

The Impact of Proximal Vessel Tortuosity on the Outcomes of Chronic Total Occlusion Percutaneous Coronary Intervention: Insights From a Contemporary Multicenter Registry

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ABSTRACT: Introduction. We examined the impact of proximal vessel tortuosity on the outcomes of chronic total occlusion (CTO) percutaneous coronary intervention (PCI). **Methods.** The baseline clinical and angiographic characteristics and procedural outcomes of 1618 consecutive CTO-PCIs performed between 2012 and 2016 at 14 United States centers in 1589 patients were reviewed. **Results.** Mean patient age was 65.3 ± 10.0 years and 85% were men. Moderate/severe proximal vessel tortuosity was present in 35.7% of target lesions. Compared with non-tortuous lesions, tortuous lesions had longer length [30 mm [interquartile range, 20-50 mm] vs 28 mm [interquartile range, 16-40 mm]; $P < .001$], more proximal cap ambiguity [36% vs 28%; $P < .01$], and more frequent utilization of the retrograde approach [52% vs 37%; $P < .001$]. Moderate/severe proximal vessel tortuosity was associated with lower technical success rates [84.1% vs 91.3%; $P < .001$] and procedural success rates [82.3% vs 89.9%; $P < .001$], but similar incidence of major cardiac adverse events [3.0% vs 2.5%; $P = .59$]. Moderate/severe tortuosity was associated with longer procedure time and fluoroscopy time, higher air kerma radiation dose, and larger contrast volume. **Conclusion.** In a contemporary multicenter registry, moderate/severe proximal vessel tortuosity was present in approximately one-third of target CTO lesions and was associated with more frequent use of the retrograde approach and lower success rates, but similar complication rates.

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KEY WORDS: tortuosity, chronic total occlusion, percutaneous coronary intervention

Coronary tortuosity can hinder vessel wiring and equipment delivery and has been associated with lower success rates and higher complications rates in percutaneous coronary intervention (PCI).¹⁻³ Coronary tortuosity affects the efficiency and success of chronic total occlusion (CTO)-PCI and is included both in the Japanese chronic total occlusion (J-CTO) score for predicting successful guidewire crossing within the first 30 minutes of the procedure,⁴ and the Progress-CTO score⁵ for predicting technical success. We examined a multicenter United States registry to determine the impact of tortuosity on outcomes of contemporary CTO-PCI.

Methods

Patient population. We examined the baseline clinical and angiographic characteristics and outcomes of CTO-PCIs performed between 2012 and 2016 at 14 United States centers: Appleton Cardiology, Appleton Wisconsin; Baylor Hamilton Heart and Vascular Hospital, Dallas, Texas; Central Arkansas VA Healthcare System, Little Rock, Arkansas; Columbia

University, New York, New York; Henry Ford Hospital, Detroit, Michigan; Massachusetts General Hospital, Boston, Massachusetts; Medical Center of the Rockies, Loveland, Colorado; Piedmont Heart Institute, Atlanta Georgia; St. Joseph Medical Center, Bellingham Washington; St. Luke's Health System's Mid-America Heart Institute, Kansas City, Missouri; Torrance Memorial Center, Torrance, California; University of Pittsburgh Medical Center, Presbyterian University Hospital, Pittsburgh, Pennsylvania; VA North Texas Health Care System, Dallas, Texas; and University of California, San Diego Healthcare System, San Diego, California.

Enrollment was performed during only part of the study period in some centers due to participation in other studies. Data collection was performed both prospectively and retrospectively and was recorded in a dedicated online database (Progress CTO: Prospective Global Registry for the Study of Chronic Total Occlusion Intervention; Clinicaltrials.gov Identifier: NCT02061436).⁵⁻⁹ The study was approved by the institutional review board of each site.

Table 1. Baseline clinical characteristics of the study patients, classified according to the presence of moderate or severe proximal vessel tortuosity.

