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## Coronary artery surgery: cardiomy suction or cell salvage?

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Published: 25 October 2007

Received: 30 May 2007

*Journal of Cardiothoracic Surgery* 2007, **2**:46 doi:10.1186/1749-8090-2-46

Accepted: 25 October 2007

This article is available from: <http://www.cardiothoracicsurgery.org/content/2/1/46>

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### Abstract

Coronary artery bypass grafting (CABG) today results in what may be regarded as acceptable levels of blood loss with many institutions avoiding allogeneic red cell transfusion in over 60% of their patients. The majority of cardiac surgeons employ cardiomy suction to preserve autologous blood during on-pump coronary artery bypass surgery; however the use of cardiomy suction is associated with a more pronounced systemic inflammatory response and a resulting coagulopathy as well as exacerbating the microembolic load. This leads to a tendency to increased blood loss, transfusion requirement and organ dysfunction. Conversely, the avoidance of cardiomy suction in coronary artery bypass surgery is not associated with an increased transfusion requirement. There is therefore no indication for the routine use of cardiomy suction in on-pump coronary artery surgery.

### Introduction

Coronary artery bypass grafting (CABG) today results in what may be regarded as acceptable levels of blood loss with many institutions avoiding allogeneic red cell transfusion in over 60% of their patients [1,2]. The results of on-pump coronary artery bypass surgery are excellent in terms of early mortality [3]. However there remains significant associated morbidity, including bleeding and secondary organ dysfunction such as neurological and renal impairment.

The cardiomy suction apparatus was introduced in the 1960s as an extension of the intracardiac vent to allow blood shed into the operative field to be returned to the cardiopulmonary bypass (CPB) circuit. The aim was to reduce blood loss and hence the need for allogeneic blood transfusions with its known risk of mortality, other sequelae [4-6] and cost. Recent evidence however, suggests that

the return of shed blood by cardiomy suction does not reduce blood loss or blood transfusion requirement in CABG [7,8]. On the other hand, it has been shown to increase the burden of microembolisation and potentiates the systemic inflammatory response.

### Pericardial shed blood

Blood which has extravasated into the pericardial or pleural cavities and which is subsequently aspirated by cardiomy suction differs markedly from intravascular blood or blood within a closed CPB circuit. Surgical trauma from opening the chest results in substantial tissue damage and release of tissue factor [9,10]. Exposure of blood to tissue factor results in rapid activation of the extrinsic pathway of the coagulation system with release of thrombin and fibrin. In addition, tissue plasminogen activator release stimulates fibrinolysis. Analysis of pericardial shed blood shows high concentrations of markers of clotting activa-

tion and fibrinolysis [11,12] and a low heparin concentration [7]. Activation of the coagulation cascade inevitably results in activation of the other inflammatory cascades. High levels of inflammatory markers such as TNF-alpha, IL-6, IL-8 and have been identified in pericardial shed blood [8,13,14].

In addition to activation of the coagulation cascade, complement system and fibrinolytic pathways, platelets are activated when extravasation occurs into the pericardial cavity. This results in aggregation, degranulation and consumption of platelets, as well as the release of further vasoactive substances [9,12].

The pericardial space also contains a mixture of debris resulting from surgical trauma, most noticeably sternal marrow fat and air microbubbles [15]. Thus, shed 'blood' is far from pure and contains a substantial fraction of potential embolic substances as well as activated platelets and vaso-active mediators. It has been shown that these additional constituents are likely to adversely affect flow characteristics in the micro-circulation with shed blood having grossly abnormal flow characteristics when passed through a 5 micron filter [16].

### **Cardiotomy suction**

Flow within the cardiotomy suction tubing differs significantly from that in the CPB circuit. The concurrent suction of air results in highly turbulent flow with high shear stresses at the air-fluid interface. This causes cellular damage as well as being a potent activator of all the humoral cascades involved in the systemic inflammatory response. Cardiotomy suction blood therefore contains an elevated level of free haemoglobin [7,13,17] due to mechanical haemolysis. High concentrations of free haemoglobin cause platelet dysfunction and direct injury to the renal tubular cells [18]. Similarly, platelet numbers are reduced in cardiotomy suction blood through the rheological trauma [19].

