The Risk of Neurological Dysfunctions after Deep Hypothermic Circulatory Arrest with Retrograde Cerebral Perfusion

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Objective: Retrograde cerebral perfusion (RCP) is a brain protection technique that is adopted generally for anticipated short periods of deep hypothermic circulatory arrest (DHCA). However, the real impact of this technique on cerebral protection during DHCA remains a controversial issue. *Methods:* For 344 (59.5%) of 578 consecutive patients (mean age, 66.9 ± 10.9 years) who underwent cardiovascular surgery under DHCA at the present authors' institution (1999-2015), RCP was the sole technique of cerebral protection that was adopted in addition to deep hypothermia. Surgery of the thoracic aorta was performed in 95.9% of these RCP patients; in 92 cases there was an aortic arch involvement. Outcomes were reviewed retrospectively. The focus was on postoperative neurological dysfunctions. *Results:* There were 33 (9.6%) in-hospital deaths. Thirty-one (9%) patients had permanent neurological dysfunctions and 66 (19.1%) transitory neurological dysfunctions alone. Age older than 74 years (odds ratio [OR], 1.88, $P = .023$), surgery for acute aortic dissection (OR, 2.57; $P = .0009$), and DHCA time longer than 25 minutes (OR, 2.44; $P = .0021$) were predictors of neurological dysfunctions. The 10-year nonparametric estimate of freedom from all-cause death was 61.8% (95% confidence interval, 57.8%-65.8%). Permanent postoperative neurological dysfunctions were risk factors for cardiac or cerebrovascular death (hazard ratio, 2.6; $P = .039$) even after an adjusted survival analysis ($P < .04$). *Conclusions:* According to the study findings, RCP, in addition to deep hypothermia, combines with a low risk of neurological dysfunctions provided that DHCA length is 25 minutes or less. Permanent postoperative neurological dysfunctions are predictors of poor late survival. **Key Words:** Aortic surgery—brain protection—deep hypothermia—neurological dysfunctions—quality of results improvement.

Introduction

Protection of the brain during operations on the aortic arch by perfusing cold oxygenated blood into the superior vena cava was first reported by Ueda et al in 1988.[1] The proposed benefits of this technique, which is known as retrograde cerebral perfusion (RCP), are to maintain cerebral hypothermia, flush out embolic debris and air, provide metabolic support, and allow for the removal of toxic metabolites and waste products. Although some clinical and experimental studies confirmed the limited capacity

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of retrograde perfusion to sustain cerebral metabolism,[2,3] RCP has proven effective at producing deep and homogeneous cooling of the brain hemispheres as well as the washout of solid particles and gaseous babbles from the arterial circulation of the brain.[4,5] To date there have been several retrospective reports of RCP series, many of which show improved results compared with historical control series.[6-10] However, in the absence of prospective randomized trials for the evaluation of RCP during deep hypothermic circulatory arrest (DHCA), the question remains whether the purported advantages of RCP are a factor of the sole RCP usage or are a reflection of better overall techniques and technologies in aortic surgery.

In the present study, outcomes of a significant number of cardiovascular operations, which were performed during DHCA with RCP, were reviewed retrospectively. The primary end points were the predictors of postoperative neurological dysfunctions and the safe duration of DHCA with RCP. The secondary end point was the impact of neurological dysfunctions on late outcomes of patients.

Patients and Methods

Study Patients

Between 1999 and 2015, 578 consecutive cardiovascular operations were carried out under DHCA (core temperature during circulatory arrest, 14°C-20°C) at the Cardiovascular Department of the University Hospital of Trieste, Italy. In 344 (59.5%) of these patients (mean age, 66.9 ± 10.9 years), RCP via the superior vena cava was the sole technique of cerebral protection that was adopted in addition to deep hypothermia; these patients were enrolled into the present retrospective study. A comparison between these RCP patients and 26 consecutive patients who underwent aortic surgery under DHCA alone (control group) was also performed.

Baseline characteristics of patients and surgical features were prospectively recorded for every patient in a computerized data registry (FileMaker Pro 12.0; FileMaker, Inc., Santa Clara, CA). These data are summarized in Tables 1 and 2. The risk profile of each patient was established preoperatively according to the European System for Cardiac Operative Risk Evaluation II (EuroSCORE II).[11]

Definitions

Unless otherwise stated, the definitions and cutoff values of the preoperative variables were those employed for EuroSCORE II.[11] Definitions of postoperative complications were in accordance with the internationally agreed definitions of complications after cardiac surgery.[12-14] All patients with new symptoms from the central nervous system were formally assessed by a neurologist. Neurological dysfunctions were arbitrarily divided into 2 categories: (1) temporary dysfunctions, which included transient ischemic attacks and reversible neurologic deficits such as seizures, confusion, and psychiatric disorders; and (2) permanent dysfunctions, which included permanent focal neurological dysfunctions (monoparesis/monoplegia, hemiparesis/hemiplegia, and aphasia/dysarthria) and heavy diffuse neurological deficits with decreased levels of consciousness or coma.[14] In patients with permanent dysfunctions, corresponding cerebral lesions were confirmed by computed tomography imaging.

Indications to Surgery

Indications to surgery were aortic dissection (acute, 81 patients; subacute, 10 patients; chronic, 2 patients), nondissecting aortic disease (237 patients), valve surgery within a porcelain aorta (11 patients), coronary surgery in the presence of a porcelain aorta (1 patient), extra-anatomic aortic bypass (1 patient), and pulmonary embolectomy (1 patient).

Surgical Techniques

Surgery was carried out through a median sternotomy with cardiopulmonary bypass. The ascending aorta and the femoral artery (especially for aortic dissection cases and reoperations) were the sites of initial arterial cannulation, although the aortic arch was occasionally used when required by patient pathological features or anatomy. Aortic cannulation was performed immediately after the epiaortic ultrasonography scan, which was done in every patient.[15] Since 2010 continuous intraoperative monitoring of cerebral oxygenation by near-infrared spectroscopy was introduced into clinical practice.[16] Myocardial protection was achieved either with multidose cold blood cardioplegia or (since July 2009) a single-dose crystalloid solution (Custodiol-HTK solution; Essential Pharma, Newtown, PA),[17] both delivered in antegrade and retrograde modes. A right-angled vena cava cannula was used for RCP, which was administered during circulatory arrest by way of the snared superior vena cava cannula with a flow rate up to 500 mL/min to a target central venous pressure of up to 25 mmHg. After completion of the distal aortic anastomosis (or of repair, when no aortic surgery was contemplated), full-flow cardiopulmonary bypass was reinstituted and the patient warmed.[7]

Surgery of the thoracic aorta was performed in 330 (95.9%) cases; in 92 (27.5%) patients there was an aortic arch involvement. A concomitant valve or coronary surgery was carried out in 207 (60.2%) and 123 (35.8%) patients, respectively (Table 2).

Follow-Up

An up-to-date clinical follow-up was obtained by a telephonic interview with the patients or their family. The occurrence of death during the follow-up period and the cause of death were recorded. The Katz Index of Independence in Activities of Daily Living, commonly referred