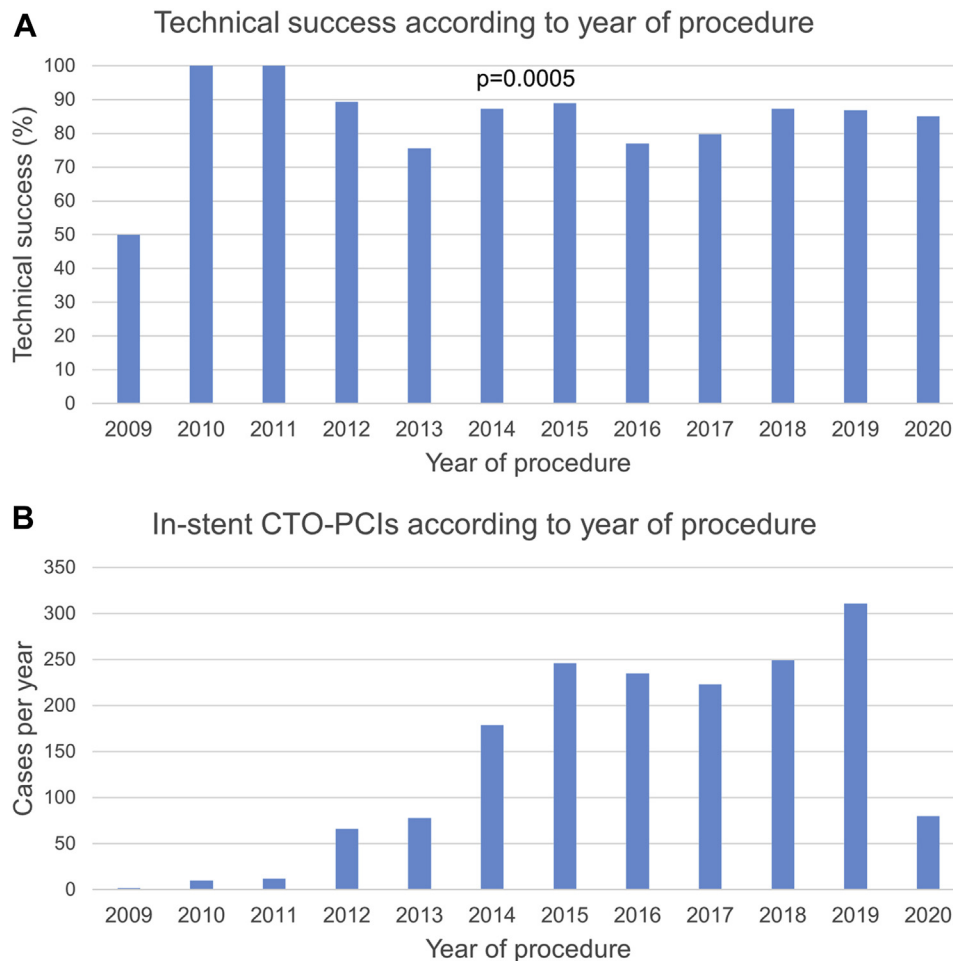
**DIFFERENCES ACROSS REGISTRIES.** There were no significant differences in technical success for ISR CTO PCI among the registries ([Figure 2A](#)). However, there were differences in various crossing strategies used during the procedure ([Figure 2B](#)), successful crossing strategies ([Figure 2C](#)), in-hospital MACE rates ([Figure 2D](#)), and contrast volume use patterns ([Figure 2E](#)).

**MULTIVARIABLE ANALYSIS.** On multivariable analysis, ISR CTO PCI was not independently associated with technical success (odds ratio [OR]: 0.96; 95% confidence intervals: 0.81 to 1.14;  $p = 0.68$ ) ([Figure 3](#)).