### **Re-transfusion of shed blood retrieved by cardiotomy suction**

Re-transfusing the vasoactive and activated inflammatory mediators in shed blood into the patient's circulation magnifies the systemic inflammatory response. In one study where shed blood was retransfused, the plasma levels of complement C3a, TNF-alpha, IL-6 were significantly elevated compared to when there was no retransfusion [8]. The clinical effect of this was demonstrated by a significant reduction in systemic vascular resistance (SVR) at the point of retransfusion [20]. This fall in SVR correlated to the concentration of TNF-alpha returned to the circulation.

Fat embolisation was known to be associated with cardiotomy suction as long ago as 1963 [21] when fat globules were noted in the urine of patients where the blood overflowed into the pericardium at operation. The authors associated this with the 'post-perfusion syndrome' and advocated discarding this shed blood. Over three decades later, Moody and colleagues demonstrated small capillary and arteriolar dilatations (SCADs) in the brains and other organs of patients who died following cardiopulmonary bypass [22], and confirmed that they were in fact fat emboli lodged within the vessels [23]. Cardiotomy suction blood is known to be saturated with fat released from the subcutaneous tissue and sternal marrow on sternotomy [24,25].

### **Alternative strategies**

There have been many attempts to reduce the problems associated with cardiotomy suction by using filters. These have been shown to reduce, but not eliminate the micro-embolic load [26,27]. Greater reductions in embolic load have been achieved with the use of serial filters [25] however filters do not have any beneficial impact upon the other problems associated with cardiotomy suction, namely derangement of coagulation and activation of inflammatory cascades.

An alternative strategy which has been employed with some success is to use controlled suction which reduces the air-fluid interface and shear stress and thereby attenuates haemolysis and the inflammatory response [19,28].

In an animal model, discarding the shed blood reduced the lipid micro-embolic load more than ten fold compared to when cardiotomy suction was used and the shed blood reinfused [23]. A number of other studies comparing the effects of cardiotomy suction plus retransfusion versus discarding the cardiotomy suction blood in primary CABG have shown a significant reduction in the systemic inflammatory response and haemolysis in the latter group [8,14,29]. Moreover, this was not associated with an increase in the transfusion requirement in the second group but rather a trend towards increased mediastinal bleeding [7,8,30], higher levels of circulating IL6, TNF and C3a [8] and increased thrombin generation, PMN elastase and beta thromboglobulin levels [14] when cardiotomy suction was used, and the shed blood reinfused.

### **Intra-operative cell salvage**

Red cell salvage has been in use in this country in cardiac surgery in a few institutions since 1976. Its use however became widespread following two Health Service Circulars issued by the Chief Medical Officer recommending cell salvage as a key component of the appropriate use of blood [31,32]. Most cardiac units now employ intraoperative cell salvage for complex cases and some use it rou-

tinely in all cardiac procedures requiring cardiopulmonary bypass.

Intraoperative autologous red cell salvage during cardiopulmonary bypass is an attractive alternative to cardiotomy suction. It allows the conservation of red blood cells whilst reducing the retransfusion of fat micro-emboli, activated coagulation and inflammatory markers. When the blood is aspirated from the pericardium, heparin is delivered at an appropriate rate to the tip of the suction cannula to minimize activation of coagulation. The salvaged blood is then stored in a reservoir containing additional heparinised saline prior to processing. During processing the red cells are retained in the bowl whilst the plasma, platelets, heparin, free haemoglobin, and inflammatory mediators are discarded with the wash solution. This process may be discontinuous or continuous, and the resulting red cells are finally resuspended at a haematocrit of 50 – 70% in normal saline, and reinfused.

Fat microembolic load is decreased by the cell saver by as much as 85% [25,26,33-35]. In an animal model of CPB; the processing of shed blood by a cell saver resulted in a significant reduction in the formation of SCADs [25]. Indeed there is some evidence that the continuous autotransfusion devices may now be capable of removing 100% of fat from cell salvage blood [33].

