REVIEW ARTICLE

Perioperative Blood Management Strategies for Total Knee Arthroplasty

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Total knee arthroplasty (TKA) often causes a significant amount of blood loss with an accompanying decline in hemoglobin and may increase the frequency of allogeneic blood transfusion rates. Unfortunately, allogeneic blood transfusions have associated risks including postoperative confusion, infection, cardiac arrhythmia, fluid overload, increased length of hospital stay, and increased mortality. Other than reducing the need for blood transfusions, reducing perioperative blood loss in TKA may also minimize intra-articular hemorrhage, limb swelling, and postoperative pain, and increase the range of motion during the early postoperative period. These benefits improve rehabilitation success and increase patients' postoperative satisfaction. Preoperative anemia, coupled with intraoperative and postoperative blood loss, is a major factor associated with higher rates of blood transfusion in TKA. Thus, treatment of preoperative anemia and prevention of perioperative blood loss are the primary strategies for perioperative blood management in TKA. This review, combined with current evidence, analyzes various methods of blood conservation, including preoperative, intraoperative, and postoperative methods, in terms of their effectiveness, safety, and cost. Because many factors can be controlled to reduce blood loss and transfusion rates in TKA, a highly efficient, safe, and cost-effective blood management strategy can be constructed to eliminate the need for transfusions associated with TKA.

Key words: Blood management; Conservation strategies; Total knee arthroplasty

Introduction

Total knee arthroplasty (TKA) is the most common elective orthopaedic surgical procedure, with more than 600 000 TKA procedures performed annually in the United States[1]. Although TKA can effectively improve joint functionality and a patient's quality of life, it is often associated with substantial blood loss and a high rate of allogeneic blood transfusion. Some centers indicate that 20%–40% of all patients who underwent TKA received blood transfusions[2,3]. Blood transfusion effectively corrects anemia, but also increases the economic burden placed on patients and society. Allogeneic blood transfusions are also associated with significant potential risks and complications, including infections, fluid overload, cardiac arrhythmia, prolonged hospitalization, and an increase in mortality[4,5]. Minimizing blood loss and blood transfusions associated with TKA is critical to avoid unnecessary expense and complications.

Preventing blood loss around the knee during TKA also minimizes hemarthrosis, limb swelling, postoperative pain, and the use of analgesics. These outcomes facilitate better outcomes when performing functional exercise during the early postoperative period, thus improving postoperative patient satisfaction.

Perioperative blood management strategies focus on minimizing blood loss and the need for blood transfusions. Preoperative anemia and significant blood loss intraoperatively and postoperatively are common factors that increase the need for postoperative blood transfusions. There are several blood conservation methods that can be utilized during TKA. However, implementation of these methods is based on subjective judgment rather than relevant evidence-based guidelines. The goal of this article is to explore the current scientific literature and to provide an overview of the effectiveness of blood management strategies in TKA.

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Method

For this review of the literature, related reports were found through searches of PubMed, OVID Medline, and the Cochrane database using the following subject terminology: "knee arthroplasty," "blood transfusion," "preoperative," "intraoperative," and "postoperative". In all, 589 articles were found. After excluding 75 non-English articles, 514 English articles were browsed and assessed. As a result, 322 articles were excluded from the analysis because they were not relevant to the subject of this study, thus leaving 192 articles for final review. Each article was strictly screened for quality using the following criteria: whether there was acceptable research design and the reputability of its journal. Ninety-three articles were screened out because the study methods were unclear or not suitable, leaving 99 research articles for inclusion in this review. This entire process is depicted in Fig. 1.

Preoperative Strategies

Iron Therapy

Approximately one-third of the world's population is anemic, mainly due to iron deficiency[6]. Current data indicates that patients undergoing major surgery may have a higher prevalence of anemia, with rates as high as 75%[7]. Various studies indicate that preoperative anemia is associated with poor prognosis[8–10]. In addition, preoperative anemia is the strongest predictor of transfusion requirements[11,12]. Therefore, preoperative correction of anemia is of great significance.

