Racial Disparities in Risk for Major Amputation or Death After Endovascular Interventions for Peripheral Artery Disease: A LIBERTY 360 Study

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Abstract

Objectives. Previous studies have suggested that Black patients with peripheral artery disease (PAD) may have worse outcomes than White patients. The aim of this study was to determine whether there are racial differences in outcomes of patients with PAD undergoing endovascular treatment. **Methods.** Data were derived from the LIBERTY 360 study (NCT01855412). Unadjusted hazard ratios (HRs) and the respective 95% confidence intervals (CIs) were synthesized to examine the association between race and all-cause mortality, target-vessel revascularization (TVR), major amputation, major adverse event (MAE), and combination of major amputation/death up to 3 years of follow-up. **Results.** We included 1150 patients with PAD (178 Black patients vs 972 White patients) treated with any United States Food and Drug Administration (FDA)-approved or cleared device. Isolated below-the-knee disease was more prevalent among Black patients (*P*=.01). Procedural success was similar between the 2 groups with no statistically significant difference in periprocedural complication rates. Among the subjects with baseline wounds, 58.8% of Black patients and 52.6% of White patients had wound healing at 6 month follow-up exam (*P*=.44). Despite similar rates of wound care and wound healing, Black patients were at higher risk for the combined endpoint of major amputation/death compared with White patients at 12-month follow-up (HR, 1.61; 95% CI, 1.03-2.50; *P*=.04) and 36-month follow-up (HR, 1.45; 95% CI, 1.04-2.04; *P*=.03). Data regarding racial disparity in outcomes after endovascular therapy of patients with PAD are sparse. In our study, Black race was associated with combined major amputation/death risk during follow-up. However, this is likely attributed to population-related characteristics rather than biological characteristics. **Conclusions.** Further studies are needed to evaluate the role of race in revascularization outcomes among patients with PAD.

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Key words: Black race, endovascular repair, peripheral vascular disease, racial disparity in healthcare, revascularization

Peripheral artery disease (PAD) affects 8-10 million patients in the United States,[1,2] with Black patients having 2-3 times higher prevalence of PAD than White patients.[3] PAD has been associated with high morbidity and mortality rates.[4-6] Endovascular intervention is a viable treatment approach for PAD, with acceptable hemodynamic improvement and safety profile.[7,8] Thus, in the last decades there has been a shift toward endovascular therapy for patients with PAD, and an associated lower overall number of open surgical revascularizations and lower-extremity amputation rates performed for PAD treatment.[9-11] However, significant racial differences remain in outcomes of PAD therapy, with Medicare and Nationwide Inpatient Sample analyses showing that Black patients with PAD are more likely to undergo amputation compared with non-Hispanic whites.[11-13]

Older studies that investigated patency and amputation rates after bypass surgery have suggested that the observed

poorer limb-salvage outcomes among Black patients with PAD undergoing revascularization procedures could be attributed to racial differences in biological pathways.[14,15] However, these studies are outdated and their results have been questioned as larger analyses have shown that Black patients are less likely to be offered revascularization attempts before amputation, indicating that racial differences in disease severity, as well as patient and/or physician decision making are the actual reasons for this observed difference in outcomes between Black patients and White patients with PAD.[13,16] Additionally, the socioeconomic status,[17-19] access to appropriate healthcare, and regional clustering of vascular services potentially constitute major confounders for the racial disparity in outcomes of endovascular procedures for patients with PAD, contributing to geographic variation in amputation rates.[10,20]

As only a few studies have evaluated the effects of race/ethnicity on the course of PAD among patients undergoing revascularization procedures, it is not yet clear to what extent race and associated population-related characteristics affect clinical outcomes after endovascular therapy for PAD. Identification of such risk factors for worse prognosis could optimize the management of populations that are potentially at a higher risk for complications.[21-25] The aim of this study was to determine whether Black race was associated with risk of adverse short- and long-term outcomes of endovascular therapy in patients with PAD. We utilized data from the LIBERTY 360 study, which is a modern, real-world cohort of patients with PAD treated with endovascular approaches.[7]

Methods

Study design and patient enrollment. LIBERTY 360 is a prospective, observational, multicenter study (ClinicalTrials.gov identifier NCT01855412) examining predictors of clinical and economic outcomes in patients with PAD undergoing lower-extremity endovascular interventions between 2013 and 2016. United States Food and Drug Administration (FDA)-approved or cleared devices were utilized. Both target lesions above and below the knee were revascularized. Target lesions were located within or extending into 10 cm above the medial epicondyle to the digital arteries. A steering committee, consisting of principal investigators, representatives from the study core laboratories, and the sponsor (Cardiovascular Systems, Inc [CSI]), developed the study protocol. CSI was responsible for approval and oversight of the protocol; the protocol for the LIBERTY 360 study was approved by the institutional review board of each participating site. Overall, 51 sites enrolled patients in the LIBERTY 360 study (Supplemental Table S1). All treated patients provided written informed consent and the trial was conducted in accordance with the Declaration of Helsinki. Details about the exact inclusion and exclusion criteria of the LIBERTY 360 study have been previously published[26] and can also be found at https://clinicaltrials.gov/ct2/show/NCT01855412?cond=NCT01855412&rank=1.

Renal disease was defined as calculated estimated glomerular filtration rate <60 mL/min/1.73m^2 (based on case report forms and Modification of Diet in Renal Disease study equation) or kidney damage of at least 3 months. *Hyperlipidemia* was defined as cholesterol levels >200 mg/dL or low-density lipoprotein >100 mg/dL, or dyslipidemia requiring medication. *Hypertension* was defined as systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg or requiring medication for blood pressure control. For the current subanalysis of the LIBERTY 360 study, patients with available demographic data regarding race were included and race-related comparisons were performed (Black patients vs White patients). A total of 1150 patients who underwent endovascular procedures for PAD were identified. For analysis purposes, patients were divided into 2 groups that included Black or African American patients (the Black group) and non-Hispanic White patients (the White group). Patient and lesion characteristics stratified by race are summarized in Tables 1 and 2, respectively.