The process of cell salvage results in the activation of white blood cells leading to the release of inflammatory mediators (IL-6, C5a, C3a, terminal complement complexes). However unlike cardiotomy suction blood, the centrifugation and washing processes reduce the concentration of white blood cells by 30 – 80% and inflammatory mediators by 90 – 95% as they are discarded in the wash solution [36].

Cell salvage is not however entirely without problems; the issue of air-fluid interfaces remains, although the avoidance of "skimming" and the presence of heparin at the tip of the suction apparatus reduces the activation of the clotting and inflammatory cascades. It is also easy to understand that if very large volumes of blood are processed through a cell saver it will deplete that volume of blood of platelets and clotting factors, careful monitoring and replacement of these may be necessary.

A small number of studies have shown no adverse effect on mediastinal drainage or transfusion requirements when a cell saver is used to replace cardiotomy suction in coronary surgery [17,30]. A small randomised clinical trial (20 vs 20), demonstrated that reinfusion of cell saved blood did not increase mediastinal blood loss or blood product usage [34]. These published studies were supported by the results of an audit in our own institution (of

first time CABG; 2004–05) in which there was a trend for blood loss or product usage to be higher in those patients managed with cardiotomy suction rather than cell salvage.

### Contemporary clinical studies

It is conceivable that many of the reported benefits attributed to mini-extracorporeal circulation (MECC) systems and off-pump CABG (decreased bleeding, decreased inflammatory response and reduced micro-emboli) may at least in part be attributable to the avoidance of cardiotomy suction. Recent developments in CPB designed to minimise its adverse effects resulted in MECC systems comprising of a short, reservoir-free, heparinised circuit with a centrifugal pump and membrane oxygenator [37]. The closed-circuit design without cardiotomy suction and vents eliminates any air-fluid interface, and pericardial shed blood is not reinfused. Several studies comparing MECC circuits to crude cardiopulmonary bypass circuits have found an attenuated systemic inflammatory response [38], reduced microembolisation [39] and reduced the need for red cell transfusion [40] associated with the former. It is likely that the elimination of cardiotomy suction contributed significantly to the improved outcome of these patients, and further studies are required to compare MECC directly to CPB without cardiotomy suction.

The elimination of CPB and cardiotomy suction altogether in off-pump coronary artery bypass (OPCAB) is also associated with a reduced systemic inflammatory response [41,42], lower transfusion rate [43] and fewer microemboli [44]. Whilst there is some evidence that the organ protective effects of MECC approximates that of OPCAB [45], a direct comparison between OPCAB and CPB without cardiotomy suction is required to ascertain whether the elimination of cardiotomy suction is enough to explain the difference.

### Summary

We know that conventional CPB induces a systemic inflammatory response and results in microembolism to the brain and other organs. Salvage of shed blood by cardiotomy suction exacerbates the inflammatory response and increases the load of lipid emboli to the brain (and by implication, all other capillary beds). Discarding shed mediastinal blood will attenuate these adverse effects but at the cost of losing red cells mass. Cell salvage is an attractive alternative although current evidence suggests that the complications associated with reinfusing shed blood may be attenuated rather than eliminated.

We hope that we have demonstrated that there is good evidence that CABG can be safely performed without the use of cardiotomy suction, with red cell salvage, and without an increase in blood loss or blood usage. Despite this

evidence, cardiomy suction continues to be indiscriminately used during coronary artery bypass surgery, and although in the presence of rapid significant blood loss its use is justified, its continuous application in the operative field is not.

### Conclusion

There is robust, published, clinical evidence that salvage of shed blood by cardiomy suction and its reinfusion is deleterious to patients undergoing coronary artery bypass surgery and we suggest that there is no indication for its routine use in this group. We conclude that cell salvage represents an acceptable alternative to cardiomy suction by attenuating the deleterious effects of the reinfusion of cardiomy suction blood whilst preserving the red cell mass.

### List of Abbreviations

CABG – coronary artery bypass graft

CPB – cardiopulmonary bypass

MECC – mini-extracorporeal circulation

OPCAB – off-pump coronary artery bypass

PMN – polymorphonuclear

SCAD – small capillary and arteriolar dilatation

SVR – systemic vascular resistance

TNF – tumour necrosis factor

### Competing interests

The author(s) declare that they have no competing interests.

