Effect of Cerebral Embolic Protection Devices on CNS Infarction in Surgical Aortic Valve Replacement A Randomized Clinical Trial

Michael J. Mack, Baylor Scott & White Health
Michael A. Acker, University of Pennsylvania
Annetine C. Gelijns, Icahn School of Medicine at Mount Sinai
Jessica R. Overbey, Icahn School of Medicine at Mount Sinai
Michael K. Parides, Icahn School of Medicine at Mount Sinai
Jeffrey N. Browndyke, Duke University
Mark Groh, Mission Health and Hospital
Alan J. Moskowitz, Icahn School of Medicine at Mount Sinai
Neal O. Jeffries, National Heart, Lung, and Blood Institute
Gorav Ailawadi, University of Virginia

Only first 10 authors above; see publication for full author list.

Journal Title: Journal of the American Medical Association
Volume: Volume 318, Number 6
Publisher: American Medical Association (AMA): JAMA | 2017-08-08, Pages 536-547
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1001/jama.2017.9479
Permanent URL: https://pid.emory.edu/ark:/25593/s8dzf

Final published version: http://dx.doi.org/10.1001/jama.2017.9479

Copyright information:
© 2017 American Medical Association. All rights reserved.

Accessed April 14, 2019 4:26 PM EDT
Effect of Cerebral Embolic Protection Devices on CNS Infarction in Surgical Aortic Valve Replacement
A Randomized Clinical Trial

Michael J. Mack, MD; Michael A. Acker, MD; Annetine C. Gelijns, PhD; Jessica R. Overbey, MS; Michael K. Parides, PhD; Jeffrey N. Browndyke, PhD; Mark A. Groh, MD; Alan J. Moskowitz, MD; Neal O. Jeffries, PhD; Gorav Ailawadi, MD; Vinod H. Thourani, MD; Ellen G. Moquete, RN; Alexander Ibanez, MD; Pierre Voisine, MD; Michel Bilello, MD, PhD; Christos Davatzikos, PhD; Ralph F. Mangus, RN-BC; Rachelle A. Winkle, RN; Peter K. Smith, MD; Robert E. Michler, MD; Marissa A. Miller, DVM; Karen L. O’Sullivan, MPH; Wendy C. Taddei-Peters, PhD; Eric A. Rose, MD; Richard D. Weisel, MD; Karen L. Furie, MD, MPH; Emilia Bagiella, PhD; Claudia Scala Moy, PhD; Patrick T. O’Gara, MD; Steven R. Messé, MD; for the Cardiothoracic Surgical Trials Network (CTSN)

IMPORTANCE Stroke is a major complication of surgical aortic valve replacement (SAVR).

OBJECTIVE To determine the efficacy and adverse effects of cerebral embolic protection devices in reducing ischemic central nervous system (CNS) injury during SAVR.

DESIGN, SETTING, AND PARTICIPANTS A randomized clinical trial of patients with calcific aortic stenosis undergoing SAVR at 18 North American centers between March 2015 and July 2016. The end of follow-up was December 2016.

INTERVENTIONS Use of 1 of 2 cerebral embolic protection devices (n = 118 for suction-based extraction and n = 133 for intra-aortic filtration device) vs a standard aortic cannula (control; n = 132) at the time of SAVR.

MAIN OUTCOMES AND MEASURES The primary endpoint was freedom from clinical or radiographic CNS infarction at 7 days (±3 days) after the procedure. Secondary end points included a composite of mortality, clinical ischemic stroke, and acute kidney injury within 30 days after surgery; delirium; mortality; serious adverse events; and neurocognition.

RESULTS Among 383 randomized patients (mean age, 73.9 years; 38.4% women; 368 [96.1%] completed the trial), the rate of freedom from CNS infarction at 7 days was 32.0% with suction-based extraction vs 33.3% with control (between-group difference, −1.3%; 95% CI, −13.8% to 11.2%) and 25.6% with intra-aortic filtration vs 32.4% with control (between-group difference, −6.9%; 95% CI, −17.9% to 4.2%). The 30-day composite end point was not significantly different between suction-based extraction and control (21.4% vs 24.2%, respectively; between-group difference, −2.8% [95% CI, −13.5% to 7.9%]) nor between intra-aortic filtration and control (33.3% vs 23.7%; between-group difference, 9.7% [95% CI, −1.2% to 20.5%]). There were no significant differences in mortality (3.4% for suction-based extraction vs 1.7% for control; and 2.3% for intra-aortic filtration vs 1.5% for control) or clinical stroke (5.1% for suction-based extraction vs 5.8% for control; and 8.3% for intra-aortic filtration vs 6.1% for control). Delirium at postoperative day 7 was 6.3% for suction-based extraction vs 15.3% for control (between-group difference, −9.1%; 95% CI, −17.1% to −1.0%) and 8.1% for intra-aortic filtration vs 15.6% for control (between-group difference, −7.4%; 95% CI, −15.5% to 0.6%). Mortality and overall serious adverse events at 90 days were not significantly different across groups. Patients in the intra-aortic filtration group vs patients in the control group experienced significantly more acute kidney injury events (14 vs 4, respectively; P = .02) and cardiac arrhythmias (57 vs 30; P = .004).

CONCLUSIONS AND RELEVANCE Among patients undergoing SAVR, cerebral embolic protection devices compared with a standard aortic cannula did not significantly reduce the risk of CNS infarction at 7 days. Potential benefits for reduction in delirium, cognition, and symptomatic stroke merit larger trials with longer follow-up.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT02389894


Supplemental content
CME Quiz at jamanetwork.com/learning

Author Affiliations: Author affiliations are listed at the end of this article.

Group Information: The members of the Cardiothoracic Surgical Trials Network (CTSN) appear at the end of the article.

Corresponding Author: Annetine C. Gelijns, PhD, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Place, Box 1077, New York, NY 10029 (annetine.gelijns@mssm.edu).

© 2017 American Medical Association. All rights reserved.
he prevalence of aortic stenosis increases with aging and the expanding number of US patients requiring surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR) is estimated to be 100 000 per year. Steady improvements in patient selection, surgical techniques, and perioperative management have improved survival and quality of life for these patients. However, concerns remain about the incidence of central nervous system (CNS) infarction, a serious complication of SAVR. Studies documented a high incidence (up to 60%) of radiographic brain infarcts on postoperative magnetic resonance imaging (MRI) scans, although the vast majority are subclinical. In a cohort study, 17% of patients undergoing SAVR (enrolled from 2008-2012) experienced clinical stroke, about 25% of which were moderate or severe. The effect of perioperative stroke on survival, quality of life, and cost is well established, whereas the effect of silent (nonsymptomatic) cerebral infarcts on these outcomes is unknown.