Study endpoints. *Primary endpoints* of the current LIBERTY 360 subanalysis were: (1) procedural success assessed by the angiographic core laboratory as <50% residual stenosis without significant angiographic complications (ie, severe dissection (type C-F), perforation, distal embolization, abrupt closure); (2) combined incidence of major amputation or death; and (3) major amputation of the target limb. *Secondary endpoints* were lesion success (<50% residual stenosis, without significant angiographic complications), major adverse events (MAEs), target-vessel revascularization (TVR), all-cause death, and wound healing during follow up. *MAE* was defined as death within 30 days of the primary procedure, unplanned major amputation of the target limb, and TVR as assessed by the angiographic core laboratory when angiographic images were available. Additional secondary outcomes included ankle brachial index (ABI) and Rutherford class (RC) at baseline and during follow-up. As the 3-year follow-up visit was a phone visit, ABI and RC were assessed only up to 2 years of follow-up.

Statistical analysis. Descriptive statistics were used for baseline demographic and lesion characteristics. Categorical variables are presented as absolute and relative frequencies (ie, percentages) and were compared with Monte Carlo approximation of the Fisher's exact test. Numeric data are presented as mean ± standard deviation and compared using analysis of variance or a paired t-test, while discrete data were compared with the Kruskal-Wallis test or Wilcoxon signed-rank test for paired data. Angiographic data were adjudicated by SynvaCor/Prairie Educational and Research Cooperative. In the analyses of this LIBERTY 360 substudy, core lab data were preferred in order to minimize any potential bias. In cases where the core lab was not able to assess significant angiographic complications, site-reported data were used. The Kaplan-Meier method was

TABLE 1. Baseline characteristics.

Characteristics	Black Patients (n = 178)	White Patients (n = 972)	*P*-Value
Age (years)	67.2 ± 10.9 (n = 178)	70.3 ± 10.7 (n = 971)	<.001
Male gender	99 (55.6%)	645 (66.4%)	<.01
Hispanic or Latino	4 (2.2%)	152 (15.6%)	<.001
Body mass index (kg/m^2)	29.3 ± 5.9 (n = 178)	28.9 ± 6.0 (n = 972)	.51
Estimated glomerular filtration rate (mL/min/1.73 m)	63.0 ± 37.1 (n = 178)	63.2 ± 27.4 (n = 971)	.93
Smoking history	113 (63.5%)	672 (69.1%)	.14
Current smoker	46 (25.8%)	177 (18.2%)	.02
Former smoker	67 (37.6%)	495 (50.9%)	<.01
Diabetes	120 (67.4%)	578 (59.5%)	.06
Hyperlipidemia	148 (83.1%)	850 (87.4%)	.12
Hypertension	168 (94.4%)	906 (93.2%)	.74
Renal disease	78 (43.8%)	320 (32.9%)	<.01
Renal disease and on hemodialysis	31 (39.7%)	53 (16.6%)	<.001
Coronary artery disease	87 (48.9%)	614 (63.2%)	<.001
Myocardial infarction	33 (18.5%)	238 (24.5%)	.10
Stroke/transient ischemic attack	37 (20.8%)	138 (14.2%)	.03
Run-off vessels before treatment (core lab)	(n = 154)	(n = 842)	<.01
3	15 (9.7%)	163 (19.4%)	<.01
2	52 (33.8%)	326 (38.7%)	.28
1	71 (46.1%)	264 (31.4%)	<.01
0	16 (10.4%)	89 (10.6%)	>.99
Run-off vessels post treatment (core lab)	(n = 137)	(n = 711)	<.01
3	22 (16.1%)	179 (25.2%)	.02
2	50 (36.5%)	287 (40.4%)	.45
1	55 (40.1%)	229 (32.2%)	.08
0	10 (7.3%)	16 (2.3%)	<.01
Previous endovascular therapy of target limb	(n = 178)	(n = 972)	.38
No	133 (74.7%)	672 (69.1%)	
Yes	44 (24.7%)	298 (30.7%)	
Unknown	1 (0.6%)	2 (0.2%)	
Previous bypass surgery of target limb	(n = 178)	(n = 972)	.52
No	171 (96.1%)	929 (95.6%)	
Yes	6 (3.4%)	41 (4.2%)	
Unknown	1 (0.6%)	2 (0.2%)	
Prior stent placed, target limb	(n = 178)	(n = 972)	.45
No	152 (85.4%)	816 (84.0%)	
Yes	25 (14.0%)	154 (15.8%)	
Unknown	1 (0.6%)	2 (0.2%)	
Previous amputations	(n = 178)	(n = 972)	.12
Target limb	11 (6.2%)	46 (4.7%)	.45
Non-target limb	12 (6.7%)	63 (6.5%)	.87
Both limbs	9 (5.1%)	21 (2.2%)	.04
None	146 (82.0%)	842 (86.6%)	.13
If previous amputations, target limb	(n = 20)	(n = 67)	.74
Toe(s) only	19 (95.0%)	65 (97.0%)	.55
Foot only	1 (5.0%)	4 (6.0%)	>.99
Antiplatelet therapy at discharge	163 (91.6%)	921 (94.8%)	.11
Aspirin	140 (78.7%)	779 (80.1%)	.68
Clopidogrel	131 (73.6%)	732 (75.3%)	.64
Dual	118 (66.3%)	658 (67.7%)	.73
Anticoagulants at discharge	13 (7.3%)	104 (10.7%)	.22
Warfarin	8 (4.5%)	65 (6.7%)	.32
Other	5 (2.8%)	40 (4.1%)	.53
Antihyperlipidemic at discharge	118 (66.3%)	793 (81.6%)	<.001
Antihypertensive at discharge	164 (92.1%)	879 (90.4%)	.58
Hospitalization	98 (55.1%)	401 (41.3%)	<.001
ICU admissions among patients hospitalized	(n = 98)	(n = 401)	.19
No	89 (90.8%)	343 (85.5%)	
Yes	9 (9.2%)	58 (14.5%)	
Time of admission to discharge (hours)	48.0 ± 103.0 (n = 178)	27.5 ± 70.2 (n = 966)	<.01

Data presented as mean ± standard deviation or n (%). ICU = intensive care unit.

TABLE 2. Lesion characteristics.

