

**The role of intra-operative cell salvage in patient blood management for revision hip arthroplasty:
a prospective cohort study**

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Summary

Cell salvage is an important component of blood management in patients undergoing revision hip surgery. However, concerns regarding efficacy and patient selection remain. The aims of this study were to describe intra-operative blood loss, cell salvage re-infusion volumes and red blood cell transfusion rates for revision hip procedures, and to identify factors associated with the ability to salvage sufficient blood intra-operatively to permit processing and re-infusion. Data were collected from a prospective cohort of 664 consecutive patients undergoing revision hip surgery at a single tertiary centre from 31 March 2015 to 1 April 2018. Indications for revision surgery were: aseptic ($n = 393$ (59%)); fracture ($n = 160$ (24%)); and infection ($n = 111$ (17%)). Salvaged blood was processed and re-infused when blood loss exceeded 500 ml. Mean (SD) intra-operative blood loss was 1038 (778) ml across all procedures. Salvaged blood was re-infused in 505/664 (76%) cases. Mean (SD) re-infusion volume was 253 (169) ml. In total, 246 of 664 (37%) patients received an allogeneic red blood cell transfusion within 72 hours of surgery. Patients undergoing femoral component revision only (OR (95%CI) 0.41 (0.23–0.73)) or acetabular component revision only (0.53 (0.32–0.87)) were less likely to generate sufficient blood salvage for re-infusion compared with revision of both components. Compared with aseptic indications, patients undergoing revision surgery for infection (1.87 (1.04–3.36)) or fracture (4.43 (2.30–8.55)) were more likely to generate sufficient blood salvage for re-infusion. Our data suggest that cell salvage is efficacious in this population. Cases where the indication is infection or fracture and where both femoral and acetabular components are to be revised should be prioritised.

Introduction

Revision hip arthroplasty is associated with significant peri-operative blood loss and high allogeneic red blood cell transfusion requirements [1]. Blood loss and red blood cell transfusion are both independently associated with increased morbidity and mortality [2, 3]. Strategies to reduce peri-operative blood loss and allogeneic red blood cell transfusion requirements include optimisation of pre-operative anaemia [4], antifibrinolytic therapy [5], and intra-operative cell salvage [6-8].

Whilst pre-operative anaemia optimisation and antifibrinolytic therapy are indicated for all patients undergoing revision hip and knee surgery, the role of intra-operative cell salvage is less well defined [8, 9]. Interpretation of currently available data is limited by heterogeneity of surgical procedures and patient characteristics, as well as uncertainties regarding estimates of blood loss and re-infusion volumes [10, 11]. A previous study of aseptic elective hip revision arthroplasty found that adequate blood for re-infusion was collected in only half of patients [12].

Current guidelines vary in their recommendations for cell salvage. The National Institute for Health and Care Excellence recommends considering intra-operative cell salvage in patients who are *“expected to lose a very high volume of blood, for example in cardiac and complex vascular surgery, major obstetric procedures, and pelvis reconstruction and scoliosis surgery”* [9], whereas the Association of Anaesthetists recommends its use when *“it can be expected to reduce the likelihood of allogeneic (donor) red cell transfusion and/or severe postoperative anaemia”* [13]. Importantly the use of cell salvage may also be limited by costs and resources [8]. Therefore, it is essential to target patients who are most likely to benefit from this intervention.

The aims of this study were to determine intra-operative blood loss, cell salvage re-infusion volumes and allogeneic transfusion rates for revision hip arthroplasty, and to identify factors associated with the ability to salvage sufficient blood intra-operatively to permit processing and re-infusion.

Methods

We performed a prospective cohort study of all patients undergoing revision hip arthroplasty who received intra-operative cell salvage at the Nuffield Orthopaedic Centre, Oxford, UK, between 31 March 2015 and 01 April 2018. Revision was defined as removal or exchange of any hip prosthesis component. Indications for revision hip surgery were categorised as either: aseptic, fracture, or infection. Aseptic indications were primarily implant wear or loosening that was causing pain or mechanical. There were no exclusion criteria. We report our findings in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement. Research Ethics Committee approval was not required as per the Health Research Authority assessment tool. The study received Caldicott Guardian approval.