These concerns stimulated the development of cerebral embolic protection devices. Currently 2 devices are approved in the United States. The Embol-X (Edwards Lifesciences) intra-aortic filtration device has been shown to be safe and capture emboli (with a heparin-coated polyester mesh filter), but not reduce stroke in a mostly low-risk population undergoing coronary artery bypass graft surgery. The CardioGard (CardioGard) device extracts both particulate and gaseous emboli through suction-based extraction. A small trial of this device among patients undergoing SAVR reported a significant reduction in the total volume and number of radiographically detected brain lesions, but the effect on cognitive outcomes was not evaluated. More rigorous data are needed on the value of cerebral embolic protection devices in reducing ischemic CNS injury documented by clinical and radiographic means.

This trial evaluated the efficacy and adverse effects of these cerebral embolic protection devices among patients undergoing SAVR, which is a high-risk setting for CNS infarction. It included clinical, radiographic, and cognitive outcomes within 90 days.

### Methods

We conducted a randomized clinical trial at 18 North American centers that compared each of 2 approved cerebral embolic protection devices vs a standard aortic cannula (control) in patients undergoing SAVR. This trial had a coordinating center, an events adjudication committee, and a data and safety monitoring board appointed by the National Institutes of Health (NIH) overseeing the trial. Participating institutional review boards approved the protocol and all patients gave written informed consent (the trial protocol appears in Supplement 1). The overall aim of the trial was to establish the effectiveness of embolic protection devices vs standard of care. At the time the trial was initially designed, patients were to be randomized to the treatment group to receive the intra-aortic filtration device or to receive a standard aortic cannula in a 1:1 ratio. Within 6 weeks after initiating the trial, the suction-based extraction device became available, and patients were then to be randomly assigned to receive the intra-aortic filtration device, the suction-based extraction device, or standard aortic cannula in a 1:1:1 ratio. The trial was not designed to directly compare devices, which would have required a substantially larger sample size.

### Patients, Interventions, and End Points

The trial randomized patients aged 60 years or older undergoing SAVR for aortic stenosis with minimal or no deficits within 7 days of randomization according to the preoperative scores on the NIH Stroke Scale (NIHSS; score ≤1) and the modified Rankin Scale (score ≤2). Key exclusion criteria included clinical stroke during the 3 months prior to randomization; cardiac catheterization; cerebral or aortic arch angiography within 3 days of planned SAVR; and active endocarditis. Patients were randomized immediately after sternotomy and stratified by center and procedure (isolated aortic valve replacement vs aortic valve replacement and coronary artery bypass graft with or without mitral valve repair). The intra-aortic filtration device uses a heparin-coated polyester mesh filter. Filter size was determined by measuring the size of the distal ascending aorta (using computed tomography or an intraoperative measurement). The suction-based extraction device has a suction port located posterior to the main port of an aortic perfusion cannula. In the control group, a standard aortic perfusion cannula was used (eAppendix 1 in Supplement 2).

Patients underwent SAVR between March 2015 and July 2016. The end of follow-up was December 2016. Patients were assessed at baseline and at postoperative days 1, 3, 7, 30, and 90; the investigators were blinded to the end point data. The primary end point was freedom from clinical or radiographic CNS infarction at 7 days (± 3 days) after the procedure. Radiographic CNS infarcts were identified using a diffusion-weighted 1.5-T or 3.0-T MRI scanner.

Imaging-based stroke ascertainment was supplemented by serial neurological assessment using the NIHSS (score at postoperative days 1, 3, and 7) and reporting of ischemic stroke adverse events detected during hospitalization. All MRIs were read by a core laboratory and stroke events with clinical findings (NIHSS score ≥2) were adjudicated by an events adjudication committee composed of vascular neurologists.

The composite secondary end point was mortality, clinical ischemic stroke (including newly MRI-detected CNS infarcts associated with focal findings by the NIHSS before postoperative day 7), or acute kidney injury within 30 days after...
Cerebral Embolic Protection in Patients Undergoing Surgical Aortic Valve Replacement

Research Original Investigation

Statistical Analysis

Patients were randomized with equal allocation to 1 of 2 cerebral embolic protection device groups or to the control group. Random permuted block sizes of 3, 6, and 9 were used. The randomization sequence was generated by a trial statistician and randomization assignment was controlled centrally through a web-based data collection system and performed in the operating room. A sample size of 165 patients in each group ensured that each comparison had a power of approximately 90% to detect a between-group difference of 17.5% from an assumed control rate of 50% in the incidence of postoperative delirium as defined by an O’Brien-Fleming spending function.11,12 The consideration of halting for futility was prespecified if conditional power was below 20% (eAppendix 3 in Supplement 2). Intention-to-treat χ² tests performed at the nominal .05 level (2-sided) were used to test hypotheses about differences between the intervention devices and the control intervention.

No adjustment was made to the type I error rate because these 2 planned comparisons are separate comparisons of each device group vs a shared control. Based on the recommendation of the data and safety monitoring board at the interim analysis, randomization but not follow-up was halted due to low conditional power of observing any between-group differences for the primary end point. At that point, 383 patients had been randomized.

The primary end point analysis used an iterative hot-deck multiple imputation approach, assuming a nonignorable missing data mechanism (eAppendix 3 in Supplement 2). The proportion of patients who experienced the composite clinical end point was compared using χ² tests. The volume of brain infarcts was compared by permutation test.

Negative binomial models were used to analyze the number of brain infarcts (instead of protocol-defined zero-inflated Poisson regression models) because model fit was better. All-cause mortality was analyzed using the log-rank test and differences in adverse event rates were tested using Poisson regression. The incidence of delirium at postoperative days 1, 3, and 7 were compared using χ² tests and the trajectory of delirium incidence over time was compared using generalized estimating equation logistic regression models.

The decline in scores for cognitive domains (decrease of 0.5 SD at 90 days) was compared between groups using logistic regression models, adjusting for baseline scores. Quality of life was assessed using t tests. Depression (presence vs absence), modified Rankin Scale scores (>2), and Barthel Index scores (≤80) were assessed using χ² tests. All statistical analyses were conducted using SAS version 9.4 (SAS Institute Inc).

Results

A total of 870 patients were screened and found eligible (Figure 1). Among 383 patients (mean age, 73.9 years; 38.4% women; 368 [96.1%] completed the trial), 118 were randomized to the suction-based extraction group, 133 to the intra-aortic filtration group, and 132 to the control group. Of the 132 patients randomized to the control group, the first 12 served as controls for the intra-aortic filtration group only because the suction-based extraction device was not yet clinically available and the other 120 served as controls for both the suction-based extraction group and the intra-aortic filtration group.