Characteristics	Black Patients (n = 235)	White Patients (n = 1244)	*P*-Value
Lesion location within the leg (summarized)	(n = 235)	(n = 1244)	.06
ATK only	66 (28.1%)	454 (36.5%)	.01
ATK and BTK	30 (12.8%)	164 (13.2%)	.92
BTK only	139 (59.1%)	624 (50.2%)	.01
Unknown	0 (0.0%)	2 (0.2%)	>.99
Lesion location within the leg	(n = 235)	(n = 1244)	.23
SFA only	13 (5.5%)	89 (7.2%)	.48
SFA to POP	25 (10.6%)	162 (13.0%)	.34
SFA to BTK	5 (2.1%)	40 (3.2%)	.53
POP only	28 (11.9%)	203 (16.3%)	.10
POP to BTK	25 (10.6%)	124 (10.0%)	.72
BTK only	139 (59.1%)	624 (50.2%)	.01
Unknown	0 (0.0%)	2 (0.2%)	>.99
Target lesion length (mm)	114.0 ± 106.9 (n = 211)	110.6 ± 106.0 (n = 1170)	.67
Target lesion length	(n = 211)	(n = 1170)	.73
<40 mm	61 (28.9%)	371 (31.7%)	.47
40–99 mm	62 (29.4%)	330 (28.2%)	.74
≥100 mm	88 (41.7%)	469 (40.1%)	.70
Distal RVD (mm)	3.1 ± 1.1 (n = 221)	3.4 ± 1.2 (n = 1196)	<.01
Preprocedural MLD (mm)	0.6 ± 0.8 (n = 228)	0.7 ± 0.8 (n = 1209)	.39
Preprocedural stenosis (%)	82.3 ± 20.0 (n = 228)	81.9 ± 19.5 (n = 1214)	.76
CTO of the lesion	93/228 (40.8%)	469/1214 (38.6%)	.55
TASC lesion type	(n = 222)	(n = 1200)	.62
A	117 (52.7%)	644 (53.7%)	.83
B	39 (17.6%)	220 (18.3%)	.85
C	40 (18.0%)	176 (14.7%)	.22
D	26 (11.7%)	160 (13.3%)	.59
Predominantly calcified plaque	116/212 (54.7%)	684/1161 (58.9%)	.26
PARC stenosis	(n = 228)	(n = 1214)	.86
Mild	18 (7.9%)	86 (7.1%)	.68
Moderate	44 (19.3%)	246 (20.3%)	.79
Severe	73 (32.0%)	413 (34.0%)	.59
Occluded	93 (40.8%)	469 (38.6%)	.55
Target-lesion access site	(n = 258)	(n = 1352)	.85
Femoral	247 (95.7%)	1267 (93.7%)	.25
Popliteal	1 (0.4%)	8 (0.6%)	>.99
Tibial	12 (4.7%)	85 (6.3%)	.39
Pedal	10 (3.9%)	55 (4.1%)	>.99
Brachial	0 (0.0%)	3 (0.2%)	>.99
Approach	(n = 258)	(n = 1352)	.12
Ipsilateral	50 (19.4%)	342 (25.3%)	.048
Contralateral	195 (75.6%)	937 (69.3%)	.04
Dual access	13 (5.0%)	73 (5.4%)	>.99
Access site position relative to lesion	(n = 258)	(n = 1352)	.75
Anterograde	232 (89.9%)	1193 (88.2%)	.52
Retrograde	13 (5.0%)	86 (6.4%)	.48
Dual access	13 (5.0%)	73 (5.4%)	>.99
Postprocedural MLD (mm)	2.2 ± 1.2 (n = 217)	2.6 ± 1.2 (n = 1177)	<.001
Acute MLD gain (%)	1.6 ± 1.0 (n = 216)	1.9 ± 1.2 (n = 1165)	<.001
Postprocedural stenosis (%)	35.1 ± 21.1 (n = 217)	31.7 ± 19.1 (n = 1180)	.02

Data presented as mean ± standard deviation or number (percentage).
ATK = above the knee; CTO = chronic total occlusion; SFA = superficial femoral artery; POP = popliteal artery; BTK = below the knee; RVD = reference vessel diameter; MLD = minimal lumen diameter; TASC = Trans-Atlantic Inter-Society Consensus Document; PARC = Consensus Definitions from the Peripheral Academic Research Consortium.

employed to estimate MAE rates through each time point; curves were compared with the log-rank test. Kaplan-Meier event rates were compared between groups using a Cox proportional hazards unadjusted model and the results are presented as the hazard ratio (HR) and 95% confidence interval (CI). All statistical analyses were performed by NAMSA. For all tests, *P*-values <.05 were considered statistically significant.

Results

Patients and lesion characteristics. A total of 1150 patients with PAD (178 in the Black group vs 972 in the White group), with 1479 treated lesions (235 lesions in the Black group vs 1244 lesions in the White group) were included. More than half of the patients were men, with a higher prevalence of men in the White group

TABLE 3. Procedure characteristics and target-lesion device use (subject level).

Characteristics	Black Patients (n = 178)	White Patients (n = 972)	*P*-Value
Procedure time (minutes)	80.1 ± 46.8 (n = 178)	77.4 ± 44.4 (n = 971)	.46
Fluoroscopy time (minutes)	25.4 ± 16.8 (n = 178)	25.3 ± 17.8 (n = 964)	.93
Contrast volume (mL)	173.4 ± 96.0 (n = 178)	166.3 ± 90.5 (n = 968)	.34
Inflow vessel disease (>50% stenosis)	73 (41.0%)	365 (37.6%)	.40
Inflow treatment performed in the target limb	(n = 119)	(n = 692)	.73
No	85 (71.4%)	505 (73.0%)	
Yes	34 (28.6%)	187 (27.0%)	
Target lesions treated per subject (core lab)	(n = 177)	(n = 968)	.55
1	130 (73.4%)	739 (76.3%)	
2	37 (20.9%)	188 (19.4%)	
≥3	10 (5.6%)	41 (4.2%)	
Devices used per subject including atherectomy, balloon, stent (n)	3.3 ± 2.0	3.3 ± 1.9	.86
Lesions treated with balloons	171/177 (96.6%)	950/968 (98.1%)	.25
Plain old balloon angioplasty	144/177 (81.4%)	819/968 (84.6%)	.27
Drug-coated balloon	14/177 (7.9%)	111/968 (11.5%)	.19
Cutting	25/177 (14.1%)	82/968 (8.5%)	.02
Focal Force	18/177 (10.2%)	148/968 (15.3%)	.08
Scoring	0/177 (0.0%)	13/968 (1.3%)	.24
Maximum nominal balloon diameter (mm)	3.7 ± 1.3 (n = 224)	4.1 ± 1.4 (n = 1187)	<.001
Maximum balloon length (mm)	126.5 ± 73.4 (n = 224)	127.2 ± 95.2 (n = 1187)	.91
Bail-out stenting	9/177 (5.1%)	47/968 (4.9%)	.85
Lesions treated with atherectomy	122/177 (68.9%)	725/968 (74.9%)	.11
Diamondback/Stealth	83/177 (46.9%)	490/968 (50.6%)	.37
Jetstream	3/177 (1.7%)	24/968 (2.5%)	.79
Laser	13/177 (7.3%)	68/968 (7.0%)	.87
Rotablator	4/177 (2.3%)	8/968 (0.8%)	.10
Turbohawk/Silverhawk/HawkOne	16/177 (9.0%)	133/968 (13.7%)	.09
Phoenix	4/177 (2.3%)	14/968 (1.4%)	.51
Bard Crosser	4/177 (2.3%)	15/968 (1.5%)	.52
Lesions treated with stent	31/177 (17.5%)	208/968 (21.5%)	.27
Drug-eluting stent	11/177 (6.2%)	63/968 (6.5%)	>.99
Bare-metal stent	20/177 (11.3%)	149/968 (15.4%)	.17
Covered	0/177 (0.0%)	10/968 (1.0%)	.38
Mean maximum stent diameter (mm)	5.1 ± 1.4 (n = 32)	5.5 ± 1.3 (n = 216)	.09
Maximum stent length (mm)	91.8 ± 47.8 (n = 32)	88.7 ± 45.9 (n = 216)	.73