Iron supplementation is an important method to optimize hemoglobin (Hb) concentration and can be administrated orally or intravenously. Oral iron is an inexpensive way to treat anemia, but the daily absorption of oral iron is limited to 2–16 mg daily. Thus, to be effective, patients must take oral iron for 3–6 months preoperatively. Unfortunately, the malabsorption and gastrointestinal side effects of oral iron further limit its application. Intestinal resection, *Helicobacter pylori* infections, antacids, and phenolic compounds also decrease the absorption of oral iron, with the likelihood of patients experiencing gastrointestinal dysfunction when taking oral iron approximately 32%[13–16].

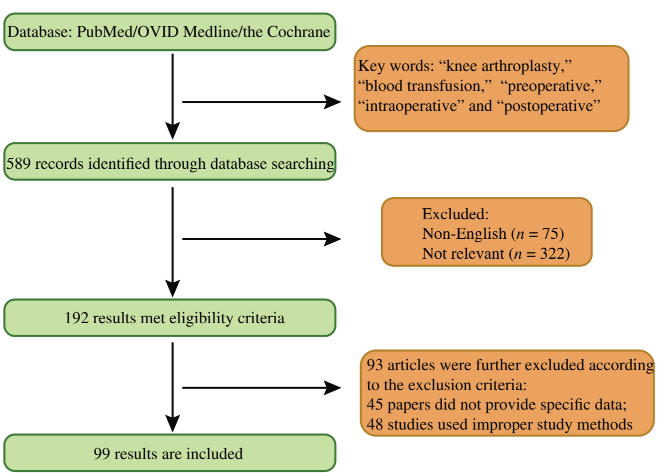

Fig. 1 Flow-chart of search of published reports showing the process of inclusion and exclusion.

Routine use of oral iron supplementation during TKA has been a controversial issue. Lachance *et al.* found that preoperative continuous iron supplementation (300 mg, 3 times/day) lasting longer than 3 weeks increased ferritin concentrations by 25.8 ng/mL ($P < 0.001$), but caused a drop in Hb by 0.14 g/dL ($P = 0.015$)[17]. However, they also report many side effects, including constipation (33.3%), heartburn (13.8%), and abdominal pain (12.6%). However, other investigators have reported that the therapeutic regimen of taking ferrous sulfate (256 mg/day), vitamin C (1000 mg/day), and folic acid (5 mg/day) 30–45 days before surgery could reduce transfusion rates (5.8% *vs* 32%; $P < 0.01$) and the units of blood transfused (1.78 U *vs* 2.22 U; $P < 0.05$) in TKA when compared with a control group[18]. A meta-analysis by Yang and his colleagues corroborates that oral iron can increase Hb levels ($P = 0.009$), but also reports that there are no significant differences in the rate and volume of transfusion ($P > 0.05$) between patients who receive iron therapy and those who do not[19].

