# Mechanical methods of reducing blood transfusion in cardiac surgery: randomised controlled trial

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ELPS

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## Abstract

**Objective** To assess the effectiveness of two mechanical methods of blood conservation in reducing the need for allogeneic red blood cells or coagulation products during cardiac surgery.
**Design** Randomised controlled trial.
**Setting** Regional cardiac centre in a teaching hospital in Southampton.
**Participants** 263 adults aged 18-80 years undergoing elective coronary artery bypass surgery entered the study, of whom 252 completed the trial. All patients received routine perioperative care. Patients were allocated to one of three treatment groups: intraoperative cell salvage, intraoperative cell salvage with acute perioperative normovolaemic haemodilution, or no mechanical blood conservation. There were 84 patients in each group.
**Main outcome measures** Numbers of patients who received allogeneic blood or coagulation products, and the mean number of units of blood transfused per patient.
**Results** Of the patients in the intraoperative cell salvage group, 26 were given a transfusion of allogeneic blood, compared with 43 in the control group (odds ratio 0.43 (95% confidence interval 0.23 to 0.80)). The mean number of units of allogeneic blood transfused per patient in the intraoperative cell salvage group was 0.68 units (SD=1.55), compared with 1.07 (1.56) units in the control group. 32 of the patients in the intraoperative cell salvage group were given any blood product, compared with 47 in the control group (odds ratio 0.47 (0.25 to 0.89); P=0.019). Combining acute perioperative normovolaemic haemodilution with intraoperative cell salvage conferred no additional benefits.
**Conclusions** An intraoperative cell salvage device should be used in elective coronary artery bypass grafting. Pharmacological strategies may achieve further reductions in blood transfusions. Yet further reductions in blood transfusions could be achieved if the lower safe limit of haemoglobin concentration in patients undergoing cardiac surgery were known.


## Introduction

The National Blood Service for England issues approximately 2.2 million units of blood a year, of which 10% are used in cardiac surgical units.[1 2] Up to 92% of patients presenting for elective cardiac surgery receive blood.[3 4] Patients who receive allogeneic blood risk contracting bloodborne or other infections or having a perioperative myocardial infarction.[5–7] To minimise the risk of transmission of variant Creutzfeldt-Jakob disease, leucodepletion of all donated blood in this country has been introduced. This has quadrupled the cost of allogeneic red blood cells. The optimal use of this scarce, expensive, and potentially infectious resource is of international importance.

Intraoperative cell salvage is the most widely used method of mechanical blood conservation in elective cardiac surgery.[8] Acute perioperative normovolaemic haemodilution is used in less than 20% of cardiac units.[9] Both techniques have cost implications and have yet to become normal practice—perhaps due to the lack of data showing their effectiveness.[10 11]

We report a randomised controlled trial in patients undergoing elective coronary artery bypass surgery. We compared a group of patients in whom intraoperative cell salvage was used with a control group and with a group in whom acute perioperative normovolaemic haemodilution was used in addition to intraoperative cell salvage.

## Materials and methods

### Selection of patients

Patients were approached on their admission the day before surgery in the cardiac unit at Southampton General Hospital. Written informed consent was sought from all patients thought to meet the inclusion criteria (box).

A total of 252 patients who met the inclusion criteria were randomised to one of the three groups. Intraoperative masking of mechanical red blood cell salvage treatment was not possible.

### Trial protocol

All patients received standard care according to a protocol (see bmj.com).

*Intraoperative cell salvage group* A cell saver (Dideco Compact, Dideco, Mirandola, Italy) was used from incision until the end of surgery. After the termination of the bypass, patients received protamine, and any shed blood and the residual cardiopulmonary bypass circuit volume were washed and centrifuged by the intraoperative cell salvage machine then retransfused.