**FOLLOW-UP OUTCOMES.** Long-term follow-up was available for 5,701 patients (48.6% of the total population). The median duration of follow-up was 306 days (IQR: 57 to 365 days). At 12 months, patients with ISR CTOs had a higher incidence of MACE (hazard ratio: 1.31; 95% confidence intervals: 1.01 to 1.70;  $p = 0.04$ ) ([Central Illustration](#)) and target vessel revascularization (hazard ratio: 1.34; 95% confidence intervals: 1 to 1.81;  $p = 0.05$ ) but similar rates of MI (hazard ratio: 1.5; 95% confidence intervals: 0.78 to 2.9;  $p = 0.23$ ) and death (hazard ratio: 1.3; 95% confidence intervals: 0.74 to 2.26;  $p = 0.36$ ) ([Figure 4](#)).

## DISCUSSION

The present study is a unique cooperation across 4 independent multinational registries and to the best of our knowledge provides the largest published patient cohort comparing the outcomes of PCI in in-stent versus de novo CTOs. The main findings were that ISR CTO PCI 1) represented 15% of all CTO interventions; 2) had similar success and in-hospital MACE rates compared with PCI of de novo CTOs; 3) was less likely to require use of the retrograde approach and antegrade dissection and re-entry techniques; and 4) was not independently associated with technical success; in addition, 5) patients with ISR CTOs had higher a incidence of MACE and target vessel revascularization during follow-up.

**FIGURE 1** Temporal Trends in In-Stent CTO PCI

**(A)** Technical success of in-stent chronic total occlusion (CTO) percutaneous coronary intervention (PCI) according to year of procedure. **(B)** Number of in-stent CTO PCIs according to year of procedure. **(C)** In-hospital major adverse cardiovascular events (MACE) associated with in-stent CTO PCIs according to year of procedure. **(D)** Median J-CTO (Multicenter CTO Registry in Japan) score of in-stent CTO PCIs according to year of procedure. The median divides the dataset into bottom and top halves. The **bottom line** and **top line** of each **box** represent quartiles 1 and 3, respectively. **Whiskers** show the 10th and 90th percentiles. In those cases in which no whisker is visible, the value of the 10th percentile coincides with the value of quartile 1. **(E)** Median contrast volume for in-stent CTO PCIs according to year of procedure. The median divides the dataset into bottom and top halves. The **bottom line** and **top line** of each **box** represent quartiles 1 and 3, respectively. **Whiskers** show the 10th and 90th percentiles. In those cases in which no whisker is visible, the value of the 10th or 90th percentile coincides with the value of quartile 1 or quartile 3, respectively.

