



## The Effects of Heart-Lung Bypass on Endothelial Function of Patients with Open Heart Surgery

Mohammad Borzouee<sup>1,2,\*</sup>, Ali Reza Nezami<sup>1</sup>, Gholamhosein Ajami<sup>1,2</sup>, Hamid Amoozegar<sup>1,2</sup>, Ahmad Ali Amirghofran<sup>1,3</sup>

<sup>1</sup> Cardiovascular Research Center, Shiraz University of Medical Sciences, Shiraz, IR Iran

<sup>2</sup> Pediatric Cardiology Division, Pediatric Department, Shiraz University of Medical Sciences, Shiraz, IR Iran

<sup>3</sup> Cardiac Surgery Division, Department of Surgery, Shiraz University of Medical Sciences, Shiraz, IR Iran

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### ABSTRACT

**Background:** Endothelium is an essential organ for maintaining an adequate vascular tone and preventing the pathological process of atherosclerosis. Heart-lung machine is a mechanical support for maintenance of blood circulation during open heart surgery. It has been shown that flow of blood through this circuit can induce complement activation, endotoxins production, and release of many inflammatory mediators.

**Objectives:** Cardiopulmonary Bypass (CPB) has some detrimental effects on endothelial function. Flow Mediated Dilation (FMD) is also a noninvasive method for evaluation of endothelial function.

**Patients and Methods:** This study was conducted on 22 patients who were admitted in cardiac surgery ward for open heart operation and met the inclusion criteria of the study. Brachial artery FMD was measured the day before and 2 days after CPB.

**Results:** The mean duration of CPB was 62.95 minutes. The mean percent of FMD changes was measured and compared before and after CPB (4.29 and 0.03 vs. 1.38 and 1.99, < 0.001). The results showed a significant relationship between CPB and brachial endothelial function.

**Conclusions:** This study revealed the influence of CPB on endothelial function. Yet, more studies are necessary to confirm this important issue, and decline in use of CPB is appreciated.

### ► Implication for health policy/practice/research/medical education:

Improvements in surgical techniques and technologies and utilization of more minimal invasive procedures reduce the negative effects of cardiopulmonary bypass.

### 1. Background

There is a significant systemic inflammatory response triggered by Cardiopulmonary Bypass (CPB) during open-heart surgery. Despite significant changes and improvements in surgical techniques, inflammation remains a significant problem (1-3). Other factors, such as anesthesia, oxidative stress, temperature, and genetic predisposition, may play a role, as well. All these factors play important roles in patients' physiological and pathophysiological status. Endothelium-

Derived Relaxing Factors (EDRFs), such as Nitric Oxide (NO), prostacyclin (PGF<sub>2</sub>), and hyperpolarizing factor (EDHF), all regulate the vascular tone. Other complex mechanisms, such as humoral and cellular immune pathways and altered flow state, are also involved. A two-staged Systemic Inflammatory Response Syndrome (SIRS) is accompanied by the organism's compensatory responses to regain homeostasis. Moreover, biomarkers, such as plasma concentrations of soluble P-selectin (sP-s), E-selectin (sE-s), tetranectin (TN), and vonWillebrand factor (vWF) levels, and Angiotensin-Converting Enzyme (ACE) activity are altered during and after cardiac surgery (4).

\*Corresponding author: Mohammad Borzouee, Cardiovascular Research Center, Research Tower, Khalili Aenue, Shiraz, Iran, Tel/Fax: +98-71136281561, E-mail: borzoeem@sums.ac.ir

## 2. Objectives

The present study aims to assess the effects of heart-lung bypass on endothelial function of patients with open heart surgery.

## 3. Patients and Methods

The present study was conducted at Nemazee Cardiac Surgery Department, Shiraz, Iran which is a tertiary center for patients with cardiovascular diseases. The study was approved by the Ethics and Research Committee of Shiraz University of Medical Sciences. Besides, all the patients provided written informed consents for taking part in the study. All the patients who were admitted for open heart surgery and use of CPB were enrolled and those who had prolonged CPB (more than 2.5 hour), severe anemia, systemic hypertension, or smoked were excluded from the study.

After taking the patients' history, their physical exam characteristics, including sex, age, weight, height, and body mass index, were recorded. Blood pressure was measured after the patients had rested for 10 minutes. Endothelial function was assessed by Flow Mediated Dilation (FMD) after 4 hours fasting on the day before and the second day of CPB.