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**Eligibility criteria**

Inclusion criteria:
- Age 18-80 years
- Ejection fraction >30%
- Serum creatinine concentration <150 μmol/l
- International normalised ratio and activated partial thromboplastin time <1.5
- Platelet count $>150 \times 10^9$/l
- Haemoglobin concentration >120 g/l
- Haematocrit >0.36
- Weight >60 kg

Exclusion criteria:
- Emergency operation
- Redo procedures and multiple procedures
- Known carotid stenosis >50%
- Myocardial infarction in past three weeks
- Heparin or warfarin taken in previous five days
- Antiplatelet treatment other than aspirin
- Cerebrovascular disease
- History of liver disease
- Jehovah's Witnesses

*Combined treatment group* After induction of anaesthesia 10 ml/kg of blood was removed from the central venous line while being replaced at the same time with an equivalent volume of modified gelatin (Gelofusine). The Harvest Blood Stream Recovery System, an autologous recovery system, was used to remove blood. The recovered blood was stored at room temperature. After protamine administration the autologous blood collected after induction of anaesthesia was retransfused. The cell saver was used in the same manner as in the intraoperative cell salvage group.

*Control group* The residual cardiopulmonary bypass circuit volume was retransfused into the patient after protamine administration.

All patients were under the care of cardiac intensivists, who were blind to the allocation of patients to study group. The threshold for transfusion of allogeneic red blood cells was the same in all groups: haemoglobin concentration <90 g/l and haematocrit <0.27. Administration of allogeneic blood coagulation products (fresh frozen plasma and platelets) was at the discretion of the cardiac intensivists.

### Statistical analysis

Percentages of patients receiving the various blood products were compared in logistic regression models, controlled for surgeon. Differences between groups in these percentages were deemed significant if they achieved significance of $P<0.025$ in the Wald test. The Kruskal-Wallis one way analysis of variance was used to compare the differences between the groups in the amounts of blood products used and in the secondary outcomes.

## Results

### Baseline characteristics

The distributions of sex, age, weight, left ventricular function, aspirin administration, and Parsonnet scores, which allow preoperative risk stratification, were similar across the three groups.

### Primary outcomes

Fewer patients in the intraoperative cell salvage group than in the control group were given allogeneic red blood cells, or any blood product, and the mean number of units of red blood cells transfused per patient was less in the intraoperative cell salvage group than in the control group (table 1). The combination of acute perioperative normovolaemic haemodilution and intraoperative cell salvage did not show any additional benefit over intraoperative cell salvage alone.

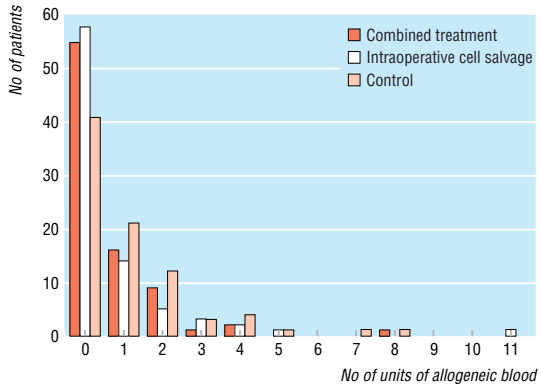
Most patients were not given allogeneic blood (figure). Nine patients needed a markedly higher amount of transfused blood (≥3 units). A surgical cause of bleeding was found in seven of these patients (three in the control group and two in each of the two treatment groups).

The variations in haemoglobin concentration from before the operation to day 3 after the operation were similar in the three groups (see bmj.com). No patient

