Procedural Outcomes of Patients Undergoing Percutaneous Coronary Intervention for De Novo Lesions in the Ostial and Proximal Left Circumflex Coronary Artery

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Ostial coronary artery lesions can be challenging during percutaneous coronary intervention (PCI) because of elastic fiber content, calcium burden, and angulation. We assessed procedural and clinical major adverse cardiac events (MACE) associated with PCI for ostial lesions, focusing on ostial left circumflex (LC) lesions compared with ostial left anterior descending artery (LAD) and right coronary artery lesions. All patients with ostial or very proximal coronary artery lesions treated with PCI at MedStar Washington Hospital Center (Washington, DC) from 2003 to 2018 were included. The primary end point was target lesion revascularization (TLR)-MACE, defined as the composite of all-cause mortality, Q-wave myocardial infarction (MI), and TLR at 1 year. A total of 4,759 patients with available 1-year follow-up were included: 2,236 ostial/very proximal LAD, 980 ostial/very proximal LC, and 1,543 ostial/very proximal right. The presenting clinical syndrome for the LC group was mainly stable or unstable angina, whereas MI was more common in the LAD. At 1 year, the TLR-MACE rate was 16.7% in the LC group versus 12.5% in the LAD and 11.8% in the right group (p = 0.001). Mortality rates were 11.2% in the LC group versus 8.4% in the LAD and 6% in the right group (p <0.001). A Cox model showed that dialysis had the highest impact on TLR-MACE. In conclusion, compared with PCI of ostial or very proximal LAD or right lesions, PCI of ostial or very proximal LC lesions was associated with higher rates of TLR-MACE. **(Am J Cardiol 2020;135:62−67)**

Ostial coronary artery lesions are defined as involving the origin of the coronary vessel, including the first 3 mm of the artery[1] with native aorto-ostial lesions involving the ostia of the right coronary artery or left main coronary artery (LMCA). However, ostial lesions are also located at the ostia of the left anterior descending artery (LAD), left circumflex artery (LC), and ramus intermedius, as well as the ostia of the branches of the major coronary arteries, such as the diagonals, marginals, posterior descending, and posterolateral branches of the right. Ostial lesions can be challenging during percutaneous coronary intervention (PCI) because of high elastic fiber content and calcium, which may increase elastic recoil during the intervention, increase the rigidity of the vessel wall, and reduce vessel distensibility.[2−5] Especially when treating ostial LAD, LC, and ramus lesions, stent positioning can be difficult such that crossover stenting to the distal left main has become standard practice, and stenting the ostial LC is additionally complicated by steep angulation of the vessel.[6] Occasionally, the ostial lesion might also involve the very proximal coronary artery segment. In this study, we assessed the procedural and clinical outcomes of PCI for ostial/very proximal LC lesions compared with PCI outcomes of similar lesions in the LAD or right.

Methods

All patients with ostial/very proximal coronary artery lesions treated with PCI at MedStar Washington Hospital Center (Washington, DC) from 2003 to 2018 were included in this analysis. In the current analysis, the definition of an ostial lesion was extended to include the segment immediately beyond the ostium. Patients with PCI of at least 1 ostial lesion and with at least 1 year of available follow-up were included in the analysis. Patients who underwent stenting for distal LMCA lesions in which the stent

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extended from the LMCA into either the ostial/proximal LAD or the ostial/proximal LC were not included. The institutional review board approved this study.

The primary end point was target lesion revascularization (TLR)-major adverse cardiac events (MACE, defined as the composite of all-cause mortality, Q-wave myocardial infarction [QWMI, new Q-waves visible on the electrocardiogram post procedure], and TLR at 1-year follow-up). Key secondary end points included rates of target vessel revascularization (TVR)-MACE, death, QWMI, TLR, and TVR.

Categorical variables have been expressed in counts and percentages. Continuous variables have been expressed as mean ± SD. Categorical variables were compared using the chi-square test and continuous variables were compared using Student's *t* test. Follow-up was restricted to at least 1 year or an event within 1 year. Cumulative incidence functions were estimated from the Kaplan-Meier estimator and presented up to 1 year. Equality of 3 cumulative incidence functions was tested with the log rank test. A p value below 0.05 was considered significant.