Many studies indicate that using intravenous iron is a safe and effective way to correct preoperative anemia[20,21]. Munoz *et al.* reveal that intravenous iron significantly reduced allogeneic blood transfusion rates (8.9% *vs* 30.1%; $P = 0.001$), shortened hospitalization periods (8.4 days *vs* 10.7 days; $P = 0.001$), and did not increase postoperative complications ($P > 0.05$)[21]. A meta-analysis by Litton *et al.* proved that intravenous iron increases the mean Hb concentration (mean difference [*MD*], 6.5 g/L; 95% *CI*, 5.1–7.9 g/L), decreasing the need for blood transfusion (risk ratio [*RR*], 0.74; 95% *CI*, 0.62–0.88), but increases the risk of infection (*RR*, 1.33; 95% *CI*, 1.10–1.64) as compared to oral iron or no iron supplementation[22]. Another meta-analysis examined 103 studies and compared patients receiving intravenous iron ($n = 10\ 390$) to patients taking oral iron ($n = 1329$), placebo ($n = 3335$), and intramuscular iron ($n = 155$) or no iron ($n = 1329$)[20]. The results showed that intravenous iron did not increase the risk of serious adverse events (*RR*, 1.04; 95% *CI*, 0.93–1.17) and was not associated with an increased risk of infection (*RR*, 1.17; 95% *CI*, 0.83–1.65), although it led to higher rates of severe infusion reactions (*RR*, 2.47; 95% *CI*, 1.43–4.28). However, the rate of serious infusion reaction was very low (1: 263) and occurred mainly in patients infused with high-molecular weight iron dextran. Despite the current limited evidence regarding the routine use of different iron formulations in TKA, preoperative anemia is the strongest predictor of blood transfusion in TKA; thus, we recommend iron supplementation to correct iron deficiency in anemia.

Erythropoietin

Erythropoietin is a natural glycoprotein secreted primarily in the kidney. It stimulates progenitor cells in bone marrow to produce red blood cells. Erythropoietin is widely used to treat various types of anemia, especially in patients with anemia secondary to chronic kidney disease. Erythropoietin is also commonly used in orthopaedic surgery, but currently its optimal dosage is unclear, with only two recommended treatment regimens. The first recommendation is to administer 300 U/kg 10 days before surgery, the day of surgery, and 4 days postoperatively[23]. The second recommendation is to inject 600 U/kg subcutaneously on days 21, 14, and 7 before surgery, and on the day of surgery[24]. Erythropoietin does have risks, including an increased risk of thromboembolism events[25]. To ensure the safety and effectiveness of erythropoietin, its use must be combined with iron to enhance the response to erythropoietin and reduce its dosage, while taking precautions to prevent thrombosis[26]. The use of erythropoietin should cease when the Hb concentration in men reaches 13 mg/dL and 12 mg/dL in women[27].

In an unrestricted transfusion standard study, Bedair *et al.* demonstrate that erythropoietin could increase the postoperative Hb level ($P < 0.001$) and lower transfusion rates (0% *vs* 41%, $P < 0.001$) but increase healthcare costs ($2632 *vs* $2284)[28]. Another study found that erythropoietin reduced blood transfusion even under restrictive transfusion criteria[29]. This study demonstrated that erythropoietin reduces blood transfusion units by 29% and blood transfusion rates by 50% but increased the cost by €785. A recent meta-analysis of 2439 TKA patients reinforced that erythropoietin can reduce the need for allogeneic blood transfusions (*RR*, 0.38; 95% *CI*, 0.27–0.53) and the amount of transfused red blood cells (*MD*, −0.57; 95% *CI*, −0.86 to −0.29), and at the same time, not increase the incidence of thrombotic and other adverse events[30]. Although current evidence indicates that erythropoietin can effectively reduce the transfusion rate in TKA, we do not recommend the routine use of erythropoietin due to cost. More investigation regarding lowering the costs of erythropoietin to promote its application is needed.

Preoperative Autologous Blood Donation

Preoperative autologous blood donation is often used for elective surgery. Autologous blood is collected and stored before the operation for reinfusion during surgery when required. Utilization of PABD for orthopaedic surgeries is popular, especially for joint replacements, but use of this approach is controversial. Some researchers have found that PABD can reduce the risk of allogeneic blood transfusion in TKA (19% *vs* 38%, $P < 0.05$)[31]. However, it can lead to 29% autologous blood wastage and increase the cost of health care ($395 *vs* $220; $P < 0.001$). A related meta-analysis points out that PABD can reduce the absolute risk of allogeneic blood transfusions by 44% (95% *CI*, −0.68 to −0.21), but it also increases the risk of total blood transfusion (allogeneic or autologous transfusion) (*RR*, 1.24; 95% *CI*, 1.02–1.51)[32].