The randomized groups had similar baseline characteristics (Table 1 and eTable 1 in Supplement 2). Preoperatively, 36.3% of patients randomized to the suction-based extraction group had severe cognitive impairment (≥2 SDs below the mean of an age-standardized population) in 1 or more of the domains specified in Table 1 vs 25.7% of patients in the control group and 29.8% of patients in the intra-aortic filtration group vs 25.8% of patients in the control group.

Most patients underwent either isolated SAVR (58%) or a combined SAVR and coronary artery bypass graft procedure (41%). Cardiopulmonary bypass times were similar in both device groups and in the control group. Three patients randomized to intra-aortic filtration and 2 patients randomized to suction-based extraction did not receive the designated device due to anatomic constraints and hemodynamic instability. Embolic debris was captured in 99% of patients in the intra-aortic filtration group and in 75% of patients in the suction-based extraction group (Table 1).

Freedom from CNS infarction at postoperative day 7 (using imputation for missing data) was not significantly different between the suction-based extraction group and the control group (32.0% vs 33.3%, respectively; between-group difference, −1.3% [95% CI, −13.8% to 11.2%]) nor between the intra-aortic filtration group and the control group (25.6% vs 32.4%, respectively; between-group difference, −6.9% [95% CI, −17.9% to 4.2%]). Sensitivity analyses assuming different missing data mechanisms appear in eTable 2 in Supplement 2. Among patients who met the primary end point, the majority did not show clinical evidence of stroke (91% in suction-based extraction group vs 90% in control group; and 87% in intra-aortic filtration group vs 90% in control group). End point analyses stratified by procedure and site are provided in the eTable 3 in Supplement 2.

The proportion of patients in the suction-based extraction device group (with or without an MRI) who had clinically...
apparent stroke was 5.1% vs 5.8% among patients in the control group (between-group difference, −0.7%; 95% CI, −6.5% to 5.1%). The proportion of patients in the intra-aortic filtration group with stroke was 8.3% vs 6.1% among patients in the control group (between-group difference, 2.2%; 95% CI, −4.1% to 8.4%). Seventy-six percent of clinically apparent strokes were detected by postoperative day 3, and there were fewer cases of severe stroke among patients who received a cerebral embolic protection device within this 3-day window in a posthoc analysis (Table 2).

Patients frequently showed evidence of multiple new CNS infarcts. The number of infarcts was not significantly different between patients in the suction-based extraction group and the control group (mean, 2.4 vs 2.3, respectively; between-group difference, 0.1 [95% CI, −0.8 to 1.0]; P = .88), nor between patients in the intra-aortic filtration group and the control group (mean, 2.8 vs 2.7, respectively; between-group difference, 0.1 [95% CI, −0.8 to 1.1]; P = .78). Total lesion volume was not significantly different between patients in the suction-based extraction group and the control group (mean, 178.5 mm³ vs 476.4 mm³, respectively; between-group difference, −297.9 mm³ [95% CI, −741.3 to 145.6 mm³]; P = .28), nor between patients in the intra-aortic filtration group and the control group (mean, 321.3 mm³ vs 484.4 mm³, respectively; between-group difference, −163.1 mm³ [95% CI, −586.0 to 259.8 mm³]; P = .49).

Figure 2 depicts the cumulative distribution of total lesion volume up to the 90th percentile. Infarct volumes were larger in patients with a clinically apparent stroke (mean, 1688 mm³) than in those without a clinically apparent stroke (mean, 236 mm³) (between-group difference, −1451.9 mm³ [95% CI, 883.0 to 2020.8 mm³]; P = .001). Data on the risk of large volume infarcts appear in the electronic figure in Supplement 2.

The proportion of patients experiencing the composite end point of death, clinically apparent ischemic stroke, or acute kidney injury within 30 days of surgery was 21.4% in the suction-based extraction group vs 24.2% in the control group (between-group difference, −2.8%; 95% CI, −13.5% to 7.9%) and 33.3% in the intra-aortic filtration group vs 23.7% in the control group (between-group difference, 9.7%; 95% CI, −1.2% to 20.5%). The individual components of the composite 30-day end point were not significantly different across groups (Table 2).
Mortality, composite neurological events, and overall serious adverse events at 90 days were not significantly different across groups (Table 2). Patients in the intra-aortic filtration group vs patients in the control group experienced significantly more acute kidney injury events (14 vs 4, respectively; between-group difference, 2.7 [95% CI, 0.4-4.9]) and cardiac arrhythmias (57 vs 30, respectively; between-group difference, 2.7 [95% CI, 0.4-4.9]) and significantly more acute kidney injury events (14 vs 4, respectively; between-group difference, 2.7 [95% CI, 0.4-4.9]) and cardiac arrhythmias (57 vs 30, respectively; between-group difference, 2.7 [95% CI, 0.4-4.9]).

The length of stay during the index hospitalization was not significantly different between patients in the suction-based extraction group and in the control group (mean, 10.4 days vs 10.3 days, respectively; between-group difference, 0.1 days [95% CI, −0.1 to 0.3 days]), nor was length of ICU stay (mean, 4.5 days vs 4.1 days, respectively; between-group difference, 0.4 days [95% CI, −0.1 to 0.2 days]). Hospital readmission rates were not significantly different between both intervention groups and the control group.

There were significant differences in the trajectories for delirium occurrence (baseline to day 7) among patients in the suction-based extraction group vs the control group (P = .03) and among patients in the intra-aortic filtration group vs the control group (P = .02; Figure 3). At postoperative day 7, 6.3% of patients in the suction-based extraction group experienced delirium vs 15.3% of patients in the control group (between-group difference, −9.1%; 95% CI, −17.1% to −1.1%) and 8.1% of patients in the intra-aortic filtration group vs 15.6% of patients in the control group (between-group difference, −7.4%; 95% CI, −15.5% to 0.6%).
Table 2. Clinical End Points and Serious Adverse Events