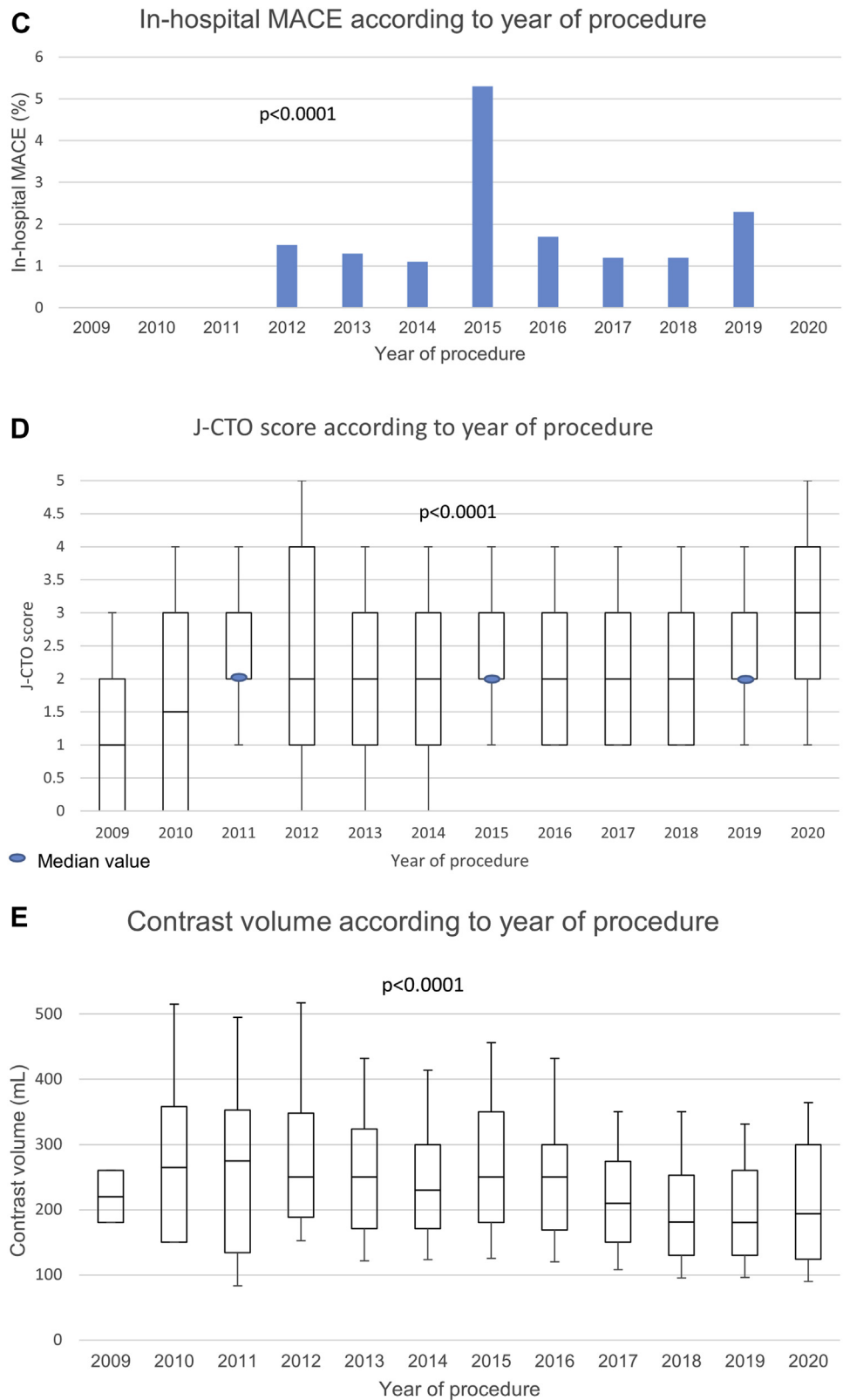
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**PREVIOUS STUDIES.** The prevalence of in-stent CTOs in our study was higher (15%) compared with the overall prevalence of in-stent lesions in the National Cardiovascular Registry (10%) (12). A number of observational studies have compared the outcomes of ISR CTO PCI, including studies whose patients were included in the present analysis (3,4,7). Initial studies, published between 2005 and 2011, by Abdel-

