Implications from neurologic assessment of brain protection for total arch replacement from a randomized trial

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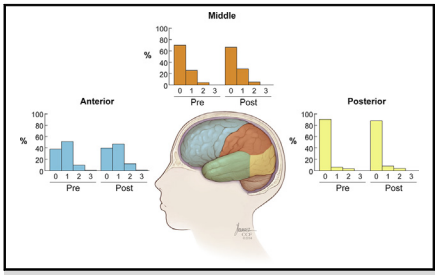
ABSTRACT

Objective: The study objective was to perform a randomized trial of brain protection during total aortic arch replacement and identify the best way to assess brain injury.

Methods: From June 2003 to January 2010, 121 evaluable patients were randomized to retrograde (n = 60) or antegrade (n = 61) brain perfusion during hypothermic circulatory arrest. We assessed the sensitivity of clinical neurologic evaluation, brain imaging, and neurocognitive testing performed preoperatively and 4 to 6 months postoperatively to detect brain injury.

Results: A total of 29 patients (24%) experienced neurologic events. Clinical stroke was evident in 1 patient (0.8%), and visual changes were evident in 2 patients; all had brain imaging changes. A total of 14 of 95 patients (15%) undergoing both preoperative and postoperative brain imaging had evidence of new white or gray matter changes; 10 of the 14 patients had neurocognitive testing, but only 2 patients experienced decline. A total of 17 of 96 patients (18%) undergoing both preoperative and postoperative neurocognitive testing manifested declines of 2 or more reliable change indexes; of these 17, 11 had neither imaging changes nor clinical events. Thirty-day mortality was 0.8% (1/121), with no neurologic deaths and a similar prevalence of neurologic events after retrograde and antegrade brain perfusion (22/60, 37% and 15/61, 25%, respectively; $P = .2$).

Conclusions: Although this randomized clinical trial revealed similar neurologic outcomes after retrograde or antegrade brain perfusion for total aortic arch replacement, clinical examination for postprocedural neurologic events is insensitive, brain imaging detects more events, and neurocognitive testing detects even more. Future neurologic assessments for cardiovascular procedures should include not only clinical examination but also brain imaging studies, neurocognitive testing, and long-term assessment. (J Thorac Cardiovasc Surg 2015;150:1140-7)



Brain imaging changes preoperatively and 4 to 6 months postoperatively according to location.

Central Message

Future neurologic assessments for cardiovascular procedures should include brain imaging studies and neurocognitive testing.

Perspective

Although this randomized trial revealed similar neurologic outcomes after RBP or ABP for total aortic arch replacement during hypothermic circulatory arrest, clinical examination for postprocedural events is insensitive, brain imaging detects more events, and neurocognitive testing detects even more. Future studies should include all these neurologic assessment modalities.

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Abbreviations and Acronyms
ABP = antegrade brain perfusion
CT = computed tomography
EEG = electroencephalography
MRI = magnetic resonance imaging
RBP = retrograde brain perfusion
TAVR = transcatheter aortic valve replacement

Supplemental material is available online.

Among cardiovascular procedures, percutaneous transcatheter aortic valve replacement (TAVR) and aortic arch replacement are considered to present the highest risk for postprocedure neurologic events.[1-15] In the Placement of AoRTic TraNscathetER (PARTNER) valve trials, risks of clinical stroke or neurocognitive deficits were 4.6% to 6.4% for transfemoral TAVR.[16,17] However, other studies have reported strokes detected by postprocedure diffusion-weighted magnetic resonance imaging (MRI) in 68% to 84% of these patients.[1,2,4] In a large retrospective study of 656 patients undergoing aortic arch replacement without adjunctive brain perfusion, the risk of clinically detectable strokes was 7%.[18] A subsequent prospective study using brain perfusion showed a 2.8% risk of stroke, but 2 to 3 weeks after surgery, 9% of patients had new neurocognitive deficits.[14] An investigation of 142 patients undergoing total arch replacement with preoperative brain MRI studies using the Scheltens scale for leukoaraiosis showed that residual focal neurologic deficits developed in 4.2%, and total white matter scores were strongly correlated with type 2 nonfocal neurocognitive changes.[10] Internet-based assessment of postoperative neurocognitive function has shown that longer duration of hypothermic circulatory arrest for these operations is associated with slow processing speed and low memory scores.[19]

