Blood transfusion in cardiac surgery – Does the choice of anesthesia or type of surgery matter?

Transfuzija krvi i operacije srca – mogući uticaji izbora anestezije i tipa operacije

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Abstract

Background/Aim. In spite of the evidence suggesting a significant morbidity associated with blood transfusions, the use of blood and blood products remain high in cardiac surgery. To successfully minimize the need for blood transfusion, a systematic approach is needed. The aim of this study was to investigate the influence of different anesthetic techniques, general as well as different surgery strategies, on-pump techniques, general study was to investigate the influence of different anesthetic fusion, a systematic approach is needed. The aim of this surgery. To successfully minimize the need for blood transfusions during perioperative period.

Methods. Eighty-two consecutive patients scheduled for coronary artery bypass surgery were randomized according to surgical and anesthetic techniques into 4 different groups: group 1 (patients operated on off-pump, under general anesthesia); group 2 (patients operated on off-pump, with combined general and high thoracic epidural anesthesia); group 3 (patients operated on using standard revascularization technique, with the use of extracorporeal circulation, under general anesthesia), and group 4 (patients operated on using standard revascularization technique, with the use of extracorporeal circulation, with combined general and high thoracic epidural anesthesia). Indications for transfusion were based on clinical judgment, but a restrictive policy was encouraged. Bleeding was considered significant if it required transfusion of blood or blood products, or reopening of the chest. The quantity of transfused blood or blood products was specifically noted. Results. None of the patients was transfused blood or blood products during the surgery, and as many as 70/81 (86.4%) patients were not transfused at all during hospital stay. No difference in postoperative bleeding or blood transfusion was noted in relation to the type of surgery and anesthetic technique applied. If red blood cells were transfused, postoperative bleeding was the most influential parameter for making clinical decision. Conclusion. No influence of off-pump surgery or epidural anesthesia on blood transfusion requirements during a perioperative period was confirmed by this study. It seems, however, that encouraging lower hemoglobin triggers in clinical decision-making could result in less transfusions during surgery or hospital stay.

Key words: blood transfusion; cardiac surgical procedures; anesthesia; perioperative care.

Apstrakt

Uvod/Cilj. Uprkos postojećim dokazima u literaturi o štetnim efektima i povećanom morbiditetu bolesnika posle transfuzije krvi, primena krvi i krvihih derivata u kardiotoraksnoj rurgiji je česta. Neophodan je sistematski pristup da bi se postigli rezultati u smanjivanju potrošnje krvi tokom perioperativnog perioda. Cilj ove studije bio je da se ispita uticaj različitih vrsta anestezije, opšte i kombinovane opšte i epiduralne anestezije, kao i različitih hirurških tehnika, on-pump i off-pump (sa ili bez primene ekstrakorporalne cirkulacije) na učestalost postoperativnog krvarjenja i potrošnju krvi. Metode. Ispitivanjem su bila obuhvaćena 82 konsekutivna bolesnika planirana za hiruršku revaskularizaciju miokarda i kompjuterski randomizovana u četiri grupe prema hirurškoj i anesteziološkoj tehnici koja je korišćena: grupa 1 (bolesnici koji se operišu na kucaju srcu (off-pump), bez primene višokompetalne epiduralne anestezije (TEA)); grupa 2 (bolesnici koji se operišu off-pump, uz primenu TEA); grupa 3 (bolesnici koji se operišu standardnom tehnikom uz primenu ekstrakorporalne cirkulacije (EKC), bez primene TEA); grupa 4 (bolesnici koji se operišu standardnom tehnikom uz primenu EKC i primenu TEA). Da li će bolesnici primiti transfuziju krvi ili ne zavisiće je od kliničke procene lekara koji su bili ohrabrivani da primene restriktivne indikacije. Značajno krvarjenje je definisano kao potreba da bolesnici...
In spite of the evidence suggesting a significant morbidity associated with blood transfusions, the use of blood and blood products remain high in cardiac surgery. Practice varies among institutions and decision to transfuse patients is still more often based on subjective opinions rather than objective evidence. Patients treated in institutions with liberal transfusion strategies were 6.5 times more likely to receive transfusion than patients treated in institutions with more conservative approaches 1, 2.

It has been shown in clinical studies that regional anesthesia is associated with certain benefits for cardiac surgery patients, such as reduced incidence of atrial fibrillation, myocardial ischemia and myocardial infarction 3. In addition, superior analgesia during a postoperative period is well proven 4 which also reduces the postoperative stress response and other related complications, including hypertension, tachycardia, increased catabolism, but also influences immune response and coagulation disturbances 5.