**Table 1** Blood products given to patients (n=84 in each group) during their perioperative course

| | | | | | Intraoperative cell salvage* *v* control | | Combined treatment *v* intraoperative cell salvage* | |
|---|---|---|---|---|---|---|---|---|
| **Blood product received** | **Control** | **Intraoperative cell salvage** | **Combined treatment** | **Kruskal-Wallis P value** | **Odds ratio (95% CI)** | **Wald test P value** | **Odds ratio (95% CI)** | **Wald test P value** |
| Allogeneic blood: | | | | | | | | |
| No of patients | 43 | 26 | 29 | | 0.43 (0.23-0.80) | 0.008 | 1.18 (0.62-2.24) | 0.622 |
| Mean (SD) No of units received per patient | 1.07 (1.56) | 0.68 (1.55) | 0.63 (1.22) | 0.015 | | | | |
| Range | 0-8 | 0-11 | 0-8 | | | | | |
| Fresh frozen plasma: | | | | | | | | |
| No of patients | 13 | 14 | 13 | | 1.1 (0.47-2.53) | 0.831 | 0.91 (0.40-2.11) | 0.831 |
| Mean (SD) No of units received per patient | 0.49 (1.25) | 0.57 (1.47) | 0.43 (1.12) | 0.952 | | | | |
| Range | 0-6 | 0-8 | 0-6 | | | | | |
| Platelets: | | | | | | | | |
| No of patients | 15 | 11 | 15 | | 0.68 (0.29-1.62) | 0.386 | 1.46 (0.62-3.47) | 0.386 |
| Mean (SD) No of units received per patient | 0.29 (0.67) | 0.20 (0.62) | 0.31 (0.81) | 0.601 | | | | |
| Range | 0-3 | 0-4 | 0-4 | | | | | |
| No of patients given any blood product | 47 | 32 | 33 | | 0.47 (0.25-0.89) | 0.019 | 1.05 (0.56-1.98) | 0.872 |

*Controlled for surgeon.




No of units of allogeneic blood transfused into patients

was given a transfusion of allogeneic blood after leaving the intensive care unit.

### Secondary outcomes

There were no differences between the groups in mediastinal drainage, time in intensive care, or length of stay in hospital. The median duration of acute perioperative normovolaemic haemodilution was 13 minutes. Patients in the combination treatment group spent the longest time in the anaesthetic room. Groups were similar with respect to total anaesthesia and surgery times, and times on cardiopulmonary bypass and with the aorta cross-clamped (see bmj.com). Perioperative complications were evenly distributed across the groups (table 2).

## Discussion

### Intraoperative cell salvage

A recent meta-analysis of cell salvage in cardiac and orthopaedic surgery found that in cardiac surgery cell salvage marginally reduced use of allogeneic blood products (relative risk 0.85 (0.79 to 0.92)).[10] However, none of the trials washed the salvaged blood before returning it to the patient, and the intraoperative cell salvage devices were used only postoperatively. Trials in which intraoperative cell salvage machines were used intraoperatively failed to meet standard eligibility criteria for the meta-analysis. Our method of intraoperative cell salvage maximised surgical salvage of red blood cells, and our washing of the residual cardiopulmonary bypass volume allowed optimal haemoconcentration, accounting for the greater efficacy of intraoperative cell salvage. Our study is the first to compare intraoperative use of intraoperative cell salvage with control treatment.

### Acute perioperative normovolaemic haemodilution

Acute perioperative normovolaemic haemodilution is not well established in cardiac surgery. A meta-analysis of the treatment across surgical specialties concluded that it reduces the need for allogeneic red blood cells (odds ratio 0.31 (0.15 to 0.62)), but that the evidence in cardiac surgery was less compelling (0.51 (0.26 to 0.99)).[11] This meta-analysis included 11 randomised controlled trials in cardiac surgery.[12–22] However, the quality of the evidence from these trials varied, only four of the trials having a transfusion protocol.[17 18 21 22] Overall the evidence for the benefit of acute perioperative normovolaemic haemodilution in reducing use of allogeneic red blood cells during cardiac surgery was equivocal.

Our results indicate that acute perioperative normovolaemic haemodilution does not confer additional benefits in terms of reduced use of allogeneic transfusion. This may be because not enough blood was removed at the start of the procedure. Given the patients' severe coronary artery disease, we decided not to exceed a predonated volume of 10 ml/kg. Removing a greater volume of blood preoperatively may expose patients to ischaemic events and decreased myocardial contractility.[23]

### Limitations

Just over half (43/84) the patients in the control group were given a transfusion—a considerably lower proportion than that reported for our institution in a previous study.[4] We believe the main reason for this was that the transfusion threshold was reduced between the two studies from a haemoglobin concentration of 100 g/l to 90 g/l.