Pre-operative assessment was performed within six weeks of surgery for elective cases and on admission to hospital for emergency cases. Routine pre-operative investigations included haemoglobin and haematocrit measurements. Haemoglobin and haematocrit were measured intra-operatively using blood gas analysis with a frequency of measurement determined by the rate of blood loss and patient haemodynamic status. A formal laboratory measurement of haemoglobin and haematocrit was also performed on the morning following surgery. All patients routinely received general anaesthesia with or without neuraxial anaesthesia followed by 1g intravenous (i.v.) tranexamic acid prior to skin incision. This was followed by a 2 g topical dose of tranexamic acid at the discretion of the operating surgeon prior to skin closure. Drains were not routinely inserted. Routine postoperative thromboprophylaxis consisted of low molecular weight heparin commenced 6 h after skin closure and thrombo-embolic deterrent stockings. There was no change in routine surgical or anaesthetic technique during the period of study.

As per our local institution's policy, we employed intra-operative cell salvage collection for all revision hip arthroplasty procedures except during first stage revision and debridement and implant retention for infection, when it was used at the discretion of the senior surgeon and anaesthetist. We did not consider infection as a contra-indication to cell salvage, but any fluid visibly contaminated by infection, cement or metallic debris was not collected. Wound irrigation was performed using saline and if chlorhexidine solution was used, it was reserved until the end of the procedure once cell salvage was complete. A leucocyte reduction filter (40µm) was used for infected cases. We commenced all procedures with the cell salvage system in 'collect only' mode. Salvaged blood was processed to resuspend red blood cells with a haematocrit of 50–60% once estimated

blood loss exceeded 500 ml. Cell salvage was performed using Sorin Xtra™ (LivaNova, London, UK) machines. Bowl size was selected based on the volume of salvaged blood (range 55–225 ml). In keeping with national guidelines [9], our haemoglobin red blood cell transfusion threshold was 70 g.l⁻¹, except for patients with acute coronary syndrome where the threshold was 80 g.l⁻¹. Red blood cell transfusions on the day of surgery were defined as those taking place before midnight.

Data were collected from local electronic patient records and cell salvage databases. Data included: patient demographics (age, sex, ASA, BMI); procedure performed and indication; cell salvage records (intra-operative blood loss, re-infused blood volume and haematocrit); haemoglobin and haematocrit measurements (pre-operative, intra-operative, and postoperative); and allogeneic red blood cell transfusion records.

Estimated intra-operative blood loss was calculated according to the following formula [14]:

$$\text{Blood loss (ml)} = \text{Estimated blood volume (ml)} * \left(\frac{\text{Hct procedure start(\%)} - \text{Hct pretransfusion(\%)}}{(\text{Hct procedure start(\%)} + \text{Hct pretransfusion(\%)})/2} \right)$$

Where estimated blood volume is 65 ml.kg⁻¹ for females and 75 ml.kg⁻¹ for males using ideal body weight, the proportion of estimated blood loss re-infused was calculated as:

$$\text{Cell Salvage Efficiency (\%)} = \left(\frac{\text{re - infusion volume(ml)} * \text{re - infusion Hct (\%)}}{\text{Hct procedure start (\%)} * \text{estimated blood loss(ml)}} \right)$$

Estimated increase in haemoglobin concentration after re-infusing salvaged blood was calculated using the formula:

$$\text{Change in Hb} = \text{Hb pre - transfusion(g/L)} * \left(1 + \frac{\text{re - infusion volume(ml)} * \text{reinfusion Hct(\%)}}{\text{estimated blood volume(ml)} * \text{Hct pre - transfusion(\%)}} \right)$$

