Changes in muscle compartment pressure after cardiopulmonary bypass

Líney Símonardóttir¹, Bjarni Torfason¹, Einar Stefánsson² and Jónas Magnússon³

¹Department of Cardiothoracic Surgery, Landspitalinn – University Hospital, 101 Reykjavík, Iceland; ²Department of Ophthalmology, Landspitalinn – University Hospital, 101 Reykjavík, Iceland; ³Department of Surgery, Landspitalinn – University Hospital, 101 Reykjavík, Iceland

Purpose: Hemodilution and inflammation lead to edema and increased muscle compartment pressure after cardiac surgery. The aim of this study was to find whether muscle compartment pressure was affected by the addition of albumin and mannitol to the pump prime, heparin coating or leukocyte depletion. Additionally, we studied the relationship between intraocular pressure and lower leg muscle compartment pressure. Edema during and following cardiac surgery is due to hemodynamic, osmotic and inflammatory changes, according to Starling’s Law. We attempted to influence the osmotic balance and reduce the inflammatory response in order to reduce the edema. Methods: Thirty-six patients who underwent cardiac surgery were randomly allocated into four groups. Group A received albumin and mannitol into the pump prime. Group B had an, heparin-coated arterial line filter and Group D was the control group, where intraocular pressure was also measured. Results: Lower leg muscle compartment pressure increased significantly during and after cardiac surgery in all groups, but this increase was significantly less in Group A than in the control group 24 h after surgery. No correlation was found between muscular compartment pressure and intraocular pressure. The intraocular pressure profile is different from the muscular compartment pressure and recovers much faster. Conclusion: Lower leg muscle compartment pressure and intraocular pressure behave differently during and after cardiac surgery. Albumin and mannitol added to the pump prime decreases muscle compartment pressure after cardiac surgery. Perfusion (2006) 21, 157–163.

Introduction

Edema during and after cardiac surgery can be understood through Starling’s Law. Hemodynamic and osmotic changes take place and, in addition, the systemic inflammatory response increases capillary permeability, with macromolecules leaking into the tissue compartment and causing edema. The main purpose of our study was to find whether the edematous response could be reduced, either by increasing the osmotic pressure in the pump prime or by decreasing the inflammatory response through heparin lining or leukocyte depletion. In addition, we compared the tissue compartment pressure in muscle to the intraocular pressure.

In a previous study, we found that the pressure in a closed muscle compartment rises significantly during and after cardiopulmonary bypass (CPB) and remains increased up to 48 h.¹ We assumed that the inflammatory response and edema causes the pressure changes in the compartment.

Materials and methods

Patients

Forty patients undergoing elective open-heart surgery, operated on by one surgeon, were randomly divided into four groups of 10 patients each. All perfusion circuits were primed with Ringer acetate 1600 mL and heparin 7500 U. Additionally, Group A received 100 mL of 20% albumin and 250 mL of 15% mannitol in the pump prime. Group B had heparin-coated CPB circuit from tip to tip (Duraflo II, Baxter). Group C had a leukocyte-depletion arterial line filter (Leukoguard™ LG from Pall Medical) instead of a conventional arterial line filter. Group D received the conventional treatment, which was considered a control group.

Participants were patients (45–76 years of age) undergoing elective coronary artery bypass grafting or aortic valve replacement with CPB. Patient demographic data were collected and are shown in Table 1. Table 2 shows the operative data.

The exclusions criteria were: previous sternotomy, kidney disease, liver disease, inflammatory or bleeding disorder, stroke, known eye disease, insulin dependent diabetes, use of corticosteroids and aspirin <4 days before operation.
The local ethics committee approved the study. Written and oral informed consent was obtained.

Anesthesia
A standardized anesthetic procedure was used in all patients. Premedication consisted of midazolam (Dormicum, 7.5–15 mg po) and a combination of morphine 5–10 mg im and scopolamine 0.3 mg im. Anesthesia was induced with propofol 1–3 mg/kg and fentanyl 5–10 mg/kg, followed by pancuronium 0.1 mg/kg for muscle relaxation. Anesthesia was then maintained with a combination of fentanyl (10–30 μg/kg) and isoflurane.

Perfusion
Heparin (300 U/kg bodyweight) was given intravenously prior to bypass. Activated clotting time (ACT) was maintained at over 480 sec throughout the bypass. A HL-20 roller pump from Jostra was used with non-pulsatile flow. Alpha-stat acid-base blood gas management was used during bypass. The CPB circuit consisted of a Univox® oxygenator, hard-shell venous reservoir, tubing, arterial line filter and cannulae from Baxter Bentley®. The priming solution consisted of 1600 mL Ringer acetate (Lyfjaverslun Islands pH ~6 and osmolarity ~280 mOsm/L), heparin (7500 U) and cloxacillin sodium (1 g). The crystalloid cardioplegia was modified St. Thomas’ solution (160 mEq/L Mg²⁺, 80 mEq/L K⁺, 1.36 g procaine in 1000 mL Ringer; Martindale Pharmaceuticals, Romford, UK). Mild hypothermia (32–34°C venous blood) was maintained during bypass. Cannulation was standard: two-stage venous cannulae and aortic root cannulae (Baxter®).