A multivariate Cox model was constructed to identify independent predictive factors of events. Hazard ratios (HR) and their 95% confidence intervals were presented for each variable with respect to TLR-MACE. In addition to the location of the lesion, a group of potentially significant covariates was selected from a pool of clinically relevant variables, including gender, age, length of stay, history of MI, history of coronary artery bypass surgery, history of PCI, diabetes mellitus (DM), chronic renal insufficiency (CRI) with and without dialysis, congestive heart failure, insulin-dependent DM, peripheral arterial disease, stent length and diameters of a drug-eluting stent (DES), number of stents implanted, baseline creatinine, and postprocedural acute renal failure. Statistical analyses were performed using SAS 9.2 (SAS Institute, Cary, NC).

Results

A total of 4,759 patients with available 1-year follow-up had PCI for ostial/proximal lesions and were included in this analysis: 2,236 LAD, 980 LC, and 1,543 right. The age of this cohort was 66 ± 26 years, and 64.8% were men. A history of hypertension, DM, hypercholesterolemia, MI, PCI, coronary artery bypass surgery, peripheral arterial disease, congestive heart failure, or CRI was more common in the LC group. The clinical presentation for the LC group was mainly stable or unstable angina, whereas MI was more common as the presenting symptom in the LAD group (Table 1).

Balloon predilation and postdilation were utilized more in the LC group, whereas direct stenting was performed in only 28.4% of cases (Table 2). The use of DES, intravascular ultrasound, and intra-aortic balloon pump was more

Table 1
Characteristics of the patients at baseline

Variable	Coronary artery			p Value
	LC (n = 980)	LAD (n = 2,236)	Right (n = 1,543)	
Age (years)	67.6 ± 11.5	63.3 ± 11	65.6 ± 11.5	0.28
Men	661 (67.4%)	1498 (67%)	926 (60%)	0.001
White	656 (67%)	1514 (67.7%)	974 (63.1%)	0.012
Black	258 (26.3%)	543 (24.3%)	457 (29.6%)	0.001
Asian	25 (2.5%)	78 (3.5%)	49 (3.2%)	0.35
Hispanic	8 (0.8%)	18 (0.8%)	15 (1%)	0.84
Native American	4 (0.4%)	4 (0.2%)	0	0.06
Body mass index (kg/m^2)	29.18 ± 5.96	29.46 ± 6.36	29.55 ± 6.17	0.34
Diabetes mellitus	414 (42.2%)	695 (31.1%)	559 (36.2%)	0.001
Insulin dependent diabetes	162 (16.5%)	224 (10%)	204 (13.2%)	<0.001
Hypertension	875 (89.3%)	1829 (81.8%)	1341 (86.9%)	0.001
Hypercholesterolemia	864 (88.2%)	1867 (83.5%)	1327 (86%)	0.002
Prior PAD	196 (20%)	237 (10.6%)	289 (18.7%)	<0.001
Smoker	484 (49.4%)	1053 (47.1%)	855 (55.4%)	<0.001
Prior myocardial infarction	276 (28.2%)	364 (16.3%)	321 (20.8%)	<0.001
Prior coronary bypass	313 (32%)	177 (7.9%)	255 (16.5%)	<0.001
Prior PCI	355 (36.2%)	472 (21.1%)	474 (30.7%)	<0.001
Family Hx of CAD	428 (43.7%)	1029 (46%)	705 (45.7%)	0.48
Prior heart failure	197 (20.1%)	364 (16.3%)	279 (18.1%)	0.028
Chronic renal insufficiency	171 (17.4%)	277 (12.4%)	211 (13.7%)	<0.001
Dialysis	37 (3.8%)	60 (2.7%)	45 (2.9%)	0.25
Left ventricular ejection fraction	0.47 ± 0.14	0.46 ± 0.16	0.49 ± 0.14	<0.01
Presenting clinical syndrome				
Stable angina pectoris	387 (39.5%)	762 (34.1%)	566 (36.7%)	0.012
Unstable angina pectoris	436 (44.5%)	881 (39.4%)	623 (40.4%)	0.026
Acute myocardial infarction	196 (20%)	550 (24.6%)	367 (23.8%)	0.018

CAD = coronary artery disease; DES = drug-eluting stent; IVUS = intravascular ultrasound; LAD = left anterior descending; LC = left circumflex; PAD = peripheral arterial disease; PCI = percutaneous coronary intervention; TLR = target lesion revascularization; MACE = major adverse cardiovascular events.

