Institutional report - Cardiopulmonary bypass

A new extracorporeal vacuum-assisted device to optimize cardiopulmonary bypass. Comparison with the conventional system

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Abstract

Miniaturized cardiopulmonary bypass (CPB) systems, though more biocompatible, are limited by not being adaptable to all cardiac surgical operations. We evaluate a versatile CPB system (extracorporeal vacuum-assisted device optimized (EVADO)) based on the elimination of roller pumps, separation of extracavitary suctioned blood and state-of-the-art technology for oxygenator systems and digital control. We randomized 165 patients to either EVADO or conventional CPB (cCPB). Surgery could be completed in all cases without conversion to cCPB. The use of EVADO significantly reduced the intraoperative haemolysis (lesser increase in free hemoglobin, \( P<0.001 \) vs. control, and lesser decrease in haptoglobin levels, \( P=0.001 \) vs. control). Among patients who were submitted to EVADO, postoperative bleeding (\( P=0.004 \)), transfusions (\( P=0.046 \)), rate of revision for bleeding (\( P=0.03 \)), rate of postoperative atrial fibrillation (\( P=0.007 \)), time to extubation (\( P=0.02 \)) and ICU stay (\( P=0.04 \)) were reduced. The clinical benefits associated with the EVADO may be due to better end-organ perfusion, lesser impairment of the coagulation and inflammatory reaction.

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Keywords: Cardiopulmonary bypass, components; Cardiopulmonary bypass, complications; Outcomes

1. Introduction

The conventional cardiopulmonary bypass (cCPB) is associated with haemodilution, systemic inflammatory reaction and transfusion of blood products [1]. The miniaturized cardiopulmonary bypass (mCPB) circuits have been proposed to minimize such effects. However, their employment is limited due to the possibility of air leakage into the circuit [2]. CPB-related morbidity is a major issue given the worsening risk profile of the surgical candidates. We propose a combination of standard-of-care technologies for cCPB [extracorporeal vacuum-assisted device optimized (EVADO)] aimed at optimizing the biocompatibility of CPB [3–6].

We report the results of a randomized study aimed at comparing EVADO with cCPB in patients undergoing a miscellaneous of cardiac operations.

2. Materials and methods

We aimed to analyse the impact of the EVADO on perioperative haemolysis and blood loss vs. cCPB. Study endpoints were: 1) free haemoglobin (FHB) levels; 2) haptoglobin (HPT) levels; 3) hourly and total rates of mediastinal bleeding; and 4) rate of transfusion of blood products.

We prospectively selected patients according to the following criteria:

- Elective, primary cardiac surgery (either coronary, valvular, aortic or combined). Complete CPB and cardiopulmonary arrest had to be foreseen.
- We excluded patients with renal or liver failure, obesity, uncompensated diabetes, autoimmune disease, active infection, any immunosuppressant therapy or coagulation disorder. Patients undergoing surgery with circulatory arrest and/or more than mild systemic hypothermia, or having preoperative haematocrit (Hct) <27% were also excluded.

The enrolled patients were randomized to surgery using either the EVADO (group B) or a cCPB (group A, control). The patients who received perioperative transfusion of blood products or exhibited procalcitonin levels >0.5 ng/ml were excluded from the assessment of the biochemical parameters. HPT is known to be significantly affected by elevated procalcitonin plasma concentrations.

The present investigation was approved by the Institutional Review Board and a written informed consent was obtained from each patient. There are no conflicts of interest in connection with the study.
The EVADO is a combination of state-of-the-art cCPB technologies, designed to minimize its side effects. Blood–air interface is present within the circuit reservoir. The system components are listed below.

- The ADMIRAL oxygenator (Eurosets, Medolla, Italy). This is characterized by low priming volume (190 ml), limited (1.35 m²) contact surface area and separation of the pericardial blood from the intracavitary suction blood. The pericardial blood is collected separately, and can be processed or re-injected, if needed. The oxygenating module is treated with phosphorylcholine.
- The HARMONY Smart Suction System (Haemonetics, Braintree, MA, USA). This automatically regulates the flow rate and pressure of aspiration of extracavitary blood. The flow rates may vary between 0.5 and 4 l/min.
- A pumpless, vacuum-assisted venous drainage (VAVD) system. This module is managed by an Amvex 100 digital controller, which regulates both the venous return flow and the intracavitary vent flow (pressures ranging between –20 and –45 mmHg).
- Heparin-coated circuits.
- Centrifugal pumps. No roller pumps are used for the suckers.