Measurements
The MTC® microtransducer (Dräger Medical Electronics) was placed, using antiseptic techniques, in the anterior tibia muscle compartment after induction of anesthesia and connected to a Viridia M3 monitor (Hewlett Packard). The 3-F electronic transducer was passed through Venflon cannulae (1.7 mm). The cannulae were removed, but the transducer remained in the muscle for the next 24 h. Zeroing was performed prior to insertion. The muscle compartment pressure was measured every 15 min (average of three measurements taken every 5 min). The first 15 min after connection was set as the normal value for each person and changes from that value were used for statistical measurements. The transducer was placed in the non-vein-harvested leg. Blood samples for colloid osmotic pressure measurement were placed in heparin tubes before and after CPB. The samples were placed in a refrigerator, approximately 10°C, until the sample was measured, which was within 48 h. The first sample (1) was obtained before induction of anesthesia, the second sample (2) was obtained 5 min after the crossclamping of the aorta, the third sample

<table>
<thead>
<tr>
<th>Table 1 Preoperative data of the patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Gender (M/F)</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>BSA (m²)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
</tr>
<tr>
<td>WBC (× 10⁹ L)</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
</tr>
</tbody>
</table>

Group A, albumin and mannitol; Group B, heparin-coated system; Group C, leukocyte depletion filter; Group D, control group. SEM, standard error of the mean; BSA, body surface area; EF, ejection fraction; WBC, white blood cells.

Table 2 Operative data of the patients

<p>| |</p>
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Bypass time (min)</td>
</tr>
<tr>
<td>Aortic crossclamp time (min)</td>
</tr>
<tr>
<td>Lowest bladder temperature (°C)</td>
</tr>
</tbody>
</table>

Group A, albumin and mannitol; Group B, heparin-coated system; Group C, leukocyte depletion filter; Group D, control group. SEM, standard error of the mean.
(3) 10 min after the crossclamp removal, the fourth
sample (4) 10 min after protamin injection started,
the fifth sample (5) 2 h after sample 4 and the last
sample (6) 24 h after the operation started. Samples
were obtained from the arterial line catheter before
and after bypass, but from the arterial line in the
bypass circuit while on bypass. At the same time-
points, muscle compartment pressure was registered
and intraocular pressure was measured in Group D
with a Schiotz tonometer (also reported in Group A).
Volume balance was calculated based on volume
administered (crystalloids, volume expanders and
blood products) against volume lost (bleeding via
drains and urine output) after the bypass and again
after 24 h.

Statistics
Wilcoxon signed ranks test was used to test if the
samples were significantly different from their
starting value, sample one. The non-parametric
Mann–Whitney U-test was used to compare the
groups with the control group. The area under
the curve for muscle compartment pressure was
measured for each participant and distributed for
mean values in each group (AUCN = ΔT•MCP
meanN). The group distribution was performed
with Kruskal–Wallis test and compared with the
Mann–Whitney U-test. A p value of 0.05 was
considered statistically significant.

Results
Patients were randomized into four groups, A, B, C
and D (Table 1). In Group A, three participants were
excluded after enrolment leaving seven participants
in Group A for analysis (one patient developed an
anaphylactic shock when anesthetized, one patient
developed hemolysis because of suction blood in
the pre-bypass filter before bypass and the third
patient had a penicillin allergy which he had not
disclosed before the operation). In Group B, one
patient was excluded because the heparin-coated
system had expired. In Groups C and D, 10 patients
concluded the study as planned.

There were no significant differences in intrao-
perative volume balance among the groups.

All patients who were given volume expanders
during surgery received Hemohes®. Of the 24
patients in the 24 h recovery period, 19 patients
received only Hemohes®, two patients Hemohes®
and plasma, and three patients blood products
(plasma and platelets). In Group A, four out of seven
patients received volume expanders (57%), in
Group B, five out of nine (55%), in Group C
eight out of ten (80%) and in Group D eight out of
ten (80%). The volume balance is shown in Tables 3
and 4.

No significant difference was demonstrated in
postoperative volume balance among the groups.

Muscle compartment pressure measurement was
divided into two periods: firstly, during the opera-
tion (Figure 1) and secondly, postoperatively up to
24 h (Figure 2). The area under the curve was
measured postoperatively and the mean value for
each participant was used to find out if there was a
statistical difference among the four groups. Group
A was different from the control Group D (p = 0.025),
whereas B and C groups were not (Figure 3, box
plot).