The volume of salvaged blood was standardised to haematocrit 60%. Two outcomes of interest were assessed: whether a sufficient volume of blood was salvaged intra-operatively to allow for processing and re-infusion; and standardised volume of re-infused blood (haematocrit 60%). We performed logistic and univariate linear regression analyses to explore associations between patient demographics, pre-operative anaemia, procedure performed and indication for surgery with each

outcome of interest, respectively. Factors that demonstrated a statistically significant relationship in univariate analysis were included in multivariable regression models. Total femoral replacement was included as revision of the femoral and acetabular component. A p value less than 0.05 was considered statistically significant.

Results

A total of 664 patients were included in our analysis. Mean intra-operative blood loss exceeded 500 ml for all revision hip procedures and 1000 ml for procedures where the femoral and acetabular components were revised (Tables 1 and 2). Thirty-seven percent (244/664) of patients required an intra-operative or postoperative allogeneic red blood cell transfusion within 72 h of surgery (Fig. 1). A median (IQR [range]) of 2 (2–3 [0–12]) units were transfused per patient. Eight patients (1.2%) required more than four units of red blood cells on the day of surgery (range 0–12 units). There was no change in pre-operative and postoperative haemoglobin concentration or allogeneic red blood cell transfusion rates over the course of the study (Supporting Information Figure S1).

A sufficient volume of blood was salvaged to allow re-infusion in 76% (505/664) of procedures. There was no difference in patient characteristics for patients where sufficient blood was salvaged for re-infusion compared with patients where it was not (see Supporting Information Table S1). Mean (SD) re-infusion volume was 253 (169) ml (standardised haematocrit 60%) (Fig. 2), equating to an estimated mean (SD) increase in haemoglobin of 10.2 (6.8) g.l⁻¹ per patient receiving autologous blood. An estimated one-third of blood volume lost intra-operatively was returned to the patient (Tables 1 and 2). Patient factors age, sex, BMI and haemoglobin concentration at the start of the procedure were not statistically associated with the ability to salvage sufficient blood for re-infusion.

Patients undergoing femoral component revision only (OR (95%CI) 0.41 (0.23–0.73)) or acetabular component revision only (OR 0.53 (0.32–0.87)) were less likely to generate sufficient blood salvage for re-infusion when compared with when both the femoral and acetabular components were revised. Compared with aseptic indications, patients undergoing revision surgery for infection (OR 1.87 (1.04–3.36)) or fracture (OR 4.43 (2.30–8.55)) were more likely to generate sufficient blood salvage for re-infusion (Table 3).

Smaller blood volumes were re-infused with increasing age (coefficient (95%CI) -1.9 (-2.9–0.8)) and higher volumes were re-infused in males (coefficient 52.0 (25.0 to 79.0)). A smaller volume of blood

was re-infused when only revising a single component, whereas the indication for surgery was not statistically associated with re-infusion volume (Table 4).

Discussion

In this study, the mean intra-operative blood loss for each revision hip procedure exceeded 500 ml; intra-operative cell salvage provided sufficient autologous blood for re-infusion in over three-quarters of these patients. Where sufficient blood was salvaged for processing and re-infusion, this equated to nearly one unit of packed red blood cells per patient, yet still more than one-third of patients required a peri-operative allogeneic red blood cell transfusion. Patients undergoing revision hip arthroplasty for infection or fracture and those where both femoral and acetabular components were revised, were more likely to generate sufficient blood salvage for re-infusion. We found no association between patient characteristics and pre-operative haemoglobin concentration, and the utility of cell salvage.