In order to avoid complications related to extracorporeal circulation, among them postoperative bleeding, thromboembolic events, organ dysfunction and fluid retention being the most important, interest for off-pump cardiac surgery has increased in recent years 6.

Preoperative assessment and medication was standard for all patients. Induction of anesthesia was done intravenously, with midazolam (up to 5 mg), bolus doses of propofol, fentanyl and pancuronium. To maintain an adequate depth of general anesthesia continuous infusion of propofol together with bolus doses of fentanyl and pancuronium were used.

In patients with TEA, epidural catheter was placed at the scheduled operation with the use of extracorporeal circulation, under general anesthesia), and group 2 [patients operated on off-pump with combined general and high thoracic epidural anesthesia (TEA)]; group 3 (patients operated on using standard revascularization technique with the use of extracorporeal circulation, under general anesthesia), and group 4 (patients operated on using standard revascularization technique with the use of extracorporeal circulation, with combined general and TEA).

In case of conversion of the off-pump procedure into standard operation with the use of extracorporeal circulation, patients were newly assigned to the group according to the surgical technique, matching the anesthetic technique.

Initially, the study was designed for larger number of patients, but for technical reasons enrollment of patients was stopped earlier (82 patients).

The inclusion and exclusion criteria for the study are shown in Table 1.

Table 1

<table>
<thead>
<tr>
<th>Study inclusion and exclusion criteria</th>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inclusion criteria</strong></td>
<td>More than one graft</td>
<td>Acute infections</td>
</tr>
<tr>
<td></td>
<td>Ejection fraction &gt; 30%</td>
<td>Immunological diseases</td>
</tr>
<tr>
<td></td>
<td>No contraindications for TEA</td>
<td>Myocardial infarction up to one month before surgery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Diabetes mellitus type 1</td>
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<tr>
<td></td>
<td></td>
<td>Acute or chronic renal failure</td>
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<tr>
<td></td>
<td></td>
<td>Chronic lung diseases</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Stroke or transitory ischemic attack</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Coagulation disorders</td>
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</table>

**TEA – thoracic epidural anesthesia**

To successfully minimize the need for blood transfusion, a systematic approach is needed.

The aim of this study was to investigate the influence of different anesthetic techniques, general and combine epidural and general anesthesia, as well as different surgery strategies, on-pump versus off-pump, on postoperative bleeding complications and need for blood transfusions during the perioperative period.
transfusion was indicated when hemoglobin concentration was more than 7 g/dL.

Demographics, comorbidity, pre- and intraoperative therapy, operation and cardiopulmonary bypass duration, ischemic time, number of grafts as well as the number and reasons for conversion from off-pump to standard procedure were noted.

Quality of postoperative recovery, outcomes, all postoperative complications, length of intensive care unit (ICU) and hospital stay were also noted.

Bleeding was considered significant if it required transfusion of blood and blood products or reopening of the chest.

Laboratory investigations such as complete blood count, clotting function tests, biochemical tests (serum glucose, electrolytes, and renal and liver function tests) were monitored five times perioperatively: at the induction of anesthesia, 30 min after weaning off cardiopulmonary bypass or finishing the last anastomosis in off-pump coronary artery-by-pass (OPCAB) surgery, and 4, 12 and 48 h after the end of the surgery. Quantity of transfused blood or blood products was specifically noted.

When examining the differences between the defined groups, the t-test and analysis of variance (ANOVA) for numeric features and χ²-square test for attribute characteristics were used. Analysis of variance with repeated measurements (MANOVA) was used to analyze the parameters monitored in five different time points during the study.

Results

Eighty-two patients were included in the study. One of the patients had incomplete data and was excluded from further statistical analysis. According to the computer randomization, all other patients (81) were assigned into four previously described groups: group 1 (19 patients); group 2 (17 patients); group 3 (27 patients); group 4 (18 patients).

There were three conversions from off-pump to standard surgery and cardiopulmonary bypass, and these patients were assigned to different groups according to the anesthetic technique applied: 2 patients into the group 3, and 1 patient into the group 4.

Table 2 shows the characteristics of the patients.

