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Research article

Intraoperative cell salvage use reduces the rate of perioperative allogenic blood transfusion in patients undergoing periacetabular osteotomy

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ABSTRACT

Blood loss during periacetabular osteotomy (PAO) is variable, with losses ranging from 100 to 3900 ml in published series. Perioperative allogenic blood transfusion is frequently utilized although is associated with significant risk of morbidity. Cell salvage (CS) is a common blood conservation tool; however, evidence supporting its use with PAO is lacking. Our aim was to assess whether CS affects perioperative allogenic blood transfusion rate in patients undergoing PAO. The clinical records of 58 consecutive PAOs in 54 patients (median age 24.7 years, interquartile range 17.8–29.4 years) performed by a single surgeon between 1 January 2016 and 30 April 2018 were reviewed. Autologous blood pre-donation and surgical drains were not used. Due to variable technician availability, CS was intermittently used during the study period. PAOs were allocated into a CS group or no cell salvage group (NCS group), according to whether an intraoperative CS system was used. There was no significant difference in patient age, gender, body mass index, dysplasia severity, regional anesthetic technique, tranexamic acid administration, surgical duration or estimated blood loss (all $P > 0.05$) between the two groups. The CS group had a lower preoperative hemoglobin compared to the NCS group (median, 13.4 g/dl versus 14.4 g/dl, $P = 0.006$). The incidence of allogenic blood transfusion was significantly lower in the CS group compared to the NCS group (2.5% versus 33.3% patients transfused, $P = 0.003$). Multivariate modeling showed CS use to be protective against allogenic blood transfusion ($P = 0.003$), with an associated 80-fold reduction in the odds of transfusion (odds ratio, 0.01; 95th% CI, 0–0.57). To our knowledge, this is the first study to assess the effect of CS use on allogenic transfusion rate in patients undergoing PAO. Our results demonstrate CS to be a mandatory component of blood conservation for all patients undergoing PAO.

INTRODUCTION

Periacetabular osteotomy (PAO) is the primary surgical treatment of symptomatic developmental hip dysplasia in adolescents and young adults, and has been shown to provide satisfactory long-term functional outcomes in appropriately selected patients [1–4]. Perioperative blood loss in patients undergoing PAO is highly variable with losses ranging from 100 to 3900 ml in published series [5, 6]. While over 90% of patients undergoing PAO will require blood transfusion with either autologous pre-donated blood, intraoperative cell salvage (CS) or allogenic transfusion [7], the incidence of allogenic blood transfusion in PAO patients ranges from 16% to 41% [7–10]. Hypotensive anesthesia, regional anesthesia, preoperative autologous blood donation [10], intraoperative blood salvage [5, 7] and pharmacological agents, such as tranexamic acid (TXA) [9], are widely used to reduce blood loss and decrease the need for allogenic transfusion in patients undergoing PAO. Despite this multitude of blood conservation strategies, there is currently no standardized blood

conservation protocol in widespread use for patients undergoing PAO.

Allogenic blood transfusion carries significant risk of patient morbidity [11–19]. Although the risk of viral or bacterial transmission via allogenic transfusion is exceedingly small [11], allergic reactions, which range from mild to life threatening, occur in 1–3% of all transfusions [12]. The rate of severe immunogenic complications, such as transfusion-associated lung injury may be as high as 1:5000 transfusions [13]. In orthopedic surgery, patients receiving allogenic blood transfusion have 1.5–3.5 times greater risk for developing perioperative infections, including wound infection [14–17]. Furthermore, allogenic transfusion has been associated with an increased long-term risk of malignancy, potentially due to transmission of occult carcinogenic factors [19] or the induction of impaired immune surveillance [18]. In females of childbearing age, allogenic blood has the potential to induce Rhesus D (RhD) alloimmunization which can have implications during subsequent prengnacies [20]. This deserves special consideration in the setting of PAO, which is most commonly performed in female patients. Due to these factors many practitioners advocate for the restrictive use of allogenic blood during the perioperative period [21, 22].