Our estimated intra-operative blood loss was comparable with other studies with an average of 1000 ml across all procedures [15], as was the average volume of re-infusion of 250 ml, although studies frequently do not specify the haematocrit of the re-infused blood [12, 15]. The proportion of patients with sufficient blood salvage for re-infusion in our study is comparable or higher than in other studies [12, 15]. In a cohort of 298 patients undergoing aseptic revision hip arthroplasty, re-infusion was only possible in 54% of patients [12]. In a cohort of 210 patients undergoing revision hip arthroplasty for a range of indications, cell salvage was used for 88 cases of which 68 had sufficient blood salvage for re-infusion [15]. Potential reasons for an increased salvage yield in our study include more fastidious suctioning, salvage from swabs or possibly a different set-up and performance of cell salvage machines.

Our red blood cell transfusion rates are lower than those reported in other studies, where rates of 57% [12] and 58% [15] have been described. The mean pre-operative haemoglobin in our cohort was 124 g.l⁻¹, which is similar to other studies [15]. Our lower allogeneic red blood cell transfusion rates may reflect: more efficient cell salvage; a smaller volume of blood loss secondary to surgical technique; preference for combined general and spinal anaesthesia together with the effects of the current emphasis on patient blood management including use of antifibrinolytic agents (such as tranexamic acid); and adherence to restrictive transfusion thresholds. The highest rate of red blood cell transfusion was for patients undergoing exploration and modular exchange, this procedure had the

lowest intra-operative blood loss of all procedures; as such, fewer patients had sufficient blood collection to allow re-infusion.

An estimated 35% of intra-operative blood loss was salvaged and re-infused during surgery. The greatest efficiency was achieved during second stage revision, perhaps due to the absence of contaminated blood as the implant has previously been removed and infection eradicated. The lowest efficiency was during total femoral replacement, likely due to difficulty containing blood loss within an extensive surgical field. The ability to salvage sufficient blood loss for re-infusion is dependent on the volume of intra-operative blood loss; however, the decision to employ cell salvage should be based on information available pre-operatively. Data from our study suggests that patient factors are not important determinants of the ability to collect sufficient blood for re-infusion. Pre-operative anaemia was not associated with the ability to collect sufficient blood for re-infusion or the volume of re-infused blood. As observed previously, smaller volumes of blood were salvaged with increasing age [12] and re-infusion volumes were greater in males than females, which is thought to reflect greater circulating volumes in males.

The most important determinants of whether sufficient blood is salvaged for re-infusion was the procedure performed and the indication for surgery. The odds of collecting sufficient blood were halved when revising a single component compared with revising the acetabular and femoral components. The odds of collecting sufficient blood were almost four times greater when the indication was an emergency revision periprosthetic fracture compared with an elective revision for an aseptic indication. These findings can help allocate cell salvage when there is limited resource, which is an important barrier to widespread utilisation [8].

Recent Association of Anaesthetists guidelines on cell salvage for peri-operative blood conservation recommend employing cell salvage whenever anticipated blood loss exceeds 500 ml [8]. The results of our study provide surgical teams with an estimation of intra-operative blood loss for different revision hip arthroplasty procedures, although we recognise that may be considerable variation between patients and centres. The proposed threshold of 500 ml for using cell salvage is lower than suggested in existing guidelines [9, 16]. As a result, there will be an increased number of cases when insufficient blood is salvaged for re-infusion, reducing the cost-effectiveness of this intervention. Costs can be reduced by setting up the cell salvage machine in 'collect only' mode [8], as practised in our institution, although consumable and staff costs will remain. There is a need for an updated

analysis of the cost effectiveness of cell salvage when used alongside other blood conservation strategies.

A revision hip arthroplasty procedure where cell salvage may not be warranted is prosthesis exploration and modular exchange, when only 35% of patients received salvaged blood. The odds of collecting sufficient blood for re-infusion during this procedure were one-seventh of those when revising femoral and acetabular components. The presence of tumour or infection is not a contra-indication for cell salvage at our institution and this is supported by an increasing number of studies [17,18]. Instead, revision hip procedures performed for infection are associated with higher blood loss and cell salvage re-infusion volumes than for aseptic indications. During our study period, cell salvage was employed for an increasing proportion of infected cases, hence the smaller number of first stage revisions than second stage revisions in the cohort.

