Does Sex Matter? Thirty-Day Stroke and Death Rates After Carotid Artery Stenting in Women Versus Men

Results From the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST) Lead-in Phase

Virginia J. Howard, PhD; Jenifer H. Voeks, PhD; Helmi L. Lutsep, MD; Ariane Mackey, MD, FRCPC; Genevieve Milot, MD, FRSC(C); Albert D. Sam II, MD; MeeLee Tom, MS; Susan E. Hughes, BSN; Alice J. Sheffet, PhD; Mary Longbottom, BA; Jason B. Avery, MPH; Robert W. Hobson II, MD†; Thomas G. Brott, MD

Background and Purpose—Several carotid endarterectomy randomized, controlled trials and series have reported higher perioperative stroke and death rates for women compared with men. The potential for this same relationship with carotid artery stenting was examined in the lead-in phase of the Carotid Revascularization Endarterectomy versus Stenting Trial (CREST).

Methods—CREST compares efficacy of carotid endarterectomy and carotid artery stenting in preventing stroke, myocardial infarction, and death in the periprocedural period and ipsilateral stroke over the follow-up period. CREST included a “lead-in” phase of symptomatic (≥50% stenosis) and asymptomatic (≥70% stenosis) patients. Patients were examined by a neurologist preprocedure, at 24 hours, and at 30 days. Review of stroke and death was by an independent events committee. The association of sex with periprocedural stroke and death was examined in 1564 patients undergoing carotid artery stenting (26.5% symptomatic).

Results—Women comprised 37% of the lead-in cohort and did not differ from men by age, symptomatic status, or characteristics of the internal carotid artery. The 30-day stroke and death rate for women was 4.5% (26 of 579; 95% CI, 3.0% to 6.5%) compared with 4.2% (41 of 985; 95% CI, 3.0% to 5.6%) for men. The difference in stroke and death rate was not significant nor were there any significant differences by sex after adjustment for age, arterial characteristics, or cardiovascular risk factors.

Conclusions—These results do not provide evidence that women have a higher carotid artery stenting stroke and death rate compared with men. The potential differential periprocedural risk by sex will be prospectively addressed in the randomized phase of CREST. (Stroke. 2009;40:00-00.)

Key Words: carotid artery stenting ■ carotid stenosis ■ complications ■ gender differences ■ sex ■ women

Sex has been identified as a factor potentially affecting perioperative stroke and death rates associated with carotid endarterectomy (CEA), the gold standard treatment for severe symptomatic extracranial carotid occlusive disease1 and recommended in highly selected asymptomatic patients.2 The Asymptomatic Carotid Atherosclerosis Study (ACAS) was the first clinical trial of CEA to suggest this increased risk, although the difference between men and women was not statistically significant; the perioperative stroke and death rate for women was 3.6% (10 of 281) compared with 1.7% (9 of 544) in men (P=0.12).3,4 This has been confirmed in the Asymptomatic Carotid Surgery Trial (ACST)5 as well as retrospective asymptomatic series.6–8 Of symptomatic trials, the European Carotid Surgery Trial (ECST) found a significantly increased periprocedural risk for women compared with men (11.1% versus 6.4%, P=0.002) who underwent CEA.9 Why women should be at greater operative risk than men remains speculative. Rothwell et al suggested it may be because women, on average, have 40% smaller internal carotid arteries than men, thus making...
CEA technically more difficult. The type of closure used in the procedure may also put women more at risk, because primary closure of the arteriotomy (versus patch angioplasty) is more prone to technical error.

The carotid artery stent procedure (CAS) has recently become another option for the management of carotid atherosclerosis, especially for persons who are considered at high surgical risk. Case series and clinical trials are beginning to be published, but few reports have described results by sex.

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) is a National Institutes of Health-funded randomized clinical trial designed to contrast the relative efficacy of CAS versus CEA in preventing stroke, myocardial infarction, and death during a 30-day periprocedural period and stroke ipsilateral to the study artery over the follow-up period in patients with symptomatic and asymptomatic extracranial carotid stenosis. A lead-in phase was built into CREST. This provided a startup and credentialing period during which each eligible interventionalist applying to participate in the clinical trial phase would perform up to 20 CAS procedures and submit data to the CREST Interventional Management Committee for review and approval to move to the randomized phase. This report describes the 30-day complication rate in women compared with men in the lead-in phase.