<table>
<thead>
<tr>
<th>Clinical End Points Within First 7 d, No./Total (%)</th>
<th>Intra-Aortic Filtration (n = 133)</th>
<th>Control (n = 132)</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary end point</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Imputed, % (95% CI)</td>
<td>68.0 (59.1 to 76.8)</td>
<td>67.7 (58.4 to 76.8)</td>
<td>1.3 (-1.2 to 3.8)</td>
<td>.22</td>
</tr>
<tr>
<td>Observed</td>
<td>68/101 (67.3)</td>
<td>71/111 (64.0)</td>
<td>8.5 (−1.5 to 14.3)</td>
<td>.15</td>
</tr>
<tr>
<td><strong>Died within 7 d</strong></td>
<td>0/117</td>
<td>1/120 (0.8)</td>
<td>1.4 (−0.1 to 3.1)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Radiographic infarct</td>
<td>66/101 (65.3)</td>
<td>71/111 (64.0)</td>
<td>0.1 (−15.5 to 15.9)</td>
<td>.99</td>
</tr>
<tr>
<td>Clinically apparent stroke within 7 d, % (95% CI)</td>
<td>6/117 (5.1)</td>
<td>7/120 (5.8)</td>
<td>1.2 (−14.6 to 16.8)</td>
<td>.65</td>
</tr>
<tr>
<td>AKI (stage 1-3, serious, and nonserious)</td>
<td>19/117 (16.2)</td>
<td>24/120 (20.0)</td>
<td>−4.8 (−13.5 to 4.0)</td>
<td>.38</td>
</tr>
</tbody>
</table>

(continued)
<table>
<thead>
<tr>
<th>Serious Adverse Events by 90 d, No. of Events (Rate/100 Patient-Months)</th>
<th>Suction-Based Extraction (n = 118)</th>
<th>Control (n = 120)</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
<th>Intra-Aortic Filtration (n = 133)</th>
<th>Control (n = 132)</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AKI</td>
<td>3 (0.9)</td>
<td>4 (1.2)</td>
<td>−0.3 (−1.8 to 1.3)</td>
<td>.74</td>
<td>14 (3.8)</td>
<td>4 (1.1)</td>
<td>2.7 (0.4 to 4.9)</td>
<td>.02</td>
</tr>
<tr>
<td>Stage 1</td>
<td>1 (0.3)</td>
<td>0</td>
<td>0.3 (−0.3 to 0.9)</td>
<td>.32</td>
<td>3 (0.8)</td>
<td>0</td>
<td>0.8 (−0.1 to 1.7)</td>
<td>.08</td>
</tr>
<tr>
<td>Stage 2</td>
<td>0</td>
<td>2 (0.6)</td>
<td>−0.6 (−1.4 to 0.2)</td>
<td>.16</td>
<td>4 (1.1)</td>
<td>2 (0.5)</td>
<td>0.5 (−0.8 to 1.8)</td>
<td>.42</td>
</tr>
<tr>
<td>Stage 3</td>
<td>2 (0.6)</td>
<td>2 (0.6)</td>
<td>0 (−1.2 to 1.2)</td>
<td>.97</td>
<td>7 (1.9)</td>
<td>2 (0.5)</td>
<td>1.3 (−0.2 to 2.9)</td>
<td>.10</td>
</tr>
<tr>
<td>Bleeding</td>
<td>8 (2.5)</td>
<td>6 (1.8)</td>
<td>0.7 (−1.5 to 2.9)</td>
<td>.55</td>
<td>5 (1.3)</td>
<td>6 (1.6)</td>
<td>−0.3 (−2.0 to 1.5)</td>
<td>.75</td>
</tr>
<tr>
<td>Cardiac arrhythmias</td>
<td>31 (9.5)</td>
<td>25 (7.4)</td>
<td>2.1 (−2.3 to 6.6)</td>
<td>.35</td>
<td>57 (15.3)</td>
<td>30 (8.1)</td>
<td>7.2 (2.3 to 12.1)</td>
<td>.004</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>0</td>
<td>1 (0.3)</td>
<td>−0.3 (−0.9 to 0.3)</td>
<td>.32</td>
<td>6 (1.6)</td>
<td>2 (0.5)</td>
<td>1.1 (−0.4 to 2.6)</td>
<td>.16</td>
</tr>
<tr>
<td>Conduction abnormalities or sustained bradycardia with permanent pacemaker placement</td>
<td>25 (7.7)</td>
<td>22 (6.5)</td>
<td>1.2 (−2.9 to 5.2)</td>
<td>.58</td>
<td>43 (11.6)</td>
<td>25 (6.8)</td>
<td>4.8 (0.4 to 9.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Major infection</td>
<td>10 (3.1)</td>
<td>12 (3.6)</td>
<td>−0.5 (−3.3 to 2.3)</td>
<td>.73</td>
<td>15 (4.0)</td>
<td>15 (4.1)</td>
<td>0 (−2.9 to 2.9)</td>
<td>.98</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>0</td>
<td>3 (0.8)</td>
<td>.0</td>
<td>0</td>
<td>0</td>
<td>0.8 (−0.1 to 1.7)</td>
<td>.08</td>
</tr>
<tr>
<td>Neurological dysfunction</td>
<td>4 (1.2)</td>
<td>10 (3.0)</td>
<td>−1.7 (−3.9 to 0.5)</td>
<td>.12</td>
<td>7 (1.9)</td>
<td>12 (3.3)</td>
<td>−1.4 (−3.7 to 0.9)</td>
<td>.24</td>
</tr>
<tr>
<td>Transient ischemic attack</td>
<td>0</td>
<td>1 (0.3)</td>
<td>−0.3 (−0.9 to 0.3)</td>
<td>.32</td>
<td>0</td>
<td>1 (0.3)</td>
<td>−0.3 (−0.8 to 0.3)</td>
<td>.32</td>
</tr>
<tr>
<td>Ischemic stroke</td>
<td>3 (0.9)</td>
<td>3 (0.9)</td>
<td>0 (−1.4 to 1.5)</td>
<td>.97</td>
<td>4 (1.1)</td>
<td>4 (1.1)</td>
<td>0 (−1.5 to 1.5)</td>
<td>.99</td>
</tr>
<tr>
<td>Toxic metabolic encephalopathy</td>
<td>1 (0.3)</td>
<td>1 (0.3)</td>
<td>0 (−0.8 to 0.8)</td>
<td>.98</td>
<td>2 (0.5)</td>
<td>1 (0.3)</td>
<td>0.3 (−0.6 to 1.2)</td>
<td>.57</td>
</tr>
<tr>
<td>Seizure</td>
<td>0</td>
<td>2 (0.6)</td>
<td>−0.6 (−1.4 to 0.2)</td>
<td>.16</td>
<td>0</td>
<td>3 (0.8)</td>
<td>−0.8 (−1.7 to 0.1)</td>
<td>.08</td>
</tr>
<tr>
<td>Other</td>
<td>0</td>
<td>3 (0.9)</td>
<td>−0.9 (−1.9 to 0.1)</td>
<td>.08</td>
<td>1 (0.3)</td>
<td>3 (0.8)</td>
<td>−0.5 (−1.6 to 0.5)</td>
<td>.31</td>
</tr>
<tr>
<td>Renal failure</td>
<td>0</td>
<td>2 (0.6)</td>
<td>−0.6 (−1.4 to 0.2)</td>
<td>.16</td>
<td>1 (0.3)</td>
<td>2 (0.5)</td>
<td>−0.3 (−1.2 to 0.6)</td>
<td>.56</td>
</tr>
<tr>
<td>Respiratory failure</td>
<td>3 (0.9)</td>
<td>9 (2.7)</td>
<td>−1.8 (−3.8 to 0.3)</td>
<td>.09</td>
<td>8 (2.2)</td>
<td>11 (3.0)</td>
<td>−0.8 (−3.1 to 1.5)</td>
<td>.48</td>
</tr>
<tr>
<td>Heart failure</td>
<td>4 (1.2)</td>
<td>8 (2.4)</td>
<td>−1.1 (−3.2 to 0.9)</td>
<td>.27</td>
<td>2 (0.5)</td>
<td>9 (2.4)</td>
<td>−1.9 (−3.7 to −0.1)</td>
<td>.03</td>
</tr>
<tr>
<td>Venous thromboembolism event</td>
<td>1 (0.3)</td>
<td>2 (0.6)</td>
<td>−0.3 (−1.3 to 0.7)</td>
<td>.58</td>
<td>4 (1.1)</td>
<td>2 (0.5)</td>
<td>0.5 (−0.8 to 1.8)</td>
<td>.42</td>
</tr>
<tr>
<td>All serious adverse events</td>
<td>91 (28.0)</td>
<td>112 (33.3)</td>
<td>−5.3 (−13.7 to 3.2)</td>
<td>.22</td>
<td>157 (42.2)</td>
<td>126 (34.2)</td>
<td>8.0 (−0.8 to 16.9)</td>
<td>.08</td>
</tr>
<tr>
<td>Hospital readmissions</td>
<td>24 (8.4)</td>
<td>20 (6.8)</td>
<td>1.7 (−2.8 to 6.1)</td>
<td>.47</td>
<td>30 (9.3)</td>
<td>23 (7.1)</td>
<td>2.2 (−2.3 to 6.6)</td>
<td>.34</td>
</tr>
</tbody>
</table>
### Table 2. Clinical End Points and Serious Adverse Events (continued)