Colloid osmotic pressure decreased significantly
(p < 0.05) from its starting value in all samples
except the last sample in Group A (p = 0.063). No
significant difference was found among the four
groups (Figure 4).

In Group D, we measured intraocular pressure and
compared it with the compartment pressure at the
same time. Intraocular pressure in samples 2 (p =
0.005) and 5 (p = 0.05) were significantly different
from sample 1, the other samples, 3, 4, and 6, were
not. There was no correlation between changes in
intraocular pressure and muscle compartment pres-
sure (Figure 5).

Table 3 Intraoperative volume balance

<table>
<thead>
<tr>
<th>Volume given:</th>
<th>Group A</th>
<th>SEM</th>
<th>Group B</th>
<th>SEM</th>
<th>Group C</th>
<th>SEM</th>
<th>Group D</th>
<th>SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloids (mL)</td>
<td>5709</td>
<td>662</td>
<td>5356</td>
<td>407</td>
<td>4855</td>
<td>818</td>
<td>4583</td>
<td>602</td>
</tr>
<tr>
<td>Volume expanders (mL)</td>
<td>43</td>
<td>43</td>
<td>111</td>
<td>73</td>
<td>350</td>
<td>150</td>
<td>175</td>
<td>75</td>
</tr>
<tr>
<td>Packed red blood cells (mL)</td>
<td>113</td>
<td>84</td>
<td>33</td>
<td>33</td>
<td>120</td>
<td>80</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Auto-transfusion (mL)</td>
<td>981</td>
<td>88</td>
<td>900</td>
<td>33</td>
<td>772</td>
<td>49</td>
<td>880</td>
<td>29</td>
</tr>
<tr>
<td>Urine (mL)</td>
<td>721</td>
<td>93</td>
<td>682</td>
<td>109</td>
<td>940</td>
<td>189</td>
<td>859</td>
<td>382</td>
</tr>
<tr>
<td>Bleeding (mL)</td>
<td>969</td>
<td>261</td>
<td>1130</td>
<td>129</td>
<td>1227</td>
<td>182</td>
<td>1010</td>
<td>110</td>
</tr>
<tr>
<td>Intra op volume balance (mL)</td>
<td>5151</td>
<td>565</td>
<td>4532</td>
<td>386</td>
<td>3892</td>
<td>555</td>
<td>3769</td>
<td>650</td>
</tr>
</tbody>
</table>

Group A, albumin and mannitol; Group B, heparin-coated system; Group C, leukocyte depletion filter; Group D, control group.
Discussion

By going on CPB, hemodilution is inevitable. Therefore, it is very common to use mannitol in the prime fluid to increase the intravascular osmolarity to decrease the extravascular fluid shifts. Mannitol is known to be very effective as an osmotic diuretic and it is also a free radical scavenger. The aldehyde moiety of mannitol binds the free radical, which then cannot react with proteins or lipids on the endothelium and, therefore, diminishes reperfusion injury. Albumin, on the other hand, has mostly been used to increase colloids and colloid osmotic pressure in the pump prime. Albumin has proven to have many other positive effects on CPB.

In this study, we increased the albumin concentration in the pump prime in Group A, but we did not obtain significantly higher colloid osmotic pressure values following bypass, so we must assume that the albumin is sitting on the surface of the oxygenator and tubing. It is most likely that albumin adhering on the artificial surface inhibits other protein and platelet adhesion and activation, and possible fibrinogen adhesion later.

All patients except one had a muscle compartment pressure starting value of <8 mmHg, which is within the normal range in a resting muscle. All 36 participants in this study increased their muscle compartment pressure significantly during and after CPB (Figures 1 and 2), but no one reached the criterion for compartment syndrome (>30 mmHg). On bypass and shortly after, the muscle compartment pressure was very unstable. Pressure changes in a muscle are related to the changes in both venous and arterial blood pressure, so, with low arterial blood pressure and non-pulsatile blood flow, as we usually have on bypass, we expected unstable pressure in the muscle compartment.

With only seven patients in Group A, the albumin and mannitol group, we still obtained a significantly lower increase of compartment pressure postoperatively. In an animal study, it was concluded that decreased colloid osmotic pressure increased the edema after CPB much more in the skeletal muscles and duodenum than other body compartments. This is possibly one of the reasons why we have this significant difference in compartment pressure in the muscle compartment, even though the colloid

| Table 4 Volume balance for the 24 h post-operative |
|---------------------------------|-----|-----|-----|-----|-----|-----|
| Volume given:                   |     |     |     |     |     |     |
| Crystalloids (mL)               | 1777| 297 | 1259| 259 | 1674| 529 |
| Volume expanders (mL)           | 413 | 156 | 478 | 188 | 580 | 183 |
| Packed red blood cells (mL)     | 375 | 233 | 0   | 300 | 95  | 240 |
| Auto-transfusion (mL)           | 444 | 146 | 227 | 102 | 325 | 103 |
| Volume output:                  |     |     |     |     |     |     |
| Urine (mL)                      | 1760| 248 | 1980| 288 | 1847| 584 |
| Bleeding (mL)                   | 1334| 321 | 887 | 210 | 1047| 331 |
| Volume balance                  | −85 | 603 | −904| 355 | −15 | −5 |
| Post op − 24 h (mL)             | 5065| 855 | 3629| 561 | 3878| 1226|
| After 24 h (mL)                 |     |     |     |     |     |     |