Variable	Overall (n = 1589)	Moderate or Severe Tortuosity (n = 566)	Mild or No Tortuosity (n = 1023)	P-Value
Age [years]	65.3 ± 10.0	65.1 ± 10.0	65.4 ± 10.0	.59
Men	85%	88%	84%	.02
Body mass index [kg/m ²]	30.6 ± 6.0	30.9 ± 6.0	30.5 ± 6.0	.30
Diabetes mellitus	44%	48%	42%	.02
Hypertension	91%	91%	90%	.78
Dyslipidemia	95%	96%	95%	.51
Smoking [current]	26%	26%	26%	.96
Left ventricular ejection fraction [%]	50 ± 14	49 ± 14	50 ± 14	.55
Family history of coronary artery disease	30%	31%	29%	.63
Congestive heart failure	30%	32%	28%	.09
Prior myocardial infarction	43%	47%	41%	.03
Prior coronary bypass	36%	46%	31%	<.001
Prior cerebrovascular disease	11%	11%	11%	.88
Prior peripheral vascular disease	17%	17%	16%	.66
Baseline creatinine [mg/dL]	1.0 [0.9-1.3]	1.1 [0.9-1.3]	1.0 [0.9-1.2]	.04

Data provided as mean ± standard deviation, percentage, or median (interquartile range).

Definitions. Coronary CTOs were defined as coronary lesions with Thrombolysis in Myocardial Infarction (TIMI) grade 0 flow of at least 3-month duration. *Estimation of the occlusion duration* was based on first onset of anginal symptoms, 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), or 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.

The *J-CTO score* was calculated as described by Morino et al.⁴ The *Progress CTO score* was calculated as described by Christopoulos et al.⁵ *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 achievement of technical success with no in-hospital major adverse cardiac event (MACE). *In-hospital MACE* included any of the following adverse events prior to hospital discharge: death, myocardial infarction, urgent repeat target-vessel revascularization with either PCI or coronary artery bypass graft (CABG) surgery, tamponade requiring either pericardiocentesis or surgery, and stroke. *Myocardial infarction* was defined using the Third Universal Definition of Myocardial Infarction.¹⁰

Statistical analysis. Comparisons were performed between CTO-PCI procedures classified into two groups according to whether moderate or severe proximal tortuosity was present in the CTO target vessel or not. Continuous

variables were presented as mean ± standard deviation or median (interquartile range) and were compared using the Student's t-test or Wilcoxon rank-sum test, as appropriate. Categorical data were reported as frequencies or percentages and compared using the Chi-squared test or Fisher's exact test, as appropriate. Logistic regression analysis was performed to identify clinical and angiographic parameters associated with technical success. Variables with $P < .10$ on univariate analysis (age >70 years, gender, hypertension, dyslipidemia, left ventricular ejection fraction in units, congestive heart failure and myocardial infarction, prior CABG, peripheral arterial disease and cerebrovascular disease, presence of moderate or severe calcification, proximal cap ambiguity, prior failed CTO-PCI, presence of interventional collaterals, moderate or severe proximal vessel tortuosity, and CTO target vessel) were included in a multivariate model. All statistical analyses were performed with JMP 11.0 (SAS Institute). Two-sided P -values <.05 were considered statistically significant.

Results

Baseline clinical characteristics. We analyzed 1618 consecutive CTO-PCIs performed in 1589 patients. The baseline clinical characteristics of the study patients are presented in Table 1. Mean age was 65.3 ± 10.0 years and 85% of the study subjects were men. Nearly one-half of the patients had diabetes mellitus or prior myocardial infarction and approximately one-third had prior heart failure and prior CABG. Patients with moderate/severe tortuosity were more likely to have diabetes mellitus and prior CABG.

Table 2. Angiographic characteristics of the study lesions, classified according to proximal vessel tortuosity.

