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The role of cell savers and filters in cardiac surgery

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Chapter 7

Summary, general discussion and future perspectives

Summary

This thesis investigated whether the use of a cell saver and the use of leukocyte depletion filters or a combination of these, could serve as a strategy to reduce allogeneic blood transfusions in adult cardiac surgery. Furthermore, we looked at the effect of cell savers and the filters on the quality of processed and retransfused blood.

Chapter 1 serves as an introduction into the different possibilities and difficulties in the current blood sparing strategies used in adult on-pump cardiac surgery, with particular attention to the standard use of cardiotomy suction.
There appears to be little to no evidence for cardiotomy suction use during CPB as a blood conserving strategy in routine cardiac surgery. Furthermore the quality of the cardiotomy suction blood is not optimal as this blood contains potential embolic substances, haemolytic blood, activated platelets and pro-inflammatory substances that can impair haemostasis and increase the inflammatory response.
The main focus of the thesis on improving or eliminating cardiotomy suction blood by filtration with leukocyte depletion filters or the use of a cell saver device is introduced. The current status of leukocyte depletion in cardiac surgery is described. Next the role of the cell saver, advocated in the most recent guidelines as a blood conserving strategy in adult on-pump cardiac surgery, is discussed. The aspects surrounding the controversies of the use of a cell saver during on-pump cardiac surgery are discussed with particular attention to initial reasons for cell saver deployment (blood sparing strategy or organ protection), the time frame used (during CPB only or more extensive) and during which type of surgery (low, intermediate or high risk).
Thus, the main questions in this thesis are whether the quality of collected and retransfused blood in cardiac surgery can be improved and whether cell savers, or the use of filters can reduce allogeneic blood transfusions in cardiac surgery.

Chapter 2 describes the multicentre, factorial designed study in which patients selected for elective on-pump cardiac surgery were randomized into four groups. One group with cell saver use, one group with cell saver and leukocyte depletion filters use and one group with only leukocyte depletion filter use to processes intra-operative shed

blood. The fourth group was a control group, with the use of standard cardiotomy suction. This study showed that the intra-operative use of a cell saver did not reduce the total number of blood products, but did reduce the percentage of patients that received allogeneic blood products. The finding of this trial has clinical implications, as transfusion of allogeneic blood products is associated with reduced long-term survival and increased morbidity. The combination of a cell saver with a leukocyte depletion filter did not result in a clinically relevant advantage for the patient nor did the novel approach to transfuse all unprocessed wound blood through a leukocyte depletion filter. The effect of preoperative anaemia, surgical procedures and red blood cell storage time on intra-operative transfusion and post-operative morbidity are also discussed. Our findings support the routine use of a cell saver during on-pump cardiac surgery.

Chapter 3 describes the study, which tries to answer the question if the quality of blood processed by a cell saver is affected when large quantities of blood are processed during adult on-pump cardiac surgery. The results of the present study demonstrate that multiple runs of the C.A.T.S. cell saver with shed intra-operative wound blood lead to a similar reduction in the concentration of the pro-inflammatory cytokine IL-6. Leukocytes were retained but haemoglobin, free haemoglobin, haematocrit and platelet concentrations were not different between the two processing runs. The study concludes that multiple runs with a cell saver device does not affect the quality of processed blood.

Chapter 4 describes the cohort study which investigates whether additional post-operative collection and processing of mediastinal shed blood with a new type of cell saver device that is also used intra-operatively could reduce the number of allogeneic blood transfusions in adult patients undergoing on-pump cardiac surgery compared to intra-operative cell salvage alone. The conclusion of the study is that continuing cell salvage beyond the operating rooms throughout a specific time in the intensive care unit did not reduce transfusion requirements further compared to intra-operative cell salvage alone. What is also shown is that the process of post-operative cell salvage with this cell saver elevates biomarkers as a side effect of haemolysis of the collected blood.

Chapter 5 elaborated on the performance of three different kinds of filters. Background for this study was that activated leukocytes and fat particles are associated with organ injury, especially the brain, after on-pump cardiac surgery. Performance of two specifically designed leukocyte depletions filters and one fat removal filter were compared in a clinical setting. This study showed that leukocyte removal filters were superior to fat removal filters in both leukocyte and fat removal. Furthermore there was a shorter passage time of blood when a leukocyte depletion filter was used.