In the control group, the ADMIRAL oxygenator, the VAVD plus conventional roller pumps and heparin-coated circuits were adopted. Blood aspiration from both the cardiac cavities and the extracavitary space was obtained by roller pumps and no separation of pericardial suction blood was performed.

A Stockert SIII (Sorin Group, Saluggia, Italy) heart/lung machine and the same cannulae was employed in both groups. The priming volume was 1000 ml in group A, and 700 ± 50 ml in group B \( (P<0.001) \). Mild hypothermia was employed in patients with carotid stenosis. Heparin reversal was obtained with 0.5–0.75 mg of protamine for every 100 units of heparin.

Anaesthesia was obtained by fentanyl, midazolam and rocuronium. Concentrated red cells (CRC) were transfused whenever haemoglobin (Hb) concentrations fell below 6 g/dl during surgery or below 8 g/dl during the intensive care unit (ICU) stay. Blood isothermic or cold crystalloid St. Thomas’ solution were used for myocardial protection.

Hct, Hb, FHb and HPT were measured before establishment of CPB and at five, 30 and 60 min, thereafter. HPT is a plasma glycoprotein that binds FHb; its levels decrease in the event of intravascular haemolysis. The FHb and HPT levels observed at each timepoint were expressed as the absolute FHb concentration.

Continuous variables are presented as mean ± standard deviation (S.D.) or as median and inter-quartile (IR) range. Inter-group differences were analysed with the Student’s t-test or the Mann–Whitney U-test. Categorial variables are given as percentages. Based on historical data, sample size calculation revealed that a total of 27 patients per study group would suffice to detect with a 0.9 power a statistically significant difference, if any, in FHb and HPT serum levels during CPB. Minor postoperative morbidity was defined as any of: respiratory insufficiency, renal failure, prolonged (>24 hours) inotropic support. Major postoperative morbidity was defined as either stroke or acute myocardial infarction. The occurrence of postoperative atrial fibrillation was recorded through continuous heart rhythm monitoring or telemetry until the fifth postoperative day.

The alpha level was 0.05. The SPSS 13.0 software for Windows (SPSS Inc, Chicago, IL, USA) was used.

3. Results

One hundred and sixty-nine patients were eligible for enrolment. Four patients refused the randomization, and the remainders were assigned to either study group. Fifteen patients encountered one or more posthoc exclusion criteria. Therefore, 73 and 77 subjects were included in the control (A) and EVADO (B) group, respectively, and completed the assessment of all the study endpoints. The study design is summarized in Fig. 1.

The two groups were similar with respect to the pre- and intraoperative features and to the type of surgery received (Tables 1 and 2). The operation could be successfully completed in all patients undergoing CPB with EVADO. In no instance, was the anaesthesiological team forced to reinfuse the extracavitary-suctioned blood during the operation.

The average value of the absolute FHb concentration increased from the baseline to the last available timepoint. Such an increase was statistically significant only in the control group \( (P<0.01) \), but not in the EVADO group \( (P=0.09) \). The mean HPT level increased in both groups, and the difference was statistically significant in the control group only \( (P=0.019 \text{ vs. } P=0.07) \). The percentage increase in the mean FHb levels was significantly higher in...
Control group

EV ADO group

vs. the EV ADO group

the first 12 postoperative hours was larger in the control group vs. the EV ADO group at both 30 and 60 min after the establishment of CPB (Fig. 2a). There was a significantly larger HPT percent decrease in patients receiving cCPB (P = 0.001 at both 30 and 60 min) (Fig. 2b). The average total blood loss during the first 12 postoperative hours was larger in the control vs. the EV ADO group (P = 0.004) (Fig. 3a). The difference in bleeding hourly rates was statistically significant at the first two hours after surgery (Fig. 3b). The average number of CRC units administered per patient was statistically lower in the control vs. the EV ADO group (1.85 vs. 0.95, respectively, P = 0.046). Nine vs. six patients (control vs. EVADO) required CRC transfusion intra- or postoperatively (P = 0.4). The average number of platelets and fresh frozen plasma transfused was not statistically different among groups, although both were consistently lower in the EVADO group (platelets: 0.22 vs. 0.08 units per patient; plasma: 0.36 vs. 0.1 units per patient).