### Authors' contributions

Lau, K.K.W.: Acquisition of data, Literature search and preparation of draft of manuscript

Shah, H: Acquisition of Data

Kelleher, A: Design of audit and preparation of draft of manuscript

Moat, N: Design of audit and preparation of draft of manuscript

All authors read and approved the final manuscript

### Acknowledgements

None in addition

### References

1. Stover EP, Siegel LC, Parks R, Levin J, Body SC, Maddi R, D'Ambra MN, Mangano DT, Spiess BD: **Variability in transfusion practice for coronary artery bypass surgery persists despite national consensus guidelines: a 24-institution study.** *Institutions of the Multicenter Study of Perioperative Ischemia Research Group. Anesthesiology* 1998, **88**:327-33.
2. Moise SF, Higgins MJ, Colquhoun AD: **A survey of blood transfusion practice in UK cardiac surgery units.** *Crit Care* 2001, **5(suppl A)**:5. [<http://heartsurgery.healthcarecommission.org.uk>].
3. Mercuriali F, Inghilleri G: **Transfusion risks and limitations.** *Minerva Anestesiol* 1999, **65**:286-92.
4. Kuduvali M, Oo AY, Newall N, Grayson AD, Jackson M, Desmond MJ, Fabri BM, Rashid A: **Effect of peri-operative red blood cell transfusion on 30-day and 1-year mortality following coronary artery bypass surgery.** *Eur J Cardiothorac Surg* 2005, **27**:592-8.
5. Rogers MA, Blumberg N, Saint SK, Kim C, Nallamothu BK, Langa KM: **Allogeneic blood transfusions explain increased mortality in women after coronary artery bypass graft surgery.** *Am Heart J* 2006, **152**:1028-34.
6. de Haan J, Boonstra PW, Monnick SH, Ebels T, van Oeveren W: **Retransfusion of suctioned blood during cardiopulmonary bypass impairs hemostasis.** *Ann Thorac Surg* 1995, **59**:901-7.
7. Westerberg M, Bengtsson A, Jeppsson A: **Coronary surgery without cardiomy suction and autotransfusion reduces the postoperative systemic inflammatory response.** *Ann Thorac Surg* 2004, **78**:54-9.
8. Johnell M, Elgue G, Larsson R, Larsson A, Thelin S, Siegbahn A: **Coagulation, fibrinolysis, and cell activation in patients and shed mediastinal blood during coronary artery bypass grafting with a new heparin-coated surface.** *J Thorac Cardiovasc Surg* 2002, **124**:321-32.
9. Paparella D, Galeone A, Venneri MT, Coviello M, Scarscia G, Marraudino N, Quaranta M, de Luca Tuppiti Schinosa L, Brister SJ: **Activation of the coagulation system during coronary artery bypass grafting: comparison between on-pump and off-pump techniques.** *J Thorac Cardiovasc Surg* 2006, **131**:290-7.
10. Tabuchi N, de Haan J, Boonstra PW, van Oeveren W: **Activation of fibrinolysis in the pericardial cavity during cardiopulmonary bypass.** *J Thorac Cardiovasc Surg* 1993, **106**:828-33.
11. Flom-Halvorsen HI, Ovrum E, Tangen G, Brosstad F, Ringdal MA, Oystese R: **Autotransfusion in coronary artery bypass grafting: disparity in laboratory tests and clinical performance.** *J Thorac Cardiovasc Surg* 1999, **118**:610-7.
12. Reents W, Babin-Ebell J, Misoph MR, Schwarzkopf A, Elert O: **Influence of different autotransfusion devices on the quality of salvaged blood.** *Ann Thorac Surg* 1999, **68**:58-62.
13. Aldea GS, Soltow LO, Chandler WL, Triggs CM, Vocelka CR, Crockett GI, Shin YT, Curtis WE, Verrier ED: **Limitation of thrombin generation, platelet activation, and inflammation by elimination of cardiomy suction in patients undergoing coronary artery bypass grafting treated with heparin-bonded circuits.** *J Thorac Cardiovasc Surg* 2002, **123**:742-55.
14. Solis RT, Noon GP, Beall AC Jr, DeBakey ME: **Particulate microembolism during cardiac operation.** *Ann Thorac Surg* 1974, **17**:332-44.
15. Appelblad M, Engstrom G: **Fat contamination of pericardial suction blood and its influence on in vitro capillary-pore flow properties in patients undergoing routine coronary artery bypass grafting.** *J Thorac Cardiovasc Surg* 2002, **124**:377-86.
16. Svenmarker S, Engstrom KG: **The inflammatory response to recycled pericardial suction blood and the influence of cell-saving.** *Scand Cardiovasc J* 2003, **37**:158-64.
17. Rother RP, Bell L, Hillmen P, Gladwin MT: **The clinical sequelae of intravascular hemolysis and extracellular plasma hemoglobin: a novel mechanism of human disease.** *JAMA* 2005, **293**:1653-62.
18. Boonstra PW, van Imhoff GW, Eysman L, Kootstra GJ, van der Heide JN, Karliczek GF, Wildevuur CR: **Reduced platelet activation and improved hemostasis after controlled cardiomy suction during clinical membrane oxygenator perfusions.** *J Thorac Cardiovasc Surg* 1985, **89**:900-6.