Chapter 6 describes the study, which investigates whether the use of a cell saver device during adult on-pump cardiac surgery influences red blood cell function and if the retransfusion of this salvaged blood affects the red blood cell function in patients. What is shown is that the cell salvage procedure reduces the red blood cell deformability and the 2,3-DPG content of red blood cells, indicating a reduction in red blood cell function. But retransfusion of this processed blood by a cell saver does not further compromise the RBC function in adult patients undergoing cardiac surgery with cardiopulmonary bypass.

General discussion and conclusions

The principal results of the combined studies in the present thesis paints a picture of the use of cell saver devices and leukocyte depletion filters in adult on-pump cardiac surgery. Alas it is not a crystal clear picture.

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Cell salvage of cardiotomy suction blood and blood quality aspects

The present thesis shows that collecting and processing cardiotomy blood in cardiac on-pump surgery with a cell salvage device negatively affects the red blood cell deformability and the 2,3-DPG content of collected blood. The reduction in red blood cell deformability or 2,3-DPG was also found in other studies in on pump cardiac surgical patients [1,2], but not in two other clinical trials [3,4]. One study found an increase in 2,3-DPG content when a cell saver processed residual CPB blood [3]. Two recent clinical trials, showed that retransfusion of the processed blood did not negatively affect the red blood cell function in vivo [2,4]. Although cell saving can reduce the red

blood cell function, it is important to realise that this reduction is still less then is seen with transfusing allogeneic red blood cells [4]. As the transfusing of allogeneic blood products is associated with increased morbidity and mortality in patients undergoing cardiac surgery [8,9], cell salvage remains an attractive option to reduce transfusion of allogeneic blood products in cardiac surgical procedures.
Processing large amounts of blood with a continuous device does not affect the ability of the device to remove pro-inflammatory cytokines. Processing cardiotomy blood with a cell saver might in this way reduce the systemic inflammatory associated with on-pump cardiac surgery [5-7].

Leukocyte depletion filters as blood transfusion sparing strategy
As mentioned in the introduction, the use of a leukocyte depletion filter during CPB is not recommended in the current guidelines [10]. Although leukocyte depletion is often reported as a successful method in reducing inflammation, nearly all of the clinical trials have failed to demonstrate clinical benefits on overall patient outcomes such as morbidity, mortality, and hospital stay [11-14]. What is shown in the present thesis is that these filters are effective in their task, are safe and can be used in a clinical setting. Blood retransfused with a leukocyte depletion filter has potential plasma saving effect, i.e. the plasma fraction of the retransfused blood is retained contrary to the use of a cell saver. But the use of a leukocyte depletion filter to improve the quality of the intra-operatively shed blood does not reduce transfusion requirements. We have not been able to show that using a leukocyte filter improves patient outcome compared to standard care or the use of a cell saver. Therefore we cannot recommend the use of leukocyte depletion filters in routine adult on-pump cardiac adult surgery as a blood transfusion sparing strategy.

Cell savers as blood transfusion sparing strategy
The present thesis also shows that the use of cell savers in on-pump cardiac surgery, instead of the standard care cardiotomy suction, reduced the percentage of patients transfused allogeneic blood products by 10%. However the total amount of blood products transfused was not reduced. This appears to be a paradox. The probable explanation is that the amount of red blood cell transfusions spared is offset by an

increase in the amount of FFP's or platelets transfused since these are completely eliminated during the washing process with the cell saver.

Earlier studies that primarily focussed on processing cardiotomy suction blood found that more patients in the cell saver group received FFP [15,16]. The cell saver initial main deployment was as organ protection for the brain. In our study we did not observe that more patients received FFP despite the fact that the cell saver was used during the entire operation and processed larger quantities of shed blood [17]. Other studies using cell savers in combination with cardiotomy suction had similar results as our study regarding the transfusion of FFP's [18,19].