Variable	Overall (n = 1618)	Moderate or Severe Tortuosity (n = 578)	Mild or No Tortuosity (n = 1040)	P-Value
CTO target vessel				
Right coronary artery	56%	57%	55%	<.001
Left anterior descending	23%	10%	30%	
Left circumflex	21%	32%	14%	
Left main	0.01%	0.0%	0.2%	
Other	0.03%	0.9%	0%	
J-CTO score	2.51 ± 1.24	3.21 ± 1.05	2.11 ± 1.16	<.001
Progress CTO score	1.11 ± 1.00	1.94 ± 0.87	0.65 ± 0.74	<.001
Calcification (moderate/severe)	57%	72%	48%	<.001
Proximal cap ambiguity	31%	36%	28%	<.01
In-stent restenosis	15%	14%	16%	.27
Prior failure to open CTO	18%	20%	16%	.047
Interventional collaterals	57%	52%	60%	.01
Side branch at the proximal cap	47%	48%	46%	.64
Blunt/no stump	64%	67%	63%	.10
Vessel diameter (mm)	3.0 [2.5-3.0]	3.0 [2.5-3.0]	3.0 [2.5-3.0]	.42
Occlusion length (mm)	30 [20-45]	30 [20-50]	28 [16-40]	<.001
Successful crossing strategy				
Antegrade wiring	41%	32%	46%	<.001
Retrograde	25%	31%	22%	
Antegrade dissection and reentry	23%	23%	22%	
None	11%	14%	9%	
First crossing strategy				
Antegrade wiring	69%	66%	71%	.02
Retrograde	19%	23%	16%	
Antegrade dissection and reentry	12%	11%	12%	
Retrograde crossing attempt	42%	52%	37%	<.001
Stents used (n)	2.5 ± 1.2	2.8 ± 1.2	2.4 ± 1.1	<.001
Guide-support techniques				
Guide-extension catheter	22%	24%	21%	.08
Side-branch anchor	3%	5%	2%	<.01
Distal anchor	1%	2%	0.5%	<.01
Other	1%	0.4%	1%	.12

Data provided as mean ± standard deviation, percentage, or median [interquartile range].

CTO = chronic total occlusion; J-CTO score = Japan chronic total occlusion score; Progress-CTO score = progress chronic total occlusion score.

Angiographic characteristics. The angiographic characteristics of the CTO target lesions are summarized in Table 2. Moderate or severe proximal vessel tortuosity was present in 35.7%. The most common target vessel was the right coronary artery (56%) followed by the left anterior descending artery (23%) and the circumflex (21%). The most common final successful crossing strategy was antegrade wire escalation (41%) followed by retrograde (25%) and antegrade dissection

and reentry (23%). Moderate or severe calcification was present in more than one-half of the lesions (57%), and interventional collaterals were present in 57%.

Lesions with moderate or severe proximal vessel tortuosity were more complex, with higher J-CTO and Progress CTO scores and moderate or severe calcification. Moreover, tortuous lesions were longer and more likely to exhibit proximal cap ambiguity and to require retrograde crossing attempts (Table 2).

Table 3. Procedural outcomes of the study patients, classified according to proximal vessel tortuosity.

Variable	Overall (n = 1589)	Moderate or Severe Tortuosity (n = 566)	Mild or No Tortuosity (n = 1023)	P- Value
Technical success	88.7%	84.1%	91.3%	<.001
Procedural success	87.2%	82.3%	89.9%	<.001
Procedural time [min]	129 [90-194]	153 [108-210]	120 [82-184]	<.001
Fluoroscopy time [min]	48 [29-77]	60 [38-94]	41 [26-68]	<.001
Air kerma radiation dose [Gray]	3.24 [2.00-5.26]	3.85 [2.35-5.54]	2.95 [1.70-5.07]	<.001
Contrast volume	275 [200-370]	293 [214-400]	263 [200-360]	<.001
Major adverse cardiac events	2.70%	3.00%	2.54%	.59
Death	0.57%	0.53%	0.59%	.89
Acute Q-wave myocardial infarction	0%	0%	0%	–
Acute myocardial infarction	0.94%	0.71%	1.08%	.47
Redo PCI	0.25%	0.53%	0.10%	.01
Stroke	0.25%	0.18%	0.29%	.66
Emergency CABG	0.06%	0.18%	0.00%	.18
Pericardiocentesis	0.94%	1.24%	0.78%	.37

Data provided as percentage or median [interquartile range].
 PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft surgery.