<table>
<thead>
<tr>
<th>End Point</th>
<th>Suction-Based Extraction (n = 118)</th>
<th>Control (n = 120)</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
<th>Intra-Aortic Filtration (n = 133)</th>
<th>Control (n = 132)</th>
<th>Absolute Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quality of Life at 90 d</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>12-Item Short-Form Health Survey score, mean (95% CI)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mental health composite</td>
<td>55.4 (53.8 to 57.1)</td>
<td>55.1 (53.5 to 56.6)</td>
<td>0.4 (−1.8 to 2.6)</td>
<td>.74</td>
<td>55.2 (53.4 to 57.0)</td>
<td>54.8 (53.4 to 56.3)</td>
<td>0.3 (−2.0 to 2.7)</td>
<td>.77</td>
</tr>
<tr>
<td>Physical health composite</td>
<td>44.9 (43.2 to 46.5)</td>
<td>44.7 (43.1 to 46.3)</td>
<td>0.1 (−2.2 to 2.4)</td>
<td>.92</td>
<td>43.0 (41.1 to 45.0)</td>
<td>44.2 (42.6 to 45.8)</td>
<td>−1.2 (−3.7 to 1.3)</td>
<td>.36</td>
</tr>
<tr>
<td>Geriatric Depression Scale score &gt;10, No./total (%)</td>
<td>5/104 (4.8)</td>
<td>7/108 (6.5)</td>
<td>−1.7 (−7.9 to 4.5)</td>
<td>.60</td>
<td>13/122 (10.7)</td>
<td>9/119 (7.6)</td>
<td>3.1 (−4.2 to 10.3)</td>
<td>.40</td>
</tr>
<tr>
<td>Functional Status at 90 d, No./Total (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decline in overall neurocognition</td>
<td>24/81 (29.6)</td>
<td>27/86 (31.4)</td>
<td>1.1 (0.5 to 2.2)</td>
<td>.82</td>
<td>28/88 (28.6)</td>
<td>31/96 (22.3)</td>
<td>0.8 (0.4 to 1.5)</td>
<td>.54</td>
</tr>
<tr>
<td>Modified Rankin Scale score &gt;2</td>
<td>7/110 (6.4)</td>
<td>4/112 (3.6)</td>
<td>2.8 (−2.9 to 8.5)</td>
<td>.34</td>
<td>5/127 (3.9)</td>
<td>5/123 (4.1)</td>
<td>−0.1 (−5.0 to 4.7)</td>
<td>&gt; .99</td>
</tr>
<tr>
<td>Barthel Index ≤80</td>
<td>2/105 (1.9)</td>
<td>3/109 (2.8)</td>
<td>−0.8 (−4.9 to 3.2)</td>
<td>&gt; .99</td>
<td>2/123 (1.6)</td>
<td>4/120 (3.3)</td>
<td>−1.7 (−5.6 to 2.2)</td>
<td>.44</td>
</tr>
<tr>
<td>Mortality, No.</td>
<td>5</td>
<td>3</td>
<td>1.7 (0.4 to 7.2)</td>
<td>.45</td>
<td>4</td>
<td>3</td>
<td>1.3 (0.3 to 5.9)</td>
<td>.71</td>
</tr>
</tbody>
</table>

Abbreviations: AKI, acute kidney injury; NIHSS, National Institutes of Health Stroke Scale.

a The number of patient-months was 324.7 and there were 284.8 patient-months outside the hospital.

b The first 12 patients randomized to the control group served as controls for the intra-aortic filtration group only and the other 120 patients served as controls for both the suction-based extraction group and the intra-aortic filtration group.

c The number of patient-months was 336.3 and there were 295.6 patient-months outside the hospital.

d For decline in overall neurocognition, the odds ratio (95% CI) is given because the analysis is based on a logistic model adjusting for baseline score. For mortality, the hazard ratio (95% CI) is given because the analysis was time to event.

e Calculated using the x² test or the Fisher exact test for the clinical, modified Rankin Scale, Barthel Index, and Geriatric Depression Scale end points; using Poisson regression for serious adverse events and hospitalizations; using t tests for 12-Item Short-Form Health Survey scores; using a logistic regression model (adjusted for baseline score) for neurocognitive decline; and using the log-rank test for mortality.

f The number of patient-months was 372.0 and there were 322.7 patient-months outside the hospital.

g Freedom from clinical or radiographic central nervous system infarction measured by diffusion-weighted magnetic resonance imaging (MRI) at 7 days (± 3 days) after the procedure. Deaths were counted as treatment failures. The denominator for the observed primary end point is the number of patients with a nonmissing MRI image or evidence of a clinical stroke or death before 7 days.