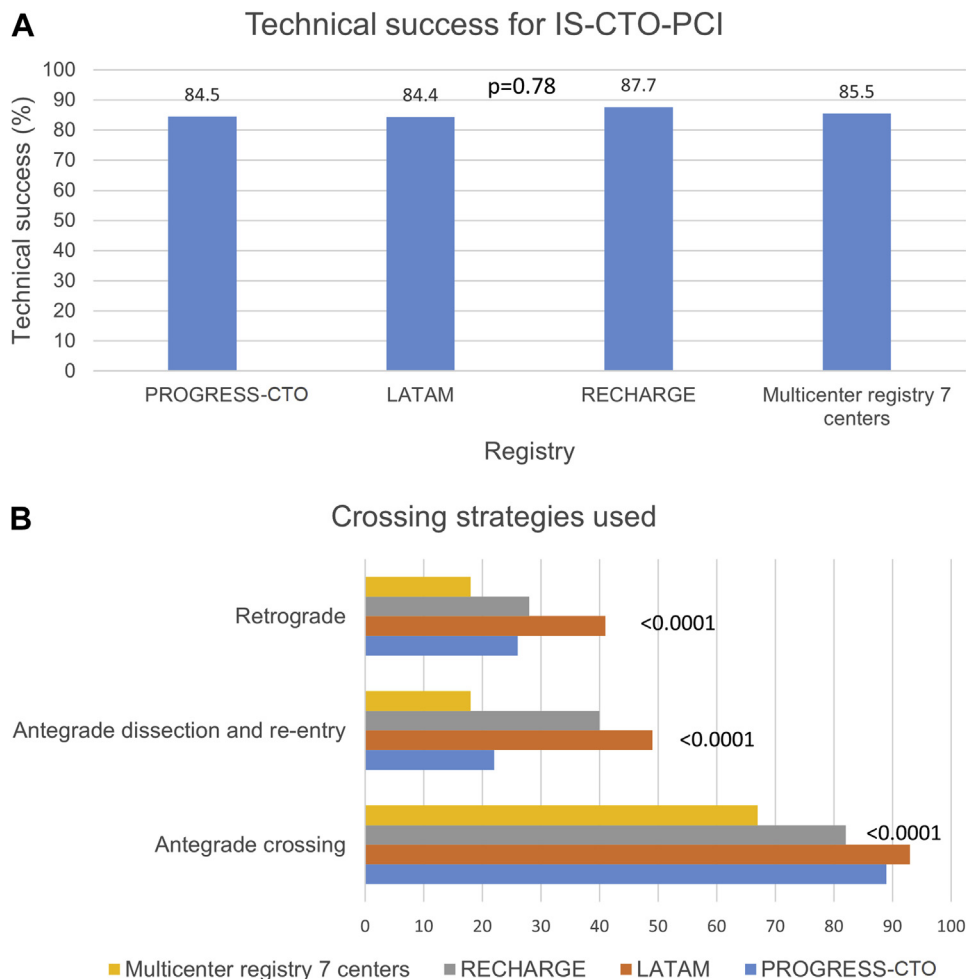
Karim *et al.* (13), Abbas *et al.* (1), and Werner *et al.* (14), showed that success rates of ISR CTO PCI were lower compared with PCI of de novo CTOs, likely because of the use of limited equipment and techniques. However, contemporary studies showed no difference in technical success rates between ISR and de novo CTO PCI (3-7,15), as confirmed by our analysis. The high success rates are likely the result of



FIGURE 1 Continued





**FIGURE 2** Inter-Registry Differences for IS CTO PCIs

(A) Technical success of in-stent (IS) CTO PCIs according to registry. (B) Crossing strategies of IS CTO PCI according to registry. (C) Successful crossing strategy used for IS CTO PCIs according to registry. (D) In-hospital MACE associated with IS CTO PCIs according to registry. (E) Median contrast volume use associated with IS CTO PCIs according to registry. The median divides the dataset into bottom and top halves. The **bottom line** and **top line** of each **box** represent quartiles 1 and 3, respectively. **Whiskers** show the 10th and 90th percentiles. LATAM = Latin American registry; PROGRESS-CTO = Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; RECHARGE = Registry of CrossBoss and Hybrid Procedures in France, the Netherlands, Belgium, and United Kingdom; other abbreviations as in [Figure 1](#).

