Novel Emboli Protection System During Cardiac Surgery: A Multi-Center, Randomized, Clinical Trial

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Background. **Stroke is a major cause of morbidity and mortality during open-heart surgery. Up to 60% of intraoperative cerebral events are emboli induced. This randomized, controlled, multicenter trial is the first human study evaluating the safety and efficacy of a novel aortic cannula producing simultaneous forward flow and backward suction for extracting solid and gaseous emboli from the ascending aorta and aortic arch upon their intraoperative release.**

Methods. **Sixty-six patients (25 females; 68 ± 10 years) undergoing elective aortic valve replacement surgery, with or without coronary artery bypass graft surgery, were randomized to the use of the CardioGard (CardioGard Medical, Or-Yehuda, Israel) Emboli Protection cannula ("treatment") or a standard ("control") aortic cannula. The primary endpoint was the volume of new brain lesions measured by diffusion-weighted magnetic resonance imaging (DW-MRI), performed preoperatively and postoperatively. Device safety was investigated by comparisons of complications rate, namely neurologic events, stroke, renal insufficiency and death.**

Results. **Of 66 patients (34 in the treatment group), 51 completed the presurgery and postsurgery MRI (27 in the treatment group). The volume of new brain lesion for the treatment group was (mean ± standard error of the mean) 44.00 ± 64.00 versus 126.56 ± 28.74 mm^3 in the control group ($p = 0.004$). Of the treatment group, 41% demonstrated new postoperative lesions versus 66% in the control group ($p = 0.03$). The complication rate was comparable in both groups.**

Conclusions. **The CardioGard cannula is safe and efficient in use during open-heart surgery. Efficacy was demonstrated by the removal of a substantial amount of emboli, a significant reduction in the volume of new brain lesions, and the percentage of patients experiencing new brain lesions.**

(Ann Thorac Surg 2014;98:1627–34)

Cardiac surgery may cause a wide spectrum of neurologic injuries, including ischemic stroke, encephalopathy, neurocognitive dysfunction and increased mortality, hospital costs, and impaired quality of life [1–3]. Embolism is considered the main mechanism of postsurgery neurologic injury [4].

Thirty percent to 50% of perioperative strokes detected with brain imaging are due to cerebral macroembolism, which can occlude flow in arteries larger than 200 μm in diameter [5–7]. Encephalopathy and neurocognitive dysfunction are believed to result primarily from cerebral microembolism [8, 9]. In such cases, flow is blocked in arteries of less than 200 μm in diameter, and the emboli are either gaseous or solid particles in composition [2]. An increased flow of macroembolism and microembolism into the cerebral circulation has been detected during various aortic manipulations performed during cardiac surgery [1, 10–12].

Several approaches have been employed to diminish the number and potential pathologic consequences of emboli released during on-pump open heart surgery, including extraaortic ultrasonic and intraaortic mechanical embolic diverting devices, and an intraaortic filtration device [13–16]. However, these devices have had

Accepted for publication June 17, 2014.

Presented at the Fiftieth Annual Meeting of The Society of Thoracic Surgeons, Orlando, FL, Jan 25–29, 2014.

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Drs Bolotin and Taggart disclose financial relationships with CardioGard.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2014.06.061

Abbreviations and Acronyms

AVR = aortic valve replacement
CABG = coronary artery bypass grafting
CVA = cerebrovascular accident
DW-MRI = diffusion-weighted magnetic resonance imaging
MMSE = Mini-Mental State Examination
NIHSS = National Institutes of Health Stroke Scale
RIFLE = risk, injury, failure, loss of kidney function, and end-stage kidney disease
TCD = transcranial Doppler

unwarranted side effects and, crucially, none have had their potential efficacy objectively evaluated by comparing preoperative and postoperative magnetic resonance imaging (MRI) scans.

The current randomized, controlled, multicenter trial is the first human study evaluating the safety and efficacy of a novel aortic cannula that produces simultaneous forward flow and backward suction to extract solid and gaseous emboli from the distal ascending aorta upon their intraoperative release. The efficacy of the novel cannula was assessed by the volume of new brain lesions measured by diffusion-weighted (DW) MRI, performed preoperatively and 5 to 7 days postoperatively.