CS systems are used to collect and then reinfuse blood lost intraoperatively [23]. Blood is collected from the surgical site with a closed suction system, then mixed with anticoagulant and stored in a reservoir before it is centrifuged to separate red blood cells from plasma [23, 24]. The blood is then washed with saline, which removes fat particles [25] and free hemoglobin [26], resulting in a product which may be transfused back into the patient. CS use has been shown to significantly reduce the requirement for allogenic blood transfusion in patients undergoing non-urgent surgery, with an average saving of 0.68 units of red blood cells per patient, without any adverse effect [27]. This avoids the risks associated with allogenic transfusion [28], and prevents alloimmunization which may complicate future transfusion [23].

There is good evidence to support the use of CS systems in patients undergoing hip and knee arthroplasty [29–32], revision hip arthroplasty [33, 34], and acetabular fracture fixation [35, 36]; however, research on the efficacy of CS use on transfusion requirements in spinal surgery has yielded conflicting results [37–39]. There are currently no studies investigating the impact of CS on perioperative allogenic transfusion requirements in patients undergoing PAO. We have performed a retrospective comparative analysis of patients undergoing PAO with or without the use of a CS system, in order to assess the impact of CS on allogenic blood transfusion rate.

MATERIALS AND METHODS

Methodological considerations

After a National Health and Disability Ethics Committee exemption was obtained, the clinical records of 60 consecutive PAOs performed by a single fellowship-trained hip preservation surgeon between 1 January 2016 and 30 April 2018 were retrospectively reviewed. The patients' demographic data were merged with perioperative information from surgical and anesthesiology records which was relevant to the analysis. Due to variations in hospital policy and technician availability, CS was intermittently used during the study period. Cases were allocated into CS and no cell salvage (NCS) groups, according to whether or not a CS system was used during the PAO. The two patient groups were then compared with respect to the primary outcome of perioperative allogenic blood transfusion rate, in addition to baseline variables [patient age, gender, body mass index (BMI)], surgical duration, anesthetic variables (ASA grading, epidural or spinal anesthesia use), hematologic variables (TXA use, estimated blood loss, preoperative and postoperative hemoglobin, change in hemoglobin), radiographic variables (preoperative and postoperative lateral center-edge angle) and clinical outcomes (time to first mobilization and duration of hospital admission). The decision to transfuse allogenic blood was at the discretion of the attending surgeon and anesthesiologist in accordance with the New Zealand Blood Service (NZBS) transfusion guidelines for patients undergoing elective surgery [21].

Surgical technique

All PAOs were performed according to the technique developed by Ganz *et al.* [40] and modified by Millis and colleagues [41]. In brief, a single-incision modified Smith–Petersen approach with preservation of the rectus femoris tendon and of the abductor musculature was used in all cases. First, an incomplete osteotomy of the anterior ischium was performed at the infracotyloid groove, followed by a complete osteotomy of the superior pubic ramus. A bicortical iliac osteotomy was then performed from just distal to the anterior superior iliac spine to 10 mm anterior to the arcuate line. The posterior column was then split midway between the posterior acetabular border and the greater sciatic notch. Finally, the posterior column split was connected to the ischial cut, completing the osteotomy and freeing the acetabular fragment. The acetabular fragment was then repositioned using image intensifier guidance, and was secured with three to four 3.5- or 4.5-mm antegrade screws. All PAOs were performed under general anesthesia with local anesthetic blockade (epidural catheter

or subarachnoid block) and appropriate antibiotic prophylaxis. All cases were performed by a single fellowship-trained orthopedic surgeon with another orthopedic surgeon, orthopedic residents and/or nurses serving as assistants. The assistants did not perform any substantive components of the procedure. Autologous blood predonation, surgical drains, hypotensive anesthesia and biologically active hemostatic agents (fibrin sealants or platelet gels) were not used. Patients were mobilized from day 1 postoperatively, touch weightbearing with two crutches. Venous thromboembolism prophylaxis included weight-adjusted doses of low molecular weight heparin (Enoxaparin) during hospital admission, followed on discharge by acetyl-salicylic acid (aspirin 100 mg daily) in low-risk adult patients or rivaroxaban in high-risk adult patients.

