The merits of cell salvage in arthroplasty surgery: an overview

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Arthroplasty entails considerable exposure to allogenic blood transfusion. Cell salvage with washing is a contemporary strategy that is not universally used despite considerable potential benefits. We searched Embase and Medline to determine if blood salvage with washing during primary and/or revision hip and knee arthroplasty results in lower rates of transfusion and postoperative complications. We included 10 studies in our analysis, which we rated according to Downs and Black criteria. With primary knee arthroplasty, there was a reduction in transfusion rate from 22% to 76% and a 48% reduction in transfusion volume (n = 887). With primary hip arthroplasty, there was a reduction from 69% to 73% in transfusion rate and a 31% reduction in transfusion volume (n = 239). There was a significant decrease in length of hospital stay (9.6 v. 13.6 d). Studies of revision arthroplasty reported a 31%–59% reduction in transfusion volume (n = 241). The available evidence demonstrates reduced exposure to allogenic blood with the use of salvage systems. Studies have been underpowered to detect differences in infection rates and other postoperative complications. Future cost analysis is warranted.

L'arthroplastie suppose une exposition considérable à des transfusions de sang allogénique. La récupération et le lavage du sang épanché est une stratégie moderne qui n'est pas universellement utilisée malgré ses immenses avantages potentiels. Nous avons interrogé les bases de données Embase et Medline afin de déterminer si la récupération du sang et son lavage durant l'intervention primaire et(ou) la révision d'arthroplastie de la hanche et du genou réduisait les taux de transfusions et de complications postopératoires. Nous avons inclus 10 études dans notre analyse et nous les avons évaluées selon les critères de Downs et Black. En ce qui concerne l'arthroplastie primaire du genou, on a noté une réduction de 22 % à 76 % du taux de transfusions et une réduction de 48 % du volume de sang transfusé (n = 887). En ce qui concerne l'arthroplastie primaire de la hanche, on a noté une réduction de 69 % à 73 % du taux de transfusions et une réduction de 31 % du volume de sang transfusé (n = 239). Le séjour hospitalier a été significativement plus bref (9,6 c. 13,6 j). Les études sur les révisions d'arthroplastie ont quant à elle fait état d'une réduction de 31 %–59 % du volume de sang transfusé (n = 241). Les preuves existantes témoignent d'une exposition moindre au sang allogénique lors de l'utilisation de systèmes de récupération. Les études n'étaient toutefois pas dotées d'une puissance statistique suffisante pour détecter des différences quant aux taux d'infection ou autres complications postopératoires. D'éventuelles analyses de coût sont justifiées.

Allogenic blood transfusion is associated with a number of risks, with recipients having increased susceptibility to postoperative infections, fluid overload, increased length of stay in hospital (LOS) and other postoperative complications.[1,2] Hospital stay has been reported to increase by 1.3% per unit of blood transfused.[3] In addition, costs associated with allogenic transfusion have increased owing to increased preparation and enhanced screening of blood.[4] Unnecessary exposure to allogenic blood may result in the development of autoantibodies, increasing the risk of transfusion-associated acute lung injury, and making future crossmatching of blood increasingly difficult.[5] Furthermore, patients may have religious concerns about receiving allogenic or banked blood but may be open to autogenous blood that is reinfused immediately.

With increased awareness of the postoperative complications and the potential detrimental effects of allogenic blood transfusion, there has been reconsideration of blood transfusion practices. Strategies to decrease exposure

to allogenic blood have included the implementation of increasingly restrictive transfusion protocols, correction of preoperative anemia through use of recombinant human erythropoietin and intravenous iron, and use of pharmacologic agents, such as aprotinin and tranexamic acid, to reduce perioperative blood loss.[6] Preoperative autogenic donation (PAD) is speculated to place patients at greater risk of a perioperative cardiac complication, as they have insufficient time to regenerate hemoglobin to predonation levels, leaving patients in a state of relative anemia. In addition, lower levels of nitric oxide in banked blood have been associated with an increased risk of heart attack and stroke.[7] In addition, there is potential for significant waste, bacterial contamination, hemolysis related to errors in handling and economic considerations associated with the collection and storage of autogenous blood.[2,8]

Cell salvage is the process by which autologous blood is collected, processed and reinfused in the perioperative period. Various forms of cell salvage have been used since the 1970s, when it was popularized in major thoracic or abdominal procedures.[4,9] Salvaged, unwashed blood has been shown to be substandard, as it is diluted and may contain a high concentration of hemolyzed red blood cells, cytokines and clotting factors.[10] Further risks with the reinfusion of hemolyzed blood include renal failure; disseminated intravascular coagulation (DIC) due to activated clotting or fibrinolytic factors; and risk of fat embolism due to debris, such as fat particles.[10–12] Contemporary cell salvage allows for effective reduction of contaminants by cell separation and washing, resulting in an autologous red blood cell concentrate of normal function and viability.[11] Salvaged blood may be collected intraoperatively or postoperatively with the use of drains. Postoperative salvage with drains is more commonly used in patients undergoing revision arthroplasty or total knee arthroplasty (TKA) with tourniquets.