Table 2

| Demographics of all the patient groups and the average duration of the surgery |
|----------------------------------|------------------|------------------|------------------|------------------|
| Sex (male/female), n             | Group 1          | Group 2          | Group 3          | Group 4          |
| Age (years), X ± SD              | 51.9 ± 7.6       | 59.9 ± 8.5       | 55.4 ± 7.9       | 55.0 ± 7.8       |
| Weight (kg), X ± SD              | 80.1 ± 11.6      | 85.9 ± 11.6      | 84.9 ± 10.6      | 83.8 ± 15.5      |
| Height (cm), X ± SD              | 173.2 ± 7.1      | 173.9 ± 6.3      | 170.7 ± 8.2      | 170.6 ± 9.2      |
| BMI (kg/m²), X ± SD              | 26.8 ± 3.1       | 28.4 ± 3.0       | 29.2 ± 3.2       | 28.8 ± 4.7       |
| EF † (%), X ± SD                 | 55.3 ± 7.8       | 53.0 ± 10.1      | 46.9 ± 9.5       | 49.6 ± 8.8       |
| NYHA class, X ± SD               | 1.8 ± 0.4        | 1.9 ± 0.5        | 1.9 ± 0.5        | 1.9 ± 0.3        |
| Duration of the surgery (min)    | 159.1 ± 36.8     | 179.4 ± 39.5     | 184.8 ± 44.8     | 183.2 ± 51.7     |

BMI = body mass index; EF = ejection fraction; NYHA = New York Heart Association;
† p < 0.05 between groups (ANOVA)
Group 1 = patients operated on off-pump, under general anesthesia; group 2 = patients operated on combined general and high thoracic epidural anesthesia (TEA); group 3 = patients operated on using standard revascularization technique with the use of extracorporeal circulation, under general anesthesia; group 4 = patients operated on using standard revascularization technique with the use of extracorporeal circulation, with combined general and TEA.

Although ejection fraction (EF) showed statistical difference between the groups, data indicate that the difference is not clinically significant and not representing the difference in severity of illness or the predicted outcome.

Planned coronary artery by-pass grafting (CABG) surgery was done in all patients. Average duration of surgery was not statistically different between the groups (Table 2), p = 0.225, ANOVA.

The majority of patients were hemodynamically stable during the procedure.

Table 3 shows the changes in hemoglobin levels that were monitored intra- and postoperatively in five different time points.
Multivariate tests for interaction between various points in time and the groups revealed that hemoglobin values changed significantly in all times comparing with the initial value, with the decrease in hemoglobin concentrations at the first and second monitored time, followed with the increase in the hemoglobin concentrations postoperatively ($p < 0.001$). Hemoglobin concentrations have changed in all the groups in the same manner (Figure 1).

Multivariate tests for interaction between time and the groups showed that platelet count did change over time, but in a different manner in different groups. There was a decrease in the platelet count in all the groups in the second and third monitored time, with the increase in the fourth and fifth time, and than again slight decrease in the sixth time (Figure 2).

A decrease in platelet count in the third time was statistically significant ($p = 0.006$). Platelet count was signifi-

<table>
<thead>
<tr>
<th>Time point Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLT0, $\bar{x} \pm SD$</td>
<td>217.3 ± 41.3</td>
<td>213.6 ± 56.9</td>
<td>249.9 ± 69.4</td>
</tr>
<tr>
<td>PLT1, $\bar{x} \pm SD$</td>
<td>191.4 ± 34.5</td>
<td>176.5 ± 33.1</td>
<td>208.1 ± 56.7</td>
</tr>
<tr>
<td>PLT2, $\bar{x} \pm SD$</td>
<td>155.9 ± 39.8</td>
<td>139.6 ± 32.6</td>
<td>143.2 ± 50.4</td>
</tr>
<tr>
<td>PLT3, $\bar{x} \pm SD$</td>
<td>212.6 ± 40.2</td>
<td>176.6 ± 42.1</td>
<td>216.6 ± 61.4</td>
</tr>
<tr>
<td>PLT4, $\bar{x} \pm SD$</td>
<td>210.9 ± 47.6</td>
<td>195.0 ± 48.6</td>
<td>205.1 ± 52.8</td>
</tr>
<tr>
<td>PLT5, $\bar{x} \pm SD$</td>
<td>173.1 ± 33.2</td>
<td>180.5 ± 53.5</td>
<td>192.4 ± 48.9</td>
</tr>
</tbody>
</table>

Table 4 shows the changes in platelet count in different time points.
cantly higher in the third time in the group 1, as compared to other groups ($p = 0.030$).