h Of 334 patients, the sites used a diffusion-weighted 1.5 T MRI scanner for 210 (63%) and a diffusion-weighted 3-T MRI scanner for 124 (37%).

i Five patients had evidence of a clinical infarction and either did not undergo diffusion-weighted MRI or had no lesions (2 in suction-based extraction group, 2 in intra-aortic filtration group, and 1 in the control group).

j Measured by Confusion Assessment Method assessment at baseline and at days 1, 3, and 7.

k Clinically apparent stroke, AKI, or death within 30 days of surgery.

l The AKI stage definitions appear in Appendix 2 in Supplement 2.

m Defined as a new infection accompanied by pain, fever, drainage, or leukocytosis that is treated with an antimicrobial agent (nonprophylactic). A positive culture from the infected site or organ should be present unless strong clinical evidence indicates the need for treatment despite negative cultures.

n Deep vein thrombosis, pulmonary embolism, or other.

o A higher score indicates a better health state. Values are normed as t scores (mean, 50 [SD, 10]).

p A score of 10 or less indicates no depression, whereas a score of 11 or greater indicates depression.

q Defined as the number of patients whose z score (computed relative to the study population at baseline, adjusting for age, education, and sex) at day 90 had decreased by 0.5 SD relative to the baseline score.

r A score of 3 to 5 corresponds to moderate disability; score of 6, death.

s A score of 80 or less corresponds to mild to moderate or greater disability.
The 12-Item Short-Form Health Survey composite physical and mental health scores were not significantly different between the 2 device intervention groups and the control group (Table 2). Moreover, no differences were observed in the overall cognition scores for the 2 device intervention groups and the control group (Table 2). However, the decline in overall cognition scores was greater for patients experiencing clinically apparent stroke than for other patients (71.4% vs 28.0%; between-group difference, 43.5% [95% CI, 19.2%-67.7%]). With the exception of executive function, which showed less decline among patients in the intra-aortic filtration group vs patients in the control group, there were no differences among the neurocognitive domain comparisons (eTable 4 in Supplement 2).

**Discussion**

Despite the fact that debris was captured in most patients who received a cerebral embolic protection device, rates of clinical and radiographic infarction were not reduced. Nearly 69% of patients who underwent SAVR experienced clinical or radiographic stroke. However, the majority of these events was only detectable by postoperative diffusion-weighted MRI, with just 9% of patients exhibiting clinical findings. Neither the number of MRI lesions nor total lesion volume differed between patients receiving either of the cerebral embolic protection devices and the patients in the control group.
However, the infarct volume pattern suggested a possible differential effect of devices compared with the control intervention, with larger volume infarcts more numerous in patients in the control group. This observation may be important because the risk of clinically evident stroke increases with infarct volume.

The reported incidence of newly detected clinical and radiographic infarcts after cardiac surgery has varied across observational studies likely in relation to cohort size, patient characteristics, approaches to clinical assessment, and imaging techniques. The volume of radiographic infarcts seen in this study (the majority of which were small with a median infarct volume of 48.7 mm³) is concordant with that reported in prior studies using MRI after patients underwent SAVR. Imaging studies in the general population have reported that clinically silent brain infarction (including microinfarction <3 mm) is associated with dementia, mortality, and risk of future stroke and death; however, it is not clear whether these same associations pertain to periprocedural infarcts that are clinically silent.

The proportion of patients with clinical stroke findings at day 7 (with or without MRI evidence of infarction) were not significantly different between patients in the suction-based extraction group and the control group (5.1% vs 5.8%, respectively) nor between patients in the intra-aortic filtration group and the control group (8.3% vs 6.1%, respectively). However, the majority of clinical stroke findings were detected by postoperative day 3, suggesting that many cases of perioperative stroke may be preventable with use of a cerebral embolic protection device.

In a post hoc analysis, there were numerically fewer patients with severe clinical stroke (NIHSS score >20) among patients receiving a cerebral embolic protection device compared with patients in the control group at days 0 through 3. Given that severity (defined by NIHSS score) at onset is one of the strongest predictors of long-term outcome after acute stroke, a reduction in the risk of severe stroke during the early perioperative period might be a tangible benefit of cerebral embolic protection device use during SAVR, and may justify a larger trial.

The rate of clinically apparent stroke (6.5%) in this trial is much higher than the 7-day stroke incidence of 1% to 3% reported in several prior studies, and is most likely attributable to active ascertainment with early repeated neurological assessments. However, there was a lower incidence of stroke with clinical findings than the 17% seen in a previously reported cohort study, perhaps related to a treatment shift from SAVR to TAVR among high-risk patients that occurred during the course of this trial. There was a large difference in this trial between observed cases of stroke during the course of clinical care and cases of stroke detected through protocol-specified, routine NIHSS screening, suggesting that many clinical events are undetected or underreported in practice.

Delirium (defined as a disturbance of consciousness and cognition that can develop acutely after surgery) is common and occurs in 11% to 46% of patients after surgery. Prior studies have shown that cerebral embolization is associated with delirium, a condition that is costly and associated with poor outcomes, including prolonged hospitalization, readmissions, long-term cognitive decline, and mortality. Longitudinally (over 7 days postoperatively), there was a significant difference between patients who received one of the device interventions and patients in the control group. At day 7 (when perioperative medications are less of a factor), fewer patients who received a device experienced in-hospital delirium than patients in the control group and the difference achieved statistical significance with the suction-based extraction device. This difference may be related to the fact that, in addition to particulate matter, the suction-based device also extracts gaseous microemboli, which have been shown to affect neuropsychological functioning early during the postoperative phase among patients undergoing cardiac surgery.

More than 25% of patients had severe cognitive impairment on baseline testing in 1 domain compared with age-adjusted norms, especially in verbal memory and executive functioning. These domains are associated with late-onset Alzheimer-related pathology and cerebrovascular disease. Similar findings have been reported with TAVR. Given the advanced age of patients with aortic stenosis and the increased incidence of cerebrovascular disease, higher rates of postoperative cognitive impairment in populations undergoing SAVR and TAVR is not unexpected. These findings underscore the importance of evaluating cognitive impairment during risk assessment given its association with postoperative delirium and late-onset dementia.

Baseline performance-adjusted cognitive outcomes at 90 days were not significantly different between the patients in the device groups and the control group with the exception of a reduced decline in executive functioning in the intra-aortic filtration group. This finding requires more investigation, but might relate to the lower incidence of delirium observed among patients in the device treatment groups compared with patients in the control group. There was evidence of an increased incidence of acute kidney injury and a higher rate of cardiac arrhythmias among patients in the intra-aortic filtration group compared with the control group. These findings merit further investigation, but need to be interpreted in the context of multiple statistical comparisons for adverse events, which increases the likelihood of finding abnormalities due to random variation alone.