Methods

The lead-in phase of CREST was active from December 2000 to February 2008. During this period, 1564 participants from 97 clinical sites were enrolled. The protocol was approved by the Institutional Review Boards at all patient enrolling sites and all participants provided signed informed consent.

For approval to participate in the lead-in, each site had to have at least one CREST-approved interventionalist and neurologist. The interventionalists were required to submit data from their last 10 to 30 CAS procedures performed with any device. These data were reviewed by the CREST Interventional Management Committee. After initial approval, interventionalists who had no experience with the study devices were required to participate in a CREST-specific Carotid Stent Operator Certification Program. Further details on this approval process are described elsewhere. Approval for the lead-in study end points were stroke, death, or myocardial infarction (MI) during the periprocedural period (30 days after the index procedure) or any stroke ipsilateral to the study artery up to 1 year after the procedure. This report focuses on 30-day strokes and deaths to be comparable to the multicenter CEA trials that did not include MI as an end point. An independent clinical events committee reviewed all deaths and potential strokes and MIs.

The association between sex and the combined periprocedural complications of stroke and death within 30 days of CAS was assessed by univariate logistic methods. Then incremental multivariable methods were applied first adjusting for demographic factors (age and race), then adjusting for characteristics of the study artery (reference diameter and symptomatic status), and further adjusting for major modifiable cardiovascular risk factors (hypertension, dyslipidemia, diabetes, and current cigarette smoking). In each model, 2-way interactions between the potential covariates and sex were assessed to evaluate any potential differential impact of the confounding factor (ie, effect modification).

Results

The study population was 579 (37%) women and 985 men. Women did not differ from men by age, symptomatic status, risk factors, or reference diameter of the internal carotid artery (Table 3). The only difference in risk factors between women and men was in current smoking status; women were more likely to be current smokers (20.9% versus 16.7%, P=0.038).

Table 4 shows the 30-day postprocedural complications of stroke and death by sex and symptomatic status. The overall 30-day stroke and death rate was 4.3% (67 of 1564), 5.8% (24 of 414) in symptomatic patients versus
### Table 2. Inclusion and Exclusion Criteria for Participant Selection

**Inclusion criteria**

1. Patient age ≥18 and ≤79 years old (upper age limit was added March 2004)
2. Symptomatic patient as evidenced by transient ischemic attack (TIA), amaurosis fugax, minor or nondisabling stroke (in the hemisphere supplied by the target vessel) within 180 days of the treatment date or asymptomatic patients meeting angiographic criteria (≥70% stenosis)
3. Patient has no childbearing potential or has a negative pregnancy test within 1 week before the study procedure
4. Patient and the patient’s physician agree to have the patient return for all required clinical contacts after study enrollment
5. Patient has been informed of the nature of the study and has provided written informed consent
6. Patient has a discrete lesion located in the internal carotid artery (ICA; with or without involvement of the contiguous common carotid artery [CCA])
7. Carotid stenosis ≥50% defined by angiography in symptomatic patients or ≥70% in asymptomatic patients (based on NASCET criteria)
8. Target ICA vessel reference diameter must be measured to be ≥4.0 mm and ≤9.0 mm; target ICA may be reasonably estimated by angiography of the contralateral artery
9. Expected ability to deliver the stent to the lesion (absence of excessive tortuosity)