Data presented as mean ± standard deviation or number (percentage).

TABLE 4. Periprocedural complications.

Characteristics	Black Patients	White Patients	*P*-Value
Procedural success (<50% residual stenosis, without significant angiographic complications)	132/163 (81.0%)	706/907 (77.8%)	.41
Lesion success (<50% residual stenosis, without significant angiographic complications)	184/218 (84.4%)	953/1188 (80.2%)	.20
Angiographic complications	16/235 (6.8%)	125/1231 (10.2%)	.28
Severe dissection (type C-F)	3/235 (1.3%)	34/1241 (2.7%)	.12
Perforation	2/235 (0.9%)	20/1241 (1.6%)	.28
Distal embolization	11/235 (4.7%)	64/1230 (5.2%)	.44
Abrupt closure	2/235 (0.9%)	18/1241 (1.5%)	.38

Data presented as number (percentage).

TABLE 5. Hazard ratios and 95% confidence intervals of outcomes during follow-up (Black patients vs White patients).

Outcomes	HR (95% CI)	*P*-Value
1 month		
Major adverse event	1.75 (0.79-3.85)	.17
Death	1.82 (0.36-9.09)	.47
Major amputation	1.37 (0.29-6.25)	.70
Target-vessel revascularization	1.67 (0.55-5.26)	.36
Major amputation/death	1.67 (0.55-5.26)	.37
6 months		
Major adverse event	1.23 (0.81-1.89)	.32
Death	1.45 (0.75-2.86)	.27
Major amputation	1.20 (0.46-3.13)	.71
Target-vessel revascularization	1.20 (0.75-1.92)	.43
Major amputation/death	1.45 (0.84-2.50)	.18
12 months		
Major adverse event	1.19 (0.85-1.67)	.30
Death	1.39 (0.80-2.38)	.24
Major amputation	2.00 (0.98-4.17)	.06
Target-vessel revascularization	1.12 (0.78-1.61)	.54
Major amputation/death	1.61 (1.03-2.50)	.04
36 months		
Major adverse event	1.00 (0.74-1.35)	.98
Death	1.30 (0.89-1.92)	.17
Major amputation	1.89 (0.98-3.57)	.06
Target-vessel revascularization	0.93 (0.68-1.30)	.69
Major amputation/death	1.45 (1.04-2.04)	.03

CI = confidence interval; HR = hazard ratio.

(Black 55.6% vs White 66.4%; *P*<.01). Renal disease (Black 43.8% vs White 32.9%; *P*<.01) and history for cerebrovascular accidents [ie, stroke/transient ischemic attack] were more commonly observed among Black patients (Black 20.8% vs White 14.2%; *P*=.03). In comparison, coronary artery disease was more prevalent among White patients (Black 48.9% vs White 63.2%; *P*<.001). More Black patients required hospitalization (Black 55.1% vs White 41.3%). Additionally, more Black patients presented with 1 run-off vessel at baseline, while White patients mainly presented with 2 run-off vessels. Detailed patient characteristics are presented in Table 1.

Mean target-lesion length was 114.0 ± 106.9 mm in the Black group vs 110.6 ± 106.0 mm in the White group (*P*=.67). Overall, most lesions were solely located at the infrapopliteal segment (Black 59.1% vs White 50.2%; *P*=.01), with isolated below-the-knee disease more prevalent among Black patients. More than half of all lesions treated were calcified (Black 54.7% vs White 58.9%; *P*=.26) and 39.0% were chronic total occlusions, with no significant difference between the 2 groups (Black 40.8% vs White 38.6%; *P*=.55). The average preprocedural minimal lumen diameter (MLD) was 0.6 ± 0.8 mm in the Black group and 0.7 ± 0.8 mm in the White group, with no statistically significant difference between the 2 groups (*P*=.39), corresponding to 82.3% ± 20.0% and 81.9% ± 19.5% mean preprocedural stenosis in Black patients and White patients, respectively. However, mean distal reference vessel diameter was significantly smaller in Black patients vs White patients (3.1 ± 1.1 mm vs 3.4 ± 1.2 mm, respectively; *P*<.01), reflecting the poorer run-off among Black patients. Detailed lesion characteristics are summarized in Table 2.

Procedure characteristics and short-term outcomes. Details regarding important procedural characteristics are provided in Table 3. For almost all patients, balloon angioplasty was the preferred treatment approach (Black 96.6% vs White 98.1%; *P*=.25), with bail-out stenting occurring in 9/177 Black patients (5.1%) and in 47/968 White patients (4.9%; *P*=.85). Interestingly, although preprocedural MLD was similar between the 2 groups, postprocedural MLD was statistically lower in the Black group (Black 2.2 ± 1.2 mm vs White 2.6 ± 1.2 mm; *P*<.001), corresponding

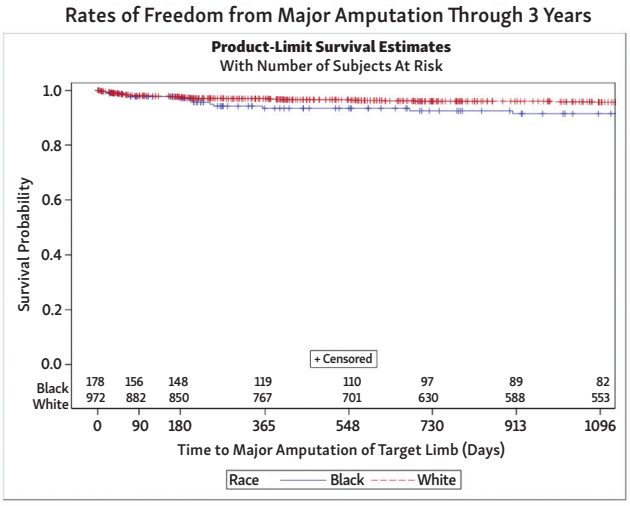

FIGURE 1. Rates of freedom from major amputation through 3 years.