20. Westerberg M, Gabel J, Bengtsson A, Sellgren J, Eidem O, Jeppsson A: **Hemodynamic effects of cardiotomy suction blood.** *J Thorac Cardiovasc Surg* 2006, **131**:1352-7.
21. Caguin F, Carter MG: **Fat embolization with cardiotomy with the use of cardiopulmonary bypass.** *J Thorac Cardiovasc Surg* 1963, **46**:665-72.
22. Moody DM, Brown WR, Challa VR, Stump DA, Reboussin DM, Legault C: **Brain microemboli associated with cardiopulmonary bypass: a histologic and magnetic resonance imaging study.** *Ann Thorac Surg* 1995, **59**:1304-7.
23. Brooker RF, Brown WR, Moody DM, Hammon JW Jr, Reboussin DM, Deal DD, Ghazi-Birry HS, Stump DA: **Cardiotomy suction: a major source of brain lipid emboli during cardiopulmonary bypass.** *Ann Thorac Surg* 1998, **65**:1651-5.
24. Brown WR, Moody DM, Challa VR: **Cerebral fat embolism from cardiopulmonary bypass.** *J Neuropathol Exp Neurol* 1999, **58**:109-19.
25. Kaza AK, Cope JT, Fiser SM, Long SM, Kern JA, Kron IL, Tribble CG: **Elimination of fat microemboli during cardiopulmonary bypass.** *Ann Thorac Surg* 2003, **75**:555-9.
26. de Vries AJ, Gu YJ, Douglas YL, Post WJ, Lip H, van Oeveren W: **Clinical evaluation of a new fat removal filter during cardiac surgery.** *Eur J Cardiothorac Surg* 2004, **25**:261-6.
27. Whitaker DC, Newman SP, Stygall J, Hope-Wynne C, Harrison MJ, Walesby RK: **The effect of leucocyte-depleting arterial line filters on cerebral microemboli and neuropsychological outcome following coronary artery bypass surgery.** *Eur J Cardiothorac Surg* 2004, **25**:267-74.
28. Mueller XM, Tevaearai HT, Horisberger J, Augstburger M, Boone Y, von Segesser LK: **Smart suction device for less blood trauma: a comparison with Cell Saver.** *Eur J Cardiothorac Surg* 2001, **19**:507-11.
29. Skrabal CA, Khosravi A, Choi YH, Kaminski A, Westphal B, Steinhoff G, Liebold A: **Pericardial suction blood separation attenuates inflammatory response and hemolysis after cardiopulmonary bypass.** *Scand Cardiovasc J* 2006, **40**:219-23.
30. Nuttall GA, Oliver WC, Fass DN, Owen WG, Dinunno D, Ereth MH, Williams BA, Dearani JA, Schaff HV: **A prospective, randomized platelet-function study of heparinized oxygenators and cardiotomy suction.** *J Cardiothorac Vasc Anesth* 2006, **20**:554-61.
31. **Health Service Circular Better Blood Transfusion.** Department of Health (HSC 1998/224).
32. **Health Service Circular Better Blood Transfusion: appropriate use of blood.** Department of Health (HSC 2002/009).
33. Booke M, Fobker M, Fingerhut D, Storm M, Mortlemans Y, Van Aken H: **Fat elimination during intraoperative autotransfusion: An in vitro investigation.** *Anesth Analg* 1997, **85**:959-962.
34. Jewell AE, Akowuah EF, Suvarna SK, Bradley P, Hopkinson D, Cooper G: **A prospective randomised comparison of cardiotomy suction and cell saver for recycling shed blood during cardiac surgery.** *Eur J Cardiothorac Surg* 2003, **23**:633-6.