Group A, albumin and mannitol; Group B, heparin-coated system; Group C, leukocyte depletion filter; Group D, control group.

![Figure 1](image1.png) Intraoperative muscle compartment pressure. Median values. Group A: albumin and mannitol, Group B: heparin coating, Group C: LG-6 arterial leukocyte depletion filter and Group D: a control group.

![Figure 2](image2.png) Muscle compartment pressure 24 h post-op, median values. Group A: albumin and mannitol, Group B: heparin coating, Group C: LG-6 arterial leukocyte depletion filter and Group D: a control group.
osmotic pressure is not significantly higher, as in Group A. The concentration of colloid and crystals are still higher in the pump prime in Group A, even though the albumin adheres to the surface area shortly after the onset of bypass instead of floating in the bloodstream. In Group B, the heparin-coated group, we did not see any tendency towards lower muscle compartment pressure. Many researchers have reported decreased inflammatory response after using heparin-coated systems and it seems to decrease contact activation, but it does not decrease compartment pressure in this study. In our case, the reason might be the small size of our study group, which included only nine patients, but it also could be the low-risk patient selection.

Several studies have been made on the leukocyte depletion filter, LG-6, but the results are not clear. In some studies, it seems to be reducing the inflammatory response, while other studies indicate that the filter is destroying healthy cells. Where it is placed in the system, when and for how long it is running seem to make the whole difference. As a replacement for the conventional arterial filter for the whole operation, as in this study, it does not decrease muscle compartment changes.

Intraocular pressure has been reported to increase during CPB. The intraocular pressure is actively regulated. By increasing the concentration of colloids in the pump prime or by giving mannitol prior to surgery, the intraocular pressure changes decrease during and after CPB. Aqueous humor formation in the eye is both by active transport and by ultrafiltration. The outflow of aqueous humor is dependent on the intraocular pressure. Therefore, the intraocular pressure has a strong tendency to return to normal levels when increased. This probably plays a big role in the different pressure responses in the muscle compartment and in the eye and how much sooner the intraocular pressure recovers. All the patients increased their intraocular pressure significantly at the beginning (sample 2) and decreased significantly at the end (sample 5) compared to their starting value, which was rather low compared to the normal value of 16 mmHg. All of them returned to the starting value within 24 h.

Only one of the participants in the study increased the intraocular pressure more than normal fluctuation and this was a patient from Group A. He had an undisclosed penicillin allergy and, therefore,
fell out of the study. His starting value was 18.9 mmHg, which was high compared to the other participants. The intraocular pressure went down to 13.4 mmHg during the operation, but increased to 23.4 mmHg postoperatively instead of returning to normal, like the other participants, and increased further the next day up to 36.1 mmHg. The patient was treated for high intraocular pressure for 2 days.

In low-risk patients, as we have in our study, with a CPB time of <90 min, the muscle compartment pressure is mostly dependent on hemodynamic factors. The fluid shift from the capillaries into the surrounding tissues peaks when the hemodiluted patients on bypass take over their own perfusion. While on bypass, the blood flow is non-pulsatile, the arterial blood pressure is low and colloid osmotic pressure is decreased. By going off bypass, the hydrostatic pressure increases and becomes pulsatile again, but the osmotic pressure is still low, so the hydrostatic pressure is dominating the colloid osmotic pressure and, therefore, forces the fluid out of the capillaries. If the albumin is sitting on the surface of the oxygenator and tubings, it could decrease the total body inflammatory response and decrease the fluid shift from the capillaries to the surrounding tissue and diminish the muscle compartment pressure changes. The mannitol also helps by increasing osmolarity in the pump prime, increases urine output and decreases reperfusion injury.

Conclusion

Lower leg muscle compartment pressure and intraocular pressure behave differently during and after cardiac surgery. Albumin and mannitol added to the priming fluid decreases muscle compartment pressure after cardiac surgery.

References

1 Simonardottir L, Torfason B, Magnusson J. Is compartment pressure related to plasma colloid osmotic pressure in patients during and after cardiac surgery? Perfusion 2001; 16(2): 137 – 45.