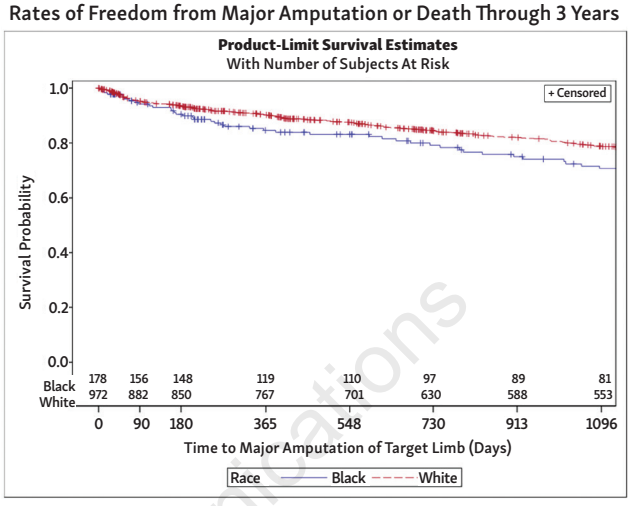

FIGURE 2. Rates of freedom from major amputation or death through 3 years.

with lower mean acute MLD gain (Black 1.6 ± 1.0 mm vs White 1.9 ± 1.2 mm; *P*<.001) and as such, higher mean postprocedural stenosis (Black 35.1 ± 21.1% vs White 31.7 ± 19.1%; *P*=.02). Overall, significant angiographic complications occurred in 9.6% of all lesions treated (16/235 Black patients [6.8%] vs 125/1231 White patients [10.2%]; *P*=.28). The observed frequencies of severe dissections (types C-F), vessel perforation, distal embolization, and abrupt closure were similar between the 2 groups. In total, target-lesion success occurred in 184/218 Black patients (84.4%) vs 953/1188 White patients (80.2%), with no statistically significant difference between the 2 groups (*P*=.20). Information regarding periprocedural complications is presented in Table 4 and Supplemental Table S2.

Follow-up outcomes. The 30-day ABI was improved compared with preprocedural values for each group, with White patients demonstrating a higher median ABI at 30-day follow-up. Median ABI value remained lower for Black patients vs White patients at 1 year post index procedure; however, both groups had similar ABI values at 2 years. The median RC at 30 days was similar in both groups. No statistically significant difference in median RC was detected between groups at 2 years. Details about categorical and continuous ABI and RC values during follow-up are presented in Supplemental Table S3.

Black patients had a higher risk than White patients for the combination of major amputation or death during the first 12 months of follow-up (HR, 1.61; 95% CI, 1.03-2.50; *P*=.04). The 12-month risk for all-cause mortality was similar between the 2 groups (HR, 1.39; 95% CI, 0.80-2.38; *P*=.24). A trend for higher risk of 12-month major amputation was observed among Black patients; however, no statistical significance was reached (HR, 2.00; 95% CI, 0.98-4.17; *P*=.06). At 36-month follow-up, Black patients were at higher risk for major amputation or death combined (HR, 1.45; 95% CI, 1.04-2.04; *P*=.03), which was likely driven by higher risk for major amputation (HR, 1.89; 95% CI, 0.98-3.57; *P*=.06) rather than the risk for all-cause mortality (HR, 1.30; 95% CI, 0.89-1.92; *P*=.17). The MAE, TVR, and mortality risk rates were similar between the 2 groups and did not change during 36 months of follow-up. The 36-month Kaplan-Meier estimates for freedom from major amputation and major amputation/death combined were 91.5% vs 95.6% and 70.7% vs 78.9% among Black and White patients, respectively. The corresponding Kaplan-Meier curves for freedom from major amputation and freedom from major amputation or death combined are illustrated in Figures 1 and 2, respectively. The HRs and Kaplan-Meier estimates of primary and secondary outcomes at several follow-up points are reported in Table 5 and Supplemental Table S4, respectively.

Wound-healing rates. At baseline, 243/972 White patients (25.0%) and 51/178 Black patients (28.7%) were seeing a wound-care specialist for wounds on the target limb, and more Black patients than White patients presented with wounds (79/178 Black patients [44.4%] vs 324/972 White patients [33.3%]; *P*<.01). The toes were the most common wound location (46/178 Black patients [25.8%] vs 176/972 White patients [18.1%]; *P*=.02) followed by the foot (26/178 Black patients [14.6%] vs 148/972 White patients [15.2%]; *P*=.91). The average wound area was 4.3 ± 14.1 cm^2 in Black patients vs 3.9 ± 19.9 cm^2 in White patients, with no statistical difference detected (*P*=.76). The mean number of wounds on the target limb was similar between the 2 groups as well (0.79 ± 1.16 in Black patients vs 0.64 ± 1.18 in White patients). At 6-month follow-up, 23 Black patients and 110 White patients were seeing a wound-care specialist for wounds on the target limb. Among the subjects with baseline wounds, 30/51 Black patients (58.8%) and 122/232 White patients (52.6%) had wound

healing at 6-month follow-up (*P*=.44), while 35/45 Black patients (77.8%) and 160/219 White patients (73.1%) experienced wound healing at 12-month follow-up, with no statistically significant difference detected between the 2 groups (*P*=.58).

Discussion

This study utilized data from the multicenter LIBERTY 360 trial[7,27] in order to investigate the association of race with limb and cardiovascular outcomes after endovascular procedures performed for PAD treatment. Our study is one of the few to investigate the impact of racial disparity on limb-related risk after endovascular therapy for PAD. Based on real-world data, separate analyses at several time intervals after the primary procedure demonstrated that Black patients were at statistically significantly higher risk for the combined outcome of major amputation or all-cause death, indicating that race might have played a role in the disease prognosis.