Table 5 shows the INR values in different time points.

### Table 5

<table>
<thead>
<tr>
<th>Time point</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>INR1, $\bar{x} \pm SD$</td>
<td>1.1 $\pm$ 0.3</td>
<td>1.2 $\pm$ 0.2</td>
<td>1.1 $\pm$ 0.2</td>
<td>1.1 $\pm$ 0.2</td>
</tr>
<tr>
<td>INR3†, $\bar{x} \pm SD$</td>
<td>1.4 $\pm$ 0.3</td>
<td>1.5 $\pm$ 0.4</td>
<td>1.3 $\pm$ 0.3</td>
<td>1.4 $\pm$ 0.3</td>
</tr>
<tr>
<td>INR5, $\bar{x} \pm SD$</td>
<td>1.2 $\pm$ 0.2</td>
<td>1.2 $\pm$ 0.2</td>
<td>1.2 $\pm$ 0.2</td>
<td>1.3 $\pm$ 0.2</td>
</tr>
</tbody>
</table>

INR1 – values at the induction of anaesthesia; INR3 – 4 h after surgery; INR5 – 48 h after surgery; † $p < 0.05$ compared to initial value

Group 1 – patient operated on off-pump, under general anesthesia; group 2 – patients operated on off-pump with combined general and high thoracic epidural anesthesia (TEA); group 3 – patients operated on using standard revascularization technique with the use of extracorporeal circulation, under general anesthesia; group 4 – patients operated on using standard revascularization technique with the use of extracorporeal circulation, with combined general and TEA

Multivariate tests for interaction between different points in time and the groups showed that INR values did change over time, but in all the groups in the same manner. INR was significantly higher in the third monitored time compared with the initial value ($p < 0.001$). In the fifth time it decreased again but stayed higher as compared to the initial value ($p = 0.022$).

Table 6 shows postoperative blood drainage.

### Table 6

<table>
<thead>
<tr>
<th>Group</th>
<th>$\bar{x} \pm SD$ (range), mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>525.6 ± 299.4 (110–1150)</td>
</tr>
<tr>
<td>2</td>
<td>580.0 ± 225.8 (300–1100)</td>
</tr>
<tr>
<td>3</td>
<td>666.0 ± 408.2 (200–1750)</td>
</tr>
<tr>
<td>4</td>
<td>648.7 ± 216.7 (350–1750)</td>
</tr>
</tbody>
</table>

Group 1 – patient operated on off-pump, under general anesthesia; group 2 – patients operated on off-pump with combined general and high thoracic epidural anesthesia (TEA); group 3 – patients operated on using standard revascularization technique with the use of extracorporeal circulation, under general anesthesia; group 4 – patients operated on using standard revascularization technique with the use of extracorporeal circulation, with combined general and TEA

Drainage was not different between the groups ($p = 0.491$).

Reopening the chest due to postoperative bleeding was done in three patients (3.7%). These patients were operated on using standard on-pump surgery with cardiopulmonary bypass and general anesthesia.

None of the patients was transfused blood or blood products during the surgery, and as many as 70/81 (86.4%) patients were not transfused at all during hospital stay. If red blood cells were transfused, postoperative bleeding was the most influential parameter for making clinical decision.

Two of the patients with chest reopening for postoperative bleeding had both transfusion of packed red blood cells and fresh frozen plasma. The third one was returned to the operating theatre shortly after surgery and received only blood from cell saver, without additional blood or blood products. Only three patients were transfused fresh frozen plasma. No patient was given platelet transfusion.

There was only one death in the studied patients. The patient died due to multi-organ failure 53 days after the surgery; he received transfused blood and other blood products according to the clinical indications.

### Discussion

Red blood cell transfusion is a common in cardiac surgery patients. Proportion of patients that receive blood transfusion during perioperative period varies in the literature: from up to 95% of patients ten years ago, to 49% of CABG patients more recently 7.

It is well known that red blood cell transfusion can be life-saving intervention. Transfusions improve systemic oxygen capacity, ameliorate vasomotor regulation, improve myocardial oxygen delivery and improve short-term survival in myocardial ischemia 5.

On the other hand, existing literature highlights that the harms of transfusion are probably more serious than has been appreciated and that transfusion is used more frequently than necessary.

Even one unit of transfused blood is associated with significant risk of serious postoperative morbidity and immediate aim should be to avoid transfusing simply to treat low hemoglobin levels, which is usual practice in up to 50% of all transfused patients 7.