The rates of major and minor postoperative morbidity were comparable among the groups, except for the rate of revision for bleeding (five in the control group vs. zero in the EVADO group, P = 0.02), and for postoperative atrial fibrillation. This occurred in 31 (42%) cases of the control group vs. 11 (14%) cases of the EVADO group (P < 0.001). The EVADO was also associated with a shorter ICU stay (38.9 vs. 34.9 hours, P = 0.04) and a shorter time to extubation (10.2 vs. 8.9 hours, P = 0.02). There were no cases of operative mortality.

Table 1. Clinical characteristics of the study groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control group (n = 73)</th>
<th>EVADO group (n = 77)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (mean and IR)</td>
<td>67.0 (58.0–75.0)</td>
<td>68.9 (65.0–74.0)</td>
<td>0.83</td>
</tr>
<tr>
<td>Body surface area</td>
<td>1.84</td>
<td>1.83</td>
<td>0.9</td>
</tr>
<tr>
<td>NYHA class (median)</td>
<td>2</td>
<td>2</td>
<td>0.9</td>
</tr>
<tr>
<td>CCS class (median)</td>
<td>1</td>
<td>1</td>
<td>0.9</td>
</tr>
<tr>
<td>Additive EuroSCORE (median)</td>
<td>5</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>Pre-CPB haematocrit (%)</td>
<td>34.4 ± 3.3</td>
<td>33.0 ± 3.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Pre-CPB Hb (g/dl)</td>
<td>10.9 ± 1.3</td>
<td>10.3 ± 1.2</td>
<td>0.87</td>
</tr>
<tr>
<td>CPB time (min)</td>
<td>71.86 ± 20.5</td>
<td>69.23 ± 8.47</td>
<td>0.58</td>
</tr>
<tr>
<td>Aortic cross-clamp time (min)</td>
<td>51 ± 26</td>
<td>47 ± 24</td>
<td>0.6</td>
</tr>
<tr>
<td>Major postoperative morbidity</td>
<td>4</td>
<td>2</td>
<td>0.49</td>
</tr>
<tr>
<td>Minor postoperative morbidity</td>
<td>12</td>
<td>14</td>
<td>0.75</td>
</tr>
</tbody>
</table>

EVADO, extracorporeal vacuum-assisted device optimized; IR, inter-quartile; NYHA, New York Heart Association; CCS, Canadian Cardiovascular Society; CPB, cardiopulmonary bypass; Hb, haemoglobin.

Table 2. Type of intervention

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Control group (n = 73)</th>
<th>EVADO group (n = 77)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CABG</td>
<td>32</td>
<td>34</td>
<td>0.83</td>
</tr>
<tr>
<td>AVR</td>
<td>10</td>
<td>11</td>
<td>0.9</td>
</tr>
<tr>
<td>MVR</td>
<td>9</td>
<td>9</td>
<td>0.9</td>
</tr>
<tr>
<td>Mitral valve repair</td>
<td>8</td>
<td>9</td>
<td>0.9</td>
</tr>
<tr>
<td>Ascending aortic replacement</td>
<td>4</td>
<td>5</td>
<td>0.9</td>
</tr>
<tr>
<td>CABG + valve replacement</td>
<td>10</td>
<td>14</td>
<td>0.9</td>
</tr>
</tbody>
</table>

EVADO, extracorporeal vacuum-assisted device optimized; CABG, coronary artery bypass grafting; AVR, aortic valve replacement; MVR, mitral valve replacement.