The lack of a protocol on the use of allogeneic blood coagulation products means that caution is needed in interpreting differences between the groups in the use of fresh frozen plasma and platelets. Our trial involved patients undergoing elective coronary artery bypass grafting. Although intraoperative cell salvage may be useful in more complex cardiac surgery or for patients with pre-existing coagulopathy, our findings cannot necessarily be extrapolated to such patients.

Intraoperative masking of mechanical conservation technique was not possible. This might have led to transfusion practice being driven by knowledge of allocation to group. This effect would be pronounced if no transfusion protocol were used. Because the intensive care staff were blinded to allocation to group, and no protocol violations occurred, we assume that the reduction in allogeneic red blood cell transfusion is related to the efficacy of intraoperative cell salvage.

### Conclusions

The need for allogeneic red blood cell transfusion in elective coronary artery bypass grafting can be reduced by using intraoperative cell salvage. Acute perioperative normovolaemic haemodilution with intraoperative cell salvage confers no additional benefit. The lower safe limit of haemoglobin concentration in patients undergoing cardiac surgery—either while they are on bypass or postoperatively—is unknown. If this limit was known, and made use of, the combination of optimal pharmacological strategies with intraoperative cell salvage could achieve yet further reductions in the numbers of patients who

**Table 2** Numbers of patients with perioperative complications (n=84 in each group)

| | Control | Intraoperative cell salvage | Combined treatment |
|---|---|---|---|
| Without complications | 42 | 46 | 46 |
| Inotropes required after 24 hours | 9 | 12 | 11 |
| Surgical bleeding | 3 | 2 | 2 |
| Cerebrovascular accident | 2 | 1 | 1 |
| Arrhythmias | 27 | 17 | 20 |
| Renal failure | 0 | 1 | 2 |
| Proven infection | 7 | 11 | 7 |
| Myocardial infarction | 10 | 5 | 4 |

## What is already known on this topic

Patients undergoing elective coronary artery bypass surgery often need a blood transfusion

Recent meta-analyses have shown that the mechanical blood conservation techniques of intraoperative cell salvage and acute perioperative normovolaemic haemodilution may reduce the need for transfusion, but flawed methods in trials mean that clear evidence in cardiac surgery is lacking

## What this study adds

Intraoperative cell salvage significantly reduces the number of patients needing an allogeneic blood transfusion

Combining acute perioperative normovolaemic haemodilution with intraoperative cell salvage does not confer any additional benefit

need to be given transfusions of allogeneic red blood cells and blood coagulation products.

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*Science commentary*

# Science commentary: Why is it important to reduce the need for blood transfusion, and how can it be done?

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Reducing the need for blood transfusions is desirable for several reasons. Since 2000 in the United Kingdom it has been mandatory to remove all white cells from donated blood to reduce the small but theoretical risk of prion disease (variant Creutzfeldt-Jakob disease). This has trebled the cost of providing donated blood. Transmission of hepatitis B, hepatitis C, and HIV by transfusion occurs in 1 in 300 000 cases, despite screening programmes.[1] However, non-fatal but serious transfusion errors occur in 1 in 16 000 transfusions.[1]

Critically ill patients are now known to do just as well with a lower haemoglobin concentration than previously thought, thus reducing the need for top-up transfusions.[2] There is also some evidence that homologous blood transfusions increase the rates of recurrence of some cancers (tumours of the bowel and oesophagus, in particular) and can increase the incidence of wound infections.[3] It is unclear why these phenomena occur.

A number of mechanical methods have been developed to help reduce the need for postoperative blood transfusions. In the United States erythropoetin injections or autologous blood donations (or both), given preoperatively, are commonly used. Both require the exact date of surgery to be known—but neither process is free from human error in labelling, storing, and administration.