Table 2
Procedural characteristics

Variable	Coronary artery			p Value
	LC (n = 980)	LAD (n = 2,236)	Right (n = 1,543)	
Lesion type				
ACC/AHA type A	75 (7.7%)	190 (8.5%)	106 (6.9%)	0.050
ACC/AHA type B1/B2	620 (63.3%)	1393 (62.3%)	929 (60.2%)	0.076
ACC/AHA type C	284 (29%)	653 (29.2%)	508 (32.9%)	0.002
Predilatation	420 (42.9%)	818 (36.6%)	647 (41.9%)	<0.001
Bare metal stent	153 (15.6%)	347 (15.5%)	290 (18.8%)	<0.001
Drug-eluting stent	730 (74.5%)	1735 (77.6%)	1156 (74.9%)	0.01
Direct stenting	278 (28.4%)	814 (36.4%)	532 (34.5%)	0.001
Postdilatation	206 (21%)	425 (19%)	284 (18.4%)	0.075
Stent diameter (mm)	3.41 ± 8.44	3.23 ± 3.46	3.33 ± 7.76	0.76
Stent length (mm)	17.64 ± 7.05	19.2 ± 6.37	19.97 ± 7.87	<0.001
Number of DESs (per patient)	1.19 ± 1.1	1.1 ± 0.99	1.28 ±1.23	0.001
IVUS performed	540 (55.1%)	1427 (63.8%)	805 (52.2%)	<0.001
Rotational atherectomy	44 (4.5%)	92 (4.1%)	65 (4.2%)	0.75
Laser atherectomy	2 (0.2%)	4 (0.2%)	6 (0.4%)	0.28
Cutting balloon	48 (4.9%)	98 (4.4%)	68 (4.4%)	0.60
IABP	54 (5.5%)	183 (8.2%)	56 (3.6%)	<0.001
Closure device	610 (62.2%)	1438 (64.3%)	935 (60.6%)	0.065
Contrast amount (ml)	176 ± 87.3	175 ± 101.3	171 ± 84.5	0.30
Procedure length (min)	69.3 ± 37.6	63.1 ± 44.1	69.8 ± 42.3	<0.001

DES = drug-eluting stent; IVUS = intravascular ultrasound; IABP = intra-aortic balloon pump; LAD = left anterior descending; LC = left circumflex.

common in the LAD group. American College of Cardiology/American Heart Association type C lesions were more common in the right group. There was no difference in the rate of mechanical atherectomy use among the 3 groups (Table 2). Vascular complications were more common in the right group, whereas in-hospital mortality was higher in the LAD group (4.2% vs 3.6% for LC and 2.3% for right, p = 0.005). Other in-hospital clinical outcomes were similar (Table 3).

The 1-year TLR-MACE rate was 16.7% in the LC group, 12.5% in the LAD group, and 11.8% in the right group (p = 0.001; Figure 1). The 1-year TVR-MACE rate was also higher in the LC group (17.8% vs 15.4% for LAD and 13.4% for right, p = 0.01). Higher mortality rates mainly drove these higher TLR-MACE and TVR-MACE rates in patients in the LC group (11.2% vs 8.4% for patients with LAD lesions and 6.0% for patients with right lesions, p <0.001). The TLR rate was similar between the LC and right groups (6.4% vs 6.0%), higher than in the LAD group (4.5%; Figure 2). The rates of TVR and MI did not show any difference among the groups (Table 4).

To identify potential predictors for TLR-MACE in addition to the location of the lesion, we applied a multivariate Cox model, including patient-level factors. The Cox model revealed that when compared with LC, the HR for LAD and right lesion location was 0.78 and 0.72, respectively. Dialysis had the highest impact on TLR-MACE with an HR of 4.03. History of CRI had a HR of 1.18. History of MI had a HR of 1.38. For patient age, the HR was 1.007, implying that each 10-year increase in age would only increase the HR by 7% (Table 5).