Fig. 2. (a) FHb in the two groups 30 and 60 min after establishment of CPB. Values are expressed as percent change relative to the baseline values (pre-CPB). Percent change is significantly higher in the control group. (b) Haptoglobin plasma levels in the two groups 30 and 60 min after establishment of CPB. Values are expressed as percent change relative to the baseline values (pre-CPB). Negative percent variation is significantly larger in the control group. FHb, free haemoglobin; EVADO, extracorporeal vacuum-assisted device optimized; HPT, haptoglobin; CPB, cardiopulmonary bypass.
4. Discussion

The cCPB systems are limited by excessive haemodilution, which adversely affects outcome [7] and may results in increased transfusion requirements [8]; mechanical injury to red blood cells induced by the roller pumps; no separation of pericardial suction blood, which mediates inflammatory response. These may cause end-organ damage, impair the coagulation system and promote haemolysis [9, 10].

We conducted a randomized study of an integrated cCPB circuit based on separation of the intracavitary from the extracavitary suction blood, minimization of priming volume, elimination of roller pumps and use of a phosphorylcholine-coated oxygenator. Our results indicate that such a system, compared with cCPB, allows a lesser degree of perioperative haemolysis in patients undergoing cardiac operations. This appears to be primarily related to the elimination of roller pumps [11, 12] and to the separation of pericardial suction blood. Lesser haemolysis has been associated with improved clinical outcomes [13, 14]. In group B, the Hct values were actually greater than in group A throughout CPB and the ICU stay, although this difference was not statistical. The perioperative need for blood transfusions was significantly reduced in the EVADO group. The reliability of our conclusions is strengthened by the fact that in no patient in group B had the extracavitary blood to be reinfused in the pump during the operation. The pericardial shed blood carries proinflammatory mediators, damaged red blood cells, which may impact the indexes of haemolysis and potentially bias our analysis. For the same reason, we excluded from the assessment of the haemolysis-related endpoints those patients who received CRC transfusion. The need for blood transfusion is frequent, and may partially offset the benefits of the EVADO in terms of reduced indexes of haemolysis. As such, we observed a lesser rate of perioperative CRC transfusion in the patients treated with the EVADO. Reasonably, a smaller priming volume and a lesser degree of haemolysis may have contributed to such effect. We observed a statistically lower bleeding rate from the chest tubes in the patients enrolled in the EVADO group, which is consistent with the lower rate of surgical revision of haemostasis in the EVADO group.

Taken together, these factors may contribute to an optimized perioperative end-organ perfusion. No coagulation- and inflammation-related endpoint was addressed, since the present investigation and its sample size were tailored on the bleeding-related endpoints.

The biochemical advantages associated with the EVADO may translate into measurable clinical benefits, as it is underscored by the shorter mean ICU stay and extubation time. The rate of postoperative atrial fibrillation was significantly lower in the EVADO group, despite that the number of patients affected by mitral valvular disease and with previous atrial fibrillation were similar among groups. Recent evidence indicates that the systemic proinflammatory status elicited by CPB is a major pathophysiological mechanism for new-onset postoperative atrial fibrillation [15]. Increased proinflammatory burden after surgery is also associated with impaired lung function and prolonged mechanical ventilation. These findings suggest that:

1. The EVADO may elicit a lesser inflammatory reaction than older cCPB systems.
2. The clinical benefits associated with mCPB may be reliably obtained with the EVADO, without paying the price of lesser surgical versatility.

Compared with mCPB, EVADO allows a comfortable performance of more complex interventions (multiple valve and thoracic aortic surgery). In fact, the patients included in the present investigation underwent a wide range of operations. We excluded patients having CPB > two hours, since the coexistence of extensive heart disease may bias the clinical results. Dedicated investigation is ongoing.

Adoption of the EVADO results in lesser haemolysis, decreased blood loss and reduced need for transfusions. The reinfusion into the pump of extracavitary-suctioned
blood and the roller pumps appear to be the major determinant of haemolysis. The EVADO is useful in reducing the occurrence of minor complications (postoperative atrial fibrillation) and is associated with a more rapid extubation and a shorter ICU stay.

References