Although several studies have demonstrated that PABD can reduce the risk of allogeneic blood transfusions, many researchers do not recommend PABD in TKA. Jakovina *et al.* found that PABD did not reduce the TKA allogeneic blood transfusion rate and caused a large quantity of autologous blood waste[33]. They also confirmed that PABD-induced iatrogenic anemia would increase the need for allogeneic blood transfusion. Another study supports these findings, stating the application of PABD in hip and knee replacement would likely not benefit patients[34]. In this study, 461 patients using postoperative cell salvage were analyzed. Among these, 182 patients used PABD at the same time. The study found that PABD led to a greater reduction in Hb concentration ($P < 0.001$) and a higher transfusion rate ($P < 0.01$). In addition, 86.3% of PABD products were wasted.

A low utilization rate of autologous blood is an important factor that restricts the use of PABD. One study reports that the waste rate of PABD units at Mayo Clinic's increased from 22.8% to 88.9% between 2004 and 2010[35]. Another factor limiting the use of PABD is the dramatic increase in medical costs. A study by Etchason and his colleagues discovered that substituting autologous for allogeneic blood had little expected health benefits (0.0002–0.00044 quality-adjusted year of life saved), and the cost per unit of autologous blood increased by 68% to $4783[36]. Therefore, we do not recommend the use of PABD on a routine basis in TKA.

Intraoperative Strategies

Acute Normovolemic Hemodilution

Acute normovolemic hemodilution is similar to PABD where a certain amount of autologous blood is collected right before the operation. At the same time, an equal volume of colloid or crystal solution is added. If necessary, this autologous blood is transfused intraoperatively or postoperatively. ANH can reduce the erythrocyte loss when an equivalent amount of blood is lost due to dilution. ANH is widely used during major surgeries to reduce the postoperative allogeneic blood transfusion rates and can effectively reduce allogeneic transfusion rates[37,38]. A meta-analysis of 2439 patients in 29 randomized controlled trials showed that patients in the ANH group received less allogeneic transfusion units (*MD* = −0.79; $P = 0.001$), with a lower allogeneic transfusion rate (42.1% *vs* 56.1%; $P < 0.0001$), and had less blood loss (388 mL *vs* 450 mL; $P < 0.0001$)[37].

Of note, there is limited literature evaluating the efficacy of ANH in TKA. A prospective randomized controlled trial of 30 patients treated with TKA demonstrated that ANH was effective in reducing allogeneic transfusion[39]. The study found that in comparison with the control group, the groups that had hemodiluted autologous blood infusions 2 h or 6 h after surgery received less allogeneic blood transfusions. In a retrospective study, Schmied *et al.* also found that ANH can reduce allogeneic blood transfusions in TKA[40]. However, other investigators report that the use of ANH does not decrease allogeneic transfusions but leads to an increase in total blood loss in TKA[41,42]. Juelsgaard *et al.* found that the use of ANH significantly increased postoperative blood loss (1306 mL *vs* 1026 mL, $P < 0.05$) compared to the control group[41]. In a randomized, single-blind study comparing the effects of ANH to tranexamic acid in reducing allogeneic blood transfusion in TKA, Zohar *et al.* found using ANH increased postoperative drainage (259 mL *vs* 110 mL; $P < 0.0008$) and the amount of allogeneic blood transfusion (19 U *vs* 2 U; $P < 0.0008$)[42]. The current literature regarding the use of ANH in TKA is limited and conflicted, so more research on the efficacy of this technique in TKA is needed.

Hypotensive Anesthesia

Hypotensive anesthesia reduces blood pressure by utilizing different drugs and methods during the period of anesthesia, typically maintaining the average arterial pressure at 55–60 mm Hg. The purpose of this technique is to reduce peripheral blood flow and blood loss during surgery. This technique also improves the surgical field of vision while sustaining normal central venous pressure, stroke volume, and cardiac output. Many researchers have confirmed that this technique can effectively reduce intraoperative blood loss[43,44].