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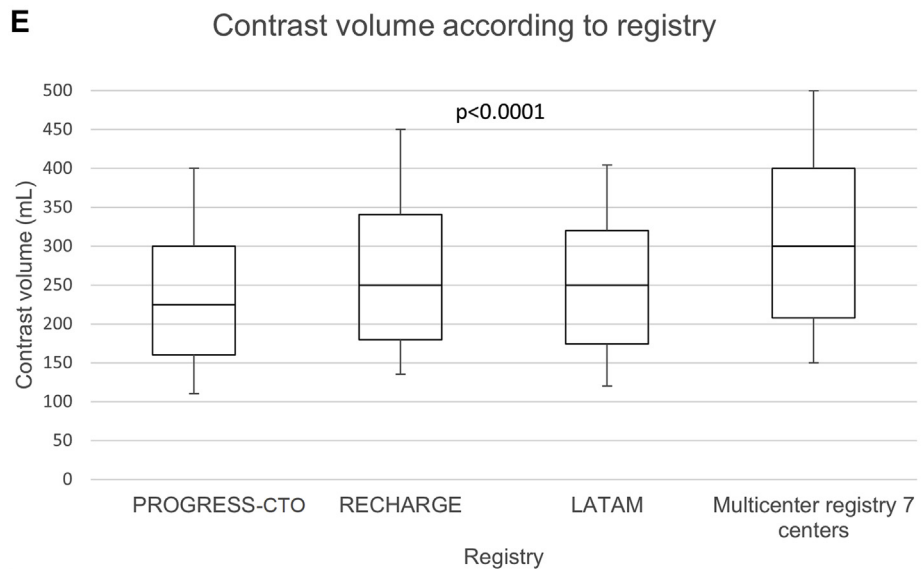
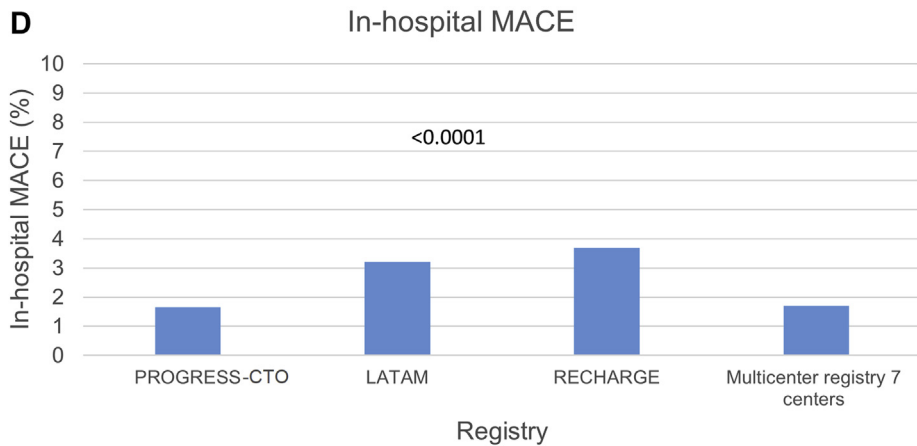
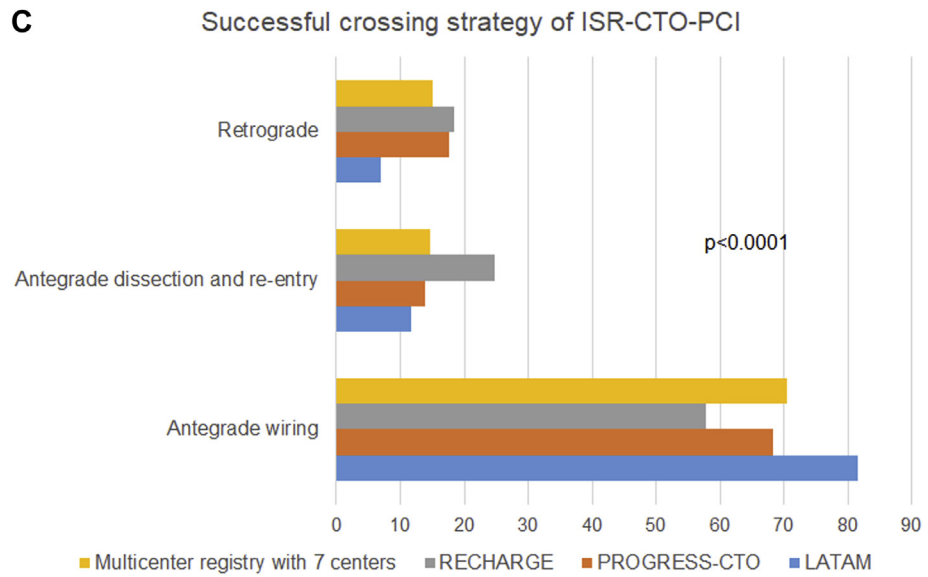
improved CTO PCI equipment and techniques and increasing operator experience, as suggested by increasing ISR CTO PCI success rates over time.