35. Kincaid EH, Jones TJ, Stump DA, Brown WR, Moody DM, Deal DD, Hammon JW Jr: **Processing scavenged blood with a cell saver reduces cerebral lipid microembolization.** *Ann Thorac Surg* 2000, **70**:1296-300.
36. Munoz M, Campos A, Munoz E, Carrero A, Cuenca J, Garcia-Erce JA: **Red cell salvage in orthopedic surgery.** *Transfusion Alternatives in Transfusion Medicine* 2006, **8**:41-51.
37. Remadi JP, Marticho P, Butoi I, Rakotoarivelo Z, Trojette F, Benamar A, Beloucif S, Foure D, Poulain HJ: **Clinical experience with the mini-extracorporeal circulation system: an evolution or a revolution?** *Ann Thorac Surg* 2004, **77**:2172-5.
38. Fromes Y, Gaillard D, Ponzio O, Chauffert M, Gerhardt MF, Deleuze P, Bical OM: **Reduction of the inflammatory response following coronary bypass grafting with total minimal extracorporeal circulation.** *Eur J Cardiothorac Surg* 2002, **22**:527-33.
39. Liebold A, Khosravi A, Westphal B, Skrabal C, Choi YH, Stamm C, Kaminski A, Alms A, Birken T, Zurakowski D, Steinhoff G: **Effect of closed minimized cardiopulmonary bypass on cerebral tissue oxygenation and microembolization.** *J Thorac Cardiovasc Surg* 2006, **131**:268-76.
40. Folliguet TA, Philippe F, Larrazet F, Dibie A, Czitrom D, Le Bret E, Bachel J, Laborde F: **Beating heart revascularization with minimal extracorporeal circulation in patients with a poor ejection fraction.** *Heart Surg Forum* 2002, **6**:19-23.
41. Schulze C, Conrad N, Schutz A, Egi K, Reichensperner H, Reichart B, Wildhirt SM: **Reduced expression of systemic proinflammatory cytokines after off-pump versus conventional coronary artery bypass grafting.** *Thorac Cardiovasc Surg* 2000, **48**:364-9.
42. Ascione R, Lloyd CT, Underwood MJ, Lotto AA, Pitsis AA, Angelini GD: **Inflammatory response after coronary revascularization with or without cardiopulmonary bypass.** *Ann Thorac Surg* 2000, **69**:1198-204.
43. Guru V, Glasgow KW, Femes SE, Austin PC, Teoh K, Tu JV: **The real-world outcomes of off-pump coronary artery bypass surgery in a public health care system.** *Can J Cardiol* 2007, **23**:281-6.
44. Abu-Omar Y, Balacumaraswami L, Pigott DW, Matthews PM, Taggart DP: **Solid and gaseous cerebral microembolization during off-pump, on-pump, and open cardiac surgery procedures.** *J Thorac Cardiovasc Surg* 2004, **127**:1759-65.
45. van Boven WJ, Gerritsen WB, Waanders FG, Haas FJ, Aarts LP: **Mini extracorporeal circuit for coronary artery bypass grafting: initial clinical and biochemical results: a comparison with conventional and off-pump coronary artery bypass grafts concerning global oxidative stress and alveolar function.** *Perfusion* 2004, **19**:239-46.

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