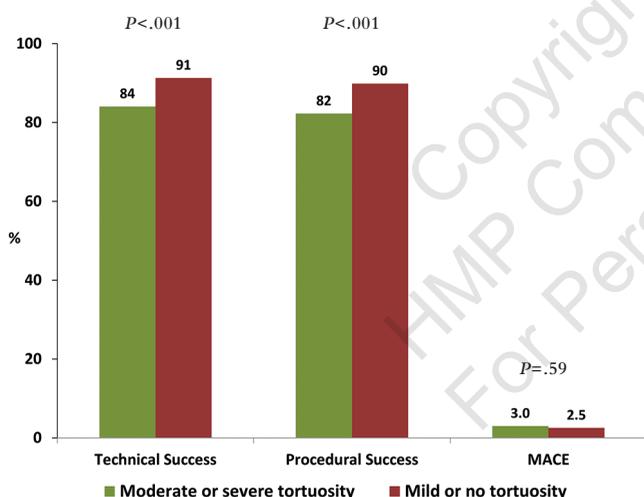


FIGURE 1. Technical and procedural success and incidence of major adverse cardiac events (MACE) among study lesions, classified according to proximal vessel tortuosity.

Procedural outcomes. Procedural outcomes are shown in Table 3 and Figure 1. Overall technical and procedural success rates were 89% and 87%, respectively, and the MACE rate was 2.7%. Lesions with moderate or severe tortuosity had lower technical success rates (84% vs 91%; $P<.001$) and procedural success rates (83% vs 90%; $P<.001$), but similar MACE rates (3.0% vs 2.5%; $P=.59$) as compared with cases with mild or no tortuosity. There was no difference between the various components of MACE

(death, myocardial infarction, repeated PCI, stroke, emergency CABG, and pericardiocentesis). However, on multivariable analysis, moderate or severe tortuosity was not independently associated with technical success (Figure 2). PCI of lesions with moderate or severe tortuosity required longer procedure and fluoroscopy times, higher air kerma radiation doses, and higher contrast volumes.

The most common guide-support technique to address proximal vessel tortuosity was use of guide-catheter extensions followed by side-branch anchor and distal-anchor techniques (Table 2; Figure 3). Among the cases with moderate or severe proximal vessel tortuosity, the most commonly used antegrade guide catheter was AL 1 (54 cases; 29.4%), while the most commonly used retrograde guide catheter was the EBU 4.0 (Figure 4).

Discussion

The main findings of this study are that significant proximal vessel tortuosity: (1) was present in approximately one-third of target CTOs; (2) was associated with lower technical and procedural success, but similar complication rates; (3) required more supportive guide catheters and guide-catheter techniques to address tortuosity; and (4) required use of the retrograde approach more frequently to obtain success.

Tortuosity is common among complex coronary lesions. Okamura et al reported 34.2% prevalence of proximal vessel tortuosity in a Japanese multicenter CTO-PCI registry.¹¹ In an analysis of 1582 retrograde CTO-PCIs from the EuroCTO club, Galassi et al reported moderate tortuosity in 28.5% and severe tortuosity in 9.7%.¹² Baykan et al reported

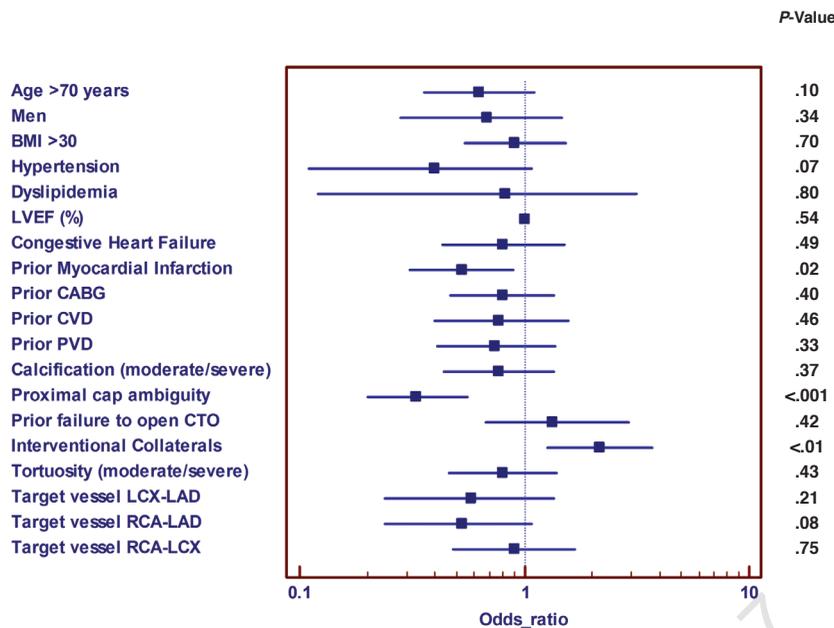


FIGURE 2. Multivariable analysis for technical success. BMI = body mass index; LVEF = left ventricular ejection fraction; CABG = coronary artery bypass graft surgery; CVD = cerebrovascular disease; PVD = peripheral vascular disease; CTO = chronic total occlusion; RCA = right coronary artery; LAD = left anterior descending coronary artery; LCX = left circumflex artery.