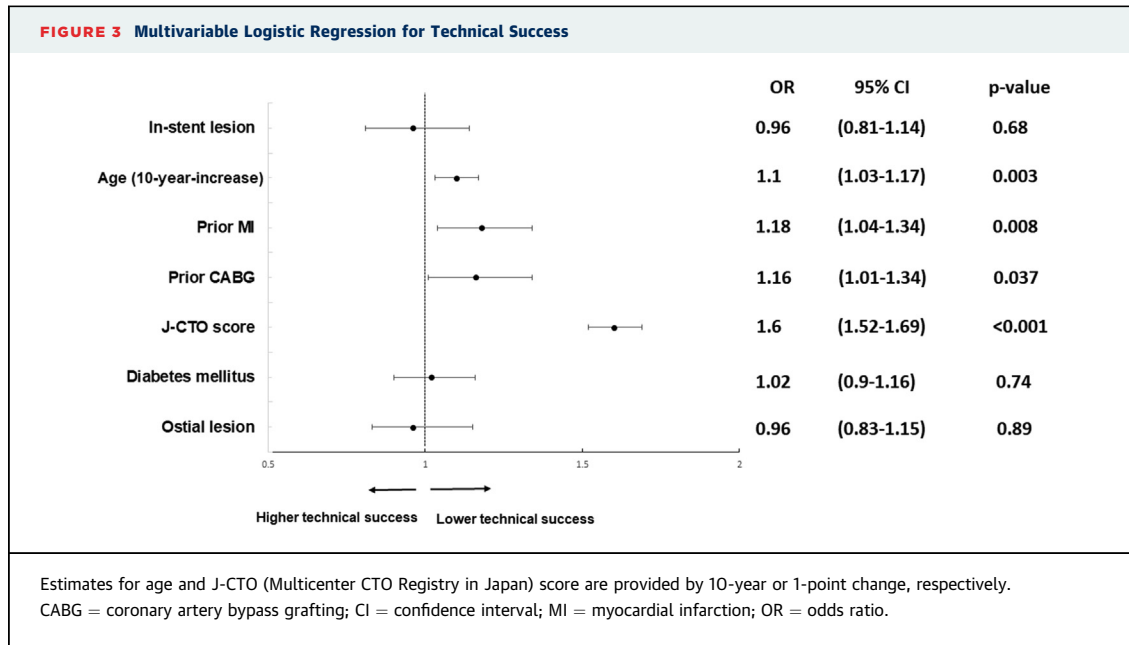
**CLINICAL CHARACTERISTICS.** Patients with in-stent CTOs were more likely to have diabetes and prior coronary artery bypass graft surgery, as anticipated given the higher risk for restenosis and target lesion failure in these patient groups. They were also more likely to have a history of prior MI, peripheral artery

disease, and coronary artery bypass graft surgery. These findings are in accordance with recent data on ISR in all comers (12), indicating a more aggressive atherosclerotic phenotype in such patients.

**INTRAVASCULAR IMAGING.** Intravascular imaging has a critical role in CTO PCI, as it can facilitate CTO crossing and ensure optimal stent deployment that reduces the risk for subsequent clinical events (16-19). The use of intravascular imaging in our