**Exclusion criteria**

1. Patient has an evolving stroke
2. Patient has history of intolerance or allergic reaction to any of the study medications, including aspirin (ASA), ticlopidine, and clopidogrel (patients must be able to tolerate a combination of ASA and ticlopidine OR ASA and clopidogrel)
3. Patient has active bleeding diathesis or coagulopathy or will refuse blood transfusions
4. Patient with a history of major ipsilateral stroke likely to confound study end points
5. Patient has severe dementia
6. Patient has a history of spontaneous intracranial hemorrhage within the past 12 months
7. Patient has had a recent (<7 days) stroke of sufficient size (on CT or MR) to place him or her at risk of hemorrhagic conversion during the procedure
8. Patient had hemorrhagic transformation of an ischemic stroke within the past 60 days
9. Patient has hemoglobin <10 g/dL, platelet count <125 000/μL, uncorrected international normalized ratio >1.5, bleeding time >1 minute beyond upper limit normal, or heparin-associated thrombocytopenia
10. Patient has any condition that precludes proper angiographic assessment or makes percutaneous arterial access unsafe. (eg, morbid obesity, sustained systolic blood pressure >180 mm Hg)
11. Patient has had neurologic illnesses within the past 2 years characterized by fleeting or fixed neurologic deficit, which cannot be distinguished from TIA or stroke (eg, partial or secondarily generalized seizures; complicated or classic migraine; tumor or other space-occupying brain lesions; subdural hematoma, cerebral contusion or other posttraumatic lesions; intracranial infection; demyelinating disease; moderate to severe dementia; or intracranial hemorrhage)
12. If a patient has vertebrobasilar insufficiency symptoms only, without clearly identifiable symptoms referable to the study carotid artery, he or she will be considered an asymptomatic patient for the lead-in phase of the study
13. Knowledge of cardiac sources of emboli (eg, left ventricular aneurysm, intracardiac filling defect, cardiomyopathy, aortic or mitral prosthetic heart valve, calcific aortic stenosis, endocarditis, mitral stenosis, atrial septal defect, atrial septal aneurysm, or left atrial myxoma)
14. Chronic atrial fibrillation known by history or present on entry examination
15. Any episode of paroxysmal atrial fibrillation within the past 6 months or history of paroxysmal atrial fibrillation requiring chronic anticoagulation
16. Patient has had a MI within previous 30 days
17. Patient has had a recent gastrointestinal bleed that would interfere with antplatelet therapy
18. Severe vascular tortuosity or anatomy that would preclude the safe introduction of a guiding catheter, guiding sheath, or stent placement
19. Presence of a previously placed intravascular stent or graft in the ipsilateral distribution
20. Presence of extensive or diffuse atherosclerotic disease involving the aortic arch and proximal common carotid artery that would preclude the safe introduction of a guiding catheter or guiding sheath
21. An intraluminal filling defect (defined as an endoluminal lucency surrounded by contrast, seen in multiple angiographic projections, in the absence of angiographic evidence of calcification) that is not associated with an ulcerated target lesion
22. Ipsilateral intracranial or extracranial arterial stenosis greater in severity than the lesion to be treated, cerebral aneurysms ≥5 mm, (arteriovenous malformation of the cerebral vasculature, or other abnormal angiographic findings that constitute contraindication to CAS
23. Bilateral carotid stenosis if intervention is planned within the 30-day perioperative period
24. Occlusion (Thrombolysis In Myocardial Infarction Trial [TIMI 0]) “string sign” >1 cm of the ipsilateral common or ICA
25. Well-delineated carotid artery dissection below the carotid siphon
26. Ostial lesion of LCCA/RCCA

NASCET indicates North American Symptomatic Carotid Endarterectomy Trial; LCCA/RCCA, left CCA/right CCA.
In univariate analysis, women had only a marginally higher risk of stroke or death (OR, 1.08; 95% CI, 0.66 to 1.79). The potential that the impact of sex could be affected (ie, confounded) by sex differences in demographic factors (age or race), characteristics of the artery (reference diameter, lesion length, percent stenosis, or symptomatic status), or stroke risk factors (hypertension, diabetes, dyslipidemia, or cigarette smoking) was assessed in a series of incremental logistic regression models (also Table 5). Caution should be applied in interpretation of specific ORs because the number of events (n=67) compared with the number of parameters in the models (3, 7, and 11, respectively) may result in unstable estimates. However, the strength of this approach is to provide estimates of the effect of sex in the presence of all potential confounding factors. Only age would be retained in any of these models had backward stepwise selection methodology been used with a P<0.05 criteria for retention. With these cautions, adjustment for age and race slightly mediated this effect (OR, 1.05; 95% CI, 0.63 to 1.76), and in this model, there was a clearly higher risk of events with increasing age (OR10-year increment, 2.31; 95% CI, 1.65 to 3.25) but little evidence of a race difference (OR, 1.07; 95% CI, 0.38 to 3.05). Tests of interaction between sex and the other covariates documented an age-by-sex interaction that was of marginal significance (P=0.081). However, considering age as 2 separate strata (≤70 and >70), after adjustment for race, sex was not significant in either strata (OR≤70 and >70, 1.93; 95% CI, 0.42 to 8.88; OR>70, 0.76; 95% CI, 0.18 to 3.23). This finding suggests that the procedure may be associated with higher risk in younger women compared with younger men but may
be associated with lower risk among older women compared with older men. This observation, however, failed to reach traditional levels of statistical significance. Further adjustment for characteristics of the artery (reference diameter and symptomatic status) reversed the direction of the effect for sex (OR, 0.97; 95% CI, 0.56 to 1.67) and only age remained a significant predictor. Further adjustment for cardiovascular risk factors (hypertension, diabetes, dyslipidemia, and cigarette smoking) had little effect on the impact of sex.