Although hypotension anesthesia is commonly used in TKA, there are few reports evaluating its effectiveness in TKA. A prospective, randomized, single-blind study of 100 patients treated with TKA showed that controlled hypotension reduced the drop in Hb levels when compared with using a tourniquet[45]. The results of the study showed that the Hb concentration in the hypotensive anesthesia group was higher at the end of surgery, and 5 and 6 days after surgery ($P = 0.043$, 0.012, 0.014 respectively). It also reduced the transfusion rate (18.4% *vs* 29.4%; $P = 0.196$) and transfusion units (19 U *vs* 33 U; $P = 0.222$). Another study found that compared with the control group, total blood loss in the controlled hypotension groups was significantly decreased (1056 *vs* 1826 mL; $P = 0.001$), blood transfusion rates were lower (42.9% *vs* 81.2%; $P < 0.05$), and the average transfusion volume was reduced (93 mL *vs* 775 mL; $P = 0.005$)[46]. Although current studies show that controlled hypotension can effectively reduce blood loss in TKA, more high-quality research is required to prove the value of hypotensive anesthesia in TKA.

Tourniquet

Using a tourniquet can effectively reduce intraoperative bleeding, provide a clear surgical visual field, and shorten operation time. Thus, it has been routinely used in TKA. Some researchers support the application of a tourniquet in TKA. In a randomized controlled study, Tai *et al.* discovered that in 72 cases of TKA where a tourniquet was utilized, there was a reduced postoperative loss of Hb (2.6 ± 0.9 g/dL *vs* 3.7 ± 1.3 g/dL) and hematocrit (7.6% ± 2.8% *vs* 10.4% ± 4.0%), and lower increases in postoperative C-reactive protein (139 ± 75 mg/dL *vs* 175 ± 55 mg/dL) and creatine phosphokinase (162 ± 104 U/L *vs* 214 ± 89 U/L)[47].

However, a significant amount of literature does not support the application of a tourniquet. A recent article reports that tourniquet use would increase the bone cement thickness (14.2 mm *vs* 13 mm; $P = 0.009$) and blood loss postoperatively (0.9 L *vs* 0.6 L; $P = 0.02$)[48]. Mori and his colleagues point out that tourniquet use was also associated with higher risk of distal deep venous thrombosis (52.9% *vs* 23.1%; $P = 0.002$)[49]. In addition, the use of a tourniquet led to the weakness of quadriceps femoris muscle and negatively affected the recovery of knee function postoperatively[50,51]. A meta-analysis examining 13 randomized controlled study with 689 patients showed that although a tourniquet reduced the intraoperative blood loss (weighted mean difference [*WMD*] = −198.21; $P < 0.01$), it did not reduce the total blood loss ($WMD = 63.20$; $P = 0.80$) and the rate of transfusion ($RR = 1.27$; $P = 0.47$)[52]. It also led to a decreased range of motion ($WMD = -10.41$; $P < 0.01$), and increased the risk of thrombotic events ($RR = 5.00$; $P = 0.02$), and other related complications ($RR = 2.03$; $P = 0.02$).

Some researchers support a shorter duration of tourniquet use to minimize the incidence of postoperative complications. Wang *et al.* compared the difference of using a tourniquet for a short and long period of time[53]. They found that longer use of the tourniquet reduced total blood loss, where shorter use helped decrease pain and limb swelling, and promoted functional recovery after the operation. However, there was no significant difference in transfusion rates between the two groups. Other investigators have pointed out that earlier release of the tourniquet would prolong the operation time and increase the rate of blood transfusion, and does not benefit patients[54]. A meta-analysis by Zan *et al.* confirmed that early release of tourniquet increased the total blood loss ($MD = 184.19$ mL; $P < 0.00001$), but may reduce the risk of various complications, including postoperative incision margin erythema, exudation, necrosis, shallow infection, and deep vein thrombosis (odds risk [*OR*] = 0.39; $P = 0.0007$), as well as other complications, including wound dehiscence, hematoma, and deep infection ($OR = 0.32$; $P = 0.05$)[55]. Overall, the use of tourniquets remains a controversial issue. Based on the current evidence we do not recommend the routine use of tourniquets in TKA.