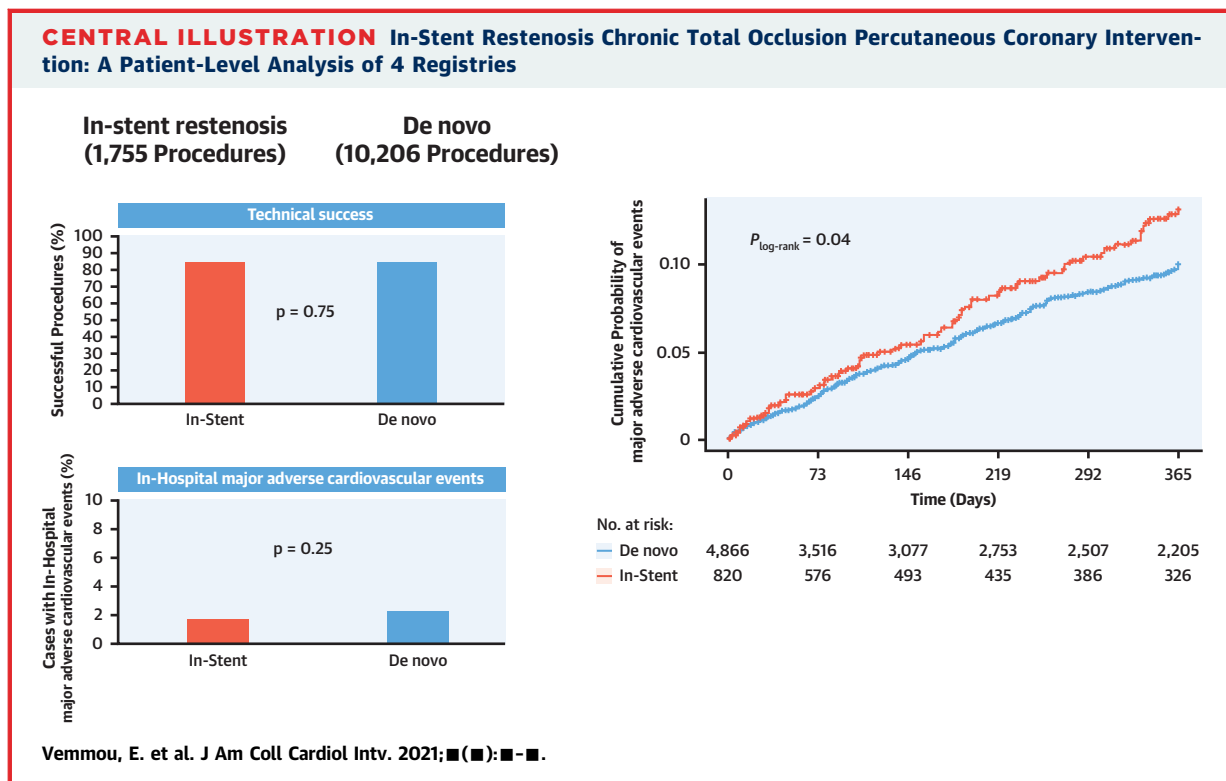
**FIGURE 2 Continued**



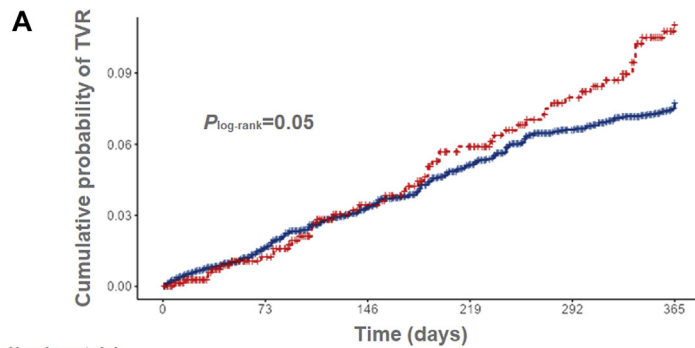


study was higher in the in-stent group (41% vs. 33%;  $p < 0.0001$ ), likely because of higher anticipated risk for repeat target vessel failure. Intravascular ultrasound or optical coherence tomography use is

especially important for ISR PCI, as it can elucidate the mechanism of prior stent failure, facilitate adequate stent choice, and optimize the final result (20).

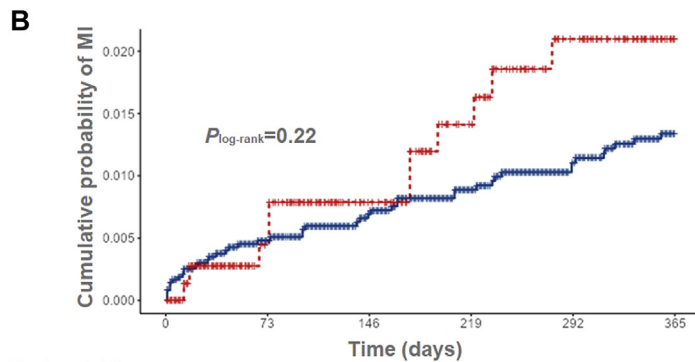


Technical success, in-hospital major adverse cardiovascular events (MACE), and 1-year MACE for in-stent versus de novo chronic total occlusion percutaneous coronary interventions.