### Discussion

In this report from a large series, 30-day stroke and death rates associated with CAS were similar among 579 women and 985 men. There was also no evidence of a differential sex effect for other outcomes, including death alone, stroke alone, MI alone, or the composite outcome of stroke–MI–death. The lack of a sex difference on any of these outcomes was also observed by symptomatic strata (ie, no apparent sex difference for either symptomatic or asymptomatic patients).

Adjustment for potential confounding factors had very little impact on the estimated sex difference in the risk of perioperative events. With the exception of one marginally significant interaction (age×sex: \( P=0.081 \)), there was no evidence of a differential impact of sex across the range of the confounding factors. In the case of this one marginally significant interaction, there was a nonsignificant trend for young women to have a poorer outcome than young men and for older women to have better outcome than older men; however, this finding should be interpreted with caution with its marginally significant probability value and the lack of any adjustment for multiple testing.

In summary, sex has little impact on the risk of events despite looking at multiple outcomes, looking within symptomatic strata, and looking for potential confounding and effect modification effects. As such, unlike CEA clinical trial data that seem to suggest a higher perioperative event rate in women, these registry data provide little evidence of a difference for CAS.

It is possible that a difference does exist but that the CREST lead-in series has an insufficient number of events to detect this true effect. This concern is introduced by the very low event rates observed in this series, specifically 6.7% in women (n=985) and men (n=579), and assuming that the true event rate in men was the 4.2% that was observed, then the true event rate in women would have to be 7.6% (1.81 relative risk) to provide 80% power to detect the difference. In addition, the observed differences are quite small in the estimated stroke and death rate—4.2% versus 5.2% (relative risk, 1.24) or only 43% power to detect a difference of 4.2% versus 6.2% (relative risk, 1.48). Although it is possible that such a large difference would exist, it seems somewhat unlikely. The power to detect smaller effects is marginal. For example, there is only 16% power to detect a difference of 4.2% versus 5.2% (relative risk, 1.24) or only 43% power to detect a difference of 4.2% versus 6.2% (relative risk, 1.48).
Table 6. 30-Day Stroke and Death Rates From CEA Arm of Major CEA Clinical Trials by Sex and Symptomatic Status

<table>
<thead>
<tr>
<th></th>
<th>Women</th>
<th>Men</th>
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</thead>
<tbody>
<tr>
<td>Symptomatic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECST</td>
<td>11.1% (49/440)</td>
<td>6.4% (70/1095)</td>
</tr>
<tr>
<td>NASCET + Aspirin</td>
<td>7.6% (57/753)</td>
<td>5.9% (107/1810)</td>
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<tr>
<td>and Carotid</td>
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<tr>
<td>Endarterectomy</td>
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<tr>
<td>Trial14</td>
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<tr>
<td>Asymptomatic</td>
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<td></td>
</tr>
<tr>
<td>ACAS14</td>
<td>3.6% (10/281)</td>
<td>1.7% (9/544)</td>
</tr>
<tr>
<td>ACST</td>
<td>3.6% (17/469)</td>
<td>2.5% (23/936)</td>
</tr>
</tbody>
</table>

reasonable statistical power. It remains a matter of speculation whether such a large effect may exist for sex.

For both women and men and similar to CEA, procedural risk with CAS was higher for symptomatic than for asymptomatic patients. Table 6 shows the 30-day stroke and death rates in the CEA arm of the major multicenter CEA trials. Only the ECST found a significantly increased periprocedural risk for women compared with men (11.1% versus 6.4%, P = 0.002). In a secondary analysis, the ECST investigators examined the effect of height, weight, body surface area, and body mass index on the 30-day operative risk of stroke and death in women versus men. Comparing clinical characteristics between the sexes, there were no differences in degree of stenosis or use of carotid patching, but women had significantly higher height, weight, and body surface area and were older.9 As Bond et al point out, most reports of 30-day events in the CEA literature do not provide data stratified by symptomatic status and sex.8