FMD is a noninvasive method for evaluation of endothelial function by sonography. Diameter of brachial artery was measured before and after a 5-minute ischemia in the forearm. Ischemia was induced by an inflated blood pressure cuff about 50 mmHg above systolic pressure for 5 minutes. Then, the cuff was released and assessment was done on the artery distal to the pressure site. Shear stress after increased arterial circulation and ischemia increases NO which induces vasodilatation. The percentage of increased brachial artery diameter to the original diameter yields the index of endothelial function. In this study, all the measurements were performed by a pediatric cardiology fellowship and the study was done by vascular probe of a Mylab 30 Gold echocardiography machine. The patients were on fasting for at least 4 hours, did not use caffeine, vasoactive, or vasodilator agents, and were at rest. They were in supine position at room temperature for 10 minutes. Brachial artery was assessed in an extended right arm and forearm 2-3 cm proximal to the elbow line and transducer in a 70 - 80 degree angle from medial of body. Electrocardiography was also obtained simultaneously.

FMD as the percentage of change in vascular diameter at hyperemia and ischemia was computed using the following formula:  $FMD = (D2 - D1)/D1 \times 100$ , where D1 was vessel diameter at rest and D2 was vessel diameter during reactive hyperemia.

The study data were analyzed using T-test and  $P < 0.05$  was considered as statistically significant. The variants in this study included brachial artery diameter at rest and after CPB, duration of ischemia and hyperemia, and percentage of difference between these measurements at 2 conditions.

## 4. Results

This study was conducted on 22 patients (10 males and 12 females) who matched the inclusion criteria. The patients' mean age was  $61 \pm 4.4$ . Among the participants, 19 had

coronary artery disease with the mean involvement duration of  $4.3 \pm 1.2$  years and were on nitroglycerin, but stopped statines and antiplatelet (aspirin for 7 days) before the operation. Three patients had valvular disease. None of the patients used inotropes and pre-operation drugs on the second day after the operation. The mean duration of CPB was  $62.9 \pm 19.1$  minutes. In addition, the mean brachial arterial diameter was  $4.68 \pm 0.56$  mm before CPB at rest and  $4.89 \pm 0.79$  mm before CPB during hyperemia. These measures were respectively obtained as  $4.9 \pm 0.74$  and  $4.97 \pm 0.79$  mm after CPB at rest and during hyperemia. The mean difference of brachial artery diameter of brachial artery was  $4.29 \pm 3.03$  before and after CPB. The results revealed no significant difference between pre- and post-CPB as well as between rest and hyperemia conditions regarding the mean brachial artery diameter ( $P = 0.068$  and  $P = 0.519$ , respectively). However, the mean percentage of differences of brachial artery diameter pre and post CPB was statistically significant ( $P < 0.001$ ).

## 5. Discussion

CPB and cardioplegic arrest remain the most popular techniques in open heart surgery (1, 3). However, both can directly or indirectly result in cardiac morbidity following surgery. The genetic background and its relationship with the inflammatory response during open heart surgery is a recent interesting development. In the present study, endothelial function was assessed by FMD in the patients before and after CPB. The study results revealed a statistically significant difference between the percentage of change in brachial artery pre- and post-CPB ( $1.38 \pm 1.99$  and  $4.29 \pm 3.03$ , respectively;  $P < 0.001$ ). Such side effects of CPB on vascular endothelium can be prevented by the use of this minimally invasive technique. It should be noted that the researchers could find no similar studies to compare the results. Up to now, numerous anti-inflammatory techniques and pharmacological agents, including corticosteroids, aprotinin, leukocyte filtration, heparin, and NO donor compounds, which largely aim at coping with CPB have been used in cardiac surgery (5-8). Selective pulmonary vasodilators; i.e. iNO and iloprost, significantly reduced PHT after weaning from CPB (1). Also, administration of sodium nitroprusside and NO donor compound at a non-vasodilatory dosage in the patients undergoing Coronary Artery Bypass Graft (CABG) on CPB reduced the myocardial inflammatory response and improved postoperative cardiac pump function (9). Overall, our study revealed that endothelial function is still an important issue and recommended to reduce utilization of CPB.

CPB remains the most popular technique during open heart surgery and FMD is an instrument for assessment of adverse effects on endothelial function. However, more studies are necessary to confirm this issue.

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### Authors' Contribution

Alireza Nezami: Data collection, Gholamhosein Ajami: Revision of the manuscript, Hamid Amoozgar: Statistical analysis of the data, Mohammad Borzouee: Performance of the study, Ahmad Ali Amirghofran: Data collection

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