**Limitations**

This trial has several limitations. First, even though the trial subscribes to the latest imaging recommendations for assessing neurological outcomes in the postcardiac surgery setting, the significance of the many small and clinically silent lesions identified by diffusion-weighted MRI cannot be established. Second, although the optimal time frame to assess the effectiveness of an intraoperative cerebral embolic protection device is within the first few postoperative days, 7-day imaging is more feasible for patients undergoing cardiac surgery. As a result, this study may have captured radiographic and clinical CNS infarctions not related to intraoperative embolization (eg, from postoperative atrial fibrillation), thus overestimating the infarct burden, whereas smaller lesions may have normalized by 7 days, underestimating the infarct burden.
Third, although the NIHSS score has been validated as a measure of stroke severity, it does not inherently inform whether a clinical stroke has occurred. However, clinical stroke end point adjudication was performed by experienced vascular neurologists who reviewed trial data to determine whether an event occurred. Fourth, randomization was halted due to low conditional power for the primary end point, diminishing the power to detect differences for the secondary end points. In addition, the long-term effects on cognition may not have been fully evident within the 90-day follow-up of the trial. Fifth, the trial was not designed to directly compare devices, which would have required a substantially larger sample size.

Conclusions

Among patients undergoing SAVR, cerebral embolic protection devices compared with a standard aortic cannula did not significantly reduce the risk of CNS infarction at 7 days. Potential benefits for reduction in delirium, cognition, and symptomatic stroke merit larger trials with longer follow-up.

ARTICLE INFORMATION

Accepted for Publication: July 6, 2017. Author Affiliations: Department of Cardiothoracic Surgery, Baylor Research Institute, Baylor Scott & White Health, Plano, Texas (Mack, Winkle); Division of Cardiovascular Surgery, Department of Surgery, University of Pennsylvania School of Medicine, Philadelphia (Ackerman); International Center for Health Outcomes and Innovation Research, Department of Population Health Science and Policy, Icahn School of Medicine at Mount Sinai, New York, New York (Gelijns, Overbey, Parides, Moskowitz, Moquete, O’Sullivan, Bagiella); Division of Geriatric Behavioral Health, Department of Psychiatry and Behavioral Sciences, Duke University Medical Center, Durham, North Carolina (Brown); Cardiovascular and Thoracic Surgery, Mission Health and Hospitals, Asheville, North Carolina (Groh, Mungas); Office of Biostatistics Research, National Heart, Lung, and Blood Institute, Bethesda, Maryland (Jeffries); Division of Thoracic and Cardiovascular Surgery, University of Virginia School of Medicine, Charlottesville (Allaway); Clinical Research Unit, Division of Cardiothoracic Surgery, Emory University School of Medicine, Atlanta, Georgia (Thourani); Cardiovascular Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire (Iribarne); Institut Universitaire de Cardiologie de Québec, Hôpital Laval, Quebec, Quebec, Canada (Vosine); Montréal Heart Institute, University of Montréal, Montréal, Quebec, Canada (Perrault); Department of Surgery, Keck School of Medicine, University of Southern California, Los Angeles (Bowdish); Department of Radiology, University of Pennsylvania, Philadelphia (Bilal, Davatzikos); Division of Cardiovascular and Thoracic Surgery, Department of Surgery, Duke University Medical Center, Durham, North Carolina (Smith); Department of Cardiothoracic Surgery, Montefiore Medical Center (Albert Einstein College of Medicine, New York, New York (Michler); Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, Bethesda, Maryland (Miller, Taddei-Peters); Department of Cardiovascular Surgery, Mount Sinai Health System, New York, New York (Rose); Peter Munk Cardiac Centre and Division of Cardiovascular Surgery, Toronto General Hospital, University Health Network and the Division of Cardiac Surgery, University of Toronto, Toronto, Ontario, Canada (Weisel); Department of Neurology, Rhode Island Hospital, Miriam Hospital and Warren Alpert Medical School, Brown University, Providence, Rhode Island (Furie); Division of Clinical Research, National Institute of Neurological Disorders and Stroke, Bethesda, Maryland (Moy); Cardiovascular Division, Brigham and Women’s Hospital, Boston, Massachusetts (O’Gara); Department of Neurology, University of Pennsylvania School of Medicine, Philadelphia (Messé).

Author Contributions: Ms Overbey and Dr Parides had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Mack and Ackerman are both first authors. Concept and design: Mack, Ackerman, Gelijns, Parides, Brown; Moskowitz, Moskowitz, Allaway, Thourani, Moquete, Iribarne, Perrault, Bowdish, Davatzikos, Winkle, Miller, Taddei-Peters, Rose, Weisel, Furie, Bagiella, Moy, O’Gara, Bagiella, O’Sullivan, Morgan, Mak, Taddei-Peters, Rose, Weisel, Hong, Parides, Brown; Moskowitz, Jeffries, Allaway, Moquete, Iribarne, Vosine, Perrault, Bello, Davatzikos, Mungas, Smith, Michel, O’Sullivan, Taddei-Peters, Rose, Weisel, Bagiella, O’Gara, Messé. Drafting of the manuscript: Mack, Ackerman, Brown; Moskowitz, Moquete, Iribarne, Bowdish, O’Sullivan, Bagiella, O’Gara. Critical revision of the manuscript for important intellectual content: Mack, Ackerman, Overbey, Parides, Brown; Groh, Moskowitz, Jeffries, Allaway, Thourani, Moquete, Iribarne, Vosine, Perrault, Bello, Davatzikos, Mungas, Winkle, Smith, Michel, Miller, Taddei-Peters, Rose, Weisel, Furie, Bagiella, Moy, O’Gara, Messé. Statistical analysis: Overbey, Parides, Brown; Groh, Jeffries, Allaway, Thourani, Moquete, Iribarne, Vosine, Perrault, Bowdish, Bello, Davatzikos, Mungas, Winkle, Smith, Michel, Miller, Taddei-Peters, Rose, Weisel, Furie, Bagiella, Moy, O’Gara, Messé. Obtained funding: Gelijns, Parides, Allaway, Bowdish, Bello, Davatzikos, Mungas, Winkle, Smith, Michel, Miller, Taddei-Peters, Rose, Weisel, Furie, Bagiella, Moy, O’Gara, Messé. Administrative, technical, or material support: Ackerman, Brown; Groh, Iribarne, Vosine, Bowdish, Bello, Davatzikos, Mungas, Winkle, Smith, Michel, Miller, Taddei-Peters, Rose, Weisel, Furie, Bagiella, Moy, O’Gara, Messé. Supervision: Mack, Ackerman, Gelijns, Groh, Moskowitz, Allaway, Thourani, Moquete, Perrault, Winkle, Michel, O’Sullivan, Weisel, O’Gara, Messé.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Mack reported having prior uncompensated research relationships with Edwards Lifesciences and Abbott Vascular, and serving on an executive board for Medtronic (uncompensated). Dr Brown; Groh reported receiving personal fees from Claret Medical Inc. Dr Bowdish reported receiving personal fees from Edwards Lifesciences. Dr Messé reported receiving personal fees from Claret Medical Inc, and receiving personal fees from the Yale Cardiovascular Research Group for serving on a clinical event committee. No other disclosures were reported.