Nonetheless, the results of the current study should be interpreted carefully due to differences in baseline characteristics between the 2 groups. More Black patients were women and had renal disease. Although the role of sex characteristics in the outcomes of PAD interventions should be further investigated,[28,29] it has been observed that women often present at an older age and later stage of PAD (eg, critical limb ischemia [CLI])[30] than men, which places them at higher limb-related and cardiovascular risk.[31,32] Hereby, a previous retrospective analysis of Vascular Quality Initiative data demonstrated that women with PAD undergoing endovascular revascularization had higher rates of reocclusion and underwent reintervention more frequently than men over a median follow-up of approximately 1 year.[33] Additionally, chronic kidney disease has been accused of higher risk for loss of patency,[34,35] likely attributed to pathophysiological mechanisms that include (but are not limited to) chronic inflammation, hypoalbuminemia, and procalcific state.[36]

Moreover, isolated infrapopliteal disease was more prevalent among Black patients, while above-the-knee disease was more commonly observed in White patients. Isolated below-the-knee lesions, which are more commonly observed in elderly, diabetic, and end-stage renal disease patients, have been associated with an additional risk for limb loss due to poor initial run-off.[37,38] In our study, more Black patients than White patients had single run-off vessel, lower mean preprocedural MLD, and worse median ABI value at baseline, which indicated that Black patients presented for treatment of PAD at a later stage, and were thus at higher risk for adverse events. Interestingly, although preprocedural MLD values were similar between the 2 groups, postprocedural MLD was statistically lower among Black patients vs White patients, corresponding to lower mean acute MLD gain and thus higher mean postprocedural stenosis. Therefore, it could be hypothesized that racial differences in disease severity and/or physician decision making (eg, device preference, intensity of treatment, etc) might influence outcomes after revascularization procedures for PAD among Black and White patients.

Several traditional risk factors have been investigated for the prognosis of endovascular treatment in patients with PAD.[6,39-42] However, only a few studies have clearly addressed the role of race on outcomes of PAD patients, providing answers to the observed racial differences in prognosis. Similar to the present study, previous reports specifically investigating the outcomes of surgical and/or endovascular interventions among Black vs White patients with PAD have shown that Black patients are more likely to experience PAD progression and undergo subsequent amputation.[16,43,44] Rivero et al reported a worse 5-year limb-salvage rate in Black patients vs White patients, which was attributed to more severe disease and more complex anatomy among Black patients at baseline.[43] Additionally, a large analysis using data from the Nationwide Inpatient Sample studied whether there was a correlation between low socioeconomic status and race with the severity of PAD at presentation and the risk for amputation.[12] The study included 691,833 patients who presented with PAD at urban hospitals and demonstrated that amputations were more prevalent among non-White and low-income patients.[12] The authors attributed the observed findings to delayed or lack of access to healthcare among economically disadvantaged patients.[12]

However, a recent retrospective study by Loja et al, who used patient discharge data from California's Office of Statewide Health Planning and Development, demonstrated that Black patients undergoing endovascular therapy for PAD had worse short- and long-term outcomes following endovascular intervention even after adjusting for disease severity at baseline, age, sex, comorbidities, and insurance status.[16] Similarly, a large retrospective analysis of data from the national Veterans Affairs Corporate Data Warehouse, investigating the impact of race and socioeconomic status on amputation risk in PAD patients, demonstrated that Black patients were at 37% higher amputation risk over a median follow-up of 5.9 years.[45] Sensitivity analysis based on socioeconomic status showed that Black race remained a risk factor for amputation within the same socioeconomic status stratum.[45] Thus, the authors suggested that Black race could have an independent effect on limb-related outcomes, unrelated to comorbidities, severity of PAD at presentation, and contemporary medical therapy.[45]

Nonetheless, the hypothesis of biological characteristics over Social Determinants of Health (SDoH) has been heavily questioned.[19,46-48] In our study, which includes real-world data, a higher risk for major amputation or death was observed among Black vs White patients at 1-year and 3-year follow-up, likely driven by a higher amputation risk for Black patients. However, isolated infrapopliteal disease and renal disease requiring hemodialysis were more frequent among Black patients,

placing them at higher risk for major amputation. Additionally, the 6-month and 12-month wound-healing rates were similar between the 2 groups, making the hypothesis of racial differences in biological characteristics very unlikely. Thus, the association of race with major amputation demonstrated by the current study was likely attributable to population-related characteristics, SDoH, and/or physician decision making rather than by underlying biological mechanisms.

SDoH include all environmental/social conditions/factors that affect the overall health, functioning, quality of life outcomes/risks and can be summarized into 5 main domains, including economic stability, education access and quality, healthcare access and quality, neighborhood and built environment, and social and community context.[49] More specifically, several studies have provided significant evidence that the likelihood of amputation: (1) is "region-correlated" especially for Medicare beneficiaries;[48,50] (2) is more common among Medicaid patients with CLI presented at low-volume hospitals;[19] (3) depends on the diagnostic testing, especially the year prior to amputation, which is based on patient, physician, and region-related factors;[47] and (4) is influenced by social cognition, and is thus subject to subconscious bias.[46] Therefore, we believe that racial differences in disease severity, patient and/or physician decision making, socioeconomic status, access to appropriate healthcare, and regional clustering of vascular services constitute a major confounder for the observed difference in major amputation rates between Black and White patients. An individualized approach to patients with PAD, with a multivariate assessment of SDoH, could provide a more accurate prediction of outcomes for Black vs White patients. Additionally, telemedicine and virtual applications could help reach high-risk populations with/without difficult access to healthcare and provide better follow-up.

Study limitations. The LIBERTY 360 study was a multicenter, core-laboratory adjudicated study; however, the results of this subanalysis should be interpreted in the context of several limitations. First, this is a *posthoc* analysis of data retrieved from the LIBERTY 360 study, which was an observational, non-randomized study of endovascular therapies, sparing open surgery.[7] Second, site and patient participation bias might be resulted, while different preferred treatment algorithms among the physicians (eg, atherectomy, drug-eluting technology utilization, etc) might have affected the outcomes. Also, this study was sponsored by a company promoting atherectomy; as such, bias could be attributed to extensive use of orbital atherectomy. Last, it was not possible to adjust for population-related characteristics and account for the influence of several SDoH; as such, inference regarding causation remained uncertain. Future research is warranted in order to better evaluate the racial disparities among patients with PAD undergoing revascularization procedures.