Table 3
In-hospital clinical outcomes

Outcome	Coronary artery			p Value
	LC (n = 980)	LAD (n = 2,236)	Right (n = 1,543)	
Clinical success	940 (95.9%)	2124 (95%)	1495 (96.9%)	0.017
Length of stay (days)	3.37 ± 4.54	3 ± 3.67	2.96 ± 3.67	0.019
Q-wave MI	3 (0.3%)	9 (0.4%)	8 (0.5%)	0.71
Stroke	4 (0.4%)	11 (0.5%)	5 (0.3%)	0.84
Vascular complication	18 (1.8%)	40 (1.8%)	46 (3%)	0.03
TLR	4 (0.4%)	16 (0.7%)	9 (0.6%)	0.60
Major bleeding	12 (1.2%)	40 (1.8%)	29 (1.9%)	0.40
Stent thrombosis	2 (0.2%)	7 (0.3%)	5 (0.3%)	0.94
Death	35 (3.6%)	94 (4.2%)	35 (2.3%)	0.005

LAD = left anterior descending; LC = left circumflex; MI = myocardial infarction; TLR = target lesion revascularization.

Discussion

The main findings from our study are as follows: (1) Patients who underwent PCI for an ostial or very proximal LC lesion had a higher prevalence of comorbid conditions, including a history of previous MI and coronary interventions, DM, and chronic kidney disease. (2) At 1-year follow-up, TLR-MACE was higher in the LC (16.7%) than in the right and LAD (11.8% and 12.5%, respectively, p <0.001), driven mainly by higher mortality rates in the LC group. (3) Among tested covariates, dialysis had the highest impact on TLR-MACE, with an HR of 4.03.

Percutaneous management of ostial lesions is challenging because of their specific histopathologic characteristics and technical issues, including pressure damping during vessel cannulation, guide-catheter-induced coronary dissection, plaque shift to an adjacent side branch, accurate stent positioning to avoid geographic miss, and stent undersizing

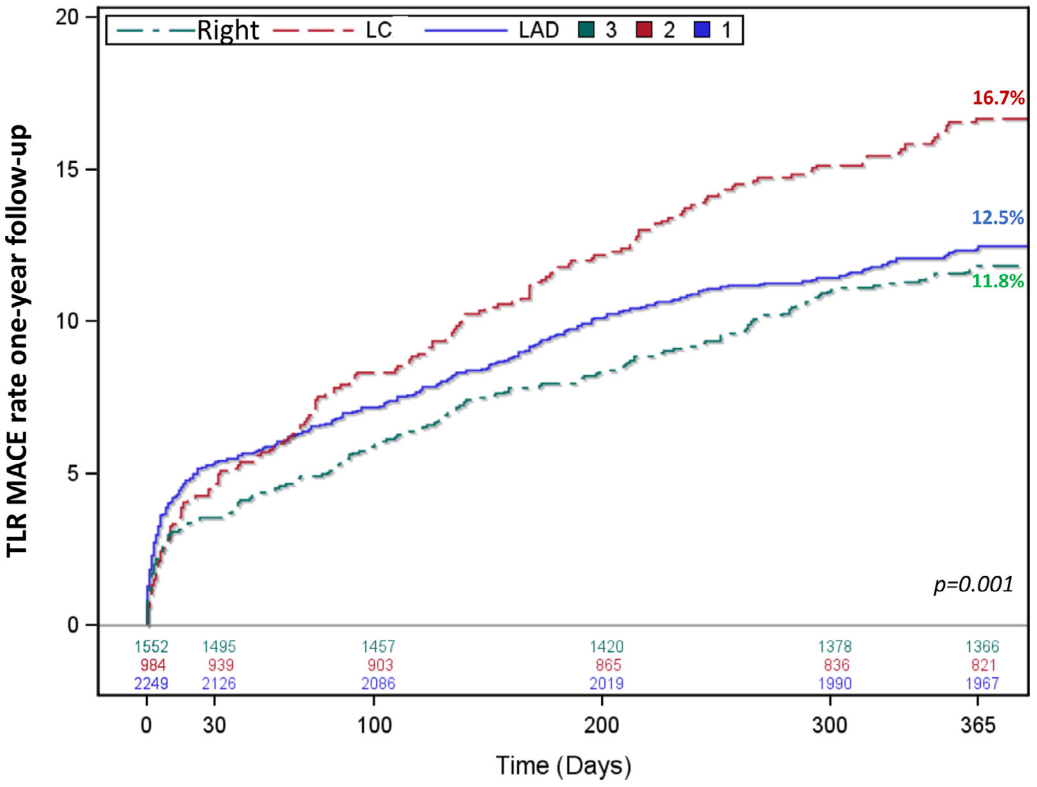

Figure 1. TLR MACE rates at 1-year follow-up. LAD = left anterior descending; LC = left circumflex; TLR MACE = target lesion revascularization major adverse cardiovascular events.