The randomized endarterectomy trials were not powered to test for interaction by sex and except for ACST, subgroup analyses by sex were post hoc and not prespecified, not following the principles for subgroup analyses as set forth by Yusuf et al.15 Women were severely underrepresented in the completed carotid artery stenting versus endarterectomy trials16–20 and it remains to be seen if sufficient enrollment of women will play out in the ongoing trials.21–26 Of the major multicenter trials of CEA versus CAS that have been completed, only the Stent-Protected Angioplasty versus Carotid Endarterectomy in Symptomatic Patients trial has reported 30-day stroke and death rates by sex: 8.2% (14 of 171) in women versus 6.4% (28 of 426) in men (P = 0.478), a slightly higher rate in women but not statistically different.16 The other trials all had less than 100 women: 55 (33%) in the Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy,17 77 (32%) in the Carotid and Vertebral Transluminal Angioplasty Study,18 72 (28%) in the Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis,19 and only 36 women (34%) in the first WALLSTENT (Boston Scientific Corp) trial.20 Given the results of the major randomized clinical trials of endarterectomy, and the burden of disease in women, a priori plans to evaluate the possibility of a differential sex effect are incumbent in trials of the management of carotid atherosclerosis. Enrollment in the clinical trial phase of CREST is complete and 884 (35%) of the 2522 participants are women. The design of CREST included targeted enrollment strategies for women and a test for interaction in the primary end point analyses.

There are some important limitations of this work. Like with all registries, because these are not consecutive patients at all participating sites, these may not be representative of all patients undergoing CAS treated at these sites, and some higher- or lower-risk patients may have been excluded. Additionally, because cerebral angiography was part of the eligibility workup, potential participants who had a major complication associated with the angiogram would not have continued with enrollment so the event rates reported here are for participants who actually had the stent procedure and strictly angiographic complications were not considered (as they were, for example, in ACAS). The randomized phase of CREST collected more data regarding clinical and angiographic risk factors than the lead-in phase, enabling secondary analyses within the randomized, controlled trial to examine other potential predictors of 30-day stroke, death, and MI. A strength of this series is that it includes 97 clinical sites from across North America, representing not only high-volume academic centers, but community medical centers. Approved interventionalists were comprised of multiple specialists, reflecting the respective representative patterns of carotid revascularization regionally.

In conclusion, our results do not provide evidence that women have a higher CAS stroke and death rate compared with men. Following the principles of subgroup analyses in randomized clinical trials, the potential for a differential periprocedural risk by sex will be examined further in the randomized phase of CREST.

Appendix

The participating centers for the Lead-in Phase of CREST, in order of the number of eligible patients entered, were as follows (with the number of patients entered for each center in parentheses):