One strength of this study is that it describes one of the largest cohort of patients undergoing revision hip arthroplasty for a broad range of indications with the use of intra-operative cell salvage. Revision hip procedures are heterogenous in nature and include cement-in-cement femoral revisions where the femoral canal is not entered, through to extended trochanteric osteotomies that increase the volume of blood loss [12]. However, the nature of the procedure performed frequently depends on intra-operative findings and our study focuses on pre-operative factors that can be used to guide resource utilisation. Our study has limitations. Calculated blood loss, cell salvage efficiency, and change in haemoglobin concentration after autologous blood re-infusion are estimations that do not account for intravenous fluid therapy and intra-operative red blood cell transfusions. Anaesthetic technique may influence blood loss, which was not explored in this study. We are unable to determine whether intra-operative cell salvage prevents red blood cell transfusion or its cost-effectiveness.

In conclusion, patients undergoing revision hip arthroplasty for infection or fracture and those undergoing revision of both femoral and acetabular components are more likely to generate sufficient blood salvage for re-infusion. Our findings may prove valuable in a clinical context of resource utilisation.

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Appendix 1

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Table 1 Patient characteristics for each procedure. Values are mean (SD) or number (proportion).

	Revise femoral and acetabular component	Revise femoral component only	Revise acetabular component only	Revision to total femur	First stage revision	Second stage revision	Exploration and modular exchange	All procedures
Number of patients	216	169	104	30	46	68	31	664
Age	70.4 (13.0)	75.1 (12.1)	68.7 (13.9)	64.6 (14.5)	67.1 (12.6)	66.2 (12.3)	68.5 (12.4)	70.3 (13.2)
Pre-operative haemoglobin (g.l ⁻¹)	125.3 (17.8)	123.2 (19.5)	123.1 (18.2)	125.9 (19.3)	115.2 (17.2)	117.5 (17.9)	120.3 (21.0)	122.6 (18.8)
Intra-operative blood loss (ml)	1069.5 (672.3)	955.6 (828.0)	762.9 (502.0)	1545.3 (1002.3)	1479.3 (1031.5)	1247.5 (819.0)	585.3 (436.9)	1037.6 (778.3)
Patients with sufficient collection for re-infusion	170 (79%)	134 (78%)	68 (65%)	29 (100%)	36 (78%)	58 (87%)	12 (39%)	507 (76%)
Volume of re-infused blood (ml)*	260.3 (163.4)	225.1 (150.9)	217.7 (135.2)	259.1 (163.1)	300.9 (227.5)	314.7 (208.3)	190.3 (64.6)	253.0 (168.8)
Proportion of blood loss salvaged	34.7 (11.5)	34.5 (10.5)	38.2 (12.6)	28.6 (10.8)	33.3 (12.7)	41.7 (13.7)	37.9 (11.6)	35.5 (12.0)
Patients receiving peri-operative red blood cell transfusion	75 (35%)	59 (35%)	33 (32%)	10 (35%)	20 (43%)	31 (46%)	16 (52%)	244 (37%)
Day 1 postoperative haemoglobin (g.l ⁻¹)	95.9 (16.0)	96.2 (14.8)	96.3 (14.3)	95.4 (18.0)	90.0 (13.1)	94.8 (12.6)	96.3 (16.3)	95.5 (15.0)

*Excludes cases where inadequate blood for re-infusion. Standardised to haematocrit 60%.

Table 2 Patient characteristics according to indication for surgery. Values are mean (SD) or number (proportion).