Tranexamic Acid

Tranexamic acid plays an important role in blood conservation strategies during TKA. Many studies show that TXA can effectively reduce blood loss and transfusion rates in TKA[56–59]. TXA can be administrated orally, through intravenous infusion, and by topical application. Although in the literature oral TXA has been reported to effectively reduce blood loss in TKA[60,61], TXA is mainly administrated by intravenous infusion and topical application. A meta-analysis of 15 randomized controlled trials reported that intravenous TXA reduced blood loss by 504.9 mL ($P < 0.00001$) and blood transfusion units by 1.43 ($P < 0.00001$), and did not increase the risk of deep vein thrombosis ($OR = 0.75$; $P = 0.48$) or pulmonary embolism ($OR = 0.65$; $P = 0.50$)[62].

Topical application of TXA in the joint cavity is also an effective approach to reduce blood loss in TKA. Gomez-

Barrena *et al.* demonstrate that 3 g of topical TXA is as effective as intravenous TXA (15 mg/kg TXA before releasing tourniquet and 3 h postoperatively)[56]. In a meta-analysis including 12 studies with 1189 patients, Yue *et al.* found that topical TXA reduced blood loss by an average of 280.65 mL ($P < 0.00001$), decreased the risk of blood transfusion (risk ratio [*RR*], 0.26; $P < 0.00001$), and was not associated with an increased risk of deep venous thrombosis or pulmonary embolism ($P > 0.05$)[63]. They recommend the dosage of topical TXA to be no less than 20 mg/kg.

Intravenous TXA combined with topical TXA is effective at reducing blood loss and transfusion rates. Recently, researchers compared the effects of 1 g of intravenous TXA combined with 3 g of topical TXA to 1 g of intravenous TXA alone in reducing blood loss in TKA[64]. The results demonstrated that compared to the control group, the combined group had decreased blood loss on postoperative day 1 (*MD*, 277 mL; $P = 0.002$) and day 2 (*MD*, 373 mL; $P = 0.003$). A meta-analysis compared intravenous or topical TXA alone to the combination of both, which revealed that the combination facilitated less total blood loss, hidden blood loss, drainage volume, a lower transfusion rate, and a lower decline of Hb level ($P < 0.05$), and was not associated with a higher risk of wound infection and deep venous thrombosis ($P > 0.05$)[65]. There is high quality evidence that favors the use of TXA in TKA. Thus, we recommend that TXA be routinely used in TKA.

Topical Hemostatic Agents

Topical hemostatic agents are primarily utilized to promote blood clotting at the surgical incision site and to reduce postoperative bleeding. Current topical hemostatic agents used to reduce bleeding in TKA include platelet-rich plasma and fibrin sealant. Platelet-rich plasma is rich in platelets, fibrinogen, thromboxane, platelet-derived growth factor and transforming growth factor beta. Therefore, platelet-rich plasma theoretically promotes hemostasis and wound healing. Mochizuki *et al.* conducted a clinical trial on reducing bleeding in TKA with platelet-rich plasma[66]. A total of 315 patients were included in the trial, and the results showed that compared to patients who did not receive platelet-rich plasma, platelet-rich plasma can effectively reduce blood loss (446.9 ± 149.7 mL *vs* 550.7 ± 178.1 mL, $P < 0.001$) and improve the Hb level ($P < 0.05$). Aggarwal *et al.* and Gardner *et al.* also found that platelet-rich plasma can effectively reduce blood loss and postoperative pain, and promote early postoperative function in TKA[67,68].