St. Michael’s Medical Center, Newark, NJ (53); Deaconess Medical Center, Spokane, Wash (51); University of Pittsburgh Medical Center/Shadyside Hospital, Pittsburgh, Pa (40); New York Presbyterian/Weill Cornell Medical Center, New York, NY (38); William Beaumont Hospital, Bingham Farms, Mich (37); St Francis Hospital, Roslyn, NY (37); Emory University, Atlanta, Ga (33); Ochsner Foundation Hospital New Orleans, La (31); University of Toledo Medical Center, Toledo, Ohio (31); Massachusetts General Hospital, Boston, Mass (30); Miami Cardiovascular Institute, Miami, Fla (30); Mayo Clinic, Jacksonville, Fla (30); Carolinas Medical Center/Sanger Clinic, Charlotte, NC (29); University of Pennsylvania, Philadelphia, Pa (29); Oregon Health Science University, Portland, Ore (27); Northwestern Memorial Hospital, Chicago, Ill (26); Iowa Heart Center, Des Moines, Iowa (26); Washington Adventist Hospital, Takoma Park, Md (26); Southern Illinois School of Medicine, Springfield, Ill (26); Vascular Interventional Project, Inc, Albany, NY (25); Cleveland Clinic Foundation, Cleveland, Ohio (24); Prairie Cardiology, Springfield, Ill (23); University of Rochester, Rochester, NY (23); Parkview Hospital, Ft Wayne, Ind (23); Mayo Clinic, Rochester, Minn (22); Rush University Medical Center, Chicago, Ill (22); Kaiser Permanente Medical Center, San Diego, Calif (21); Beth Israel Deaconess Medical Center, Boston, Mass (20); Hahnemann University Hospital, Philadelphia, Pa (20); St Luke’s Hospital, Kansas City, Mo (20); Methodist Hospital, Houston, Texas (20); Orlando Regional Healthcare, Orlando, Fla (20); Alexian Brothers Medical Center, Elgin, Ill (20); Swedish Heart Institute, Seattle, Wash (20); Providence Medical Research
Center, Spokane, Wash (20); University of South Florida, Tampa, Fla (20); Barrow Neurological Institute, Phoenix, Ariz (20); Hoag Memorial Hospital, Newport Beach, Calif (19); St Joseph’s Medical Center, Stockton, Calif (19); Vancouver General Hospital, Vancouver BC, Canada (18); St Elizabeth’s Hospital, Boston, Mass (16); Butterworth Hospital, Grand Rapids, Mich (16); New York University School of Medicine, New York, NY (15); Cape Cod Hospital, Hyannis, Mass (15); University of Alabama at Birmingham, Birmingham, Ala (15); Marshfield Clinic, Marshfield, Wis (15); St Joseph’s Hospital of Atlanta, Atlanta, Ga (14); University of Texas, Houston, Texas (14); Millard Fillmore Hospital/SUNY Buffalo, Buffalo, NY (14); Westchester Medical Center, Valhalla, NY (14); Geisinger Medical Center, Danville, Pa (14); University of Southern California, Los Angeles, Calif (13); Central Baptist Hospital, Lexington, Ky (13); University of California, Los Angeles, Calif (13); North Memorial Health Care, Golden Valley, Minn (13); Rhode Island Hospital, Providence, RI (13); University of Pittsburgh Medical Center/Presbyterian University Hospital, Pittsburgh, Pa (13); St Joseph’s Medical Center, Kansas City, Mo (13); Duke University Medical Center, Durham, NC (12); University of Calgary/Foothills Medical Center, Calgary, Alberta, Canada (12); Thomas Jefferson University Hospital, Philadelphia, Pa (12); Christiana Care Health System, Newark, Del (11); Piedmont Hospital/Fuqua Heart Center, Atlanta, Ga (11); University of Arizona, Tucson, Ariz (11); Peoria Radiology, Peoria, Ill (10); Lutheran Hospital of Indiana, Ft Wayne, Ind (9); Dartmouth Hitchcock Medical Center, Lebanon, NH (9); MidWest Cardio Surgery/Grand Rapids Hospital, Columbus, OH (9); New York Presbyterian/Columbia University Medical Center, New York, NY (8); University of Michigan, Ann Arbor, Mich (8); Loyola University Medical Center, Maywood, Il (8); Rogue Valley Medical Center, Medford, Ore (8); Wake Forest University Health Sciences, Winston Salem, NC (7); London Health Science Centre, London, Ontario, Canada (7); Charleston Area Medical Center, Charleston, W Va (6); University of Cincinnati, Cincinnati, Ohio (6); Hôpital de l’Enfant-Jésus, Quebec City, Quebec, Canada (6); Tri-State Medical Center, Beaver, Pa (6); Ottawa Hospital, Ottawa, Ontario, Canada (6); St John Hospital and Medical Center, Detroit, Mich (5); Lenox Hill Hospital, New York, NY (5); St Patrick’s Hospital, Missoula, Mont (5); Vascular Surgery Associates, Baton Rouge, La (5); Brigham & Women’s Hospital, Boston, Mass (4); Baptist Memorial Hospital of Tennessee, Memphis, Tenn (4); Toronto Western Hospital, Toronto, Ontario, Canada (4); University of Maryland, Baltimore, Md (4); Intermountain Medical Center (formerly LDS Hospital); Salt Lake City, Utah (3); Michigan Vascular Research Center, Flint, Mich (3); University of Manitoba, Winnipeg, Manitoba, Canada (3); Central Dupage Hospital, Winfield, Ill (3); South Carolina Heart Center, Columbia, SC (4); Triulum Health Centre, Mississauga, Ontario, Canada (2); Anne Arundel Medical Center, Annapolis, Md (2); Allegheny General Hospital, Pittsburgh, Pa (1); University of North Carolina, Chapel Hill, NC (4); and University of Alberta, Edmonton, Alberta, Canada (1).

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Disclosures

References


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