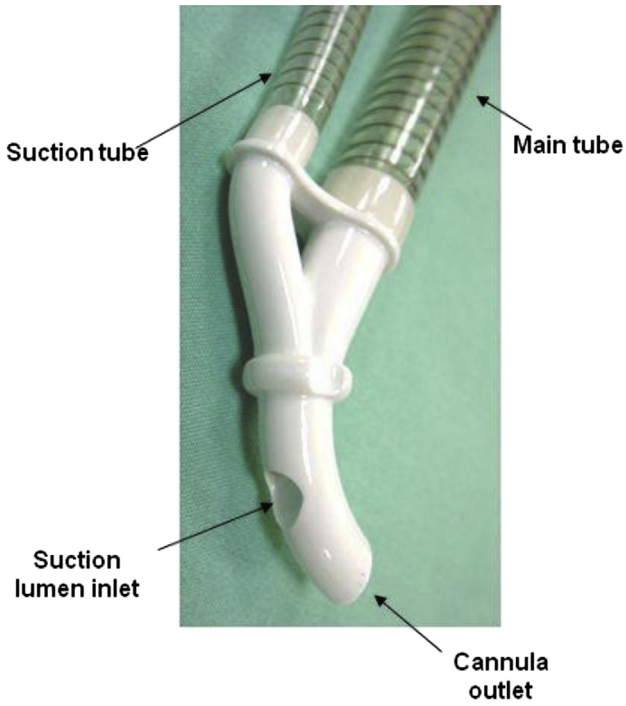

Fig 1. The CardioGard aortic cannula is a curved tip 24-French aortic perfusion cannula comprised of 2 hollow tubes, 1 for forward flow and the other for suction of embolic material.

Patients and Methods

The Institutional Review Board of all participating centers approved the study protocol in accordance with the Helsinki Declaration. All enrolled patients signed a written informed consent to participate in the study before randomization (detailed hereunder).

Aortic Cannula Description

The CardioGard aortic cannula (CardioGard Medical, Or-Yehuda, Israel) is a curved tip 24-French aortic perfusion cannula comprised of 2 hollow tubes (Fig 1). The first tube is a standard main forward-flow tube administering arterial blood into the aorta from the cardiopulmonary bypass (CPB) machine. The second tube, attached to an existing bypass vent port, is a novel element located posteriorly to the main tube; its function is to facilitate blood and particle suction, by directing the blood back to the reservoir of the CPB machine, while the retrieved embolic material is eliminated through the filter of the venous reservoir. In the current study, a 40-μm filter was attached to the suction tube lining in order to evaluate the size and weight of the emboli material captured during the procedure.

Study Design

This multicenter, prospective randomized controlled trial was the first-in-man experience with the new aortic cannula. Enrolled patients were randomized (1:1) to either CardioGard ("treatment") or standard ("control") aortic cannula, in 4 medical centers; 1 in Germany, 1 in Israel, and 2 in Switzerland.

The inclusion criteria were patients 50 years of age or older undergoing elective aortic valve replacement (AVR) or combined AVR and coronary artery bypass grafting (CABG), using CPB. Patients with fixed neurologic impairment due to previous insult were excluded.

After a preoperative assessment, which included baseline laboratory tests, neurologic evaluation, and DW-MRI, patients were randomized either to the treatment group, in which the CardioGard cannula was used, or the control group, in which a standard cannula was used. Aortic cannulation and decannulation procedures in both groups were performed using standard surgical techniques. Throughout the procedure blood flow was maintained at appropriate values. In the treatment group a constant suction rate of 1 L/minute was applied. Postoperatively, the external filter was rinsed and the captured emboli were measured for size and total weight.

Endpoints

The primary efficacy endpoint of the study was the total volume of new brain lesions measured by DW-MRI, performed preoperatively and 5 and 7 days postoperatively. The DW-MRI analysis was performed by an external core lab which was blinded to the patients' group allocation (BioImage; MRI Research & Consulting, Haifa, Israel). Additional DW-MRI related measures were the number of patients with new brain lesions, the number of new brain lesions, and the mean volume of new brain