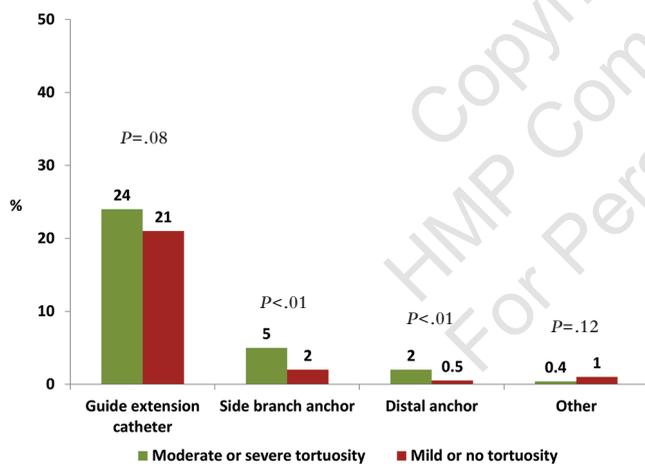


FIGURE 3. Guide-support techniques among study lesions, classified according to proximal vessel tortuosity.

a lower prevalence of severe tortuosity (10.4%) among 173 CTO-PCIs, although tortuosity was associated with technical failure (odds ratio: 0.085; 95% confidence interval, 0.013–0.579; $P=.01$), where severe tortuosity was defined as ≥ 1 bend of 90° or more, or ≥ 3 bends of 45° – 90° proximal to the diseased segment.¹

The pathogenesis of coronary tortuosity remains unclear, but tortuosity is associated with increasing age, hypertension, atherosclerosis, and genetic predisposition.^{13–16} Han created a

biomedical model of arterial buckling, demonstrating that arteries buckle due to high blood pressure, reduced axial stretch, or changes in the arterial wall stiffness and dimensions, lending support to the association of tortuosity with hypertension, aging, atherosclerosis and other pathological arterial changes.^{14,17}

Several techniques have been developed to overcome the challenges associated with PCI of tortuous lesions. Wiring of such lesions can be hindered by decreased wire torquability after passing the first curves and can be facilitated by using large size and supportive-shaped guide catheters and/or guide-catheter extensions, advancing wires through a microcatheter and using new-generation, composite-core wires or polymer-jacketed guidewires.¹⁸ Use of stiff wires, however, could straighten the vessel and possibly lead to the development of coronary “pseudolesions.”³ In our study, the most commonly used guide catheters in moderate or severe proximal vessel tortuosity were the Amplatz left and extra backup guides, which provide strong guide-catheter support. Moreover, use of dissection/reentry crossing techniques can facilitate crossing of tortuous CTOs by tracking the vessel bends with low risk of exiting the adventitia and leading to perforation. The prevalence of moderate/severe calcification was high (72%) in the majority of patients with proximal vessel tortuosity and likely contributed to the use of the retrograde approach in over one-half of the study cohort. Ultimately, the use of the above techniques resulted in $>80\%$ procedural and technical success rates in this challenging group of CTO patients.

Study limitations. There was no core laboratory analysis of the study angiograms and no independent event adjudication, and therefore assessment of angiographic characteristics was susceptible to operator-related bias. The CTO-PCI procedures were performed by centers with significant expertise in CTO-PCI; hence, these findings may not be generalizable to less experienced centers and operators. No follow-up data were available for analysis and the long-term outcomes associated with coronary tortuosity would require additional investigation. Lastly, the presence of tortuosity was determined by visual estimate.

Conclusion

In summary, moderate or severe proximal vessel tortuosity is common in CTO target lesions and is associated with lower efficiency and procedural success, but similar complication rates as compared with lesions with mild or no tortuosity.