However, other researchers have found that platelet-rich plasma does not reduce blood loss in TKA[69–72]. In a randomized controlled trial, Morishita *et al.* found that there was no significant difference in blood loss between the platelet-rich plasma group and a control group (826.2 mL *vs* 830.2 mL; $P = 0.96$) in TKA[72]. This study also demonstrated that platelet-rich plasma did not decrease postoperative pain or help improve joint function postoperatively. A related meta-analysis showed that platelet-rich plasma could reduce the amount of blood loss postoperatively (*RR*, 0.73; 95% *CI*, 0.59–0.90), but the result was highly heterogeneous ($P < 0.00001$, $I^2 = 79\%$)[73].

Fibrin sealant promotes blood coagulation reactions through fibrinogen and thrombin to reduce postoperative bleeding. Many researchers have confirmed that fibrin sealant is associated with the reduction of blood loss in TKA[74,75]. In a study of 176 patients treated with TKA, Bou Monsef *et al.* discovered that fibrin sealant could significantly decrease blood loss (603 mL *vs* 822 mL; $P < 0.005$) and blood transfusion rates (18% *vs* 38%, $P < 0.05$)[74]. A recent meta-analysis reports that fibrinogen sealant could reduce the drop of Hb levels after surgery (*MD*, −0.72; $P < 0.00001$) and led to lower drainage volumes (*MD*, −354.53; $P < 0.00001$) and transfusion rates (rate difference, −0.27; $P = 0.006$), and a lower incidence of hematomas (rate difference, −0.11; $P = 0.04$)[76]. However, Aguilera *et al.* tested two different types of fibrin sealants in their study and found that compared with the control group, fibrin sealants did not reduce the total amount of blood loss in TKA ($P > 0.05$)[77]. Recently published studies report that fibrin sealant does not reduce blood loss and the rate of blood transfusion[78–80]. There is conflicting evidence about the efficacy of topical hemostatic agents in preventing blood loss in TKA. Thus, additional research is needed to ascertain the application of platelet-rich plasma and fibrin sealant in TKA.

Postoperative Strategies

Drainage

The placement of a drainage tube followed the standard approach during TKA. Drainage tubes can prevent joint hematoma and exudation, and, thus, theoretically prevent infection and decrease limb swelling[81]. However, some researchers have discovered that using drainage tubes increases postoperative bleeding and transfusion rates ($P < 0.05$)[82]. A prospective randomized study by Jhurani *et al.* failed to find any significant difference in postoperative Hb concentrations ($P = 0.38$), blood loss ($P = 0.33$), and transfusion rates ($P = 0.52$) between patients using drainage tubes and those without in TKA[83]. Two recent meta-analyses revealed that whether or not drainage tubes were used in TKA led to no significant differences in blood loss, infection rate, hematoma formation, deep vein thrombosis, and function recovery[84,85]. Several published studies have shown that clamping the drainage tube can reduce the postoperative blood loss[86,87]. A related meta-analysis pointed out that clamping the drainage tube for 4–6 h led to a lower drop in Hb levels (*WMD*, −0.43; $P < 0.00001$) and optimized blood loss (*WMD*, −305.09; $P < 0.00001$)[87]. Based on the data, drainage tube use in TKA is a controversial issue. The current evidence shows that the usage of drainage lacks efficacy in preventing blood loss and reducing transfusion rates in TKA, while drainage clamping may optimize the outcome when drainage is used in TKA.