**FIGURE 4** Kaplan-Meier Estimates for TVR, MI, and Death at 1 Year

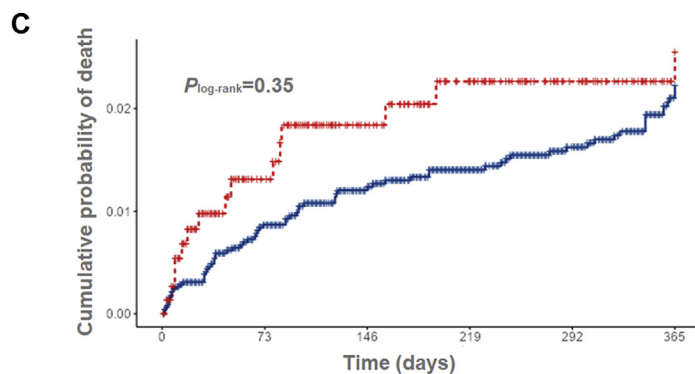
Number at risk

De novo	4867	3528	3093	2768	2524	2225
In-stent	820	577	491	434	385	324



Number at risk

De novo	4867	3564	3155	2857	2638	2330
In-stent	816	581	503	448	398	341



Number at risk

De novo	4726	3456	3069	2795	2589	2343
In-stent	793	562	489	434	386	343

(A) Kaplan-Meier estimates for target vessel revascularization (TVR) at 1 year. (B) Kaplan-Meier estimates for myocardial infarction (MI) at 1 year. (C) Kaplan-Meier estimates for all-cause death at 1 year.

ISR CTO was not independently associated with technical success, whereas age, prior MI, prior coronary artery bypass graft surgery, and J-CTO score were, as found in several prior studies (21-25), enhancing the external validity of our findings.

**TEMPORAL TRENDS.** The number of in-stent CTO PCIs increased over time, likely because of improvements in CTO PCI techniques and encouraging findings from recent studies (3-7). The technical success rates of in-stent CTO PCI varied during the study period but were high overall. During 2010 and 2011, technical success for ISR CTO PCI was 100%, and the incidence of in-hospital MACE was low, but the number of attempted in-stent cases was small (10 cases in 2010 and 12 cases in 2011), and the J-CTO scores of these lesions were low.

**SUBSEQUENT EVENTS.** As anticipated, patients who underwent PCI of in-stent CTOs had a higher incidence of MACE during follow-up, driven by a higher incidence of target vessel revascularization. Identifying and implementing strategies to improve long-term patency after occlusive ISR is therefore critical for this group of patients. Stent optimization using intravascular imaging may help reduce the risk for recurrent failure, whereas it is unclear whether routine angiographic follow-up has a favorable risk/benefit ratio.

**STUDY LIMITATIONS.** First, this was an observational, retrospective study with all inherent limitations. Second, follow-up was available for only a portion of the patient population. Third, there was no clinical event adjudication by a clinical event committee. Fourth, all procedures were performed at high-volume centers by experienced operators, limiting the generalizability of the results to other institutions with limited CTO PCI experience. Fifth, there was no information on intravascular ultrasound or optical coherence tomographic findings that could aid in understanding stent failure mechanisms in individual patients.

Finally, relevant data on the type of the occluded stent in the ISR CTO group, alternative treatments to stenting (e.g., drug-coated balloons, brachytherapy), and baseline medical therapy were not available.

## CONCLUSIONS

In-stent CTOs represented 15% of total cases in an analysis of 4 contemporary CTO PCI registries. Technical and procedural success rates were similar with de novo CTOs, as was the incidence of in-hospital MACE. However, at 1-year follow-up, in-stent

lesions were associated with higher incidence of MACE compared with de novo lesions, driven by higher incidence of target vessel revascularizations.

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## PERSPECTIVES

**WHAT IS KNOWN?** PCI of ISR CTO has been associated with lower success rates in some studies.

**WHAT IS NEW?** ISR represented 15% of total cases in an analysis of 4 multicenter CTO PCI registries. Technical and procedural success rates were similar with de novo lesions, as well as in-hospital MACE rates. However, at 1-

year follow-up, in-stent lesions were associated with a higher incidence of MACE and target vessel revascularization.

**WHAT IS NEXT?** Additional treatment options should be developed for patients with in-stent CTOs to improve long-term patency.

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