Although clinical stroke risk may seem to be acceptable for both TAVR and total arch replacement, it is likely that MRI-detected strokes occur more frequently, and it is unclear how these MRI lesions are associated with neurocognitive deficits. Because of this uncertainty about (1) the importance of clinical detection of neurologic events after cardiovascular procedures, (2) the changes noted on MRI and their potential neurocognitive consequences, and (3) whether adjunctive measures protect the brain, we have explored in depth the neurologic findings from a randomized study of brain-protection strategies during aortic arch repair to discover their implications for future studies of neurologic consequences of interventions such as TAVR and aortic arch procedures that may dislodge aortic plaque material.

MATERIALS AND METHODS

Study Design

This study is based on neurologic outcomes data from a randomized single-blinded 1:1 trial of antegrade brain perfusion (ABP) versus retrograde brain perfusion (RBP) during hypothermic circulatory arrest in patients undergoing total aortic arch replacement. The trial's individual neurologic end points were (1) clinical neurologic events, (2) brain imaging changes, and (3) reliable change index on neurocognitive testing. The complete randomized trial protocol, with details of inclusion and exclusion criteria and sample size considerations, is presented in Appendix E1.

Patients

From June 2003 to January 2010, 341 patients underwent total aortic arch operations at Cleveland Clinic, of whom 122 met inclusion and exclusion criteria and provided written consent to participate in the trial (CONSORT diagram, Figure E1). One patient died after randomization but before surgery, leaving 121 evaluable patients, 60 randomized to RBP and 61 randomized to ABP. Mean age overall was 58 ± 12 years, 48 (40%) were women, 16 (13%) had a history of stroke, and 52 (43%) had a history of carotid disease, following definitions for the Society of Thoracic Surgeons National Database (http://www.sts.org/sites/default/files/documents/STSAdultCVDataSpecificationsV2_81.pdf). Eleven patients (9%) had peripheral arterial disease in addition to their aortic disease (Table 1). Forty-seven patients (39%) had undergone previous cardiac surgery.

Surgical Context and Brain Perfusion

All 121 patients underwent total arch replacement; 74 procedures (61%) were done using the elephant trunk procedure.[12] Replacement of the total aortic arch was performed using right subclavian arterial inflow, cooling to an esophageal temperature of less than 20°C using alpha-stat strategy,[11,12,14] circulatory arrest with the patient's head down and packed in ice, and CO_2 field flooding.[14] Bispectral monitoring of anesthesia depth was routine, but not continuous electroencephalography. RBP was done by perfusing the distal superior vena cava with proximal occlusion above the azygos vein; perfusion was continuous during the period of circulatory arrest, with pressure monitoring so as not to exceed 25 to 30 cm H_2O.[18] ABP, at a pressure of 45 to 60 mm Hg, involved perfusing the brachiocephalic and carotid arteries for 5 minutes approximately 10 to 15 minutes after instituting circulatory arrest using retrograde cardioplegia balloon catheters and, if needed, perfusing again after a further 15 minutes. L.G.S. performed all operations except for 3 patients.

Patients were rewarmed to more than 36°C venous temperature and weaned from cardiopulmonary bypass. Mean cardiopulmonary bypass time was 118 ± 33 minutes, circulatory arrest time was 27 ± 13 minutes, and myocardial ischemic time was 67 ± 35 minutes (Table E1). Postoperatively, all patients were placed on chronic aspirin therapy, 162 mg daily, and statins were prescribed for all with coronary artery disease or elevated lipids.

End Points

The trial's primary end point was a composite of (1) hospital death from neurologic causes, (2) postoperative clinical stroke, (3) brain imaging changes, and (4) reliable neurocognitive decline.

Clinical neurologic events. Clinical neurologic events were recorded in-hospital after the index surgery. They included stroke, visual