Non-extracorporeal circulation for coronary artery bypass graft surgery is more beneficial than extracorporeal circulation

F.-Y. YANG\(^1\), Y.-Z. BAO\(^1\), F.-S. LIU\(^1\), Y.-C. ZHU\(^1\), J. ZHENG\(^2\), J.-H. ZHANG\(^3\), X.-F. ZHENG\(^4\), G.-C. WEI\(^1\)

\(^1\)Intensive Care Unit, The People’s Hospital of Laiwu City, Laiwu, Shandong Province, China
\(^2\)Department of Thoracic Surgery, The People’s Hospital of Laicheng District in Laiwu City, Laiwu, Shandong Province, China
\(^3\)Intensive Care Unit, Affiliated Hospital of Qingdao University, Qingdao, Shandong Province, China
\(^4\)Burn Center, Changhai Hospital Affiliated to Second Military Medical University, Changhai Road, Shanghai, China

**Abstract.** – **OBJECTIVE:** The objective of this study was to compare coronary artery bypass graft (CABG) surgery with non-extracorporeal vs. extracorporeal circulation. The study outcomes included operative time, number of graft vessels, pulmonary infection rates, and systemic inflammatory markers.

**PATIENTS AND METHODS:** 96 patients received selective CABG, either with non-extracorporeal (study group; \(n = 48\)) or extracorporeal circulation (control group; \(n = 48\)). Operative time, pulmonary infection rates, and blood levels of inflammatory markers TNF-\(\alpha\), IL-6, and IL-8 before and 4, 24, and 48 hours after the surgery were quantified. Graft vessels were quantified using computed tomography.

**RESULTS:** Operative time was significantly shorter in study group (4.58 ± 0.91 vs. 5.36 ± 1.12 hours in control group; \(p < 0.05\)). The number of graft vessels and pulmonary infection rates were comparable between both techniques. However, systemic inflammatory markers were significantly lower in study group at 4 and, partly, 24 hours after the surgery.

**CONCLUSIONS:** Extracorporeal circulation prolongs operation and can aggravate systemic inflammatory response. Therefore, CABG with non-extracorporeal circulation offers more beneficial outcomes.

**Key Words:** Pulmonary infection, Inflammation, markers, Non-extracorporeal circulation, Extracorporeal circulation, Coronary artery bypass grafting.

**Introduction**

The morbidity due to coronary heart disease has markedly increased in recent years\(^{1-3}\). One of the treatment options for coronary heart disease is coronary artery bypass grafting (CABG)\(^{4-6}\). CABG with non-extracorporeal circulation can avoid the injury associated with conventional CABG, which could be beneficial to protect cardiopulmonary function, decrease the prevalence of brain, lung and kidney complications, and minimize arrhythmias. Thus, CABG with non-extracorporeal circulation has been an effective and safe minimally invasive intervention for coronary heart disease\(^{7-10}\). However, CABG with extracorporeal circulation still remains the main therapeutic method for heart surgery. Little is known about postoperative pulmonary infection rates and systemic inflammatory response on CABG when non-extracorporeal circulation is used, especially when compared with extracorporeal circulation.

To address this knowledge gap, here we compared outcomes of CABG with non-extracorporeal vs. extracorporeal circulation. As treatment outcomes, operative time, number of graft vessels, pulmonary infection rates, and levels systemic inflammatory markers were analysed.

**Patients and Methods**

**Patients**

The study participants were 96 patients who received selective CABG in The People’s Hospital of Laiwu City, The Affiliated Hospital of Qingdao University, Changhai Hospital, and The People’s Hospital of Laicheng District in Laiwu City between October, 2012, and August, 2013, and were then transferred into intensive care units. The patients were divided into two groups that were respectively subjected to the different
surgical methods. Patients who received CABG with non-extracorporeal circulation comprised study group (n = 48; 32 male and 16 female patients), while patients who received CABG under extracorporeal circulation comprised control group (n = 48; 34 male and 14 female patients). The patient age ranged from 36-66 years, with average ages being comparable between study and control groups (respectively, [mean ± SD] 54.92 ± 5.17 vs. 56.23 ± 4.56 years).