In orthopedic surgery, the rate of exposure to allogenic blood transfusion in patients undergoing total hip arthroplasty (THA) or TKA can be substantial. In a study of 330 orthopedic surgeons' practices, reported transfusion rates were 57% in the THA (n = 3920) and 39% in the TKA (n = 5562) groups.[2] Revision arthroplasty transfusion rates may be even more impressive based on operative duration and wide soft tissue and bone exposures.

Despite these problems with alternatives and the risks associated with allogenic transfusion, cell salvage has failed to gain widespread use among orthopaedic surgeons in Canada. To our knowledge, no previous systematic review or meta-analysis comparing transfusion rates or volume in patients undergoing cell salvage with washing versus other strategies has been performed to date. The impetus for the present study was the limited local use of cell salvage, the potential to limit exposure to allogenic blood and the lack of a previous systematic review or meta-analysis on this topic. We sought to determine if intra- and/or postoperative blood salvage with washing in patients undergoing primary and/or revision TKA/THA results in a lower rate of allogenic blood transfusion. Our secondary goal was to determine whether there was an associated reduction in postoperative infection rates, other postoperative complications and LOS.

Literature search

We performed a comprehensive literature search of Embase and Medline. A health science research librarian was consulted regarding appropriate search terms and strategy. Search results were examined by 2 independent reviewers. We examined titles and abstracts of the initial search results and flagged the ones that were potentially relevant. Subsequently, we examined full-text articles to determine their suitability. Consensus was required for inclusion. Full-length articles that satisfied all inclusion criteria were critically appraised by both reviewers. References of included articles were then searched manually to ensure our literature search was comprehensive.

The inclusion criteria for the study were as follows: original research published in English from 2001 onwards; TKA and/or THA; primary and/or revision surgery; salvage system using both a washing and filtration process; primary outcome of allogenic transfusion rate and/or volume. Relevant articles were critically appraised by 2 reviewers and subjected to the Downs and Black checklist to assess methodological quality.[13]

The initial search yielded 576 studies in Medline and 233 in Embase. After review of the titles and abstracts, 24 of the studies from Medline and 17 from Embase were considered potentially relevant. Four articles in Medline and 6 in Embase satisfied all inclusion criteria. Of the articles from Embase, 3 were published only as conference abstracts. The manual search of included study references did not yield any further studies satisfying our inclusion criteria. A total of 10 studies, 1 randomized control trial, 5 prospective cohorts, 3 retrospective cohorts and 1 retrospective case series were included in the study (Table 1).

Discussion

Total knee arthroplasty

Most of the evidence pertained to primary total knee arthroplasty. In total, 2 level-2, 1 level-1 and 1 level-3 studies were included. A single-centre randomized control trial of 231 patients undergoing TKA reported transfusion rates of 7% for the salvage group and 28% for the control group ($p < 0.001$).[14] The salvage group received a total of 12 units of allogenic blood, whereas the control group received 33 units. The salvage group had an 85% reinfusion rate. In terms of other outcomes, the rate of post-hospital infectious complications was higher for the

nonsalvage than the control group (p = 0.036); however, there was no significant difference between the groups for LOS, serious adverse events or mortality.

In a retrospective cohort study of 154 patients who received TKA, transfusion rates were compared among control, PAD and cell salvage groups.[15] Data were also

Table 1. Population and clinical characteristics of studies included in our review and meta-analysis