CS system

When CS was used, an Intraoperative Haemonetics Cell Saver 5+ machine (Haemonetics Corporation, MA, USA) with a 125 ml Latham bowl was used to collect blood via a sterile suction line from the surgical field. The recovered whole blood was then centrifuged and washed in 0.9% saline with heparin (30 000 U/l) prior to reinfusion if sufficient blood was available. The processed blood was stored in bags with an integrated microaggregate filter prior to reinfusion via gravity feed. Reinfusion was at the discretion of the surgeon and anesthesiologist and was based upon blood loss during the procedure and the baseline hemoglobin.

Statistical analysis

Patient and procedural data are presented as number (percentage) and median (interquartile range) as appropriate. The Shapiro–Wilk test was used to determine if continuous data were normally distributed. Given the relatively small number of patients studied, the decision was made to utilize non-parametric statistical tests to maximize statistical power. The Fisher exact test and the Mann–Whitney *U* test were used to test for difference between discrete and continuous parameters, respectively. Statistical significance was defined as a two-tailed *P*-values of less than or equal to 0.05.

To construct the multivariate model, a backwards elimination strategy was used with allogenic transfusion as the binomial outcome variable. Candidate variables were included in the initial iteration of this model if $P < 0.10$ on univariate modeling. A two-tailed threshold of $P < 0.05$ was used to define statistical significance for tests between variables and the final multivariate model.

Statistical analysis was completed using the Statistical Package for the Social Sciences Version 25 (International Business Machines, NY, USA).

RESULTS

During the study period, 60 PAOs were performed. Two patients were excluded from the analysis due to ancillary procedures (concurrent femoral osteotomy), leaving 58 procedures performed in 54 patients. All of the procedures were unilateral; four patients in the series underwent contralateral PAO at least 6 months after their initial PAO and were included as two separate procedures. Of the 58 cases, 40 (69%) underwent PAO with the use of a CS system (CS group), and 18 (31%) underwent PAO without the use of a CS system (NCS group).

There was no statistically significant difference between the two groups with respect to patient age, gender, BMI or severity of dysplasia (all $P > 0.05$) (Table I).

Preoperative hemoglobin was lower in the CS group compared to the NCS group (median, 13.4 g/dl versus 14.4 g/dl, $P = 0.006$). There was otherwise no significant difference between the two groups with respect to surgical duration [median, 163 min (CS group) versus 179 min (NCS group), $P = 0.067$], estimated blood loss [median, 700 ml (CS group) versus 775 ml (NCS group), $P = 0.339$] or rates of intraoperative TXA administration [percent use 90.0% (CS group) versus 88.9% (NCS group), $P = 1.000$] and method of TXA administration (via bolus or infusion; $P = 0.296$). In the CS group, the mean volume of blood reinfused was 338 ± 359 ml; in 10 CS group patients (25%), the surgical blood loss was below the minimum volume required (<200–300 ml) to allow processing and therefore no blood was returned. Hematologic and anesthetic variables are further depicted in Table II.

The incidence of allogenic blood transfusion was significantly lower in the CS group compared to the NCS group (2.5% versus 33.3% of patients transfused, $P = 0.003$). The CS group experienced a smaller reduction in postoperative hemoglobin [median postoperative decrease, 2.7 g/dl (CS group) versus 3.9 g/dl (NCS group); $P = 0.004$], which resulted in similar day-one hemoglobin levels between the groups [median, 10.4 g/dl (CS group) versus 10.5 (NCS group); $P = 0.872$]. There was no significant difference in time to first mobilization or length of hospital stay between the two groups (both $P > 0.05$). Outcome variables are further depicted in Table III.

Multivariate logistic regression was performed to determine independent factors which were associated with allogenic transfusion. Sequential univariate modeling identified CS use ($P = 0.003$), estimated blood loss ($P = 0.010$) and postoperative decrease in hemoglobin ($P = 0.014$) as potential predictors of blood transfusion with *P*-values approaching statistical significance ($P < 0.10$). When entered into the multivariate model, only CS use had an

Table I Patient demographics and baseline variables

Variable[a]	*CS* (n = *40*)	*NCS* (n = *18*)	P-*value*
Patient age (years)	24.7 (17.6–29.4)	23.8 (17.9–30.2)	0.788
Female gender	33 (82.5)	11 (61.1)	0.102
BMI (kg/m^2)	25.8 (23.4–28.3)	23.5 (22.1–27.7)	0.356
Preoperative lateral center-edge angle (°)	17 (9–9)	17 (13–19)	0.516

[a]Continuous data are presented as median (interquartile range) and categoric data as number of patients (percentage of group of patients).