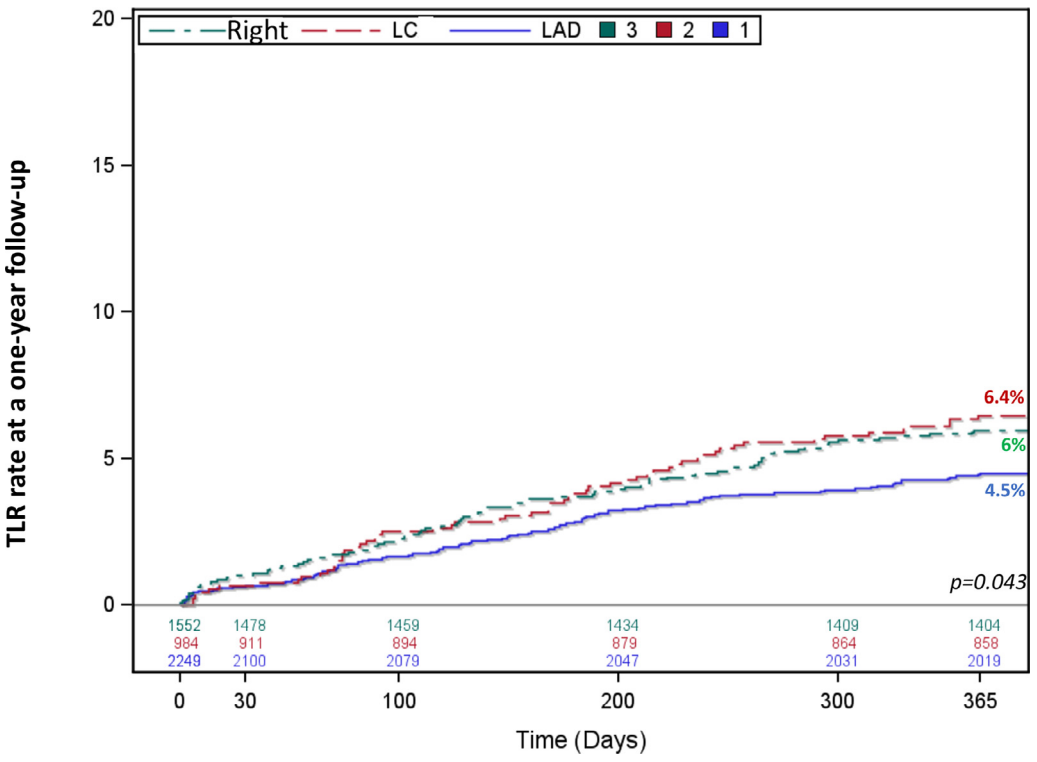

Figure 2. TLR rates at 1-year follow-up. LAD = left anterior descending; LC = left circumflex; TLR = target lesion revascularization.

Table 4
One-year clinical outcomes

Outcome	Coronary artery			p Value
	LC (n = 980)	LAD (n = 2,236)	Right (n = 1,543)	
TLR MACE	164 (16.7%)	280 (12.5%)	182 (11.8%)	0.001
TVR MACE	174 (17.8%)	344 (15.4%)	207 (13.4%)	0.011
Q-wave MI	2 (0.2%)	7 (0.3%)	9 (0.6%)	0.28
Stent thrombosis	7 (0.7%)	18 (0.8%)	9 (0.6%)	0.92
Death	110 (11.2%)	188 (8.4%)	93 (6%)	<0.001
TLR	63 (6.4%)	101 (4.5%)	93 (6%)	0.043
TVR	77 (7.9%)	174 (7.8%)	120 (7.8%)	0.99

LAD = left anterior descending; LC = left circumflex; MI = myocardial infarction; TLR MACE = target lesion revascularization major adverse cardiac events; TVR MACE = target vessel revascularization major adverse cardiac events.

Table 5
Analysis of maximum likelihood estimates for TLR MACE

Variable	Chi-square	Hazard ratio	95% CI	p Value
LAD	3.62	0.789	0.617-1.007	0.057
Right	5.6802	0.729	0.562-0.945	0.017
Age	2.4392	1.007	0.998- 1.016	0.11
Length of stay	128.1335	1.087	1.071- 1.102	<.0001
Prior MI	8.3151	1.383	1.109- 1.724	0.003
Dialysis	80.7224	4.03	2.975- 5.467	<.0001
Chronic renal insufficiency	1.1501	1.18	0.872-1.598	0.28
Stent diameter	3.9890	1.009	1.0-1.018	0.045
Number of stents implanted	18.9881	1.209	1.1-1.317	<.0001

LAD = left anterior descending; MI = myocardial infarction.

or underexpansion. A very proximal lesion might also be challenging because of the same technical issues.