Study	Population/system	Design	Level of evidence/ DB score	Findings
TKA				
Thomas et al. (2001)[14]	Primary TKA Cell Saver	Single-centre RCT salvage with and without reinfusion (control) 231 patients	Level-1 evidence DB = 25/31	Transfusion rates Salvage: 7% Control: 28% (p < 0.001) Fewer readmits and GP visits
Sinclair et al. (2009)[15]	Primary TKA OrthoPAT	Retrospective cohort Salvage/PAD/control 229 patients	Level-3 evidence DB = 22/31	Transfusion rates Salvage: 25% PAD: 18% Control: 52% High-risk and low-risk sub-analysis
Blatsoukas et al. (2010)[16]	Primary TKA Dideco Compact Advanced	Prospective cohort Salvage (intraop and postop)/salvage (postop)/control 248 patients	Level-2 evidence DB = 23/31	Transfusion rates/mean units Salvage: (intra- and postop) 62%/0.81 Salvage: (postop) 59%/0.91 Control: 79%/1.74; (p < 0.001)
THA				
del Trujillo et al. (2008)[6]	Primary THA OrthoPAT	Prospective cohort Salvage/control 108 patients	Level-2 evidence DB = 26/31	Transfusion rate/LOS Salvage: 15% / 9.6 days Control: 48% / 13.6 days (p < 0.001) Subanalysis: high/low preop Hgb Postop infection rates trended toward sign reduction (2% v. 10%; p = 0.09)
Revision				
Bridgens et al. (2007)[4]	Revision THA Cell Saver	Prospective cohort Salvage/control 94 patients	Level-3 evidence DB = 22/31	Mean transfusion units Salvage: 2.6 Control: 6.4 (p < 0.001)
Garvin et al. (2005)[17]	Revision THA OrthoPAT and Cell Saver	Retrospective case series Salvage/no salvage 147 patients	Level-4 evidence DB = 19/31	Transfusion volume 31% incremental transfusion volume when salvage used No difference between salvage systems Inappropriate control group
TKA, THA and revision				
Clark et al. (2006)[9]	Primary and revision TKA and THA OrthoPAT	Prospective cohort Salvage/control 310 patients	Level-2 evidence DB = 18/31	Transfusion rate THA 73% less likely to use allogenic blood TKA 76% less likely to have allogenic transfusion
Abstracts				
Morgenschweis et al. (2011)[18]	Primary THA and TKA Dideco Electa	Prospective cohort Salvage/control 379 patients	Level-2 evidence DB = n/a	Transfusion rates THA salvage: 9.5 THA control: 4.3% (p = 0.16) TKA salvage: 13.3 TKA control: 14.0% (p = 0.89)
White et al. (2011)[19]	Primary THA and TKA OrthoPAT	Prospective cohort Salvage/control 268 patients	Level-2 evidence DB = n/a	Transfusion rates 48% reduction in allogenic transfusion rate with salvage
Paskova (2011)[20]	Primary and revision TKA and THA OrthoPAT and Cell Saver	Retrospective cohort study Salvage/control 443 patients	Level-3 evidence DB = n/a	Transfusion rates 1) Salvage 23.1% 2) Control 35.7%

DB = Downs and Black; GP = general practitioner; n/a = not available; LOS = length of stay in hospital; PAD = preoperative autogenic donation; THA = total hip arthroplasty; TKA = total knee arthroplasty; RCT = randomized controlled trial.

analyzed according to low-risk and high-risk patients based on preoperative hematocrit levels. Transfusion rates were 52%, 25% and 18% for the control, PAD and salvage groups, respectively; the PAD ($p = 0.002$) and salvage groups ($p = 0.007$) differed significantly from controls, but not from each other. The average number of units transfused was 1.6 in the control, 0.79 in the PAD and 1.1 in the salvage group ($p < 0.001$). With subanalysis according to high- and low-risk patients, differences became more apparent for the high-risk groups. That is, higher-risk patients were even less likely to receive allogenic blood if salvage or PAD strategies were used; however, with low-risk patients, the use of salvage resulted in nonsignificant reductions in allogenic transfusion rates (36%; $p = 0.30$) while a significant protective effect remained in the PAD group (75.6%; $p = 0.05$).

A third study, which used a prospective cohort design, compared allogenic transfusion rates in 248 patients undergoing TKA who were assigned to 1 of 3 groups: combined intraoperative salvage and postoperative drainage reinfusion, postoperative drainage reinfusion only and a control group.[16] The postoperative drainage reinfusion entailed collection and reinfusion of filtered unwashed blood. Transfusion rates were 62%, 59% and 79% for combined intraoperative and postoperative drainage reinfusion, postoperative drainage reinfusion only and control groups, respectively. There was a significant difference between each salvage group and the control group ($p < 0.001$), but not between the 2 salvage groups. In addition, the number of units transfused in the 2 salvage groups differed significantly from that in the control group (combined intra- and postoperative: 0.81 ± 1.03; postoperative only: 0.91 ± 0.96; control group: 1.74 ± 1.03, $p < 0.001$), but not between the 2 salvage groups. The rate of transfusion-related complications was lower in the combined salvage/reinfusion and reinfusion only groups than in the control group, but the authors did not report whether this difference was statistically significant. The main conclusions were that postoperative drainage reinfusion results in a significant decrease in exposure to allogenic blood and that the addition of intraoperative salvage does not provide additional benefit. However, the lack of a cohort using perioperative salvage alone limits the validity of comparing perioperative salvage with washing and reinfusion of unwashed drain contents. In addition, the inclusion of cohorts in whom unwashed drained blood is reinfused is not consistent with current standards of patient care. The study raised the question of the importance of postoperative salvage in TKA. No other studies that compared perioperative to postoperative salvage for primary or revision TKA or THA could be identified.