Table II Patient hematologic and anesthetic variables

Variable[a]	*CS* (n = *40*)	*NCS* (n = *18*)	P-*value*
Preoperative hemoglobin (g/dl)	13.4 (13.0–14.1)	14.4 (13.3–14.8)	0.006
Estimated blood loss (ml)	700 (575–1000)	775 (600–1300)	0.339
Surgical duration (min)	163 (142–192)	179 (156–218)	0.067
TXA use	36 (90.0)	16 (88.9)	1.000
Regional anesthetic technique (spinal:epidural)	9:31	6:12	0.518

[a]Continuous data are presented as median (interquartile range) and categoric data as number of patients (percentage of group of patients).

Table III Patient outcomes

Variable[a]	*CS* (n = *40*)	*NCS* (n = *18*)	P-*value*
Allogenic transfusion	1 (2.5)	6 (33.3)	0.003*
Postoperative decrease in hemoglobin (g/dl)	2.7 (3.5–2.2)	3.9 (4.3–3.1)	0.004*
Time to first mobilization (h)	47.2 (27.3–72.0)	47.5 (23.1–50.7)	0.507
Length of hospital stay (days)	5.3 (5.0–6.2)	5.9 (5.1–6.2)	0.735

[a]Continuous data are presented as median (interquartile range) and categoric data as number of patients (percentage of group of patients).
*Significant.

independently significant effect on allogenic transfusion rate ($P = 0.003$), with an associated 80-fold reduction in the odds of transfusion (odds ratio, 0.01; 95th% CI, 0–0.57). Preoperative hemoglobin did not have a significant effect on allogenic transfusion rate ($P = 0.418$) using multivariate logistic regression.

DISCUSSION

We found that in patients undergoing PAO, the use of an intraoperative CS system significantly reduced the rate of allogenic blood transfusion from 33.3% to 2.5%. To our knowledge, this is the first study to specifically address this important clinical question.

PAO is a technically demanding procedure with a steep learning curve and has been associated with multiple complications, including major blood loss [6, 42]. The reported rate of allogenic transfusion in patients undergoing PAO has exceeded 40% in some series [7–10]. In our series, there was no difference in the rate of complications when patients were stratified by CS use. While a potential learning curve could influence blood loss and transfusion requirements, in a recent study from our group, we failed

to demonstrate a change in complication rates including allogenic blood transfusion across the first 50 independent PAOs performed by a single surgeon after fellowship training, indicating that significant learning and risk reduction occurs during a high volume hip preservation fellowship [43]

].Although at times lifesaving, the use of allogenic blood can be associated with significant morbidity [11–19]. Allogenic transfusion has an immunomodulatory effect, resulting in impaired T-cell-mediated immunity [18, 44], that can increase the risk of perioperative infection compared to patients receiving autologous transfusion [14–17]. This immunomodulatory effect has been attributed to transfusion of allogenic leukocytes, but with leukoreduction the risk of infection has remained [18, 45]. It is postulated that residual unfiltered leukocytes [45] and stored red blood cells rather than fresh products [18, 46] may contribute to this phenomenon. Allogenic transfusion has also been associated with increased long-term risk of malignancy, potentially due to transmission of occult carcinogenic agents [18, 19]. Patients undergoing PAO are also frequently females of childbearing age where exposure to allogenic blood risks RhD alloimmunization. Formation of RhD antibodies may compromise subsequent pregnancies for these patients and result in hemolytic disease of the fetus and newborn [20]. Furthermore, the quality of allogenic banked blood is inferior to autologous transfusion. While there is no universal measure of blood quality, 2,3-diphosphoglycerate (2,3-DPG) levels are near normal in autologous salvaged blood, whereas in allogenic blood levels can be <10% of normal values [47]. This depletion in 2,3-DPG shifts the oxygen dissociation curve to the left, thereby decreasing oxygen delivery to tissues [47]. Due to these problems, the perceived benefit of allogenic blood transfusion should be carefully weighed against the risks when making the decision to transfuse. Indeed, in a recent meta-analysis of patients undergoing major orthopedic surgery [48], restrictive transfusion policies were associated with a reduction in infection rates without any increase in adverse outcomes. It is increasingly clear that any strategy that reduces perioperative allogenic blood transfusion rate is critically important in order to optimize patient outcomes.