Conclusion

Race was not associated with periprocedural complications, with no differences observed between the 2 groups in terms of procedural/technical success and angiographic complications. At 12-month and 36-month follow-up, Black patients were at higher risk for the combined outcomes of major amputation/death compared with White patients, which was likely driven by a strong trend for higher risk of major amputation among Black patients. Nonetheless, more Black patients were women, and had renal disease, isolated infrapopliteal disease, and poorer run-off at baseline, which likely placed them at higher limb-related risk. Additionally, the likelihood of amputation is strongly dependent upon several SDoH. Thus, we believe that racial differences in disease severity, patient and/or physician decision making, socioeconomic status, access to appropriate healthcare, and regional clustering of vascular services constituted a major confounder for the observed difference in major amputation rates between Black and White patients. Additional studies should further evaluate the interaction between race and PAD, and guide the development of specific treatment strategies based on SDoH for high-risk populations.

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Supplemental Tables

SUPPLEMENTAL TABLE S1. Information about sites and principal investigators.
1. Metro Health Hospital, Wyoming, MI (Jihad Mustapha, Larry Diaz)
2. Coastal Vascular and Interventional, Pensacola, FL (Huey McDaniel)
3. Mid-Michigan Heart and Vascular Center, P.C., Mt. Pleasant, MI (John McClure)
4. Rex Hospital, Raleigh, NC (George Adams)
5. St. Luke's Medical Center, Phoenix, AZ (Mansour Assar)
6. Gotham Cardiovascular Research, PC, New York, NY (Cezar Staniloae)
7. Mission Research Institute, New Braunfels, TX (Jason Yoho, Jamison Wyatt)
8. Arkansas Heart Hospital Clinic, Little Rock, AR (Ian Cawich)
9. El Paso Cardiology Associates, El Paso, TX (Mohammad Raja)
10. Mercy Gilbert Medical Center, Chandler, AZ (Georges Nseir)
11. First Coast Cardiovascular Institute, Jacksonville, FL (Issam Moussa, Vaqar Ali)
12. St. John Hospital and Medical Center, Detroit, MI (Thomas Davis)
13. Duke University Hospital, Lumberton, NC (Schuyler Jones)
14. Houston Methodist Sugar Land Hospital, Sugar Land, TX (Imran Mohiuddin)
15. KentuckyOne Health, Lexington, KY (Kiran Saraff)
16. Premier Surgical Associates, Knoxville, TN (George Pliagas)
17. San Antonio Endovascular & Heart Institute, San Antonio, TX (Stefan Kiesz)
18. Midwest Cardiovascular Research Foundation, Davenport, IA (Nicolas Shammas)
19. Riverside Methodist Hospital/Ohio Health, Columbus, OH (John Phillips)
20. Cardiovascular Associates of East Texas, Tyler, TX (Jeffrey Carr)
21. Memorial Hospital of Carbondale, Carbondale, IL (Raed Al-Dallow)
22. Colorado Heart and Vascular, Lakewood, CO (Sameer K Mehta, John Altman)[a]
23. University Surgical Associates, Chattanooga, TN (Mark Fugate, Christopher LeSar)
24. Columbia University Medical Center, New York, NY (William Gray, Philip Green)
25. VA Eastern Colorado Health Care System-Denver VAMC, Denver, CO (Ehrin Armstrong)

SUPPLEMENTAL TABLE S1. Information about sites and principal investigators.
26. Michigan Outpatient Vascular Institute, Dearborn, MI (Elias Kassab)
27. Cardiothoracic and Vascular Surgeons/CTVS, Austin, TX (Mazin Foteh)
28. Shady Grove Adventist Hospital, Rockville, MD (Jeffrey Wang)
29. Lester E. Cox Medical Centers, Springfield, MO (Robert Vorhies)
30. Baptist Memorial Hospital DeSoto, Southhaven, MS (Stevan Himmelstein, Gilbert Zoghbi)
31. Wellmont CVA Heart Institute, Kingsport, TN (Chris Metzger)
32. Clearwater Cardiovascular & Interventional Consultants, Clearwater, FL (Richard Sola, Saihari Sadanandan)
33. Baptist Cardiac and Vascular Institute, Miami, FL (Ripal Gandhi)
34. Providence Health Center, Waco, TX (M. Wayne Falcone, Adam Falcone)
35. The Heart Institute at Largo, Largo, FL (Jesse Klein)
36. Hartford Hospital, Hartford, CT (Immad Sadiq)
37. Yale-New Haven Hospital, New Haven, CT (Jeffrey Indes, Timur Sarac)
38. Saint Luke's Hospital, Kansas City, MO (Steven Laster)
39. Sanford Research, Sioux Falls, SD (Patrick Kelly)
40. Mount Sinai Medical Center Heart Institute Miami, Miami Beach, FL (Robert Beasley)
41. Radiology and Imaging Specialists of Lakeland, P.A., Lakeland, FL (Lawrence Whitney)
42. University of Texas Medical Branch at Galveston, Galveston, TX (Michael Silva)
43. Florida Hospital Tampa, Pepin Heart Institute, Tampa, FL (Asad Sawar)
44. Florida Hospital, Orlando, FL (Mark Ranson)
45. St. John's Hospital Springfield, Springfield, IL (Jeffrey Goldstein)
46. Metropolitan Heart Institute, Coon Rapids, MN (Daniel Dulas)
47. Houston Methodist Hospital Research Institute, Houston, TX (Alpesh Shah)
48. St. John Health System, Tulsa, OK (Thomachan Kalapura)
49. Chicago Vascular Clinic, Schaumburg, IL (Parag Doshi)
50. Phoenix Heart Cardiovascular Lab, Glendale, AZ (Rajul Patel)
51. Cedars-Sinai Heart Institute, Los Angeles, CA (Guy Mayeda)
[a]Follow-up visits for some subjects enrolled at this site performed at HealthONE Clinic Services – Cardiovascular, LLC, Denver, CO (Sameer K. Mehta).

SUPPLEMENTAL TABLE S2. Odds ratio of short-term outcomes and angiographic complications (Black patients vs White patients).