A final prospective cohort of 398 consecutive patients undergoing primary and revision TKA and THA noted a significant risk reduction with the use of perioperative blood salvage without PAD in the primary TKA cohort ($n = 179$, relative risk reduction [RRR] 2.3).[9] Increased age, increased BMI and low preoperative hemoglobin or hematocrit were found to be independent risk factors for use of allogenic blood.

Total hip arthroplasty

We included 2 studies, both of level-2 evidence, related to THA. A prospective cohort study of 108 patients compared salvage with no strategy (postoperative low vacuum drainage without reinfusion) in terms of allogenic transfusion rate, infection rate and LOS.[6] The mean transfusion volume was 336 mL per patient for reinfusion. Of those patients intended to receive salvaged blood, 49 of 60 (82%) received enough reinfusion. The transfusion rates were 15% for the salvage group and 48% for the control group ($p = 0.001$). Fifteen units of blood were transfused to the salvage group and 48 were transfused to the control group. There was a significant reduction in allogenic blood transfusion regardless of whether components were cemented. When stratified based on a preoperative hemoglobin of more or less than 130 g/L, the significant difference persisted only for the high preoperative hemoglobin group. When stratified according to age older or younger than 60 years and according to use of cement, the significant difference persisted. The salvage group showed a trend toward decreased postoperative infection, with a rate of 2% versus 10% in the control group. The postoperative infection rate was higher in patients who received allogenic blood transfusion regardless of whether they were in the treatment or control group ($p = 0.046$). There were no significant differences in LOS between groups.

A previously mentioned prospective cohort study involving 398 consecutive patients who underwent primary or revision TKA or THA noted a significant risk reduction in the use of perioperative blood salvage in the unilateral primary THA cohort ($n = 131$; RRR 2.0).[9] Complication rates for the THA cohort were not reported.

Revision arthroplasty

We found 3 studies related to revision arthroplasty (2 level-2 and and 1 level-4), and their results were conflicting. The level-4 study had numerous design flaws that were detrimental to the results. One of the level-2 studies had insufficient patient data on revision TKA or THA. Therefore, only 1 study related to revision THA was included in our analysis. No studies examining revision TKA were included.

A case–control study compared 47 patients undergoing revision THA; those who received cell salvage were matched to historical controls treated before the introduction of cell salvage in terms of allogenic blood transfusion volume.[4] Controls were computer-matched based on age,

sex, surgical approach, femoral grafting, type of prosthesis removed and inserted for the femoral and acetabular components, use of cement, infection, surgeon and mode of failure. The salvage group had a mean transfusion volume of 2.6 ± 3.13 units, whereas the control group had a mean of 6.4 ± 4.5 units ($p < 0.001$). Within the salvage group 11 of 47 patients required no allogenic blood. On the other hand, within the control group only 1 patient did not require transfusion. The mean reinfusion volume with the use of salvage was 590 ± 363 mL.

A retrospective case series of 147 patients who underwent revision THA compared the use of allogenic blood to controls for revision cases in which cell salvage was used.[17] This design was inappropriate in the context of revision arthroplasty owing to the wide range of complexity affecting operative duration, blood loss and potential for allogenic blood transfusion. It can be speculated that blood salvage was used for more complex revisions with greater potential for blood loss, thereby having a significant confounding effect on the results. Therefore, it is not surprising that the results contradicted those from the bulk of the other evidence, with reported transfusion rates of 38%, 58% and 26% for the Cell Saver, OrthoPAT and no salvage groups, respectively. Ultimately, the study should be disregarded when looking at the evidence as a whole owing to the inclusion of an inappropriate control group.