Although the influence of CS use on perioperative transfusion requirements in patients undergoing PAO has not previously been addressed, our results are in concordance with multiple previous studies of patients undergoing comparable orthopedic procedures, such as revision hip arthroplasty [33, 34] and acetabular fracture fixation [35, 36]. A Cochrane review of 21 randomized, controlled trials by Carless *et al.* [27] found CS to be associated with a 58% reduction (95% CI, 46–68%) in exposure to allogenic blood, without any increase in adverse events. Bridgens *et al.* [34] presented a case-matched study of 94 patients undergoing revision hip arthroplasty, 47 with the use of CS system and 47 without. CS use was associated with a mean reduction in allogenic transfusion of 59% (median, 2 units versus 6 units, $P = 0.0006$). The authors reported an average saving of $801 (2007 USD) per patient and concluded that routine CS use is warranted. Odak *et al.* [35] presented their prospective review of 30 patients undergoing pelvic acetabular fracture fixation. In their study population, 47% required allogenic blood transfusion, and a statistically significant inverse relationship existed between volume of CS transfusion and postoperative allogenic transfusion requirement. There were no complications related to CS use, and the authors concluded that its use could save ~$130 (2013 USD) per patient. Bigsby *et al.* [36] retrospectively reviewed 80 patients undergoing acetabular fracture fixation with the use of an intraoperative CS system. Twenty-five percent of patients required allogenic blood transfusion, which is significantly lower than previous studies (rates ranging from 48% to 58% [49, 50]). The authors also concluded that the use of intraoperative CS could save an estimated $149 (2013 USD) per patient, even when allowing for the consumables related to CS use.

TXA is an anti-fibrinolytic compound derived from the amino-acid lysine. Due to associated reductions in postoperative bleeding and allogenic transfusion exposure, TXA use is widespread in orthopedic surgery [51]. For patients undergoing PAO, multiple authors have reported a reduction in both the intraoperative blood loss and perioperative allogenic blood transfusion requirements [9, 52]. In our study, despite near universal exposure to TXA in both groups, the use of CS still resulted in clinically relevant reductions in perioperative allogenic blood transfusion.

The limitations of the present study include its retrospective, non-randomized nature, which introduces an inherent risk of bias. Both groups were largely equivalent at baseline, aside from a lower baseline hemoglobin in the CS group. This difference was 1 g/dl which is clinically relevant as it approximates the increase in hemoglobin seen with one unit of allogenic blood and would decrease the tolerance for blood loss prior to transfusion thresholds being met. This factor was included in the multivariate model and was not statistically significant in the final iteration. Second, contemporary guidance from the NZBS was utilized and errs towards a restrictive transfusion threshold of 7–8 g/dl in healthy patients undergoing elective surgery. Despite the present study being a single-surgeon series, there were multiple anesthesiology and ward-based multidisciplinary providers involved in the care of these patients.

This meant that there was no one universal transfusion threshold used across all the patients in the study. Third, this study reviews the practice of a fellowship-trained hip preservation surgeon with a quaternary referral base and results may therefore not be generalizable to other surgeons or institutions.

CONCLUSION

In this retrospective study of 58 consecutive PAOs, we found that the use of a CS system significantly decreased the risk of perioperative allogenic blood transfusion. To our knowledge, this is the first study to investigate the efficacy of CS use in patients undergoing PAO. Our results demonstrate CS to be a mandatory component of blood conservation for all patients undergoing PAO.

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CONFLICT OF INTEREST STATEMENT

None declared.

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