	Aseptic	Fracture	Infection
Number of patients	393	160	111
Age	68.7 (12.7)	77.2 (11.5)	66.4 (13.8)
Pre-operative haemoglobin (g.l ⁻¹)	123.4 (18.8)	123.5 (18.5)	118.7 (18.5)
Intra-operative blood loss (ml)	945.0 (779.2)	945.9 (563.8)	1488.8 (882.8)
Patients with sufficient collection for re-infusion	271 (69%)	142 (88%)	94 (84%)
Volume of re-infused blood (ml)*	267.6 (179.2)	206.9 (127.0)	279.2 (180.8)
Proportion of blood loss salvaged	38.4 (11.9)	33.2 (10.9)	31.1 (11.9)
Patients receiving peri-operative red blood cell transfusion	137 (35%)	57 (36%)	50 (45%)
Day 1 Postoperative haemoglobin (g.l ⁻¹)	96.8 (14.5)	95.3 (15.1)	91.3 (16.3)

*Excludes cases where inadequate blood for re-infusion. Standardised to haematocrit 60%.

Table 3 Factors associated with salvaging sufficient blood for re-infusion.

	Univariate logistic regression			Multivariable logistic regression		
	OR	95%CI	p value	OR	95%CI	p value
Age	0.99	0.97 to 1.00	0.050			
Sex:						
Female		Reference	Reference			
Male	0.99	0.98 to 1.01	0.945			
BMI	0.99	0.98 to 1.01	0.583			
Pre-operative haemoglobin concentration	0.99	0.98 to 1.00	0.122			
Procedure:						
Revise femur and acetabulum	Reference	Reference	Reference	Reference	Reference	Reference
Revise femur only	0.79	0.51 to 1.25	0.320	0.41	0.23 to 0.73	0.002
Revise acetabulum only	0.42	0.26 to 0.68	<0.001	0.53	0.32 to 0.87	0.013
Exploration and modular exchange	0.14	0.06 to 0.30	<0.001	0.16	0.07 to 0.34	<0.001
Indication:						
Aseptic	Reference	Reference	Reference	Reference	Reference	Reference
Infection	2.28	1.32 to 3.94	0.003	1.87	1.04 to 3.36	0.037
Fracture	3.30	1.95 to 5.57	<0.001	4.43	2.30 to 8.55	<0.001

Table 4 Factors associated with volume of re-infusion.

	Univariate logistic regression			Multivariable logistic regression		
	OR	95%CI	p value	OR	95%CI	p value
Age	-1.9	-3.0 to -0.9	<0.001	-1.9	-2.9 to -0.8	0.001
Sex:						
Female	Reference	Reference	Reference	Reference	Reference	Reference
Male	53.1	25.3 to 81.0	<0.001	52.0	25.0 to 79.0	<0.001
BMI	1.3	-0.2 to 2.8	0.093			
Pre-operative haemoglobin concentration	-0.2	-0.6 - 1.0	0.617			
Procedure:						
Revise femur and acetabulum	Reference	Reference	Reference	Reference	Reference	Reference
Revise femur only	-52.6	-85.2 to -19.9	0.002	-39.1	-79.4 to 1.1	0.056
Revise acetabulum only	-84.4	-123.5 to -45.4	<0.001	-69.2	-109.2 to -29.3	<0.001
Exploration and modular exchange	-144.6	-210.2 to -79.0	<0.001	-143.6	-208.2 to -79.1	<0.001
Indication;						
Aseptic	Reference	Reference	Reference	Reference	Reference	Reference
Infection	63.0	24.7 to 101.4	0.001	38.1	-0.4 to 76.7	0.053
Fracture	0.3	-33.0 to 33.7	0.985	15.1	-26.5 to 56.7	0.477

Figure Legends

Figure 1: Proportion of patient cohort receiving allogeneic blood transfusions (n=644)

Figure 2: Histogram of re-infusion volumes (standardised to haematocrit 60%) (n = 507)

Supporting information

Table S1. Cohort characteristics for individuals with and without sufficient salvaged blood for re-infusion.

Figure S1: Mean pre-operative (a) and postoperative (b) haemoglobin concentration, and proportion of patients receiving allogeneic blood transfusion within 72 h of surgery (c) for each year of the study (with 95%CI).