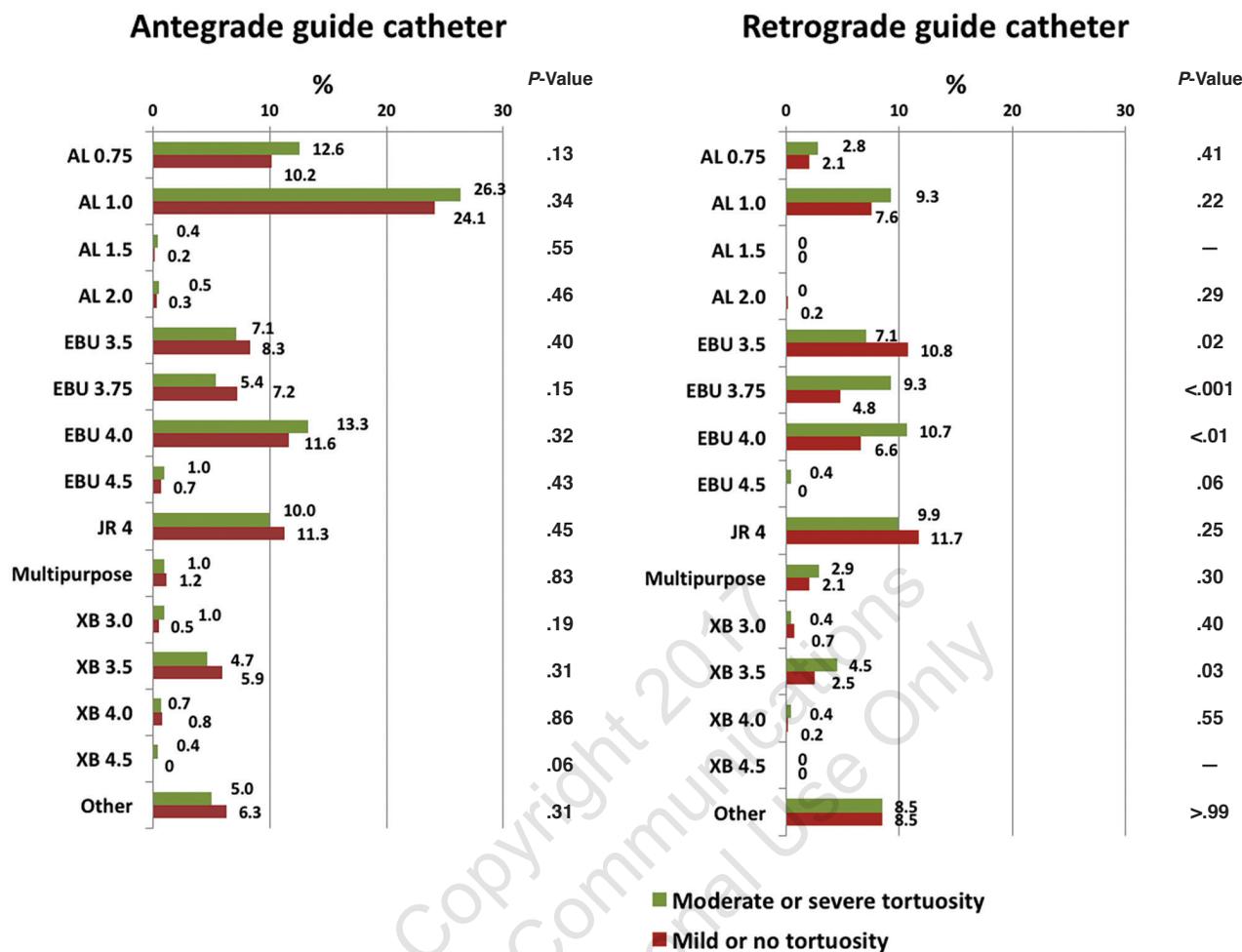


FIGURE 4. Guide catheters used among study lesions, classified according to proximal vessel tortuosity. AL = Amplatz left; EBU = Extra back-up; JR = Judkins right; XB = Extra back-up; Other = MAC 4 multi-aortic curve, sheathless Eaucath guide, right back-up, Extra back-up left anterior descending, Hockey-stick guide catheter, Judkins left, Ikari left and right guide catheter, internal mammary guide catheter, Champ 2, Voda guide catheter, right back-up catheter, power back-up guide catheter, contralateral support guide catheter.

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