Exclusion criteria were (1) preoperative pulmonary disease, (2) fever, (3) liver or kidney disease, (4) treatment with calcium channel blockers, non-steroidal anti-inflammatory analgesic, or glucocorticoids within 2 weeks before the surgery, (5) need for other surgeries (e.g., resection of ventricular aneurysm, cardiac valve replacement, etc), and (6) positive inflammatory markers (e.g., positive antistreptolysin O test).

The study protocol was approved by the Ethics Committee. All patients were informed about the advantages and disadvantages of the treatment. Then, the patients gave informed consents to participate in the study.

**Operation Technique**

Median sternotomy was used in all patients. Patients in study group were connected to extracorporeal circulation machine (SC III type artificial heart-lung machine; Berlin, Germany), which was prepared without priming. During the surgery, different coronary artery branches were exposed according to the position, and 1.0 mg/kg heparin for semi-heparinization was given after completing the internal mammary artery separation. The activated clotting time was maintained at more than 250 sec. Conventional extracorporeal circulation was established in control group, with high-potassium cold crystalloid cardioplegic solution for bridge irrigation to protect the myocardium. The rolling axial flow pump and membrane oxygenator were used. First, the distal coronary artery was anastomosed. Then, the anastomosis of the side end was completed with an aortic sidewall forceps after declamping aorta.

After surgeries were completed, protamine was used to neutralize heparin at a 1:1.3 ratio. Patients were then transferred to the intensive care units for further treatment after surgery.

**Study Outcomes**

We recorded operative time and number of graft vessels. Graft vessels were quantified by computed tomography.

In addition to the above, blood specimens were collected at 4 time points (before and 4, 24, and 48 hours after the surgery). Two ml of fasting venous blood samples were collected in the morning at the above time points and centrifuged to obtain serum. As inflammatory markers, tumor necrosis factor (TNF-α), interleukin (IL)-8, and IL-6 were quantified by respective ELISAs (Wuhan Boster Biological Engineering Co., Ltd, Wuhan, China).

Finally, we assessed the rates of pulmonary infections. To detect the pathogens, sputum samples were collected in sterile containers and immediately sent for microbiology and virology analyses. The pathogens were detected according to the guidelines of the Clinical and Laboratory Standards Institute.

**Statistical Analysis**

The SPSS version 19.0 (International Business Machines Corporation, Beijing, China) was used to analyze the study’s findings. Quantitative data were presented as mean ± SD, and differences were compared using the *t* test. Qualitative data were presented as absolute numbers and proportion of positive cases. The *p* value of < 0.05 was considered as significantly significant.

**Results**

**Operative Time and Number of Graft Vessels**

Operative time was significantly shorter in study group (4.58 ± 0.91 vs. 5.36 ± 1.12 hours in control group; *p* < 0.05, Table I). However, the number of graft vessels was comparable between study and control groups (Table I).

**Systemic Inflammatory Markers**

The levels of TNF-α, IL-6, and IL-8 did not statistically differ between study and control groups before the surgery. The levels of these markers increased significantly during the early hours after the surgery and fell back to normal levels at later time points (Table II). Specifically, the levels of TNF-α and IL-6 were significantly higher at 4 and 24 hours after the surgery in both study and control groups (*p* < 0.05 vs. before the surgery, all comparisons; Table II), and normalized at 48 hours after the surgery. IL-8 showed a more short-lived surge in blood levels, with only the levels at 4 hours after the surgery being significantly different to pre-surgery levels (Table II).
Importantly, all tested markers were markedly higher in control patients ($p < 0.05$; Table II).

**Prevalence of Pulmonary Pathogens**

Among patients of study group, there were 6 patients with virus infections, 2 patients with infections with gram positive bacteria, and 10 patients with detected Gram negative bacteria (Table III). Patients of control group showed comparable rates of pulmonary infections: 10 patients with virus infections, 6 patients with infections with gram positive bacteria, 2 patients with *Mycobacteria tuberculosis*, 6 patients with detected gram negative bacteria, and 2 patients with co-infections (Table III).

**Discussion**

Many studies demonstrated that extracorporeal circulation causes systemic inflammatory response manifested by up-regulated systemic levels of TNF-α, IL-8, and IL-6, with negative implications for the body (myocardial depression, cognitive disorder, ischemia-reperfusion injury, capillary leak syndrome, etc)\(^{11-17}\). In contrast, in CABG with non-extracorporeal circulation, these adverse reactions are avoidable\(^{18,19}\).