In our study, which is the largest cell saver study to date, we found however, that if FFP was transfused to patients in cell saver groups, more FFP was transfused compared to patient in the non-cell saver group [17]. Thus, if individual patients suffer from bleeding complications the use of a cell saver may have an adverse effect, probably by the removal of plasma with its coagulation factors and platelets. So, paradoxically, in that situation cell saving in cardiac on-pump operations with large amounts of blood loss may induce a downward spiral of bleeding and increase the total amount of blood products used.

But it is still unclear if the complex cardiac surgical procedure itself or if the use of the cell saver during the procedure is responsible for the increase in haemostatic products. In our study, higher volumes of processed cell saver blood were associated with increased transfusion rates of haemostatic products [17]. With more complex procedures, more blood is collected and processed by the cell saver. As such there is an association between the different surgical procedures, cell saver use and transfusion of haemostatic components. On the other hand, when we compared the use of haemostatic products in patients with CABG, valve surgery and combined procedures, we found no significant effect on the transfusion requirements of haemostatic products whether a cell saver was used or not. This suggests that use of a cell saver per se during the various surgical procedures is not associated with more bleeding disorders. Thus, excessive intra-operative bleeding rather than the type of operation is probably the more important factor for increased haemostatic component transfusions.

Two recent studies showed that routine use of a cell saver in low risk cardiac surgery does not reduce allogeneic transfusions [20,21]. These studies either did not use the cell saver during CPB or a large proportion of the population consisted of off-pump surgery. Contradictory to these studies, two other large studies supported the view that cell saver use in low to intermediate risk surgery reduces allogeneic RBC transfusions [22,23]. One study also showed that the use of a cell saver reduced RBC transfusions in the high-risk surgery groups [22]. The current evidence available thus favours the standard use of a cell saver device to reduce the total amount of allogeneic blood product transfused compared to cardiotomy suction, also in patients with expected little blood loss. But more evidence is needed to help guide clinicians with respect to identifying cardiac surgical patients in who cell salvage might be disadvantageous.

Future directives and implications for further research

First, as mentioned above, more evidence is needed for the use of a cell saver in operations with large amounts of blood loss or extended CPB runs. To achieve this it is important that future studies record and report the volume of cardiotomy suction blood collected and retransfused. This would give the opportunity to better characterize the specific effects of cell saving versus surgical bleeding during complex surgical procedures on transfusion of haemostatic products.

Second, currently three types of cell saver are available. Those with a fixed volume bowl system (Haemonetics (Cell saver®), Sorin (Xtra®, Electa®; BRAT 2®), Medtronics (Autolog®)), with a variable volume bowl system (Haemonetics (CardioPat®; OrthoPat®)) and the continuous, non-bowl, rotary system (Fresenius, (C.A.T.S®)). There is no recent research on the quality of the blood processed by these different types of cell savers. Furthermore not all types of cell savers systems, inherent to the type of system, are suited for use in procedures with high bleeding leading to processing of larger volumes. Whether the type of cell saver system used influences the quality of the processed blood and the need for blood transfusion in cardiac surgery is a question worth investigating.

Third, in reporting cell saver studies in adult on-pump cardiac surgery it is important that all data of the cell saver and other volumes of blood collected are presented. For an objective discussion on cell saver efficacy, studies must clearly state during which part of the surgery and CPB period the cell saver was used. It is important to note in the methods section if the cell saver was used before and after CPB, during CPB, if processing of residual CPB blood was performed and if the cell saver was used post-operatively. Then the total volume collected by the cell saver device and the volume obtained after processing (i.e. the crude extraction ratio) must be reported. This information is automatically available in all modern types of cell saving devices. To even better understand the efficacy of cell savers it would be wise to report the haematocrit of the collected and of the processed blood. The haematocrit is essential to interpret the washing process and the finished product and makes calculating the exact extraction ratio possible [24]. Initial purpose of cell saver deployment is also important to state: organ protection or blood sparing strategy.

Finally, in order to better understand blood utilization in adult cardiac surgery it is necessary to uniformly report allogeneic blood transfusions in studies in a standardized manner. Reporting the total amount of transfusions, the proportion of patients without a transfusion and how many allogeneic blood products were actually transfused per patient can help to lift the veil on the well-kept secret of blood utilization in cardiac surgery.

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