Concerns about harms of red blood cells transfusion have traditionally focused on viral and bacterial infection or hemolytic reactions that are very rare 5. However, immunosuppression, lung injury or organ dysfunction may occur in every recipient 1.

Recently, investigators from the Cleveland Clinic found that administration of red blood cells that had been stored for longer period of time (> 14 days) was independently associated with an increased risk of complications and increased estimated risk of death 10. The concept that red cells develop storage lesions over time and release cytokines, membrane fragments, free hemoglobin and oxygen radical is well-established and the probability that such injury can contribute to patient morbidity seems real.

Obviously, there is a challenge to determine the circumstances in which the benefits of transfusion outweigh the harms. Unfortunately, the existing evidence is scarce, and existing guidelines and recommendations are based on rather low levels of evidence. Convincing physicians to change their practices is not easy task and appropriate clinical judgment is used as justification for transfusions.

A number of strategies exist to minimize the likelihood that a patient will require a transfusion in the perioperative period.

Some of them are recommended by the existing guidelines ¹¹: stopping the preoperative use of antiplatelet medications, applying restrictive hemoglobin triggers for transfusing red blood cells, some form of pump salvage and reinfusion of residual pump blood at the end of CPB, use of cell saver systems, but also, off-pump CABG as one form of blood salvage technique.

The main aim of study was to investigate the influence of the type of surgery (on- vs off-pump), and anesthetic technique (TEA vs no TEA) on perioperative blood transfusions. We did use some of the transfusion reduction strategies, which would, otherwise, be able to influence our results and the number of transfused patients.

Antitplatelet therapy was stopped before surgery and was restarted postoperatively in the same manner for the majority of patients. Only the emergency patients did receive aspirin preoperatively.

Reinfusion of residual pump blood at the end of CPB and the use of cell saver systems were applied depending on the surgery technique used.

But most importantly, attending doctors were encouraged to use restrictive hemoglobin triggers to transfuse patients, which is also recommended in recent guidelines ¹¹: the patients were transfused if hemoglobin was less than 7 g/dL, and no transfusion was indicated to improve oxygen transport when hemoglobin concentration was more than 10 g/dL.

We monitored hemoglobin levels in five different time points perioperatively, and this revealed that they did drop when hemoglobin concentration was more than 10 g/dL.

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We monitored hemoglobin levels in five different time points perioperatively, and this revealed that they did drop during the procedure, recovered soon after, but did not reach the trigger for transfusion. None of the patients received blood transfusion intraoperatively, independently of the type of surgery and anesthetic technique applied.

About 20% of all CABG surgeries are now performed off-pump ¹². The use of CPB to perform CABG surgery has been associated with multiple deleterious effects, including hemodilution of coagulation factors and platelets, leading to coagulopathy that could result in excessive bleeding and the need for massive blood transfusion. Thus, off-pump would be expected to result in decreased incidence of postoperative complications, and is recommended as one of the transfusion saving strategies ¹¹.

Nevertheless, in our study no difference was noted between the groups in intra- and postoperative blood transfusions. Platelet count was monitored in five different time points, and it differed between the groups. There was a decrease in platelet count intraoperatively, followed by an increase in the immediate postoperative period. Platelet count indeed was higher in the off-pump group of patients in the third time point (30 min after cardiopulmonary bypass or finishing the last anastomosis on off-pump), but with no clinical consequences. Blood drainage after surgery was not different between the groups.

Only 13.6% of the patients received blood transfusion after the surgery and during the course of hospitalization. These decisions were mostly clinical, predominantly influenced by the rate of postoperative drainage. Even so, one of the patients with chest reopening for bleeding did not receive any, but blood from cell saver. Only three patients were back to surgery for bleeding, which is a rather small percentage.

Our study showed no influence of different surgical or anesthetic technique on the incidence of blood transfusion during the perioperative period. It seems that study design itself, with the encouragement of the attending physicians to be restrictive regarding blood transfusion, mostly influenced the number of transfused patients.

Of course, the number of enrolled patients is a limitation of our study. Since only 11 patients did receive blood transfusion, no conclusion of different influences or other correlations could be made.

Conclusion

There are different strategies in cardiac surgery to minimize transfusion requirements in a perioperative period. Our study proved no influence of OPCAB surgery or epidural anesthesia on these requirements. It seems that encouraging lower hemoglobin triggers in clinical decision-making could result in less transfusions during surgery or hospital stay.

REFERENCES


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