TNF-α, IL-8 and IL-6 are important modulators of immunity and inflammatory response\(^{13,20-21}\). Specifically, TNF-α, IL-8, and IL-6 ignite systemic inflammation, as reflected by the severity of systemic inflammatory response\(^{14,22,23}\). TNF-α is closely associated with activation of many inflammatory cells\(^{24}\). IL-8 exerts chemotactic effects on T basophil granulocytes, T lymphocytes, and neutrophils\(^{13}\). IL-6 modulates activity of B cells, T cells, hepatic cells, and macrophages\(^{25}\). In our study, systemic levels of the above inflammatory markers were significantly lower in patients undergoing CABG under non-extracorporeal circulation.

---

**Table I.** Operative time and number of graft vessels.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Patients, number</th>
<th>Operative time, hours</th>
<th>Number of graft vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study group (GABG with non-extracorporeal circulation)</td>
<td>48</td>
<td>4.58 ± 0.91*</td>
<td>3.01 ± 0.62</td>
</tr>
<tr>
<td>Control group (CABG with extracorporeal circulation)</td>
<td>48</td>
<td>5.36 ± 1.12</td>
<td>3.74 ± 0.76</td>
</tr>
</tbody>
</table>

_Footnote:_ Data are presented as mean ± SD. *$p < 0.05$ vs. CABG with extracorporeal circulation.

**Table II.** Systemic inflammatory markers before and after the surgery.

<table>
<thead>
<tr>
<th>Inflammatory factor</th>
<th>Groups</th>
<th>Before the surgery</th>
<th>After the surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 hours</td>
</tr>
<tr>
<td>TNF-α, ng/ml</td>
<td>Study group (CABG under non-extracorporeal circulation)</td>
<td>8.1 ± 4.2</td>
<td>12.5 ± 7.4* #</td>
</tr>
<tr>
<td></td>
<td>Control group (CCABG under extracorporeal circulation)</td>
<td>8.4 ± 5.3</td>
<td>47.2 ± 20.1</td>
</tr>
<tr>
<td>IL-8, ng/ml</td>
<td>Study group (CABG under non-extracorporeal circulation)</td>
<td>73.8 ± 12.8</td>
<td>95.1 ± 27.8** #</td>
</tr>
<tr>
<td></td>
<td>Control group (CCABG under extracorporeal circulation)</td>
<td>76.5 ± 24.7</td>
<td>147.4 ± 57.6</td>
</tr>
<tr>
<td>IL-6, ng/ml</td>
<td>Study group (CABG under non-extracorporeal circulation)</td>
<td>10.8 ± 25.7</td>
<td>27.3 ± 69.9* #</td>
</tr>
<tr>
<td></td>
<td>Control group (CCABG under extracorporeal circulation)</td>
<td>10.4 ± 35.4</td>
<td>48.5 ± 129.4*</td>
</tr>
</tbody>
</table>

_Footnote:_ Data are presented as mean ± SD. *$p < 0.05$ vs. before the surgery; *$p < 0.05$ vs. control group.
real circulation. Another beneficial effect of this intervention is that operative time is significantly shorter.

**Conclusions**

CABG with non-extracorporeal circulation offers more beneficial outcomes compared with the procedure utilizing extracorporeal circulation.

**Conflict of Interest**

The Authors declare that there are no conflicts of interest.

**References**


4) **BABBAKOVA IU V, KAZACHEK IA V, GRIZDEVA OV, SERGEEV T, GRIGOREV AM, VANKOV SV.** [The dynamics of C-reactive protein in the process of coronary artery bypass grafting in patients with ischemic heart disease]. Klin Lab Diagn 2013; 3-6. in Russian.


11) **KAZMIONCZAK E, GRAJEK S, KOWAL J, CHMARA E, GRYGIER M, PEDA M, BODZIANSKI P, CISELEWSIC A, JABLECKA A.** Prognostic usefulness of IL-6 and VEGF for the occurrence of changes in coronary arteries of pa-


16) Simao AP, Almeida TM, Mendonca VA, Santos SA, Gomes WF, Coimbra CC, Lacerda AC. Soluble TNF receptors are produced at sites of inflammation and are inversely associated with self-reported symptoms (WOMAC) in knee osteoarthritis. Rheumatol Int 2014; 34: 1759-1763.