Funding/Support: The trial was supported by cooperative agreement U01 HL088942 funded by the National Institute of Neurological Disorders and Stroke, the National Heart, Lung, and Blood Institute, and the Canadian Institutes for Health Research. Additional support was provided by grant R01 AG049791 from the National Institutes of Health (Dr Davatzikos). Training in use of the Embol-X (Edwards Lifesciences) and CardioGard (CardioGard) devices was provided by the companies but they did not provide financial support for the study.

Role of the Funder/Sponsor: The representatives from the National Institutes of Health were involved in study design, management, and review of the manuscript. Edwards Lifesciences and CardioGard had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript or the decision to submit for publication.

Group Information: The members of the Cardiothoracic Surgical Trials Network (CTSN) are Dennis Buxton, Nancy L. Geller, Catherine Burke, Albert Lee, and Tyrone Smith (National Heart, Lung, and Blood Institute); Iana Kogan Gombos (Canadian Institutes of Health Research); Kinjal Shah, Stephanie Pan, Alishba Aslam, Helena Chang, Melissa Chase, Kayla Dellafrate, Seth Goldfarb, Lopa Gupta, Katherine Kirkwood, Edira Dobrov, Ron Levitan, Andrea Ratner, Milena Santos, Nancy Slezd-Joyce, and Xia Ye (International Center for Health Outcomes and Innovation Research at Icahn School of Medicine at Mount Sinai; data coordinating center); Amanda Fenlon, Katherine Harrington, Kelly Hutcherson, Melissa Johnson, Jessica Jones, Megan Kolb, Sarah Lam, Lucy Miranda, Jackie Ward, Renessa Whitman, Brittany Zingler, William Ryan, Robert L. Smith, Pedro Nosnik, and Justin Whisenant (Baylor Research Institute); Edward G. Soltész, Stephanie Mick, Irene Kattzan, Brian Strippy, Shoi Smith, Michelle Garcia, and Mary Alice Bowman (Cleveland Clinic Foundation); Michael Argenziano (primary investigator), Michael Borger, Hiroo Takayama, Lyn Goldsmith, Nadia Sookraj, Talaya McCright-Gill, and Sowmya Sreekanth (Columbia University); Jock N. McCullough (primary investigator), Joseph P. DeSimone, Anthony W. DiScipio, Henry Stokes, Amanda St Ivyan, Gaylin Pett, and Jim Hart (Dartmouth-Hitchcock Medical Center); John H. Alexander, Carmelo A. Milano, Donald D. Glower, Stacey Welsh, Sarah Casalino, Victoria Johnson, Derek Smith, and Greg Tipton (Duke University); Robert Guyton, Omar Lattouf, Michael Hawk, Kim Ba, Tamara Prince, Natasha Cook, and Alexis A. Neill (Erymyan University); François Dagenais, Robert Laforce Jr, Kim O’Connor, Gladys Dussault, Manon Cauette, Hugo Tremblay, Nathalie Gagne, and...
Cerebral Embolic Protection in Patients Undergoing Surgical Aortic Valve Replacement

Original Investigation

Research

Patrick Landry (Hospital Laval), John G. Short, Reid D. Taylor, Tracy Nanny, Holly Aubart, Kristin Cross, Leslie Price, and Christina Riggsebe, and Lucy Rixey (Mission Hospital); Joseph J. Defrise Jr, Daniel J. Goldstein, Ricardo A. Bello, William Jakoboff, Kathryn Kirchhoff, Richard Zampolin, Rebecca Melli, Juan Garcia, Jon Goldenberg, and Lauren Kealy (Montefiore-Einstein Heart Center); Denis Bouchard, Michel Carrier, Jean François Tanguay, Pierre Picard, Céline Oder, Filippo Codemastri, Jonathan Lacharité, and Sophie Robichaud (Montreal Heart Institute); Keith A. Horvath (primary investigator), Philip C. Corcoran, Michael P. Siegenthaler, Mandy Murphy, Margaret Iraola, Ann Greenberg, Greg Krumkarnian, Mark Milner, and Zurab Naderashvili (National Institutes of Health Heart Center at Suburban Hospital), Bryan A. Whitson (primary investigator), Juan Crestellano, Xuan Nguyen, Mohit Datta, Asia McDavid, and Denise Fadorsen (Ohio State University Medical Center); Maral Ozouzian (primary investigator), Terry Yau, Cheryl Joaquin, Narinder Paul, Walter Kucharzyk, Nishit Fumakia, and Shakira Christie (Toronto General Hospital); John C. Mullen (primary investigator), Asvina Bissounand, and Alexandra Hipko (University of Alberta Hospital); Bradley Taylor (primary investigator), James Gammie, John Cole, Robert Morales, Kristen Mackowick, Stephanie Deasey, and Julia Collins (University of Maryland); Jesse Raiten, Cen Zhang, Mary Lou Mayer, Caitlin McDonald, Holley Fok, Breanna Moffei, Stephen Cresse, and Christine Gepty (University of Pennsylvania); Vaughn A. Starnes, David Shavale, Christi Heck, Amy Hackmann, Craig Baker, Fernando Fleischman, Mark Cunningham, Meng Law, Edward Lozano, Michelle Hernandez, and Sylvia Ramos (University of Southern California); Irving L. Cron, Karen Johnston, Ravi K. Ghanta, Leora Yarboro, Joe Carrera, Nicole Chiota-McCollum, Sandra Burks, Mike Cosner, China Ghanta, Leora Yarboro, Joe Carrera, Nicole Chiota-McCollum, Sandra Burks, Mike Cosner, China

Disclaimer: The views expressed in this article are those of the authors and do not necessarily represent the views of the National Heart, Lung and Blood Institute, the National Institutes of Health, or the US Department of Health and Human Services.

REFERENCES