Hemodynamics and vessel geometry may be associated with plaque formation because atherosclerosis tends to occur in angulated arterial segments and bifurcations. Wall shear stress has been shown to be related to the pathogenesis of atherosclerosis.[7,8] Because the right and LAD are less angulated than the LC, this may contribute to increased atherosclerosis formation in the ostium of the LC and increased event rates.

Previous studies have shown high TLR rates after ostial right interventions because these lesions are more prone to elastic recoil and stent restenosis.[2,5] Our results indicate that these findings are likely to be present, and perhaps even more problematic, at the ostium of the LC, possibly because of superimposed calcification[9] and angulation.[6] Mechanical atherectomy was used less commonly in LC procedures, even though ostial LC lesions tend to be more calcified. Although routine use of mechanical atherectomy may not improve stent-related outcomes,[10] operators tend to avoid the use of rotational atherectomy in calcified and angulated ostial lesions (eg, LC lesions) because of a higher risk of causing a dissection that may compromise blood flow to a large myocardial area.

The striking finding was a higher 1-year mortality rate in patients in the LC group than in patients in the LAD or right group, and this was the main component behind the higher TLR-MACE rates. Although we cannot isolate cardiovascular causes from other causes of mortality at 1 year (these data were not fully available), we assumed that any increased mortality was cardiovascular because it was the most common in this age group. The increased event rates in the LC could have been driven by co-morbidities more than lesion location and that ostial LC disease may be a marker as much as it is a risk factor. Our predictive model showed that dialysis had the highest impact on TLR-MACE among all covariates that were tested. The association between renal dysfunction and higher rates of unfavorable PCI outcomes has been reported previously.[11,12] Among causable factors, this might be secondary to increased coronary calcification and vascular stiffness seen in the hemodialysis population.[13] Stent underexpansion due to insufficient lesion preparation, inadequate postdilations, or more calcium may also play an important role.

The optimal treatment for ostial coronary lesions has been a concern from the earliest days of PCI. In the prestent era, balloon angioplasty resulted in higher complication rates than angioplasty of nonostial lesions.[14] This can be explained by the unique histopathologic nature of those lesions.[2] Although the use of bare-metal stents improved the acute results, increased rates of repeat revascularization were seen in patients with ostial lesions in comparison with patients who underwent nonostial, proximal PCI.[15] Compared with bare-metal stents, DES were associated with significantly lower MACE rates, with no increase in procedural complications.[16–18]

This is an observational registry study with inherent limitations. Assessment of lesion type, location, and coverage was done by operators without a core lab assessment. This is a single tertiary referral center with increased disease complexity compared with the "real world." Potential confounders might not have been identified and entered. Some patients had multivessel disease that was treated, and this might have affected the outcomes. Also, ostial left main coronary artery PCI was not included. In conclusion, PCI to ostial/very proximal LC lesions is associated with a higher rate of adverse events at 1 year, especially increased mortality, compared with similar lesions in the LAD or right. This is magnified in patients on dialysis. Special considerations should be addressed concerning whether, and how, to treat ostial lesions of the LC.

Author Contribution

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Gary S. Mintz: Conceptualization, Methodology, Validation, Formal analysis, Writing (review and editing).

Ron Waksman: Conceptualization, Formal analysis, Writing (review and editing), Supervision.

Disclosures

Toby Rogers—Consultant and proctor: Medtronic, Edwards Lifesciences; Advisory board: Medtronic. Equity interest: Transmural Systems. Ron Waksman—Advisory Board: Amgen, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Consultant: Amgen, Biotronik, Boston Scientific, Cardioset, Cardiovascular Systems Inc., Medtronic, Philips, Pi-Cardia Ltd.; Grant support: AstraZeneca, Biotronik, Boston Scientific, Chiesi; Speakers Bureau: AstraZeneca, Chiesi; Investor: MedAlliance. Gary Mintz—honoraria from Boston Scientific, Philips Volcano, Medtronic, Terumo. All other authors—None.

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