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Nadir oxygen delivery to the brain as a risk factor for post-operative neurocognitive impairment in patients undergoing coronary artery bypass grafting: A myth or fact

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ABSTRACT

Background: There are many factors that determine the best neurocognitive outcome following cardiac surgery. Optimum oxygen delivery to the tissues has always been the goal to optimum perfusion. Some patients may exhibit neurocognitive impairments in the early postoperative period; that could be easily missed clinically as they are not associated with radiographic evidence of structural brain damage. At this study we aimed to correlate the lowest oxygen delivery levels with incidence of neurocognitive impairment in the early postoperative period by Folstein test.

Methods: A non-randomized, prospective pilot study was designed to correlate the nadir oxygen delivery (DO_2) during CPB with post-operative cognitive impairment. The study included 271 patients of both sexes, an age group of 50–60 years with university level of education, scheduled for elective, isolated CABG for three vessel disease. All patients underwent pre-and post-operative neurocognitive test by a specialized neuropsychiatric doctor.

Results: with a mean nadir DO_2 of 291 mL/min/m^2 , the majority of the patients exhibited “normal” results, with a mean nadir DO_2 of 266 mL/min/m^2 92 patients showed mild impairment in their cognitive behavior, while the worst results “moderate” and “severe” were associate with means of $244,200 \text{ mL/min/m}^2$ successively.

Conclusions: The nadir oxygen delivery is a risk factor for development of post-operative neurocognitive impairment. A level below 260 mL/min/m^2 is generally associated with higher risk while a level below 220 mL/min/m^2 carries the worst prognosis.

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1. Introduction

In spite of major advances in the field of cardiopulmonary bypass (CPB) and evolvement of new techniques in renal and brain protection; there still some major debates regarding the “optimal perfusion strategy” to avoid brain and kidney CPB related adverse effects [1].

The term “optimal perfusion” itself is a little bit elusive since it depends on many co-factors reacting together differently under various pathophysiologic conditions, making the hemodilution, perfusion pressure, hematocrit and pump flow among the major players in that matter [2]. On the other hands, these factors are now agreed to have a limited role; making the tissue Oxygen delivery (DO_2) the sole most important determinant in achieving “optimal perfusion” [3].

Many authors discussed the post bypass renal impairment, a few authors illustrated brain related structural damages, but even fewer tackled the “easily missed” minor cognitive and memory impairments post cardiac surgery [4].

Postoperative cognitive dysfunction (POCD) has been reported in 14–48% of patients undergoing coronary artery bypass grafting (CABG) [5]. only a few percentage of them shows structural damage by Magnetic Resonance Imaging (MRI) [6].

Among the risk factors contributing to POCD, the truth we are operating on an aging population, with atherosclerotic disease that has its natural history affection towards medium sized arteries in the myocardium and the cerebrum. Also, the surgical procedure itself involving debris, microthrombi and manipulations all along with the circumstances of CPB.

“Mini–Mental State Examination (MMSE)” or Folstein test, is a widely used clinical instrument to detect “dementia”. Having a specificity of 86.36% and sensitivity of 86.36% in patients with 5 or more years of schooling [7].

It consists of 30 points score divided into 11 questions, covering five areas of cognitive functions: “orientation, registration, attention and calculation, recall, and language” [8] ([Appendix 1](#)).

It is used primarily for screening of dementia and differentiating organic from functional cognitive impairments. Though presence of organic dysfunction may interfere with the results, careful test conduction must be carried out by a specialized person to detect minor changes in the follow up visits [9].

At this study, we aimed to correlate between the levels of lowest DO_2 to the brain and the incidence of new neurocognitive impairment in the early post-operative period “in the absence of structural brain damage” i.e. proved radiologically.

2. Patients and methods

A non-randomized, prospective pilot study was designed to correlate the nadir DO_2 during CPB with “new” POCD. The study included 271 surviving patients, of both sexes, an age group of 50–60 years with university level of education, scheduled for elective, isolated CABG for three vessel disease (regardless of final number of grafts). All patients with history of psychiatric, neurological, diabetic and/or any other comorbidities including physical disability were excluded. The study was conducted in the Cardio-thoracic surgery Academy, Ain Shams University, Cairo, Egypt, after gaining the approval of the affiliated ethical committee and patient informed consent. The study took place from May 2014 till October 2017.

All the patients underwent full preoperative assessment as per institution protocol. All the patients underwent preoperative screening test for detection of cognitive impairment: “**Mini–Mental State Examination (MMSE) or Folstein test (MMSE)**”, conducted by the co-author in the Department of Neuropsychiatry, Faculty of medicine, Ain Shams University, Cairo, Egypt.

All anesthesia and premedication were unified in all patients, standard ECG monitoring, arterial and central venous cannulation. Usual draping and disinfection followed by median sternotomy, conduit harvesting and purse suturing for cannulation. After systemic heparinization and achieving acceptable activated clotting time, CPB was commenced and revascularization done as possible.

The CPB was conducted under moderate hypothermia 28–32 C using alpha stat bypass with tight glycemic control keeping blood sugar ≤ 200 mg/dl, Hct level was kept at an average of $24 \approx$ Hemoglobin of 8 gm/dl. The initial pump flow was set 2.4–2.8 L/minute/ m^2 and modulated by perfusionist as needed. The mean perfusion pressure was maintained from 50 to 60 mmHg.

The CPB circuit consisted of a Capiiox[®] RX15 oxygenator (Ref. 3CX*RX15RW40 Oxygenator, 1.5 m^2 surface area, 0.5–5.0 LPM flow rate, with 4000 mL hardshell reservoir with Xcoating[™] surface coating), Terumo, Tokyo, Japan. The hardware consisted of a Stöckert S5 heart-lung machine (Sorin Group, Munich, Germany) and a Stöckert S3 heart-lung machine (Sorin Group, Munich, Germany), a Stöckert Heater Cooler System 3T (Sorin Group, Munich, Germany). Priming solutions consisted of 1000 mL of Lactated Ringer solution, Mannitol 0.5–1 gm/Kg, 8.4% Sodium Bicarbonate 1 mEq/Kg and 10,000 IU of heparin. Custodiol-HTK cardioplegic solution was delivered to establish and maintain cardiac arrest. After cross-clamping of the aorta approximately 1–2 L of Custodiol-HTK was infused into the ascending aorta over 6–8 min. Additional doses of 100–200 mL

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