Outcomes	OR (95% CI)	*P*-Value
Per lesion		
Lesion success (<50% stenosis)	1.33 (0.90-1.96)	.15
Severe angiographic complications	0.65 (0.38-1.11)	.11
Per patient		
Procedural success (<50% stenosis)	1.18 (0.78-1.79)	.43
Severe angiographic complications	0.79 (0.45-1.37)	.40
Severe dissection (type C-F)	0.54 (0.16-1.79)	.31
Perforation	0.64 (0.15-2.78)	.55
Abrupt closure	0.64 (0.15-2.78)	.55
Distal embolization	1.30 (0.66-2.56)	.45

OR = odds ratio; CI = confidence interval.

SUPPLEMENTAL TABLE S3. Ankle-brachial index and Rutherford classification during follow-up.

	Black Patients	White Patients	*P*-Value
ABI at baseline	0.75 (0.55-0.97) (n = 143)	0.77 (0.60-1.00) (n = 845)	.08
Rutherford classification at baseline	4.0 (3.0-5.0) (n = 178)	4.0 (3.0-5.0) (n = 972)	.05
Patients with Rutherford class 4 / 5 / 6 at baseline (n)	33 / 56 / 21	245 / 238 / 78	.06 / .06 / .11
Categorical ABI (target limb) at baseline	(n = 161)	(n = 911)	.53
Abnormal ABI (≤0.90) at baseline	98 (60.9%)	547 (60.0%)	.86
Borderline ABI (>0.90 and <1.00) at baseline	17 (10.6%)	84 (9.2%)	.56
Normal ABI (≥1.00 and ≤1.40) at baseline	25 (15.5%)	180 (19.8%)	.23
Non-compressible (>1.40 or non-compressible) at baseline	21 (13.0%)	100 (11.0%)	.42
ABI at 30 days	0.90 (0.76-1.05) (n = 123)	0.99 [0.84, 1.10] (n = 776)	<.001
Rutherford classification at 30 days	3.0 (1.0-5.0) (n = 155)	2.0 [0.0, 5.0] (n = 876)	.14
Patients with Rutherford class 4 / 5 / 6 at 30 days (n)	13 / 34 / 16	68 / 165 / 56	.75 / .38 / .09
Categorical ABI (target limb) at 30 days	(n = 140)	(n = 828)	.03
Abnormal ABI (≤0.90) at 30 days	63 (45.0%)	275 (33.2%)	<.01
Borderline ABI (>0.90 and <1.00) at 30 days	18 (12.9%)	121 (14.6%)	.70
Normal ABI (≥1.00 and ≤1.40) at 30 days	42 (30.0%)	339 (40.9%)	.02
Non-compressible (>1.40 or non-compressible) at 30 days	17 (12.1%)	93 (11.2%)	.77
ABI at 1 year	0.88 (0.71-1.08) (n = 85)	0.95 (0.77-1.09) (n = 587)	.04
Rutherford classification at 1 year	1.0 (0.0-3.0) (n = 107)	1.0 (0.0-3.0) (n = 666)	.95
Patients with Rutherford class 4 / 5 / 6 at 1 year (n)	6 / 15 / 3	45 / 56 / 16	.83 / .07 / .74
Categorical ABI (target limb) at 1 year	(n = 98)	(n = 637)	.17
Abnormal ABI (≤0.90) at 1 year	45 (45.9%)	250 (39.2%)	.22
Borderline ABI (>0.90 and <1.00) at 1 year	8 (8.2%)	94 (14.8%)	.08
Normal ABI (≥1.00 and ≤1.40) at 1 year	29 (29.6%)	213 (33.4%)	.49
Non-compressible (>1.40 or non-compressible) at 1 year	16 (16.3%)	80 (12.6%)	.33
ABI at 2 years	0.96 (0.68-1.06) (n = 66)	0.96 (0.81-1.09) (n = 466)	.19
Rutherford classification at 2 years	1.0 (0.0-3.5) (n = 84)	1.0 (0.0-2.0) (n = 539)	.34
Patients with Rutherford class 4 / 5 / 6 at 2 years (n)	5 / 13 / 3	24 / 32 / 16	.58 / <.01 / .73
Categorical ABI (target limb) at 2 years	(n = 76)	(n = 502)	.47
Abnormal ABI (≤0.90) at 2 years	28 (36.8%)	181 (36.1%)	.90
Borderline ABI (>0.90 and <1.00) at 2 years	13 (17.1%)	83 (16.5%)	.87
Normal ABI (≥1.00 and ≤1.40) at 2 years	22 (28.9%)	179 (35.7%)	.30
Non-compressible (>1.40 or non-compressible) at 2 years	13 (17.1%)	59 (11.8%)	.19

Data presented as median (interquartile range), number (percentage), or count.

SUPPLEMENTAL TABLE S4. Kaplan-Meier estimates for late outcomes.

Outcomes	Black Patients	White Patients	Log-Rank *P*-Value
Freedom from major amputation or death			
12 months	84.6% (79.0%-90.2%)	90.3% (88.4%-92.2%)	.04
24 months	79.1% (72.6%-85.7%)	84.4% (82.0%-86.8%)	.09
36 months	70.7% (63.0%-78.3%)	78.9% (76.0%-81.7%)	.03
Freedom from all-cause death			
12 months	90.1% (85.5%-94.7%)	92.7% (91.0%-94.4%)	.24
24 months	85.5% (79.8%-91.2%)	87.5% (85.2%-89.7%)	.44
36 months	77.0% (69.9%-84.1%)	82.0% (79.3%-84.7%)	.17
Freedom from major amputation			
12 months	93.4% (89.5%-97.4%)	96.9% (95.8%-98.0%)	.05
24 months	92.5% (88.2%-96.8%)	96.0% (94.7%-97.3%)	.08
36 months	91.5% (86.8%-96.2%)	95.6% (94.2%-97.0%)	.05
Freedom from MAE			
12 months	73.4% (66.5%-80.4%)	76.6% (73.8%-79.4%)	.30
24 months	67.6% (60.0%-75.3%)	68.7% (65.5%-71.8%)	.54
36 months	67.6% (60.0%-75.3%)	64.4% (61.0%-67.7%)	.98
Freedom from TVR/TLR			
12 months	77.3% (70.6%-84.0%)	78.9% (76.1%-81.6%)	.54
24 months	71.4% (63.9%-78.9%)	71.1% (68.0%-74.3%)	.81
36 months	71.4% (63.9%-78.9%)	66.6% (63.2%-70.0%)	.69

MAE = major adverse event; TVR = target-vessel revascularization; TLR = target-lesion revascularization.