A third study examined revision arthroplasty, but small cohort sizes precluded analysis for the unilateral hip revision ($n = 38$) and unilateral knee revision ($n = 26$).[9] Despite insufficient data for these groups alone, combining the data for primary and revision THA cohorts resulted in a more impressive risk reduction than in the primary THA cohort ($n = 169$, RRR 2.7 v. $n = 131$, RRR 2.2). Complication rates were not reported for the revision arthroplasty cohorts.

Conference abstracts

We found 3 conference abstracts in Embase. A prospective cohort study of 379 patients failed to demonstrate a significant difference in transfusion rates between salvage and control groups for both primary TKA and THA.[18] Specifically, there was an increase in transfusion rate from 4.3% (control) to 9.5% ($p = 0.16$) for salvage system use in patients undergoing TKA, whereas there was a decrease from 14.0% (control) to 13.3% ($p = 0.89$) for those undergoing THA. Another prospective cohort study of 268 patients reported a 48% reduction in transfusion rate for primary TKA and THA.[19] There was an 83% reinfusion rate with the use of cell salvage and an average reinfusion of 1.17 units per patient for the salvage group. A retrospective cohort study of 443 patients evaluated the rate of allogenic blood exposure in both TKA and THA and found that there was a reduction in transfusion rate from 35.7% to 23.1% ($p < 0.01$) with the use of salvage system.[20] Of these 3 studies, 2 trials demonstrated significant reductions in transfusion rates with the use of salvage systems, whereas the other demonstrated nonsignificant changes. Despite the fact that the conference abstracts were included in this systematic review, their results must be interpreted with caution as there is insufficient detail presented to critically appraise these articles and ascertain methodological soundness.

The salvage system used did not appear to have a significant effect on the results. Five of 6 studies that used OrthoPAT and 3 of 4 studies using the Cell Saver demonstrated significant reductions in transfusion rates. One of 2 studies using Dideco devices demonstrated a significant reduction in transfusion rates. However, different models of Dideco devices were used in these studies: the Compact Advanced model was used in the positive trial, whereas the Electa model was used in the negative trial. It is plausible that the salvage system used may have had somewhat of an effect on transfusion rates. However, no studies directly compared transfusion rates among salvage systems, so it is not possible to determine the effect from the evidence available.

Only 1 study directly compared the use of drains to no drains among salvage groups within the perioperative period. In this particular study of patients undergoing TKA there was no significant difference in transfusion rates between the drain and no drain groups, but both had significantly lower rates than the control group.[16] Scarcity of evidence regarding drain use in this particular review precludes making meaningful statements regarding their utility.

Limitations

We included literature from the last 10 years in our systematic review as cell salvage with washing was rarely used before this point. A manual search of relevant articles failed to yield any further relevant studies published before 2001. However, it is conceivable that relevant studies were overlooked. Second, only English language articles were included. It is again possible that a number of non-English articles were excluded. As previously mentioned, the data from the 3 conference abstracts that met our inclusion criteria were presented but not included in the overall analysis owing to the inability to scrutinize the methodology of these studies. However, the inclusion of these studies would strengthen this systematic review by including all of the most up-to-date evidence.

Transfusion trigger varied across the studies from hemoglobin of less than 100 g/L to less than 80 g/L. Some studies had more elaborate criteria, specifying separate criteria for patients with a history of ischemic heart disease. Most studies contained a qualifier that symptomatic patients were transfused regardless of hemoglobin level.

Infection rates and complications were not universally reported across studies. Inconsistency in reporting and what constitutes an infection or complication limits the

ability to make generalizations regarding the data at this time. Most of the studies were vastly underpowered to detect differences between treatment and control groups with respect to infection rate. This detracts further from the validity of the data considered in our study.

Conclusion

There is limited arthroplasty evidence comparing cell salvage with washing to other strategies or no strategy in terms of exposure to allogenic blood. In general, published studies have low levels of evidence. In addition, studies have been underpowered to detect significant differences in postoperative infection rates with and without the use of cell salvage. Taking these factors into account, the evidence available suggests that there is a reduction in exposure to allogenic blood with the use of salvage systems in arthroplasty. The protective effect appears to be more consistent and greater for THA. The importance of risk stratification in the use of cell salvage remains unclear. Contradictory evidence exists with respect to whether low or high preoperative hemoglobin strengthens or weakens the protective effect of cell salvage. There is a lack of evidence surrounding the importance of perioperative versus postoperative cell salvage. The relative volumes collected for perioperative and postoperative periods, the use of drains and the possible effect on transfusion rates for TKA and THA should be further explored. This may be an important factor in consideration of a cost–benefit analysis of cell salvage.

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