Blood Salvage Systems

Blood salvage systems may be used intraoperatively or postoperatively to collect and reinfuse shed blood (washed or unwashed) into the patient to reduce allogeneic blood transfusion. Numerous studies report that this technique can reduce blood loss volume and allogeneic blood transfusion units in TKA[88,89]. Horstmann *et al.* found that reinfusion of autologous shed blood can optimize the Hb levels postoperatively (11.6 g/dL *vs* 11 g/dL; $P = 0.003$), and decrease blood loss (1576 mL *vs* 1837 mL; $P = 0.03$) and allogeneic blood transfusion rates (10.2% *vs* 19.6%; $P = 0.15$)[88]. A meta-analysis including 43 studies with 5631 patients demonstrated that reinfusion systems can reduce the need for allogeneic blood transfusions (*RR*, 0.51; 95% *CI*, 0.39–0.68), but an analysis of studies after 2010 indicated that reinfusing the shed blood does not reduce the rate of allogeneic blood transfusions (*RR*, 0.91; 95% *CI*, 0.63–1.31)[90]. Recently, some studies reported that using reinfusion systems does reduce allogeneic transfusion rates but instead increases the costs of health care[29,91]. So-Osman *et al.* researched the effect of reinfusing shed blood under strict standards of blood transfusion in TKA[29]. The study involving 683 patients found that reinfusing shed blood does not reduce allogeneic blood transfusions (*OR*, 1.3; $P = 0.26$) without the use of erythropoietin. However, when accompanied with erythropoietin, reinfusing shed blood significantly increases the requirement of allogeneic blood transfusions (*OR*, 2.2; $P = 0.02$). The authors also found that the use of reinfusion systems increases the medical care cost by €537 ($P = 0.03$). Thus, according to the current evidence, we do not recommend the routine use of blood salvage systems.

Postoperative Limb Positioning

Postoperative flexion of the knee joint is the most simple, economical, and effective measure to reduce postoperative bleeding in TKA[92]. A recent study reported that flexing the knee at 45° for 48 h postoperatively reduces the total blood loss (1008.4 ± 102.6 mL *vs* 1212.0 ± 113.9 mL; $P < 0.05$) and hidden blood loss (505.1 ± 28.0 mL *vs* 617.5 ± 52.4 mL; $P < 0.05$), and increases the Hb level (10.8 ± 1.1 mL *vs* 10.0 ± 1.3 mL; $P = 0.04$)[93]. Many researchers reiterate that the postoperative flexion of the knee can reduce the hidden blood loss and limb swelling, and promote the function recovery in their studies[94,95]. A meta-analysis, including 10 randomized controlled studies, supported these findings by reporting that flexing the knee postoperatively led to lower total blood loss (*MD*, −130.66 mL; $P = 0.0002$) hidden blood loss (*MD*, −73.27 mL; $P = 0.001$) and Hb level (*MD*, 0.73; $P < 0.00001$), increased the range of motion (*MD*, 3.79; $P = 0.002$), and was not associated with higher risk of deep venous thrombosis and wound infection ($P > 0.05$)[94]. Thus, we view flexing knee postoperatively as a simple and cost-effective method to decrease blood loss in TKA.

Restrictive Transfusion Thresholds

Strict transfusion thresholds are important measures of blood management in TKA, which may significantly reduce the rate of blood transfusion. In a retrospective cohort study, Loftus *et al.* demonstrated that restrictive transfusion algorithms could effectively reduce blood transfusions[96]. The study including 19 950 patients showed that patients with Hb levels higher than 7 g/dL, or who were hemostatically stable with systolic pressures no less than 100 mm Hg and heart rates no higher than 100 bpm, did not receive blood transfusions. The restrictive transfusion thresholds implemented in this study decreased the rate of blood transfusion by 44% (11.7% *vs* 20.9%, $P < 0.0001$) and the transfused blood units per 1000 patients by 41.3% (262.51 U *vs* 447.48 U, $P < 0.0001$), and decreased postoperative complications, mortality rates, the hospital length of stay and 30-day readmission rates ($P < 0.05$). The American Association of Blood Banks clinical application guidelines recommend that orthopaedic surgeons use the transfusion standard of Hb less than 8 g/dL[97]. In a meta-analysis including 31 studies with 12 587 patients, the

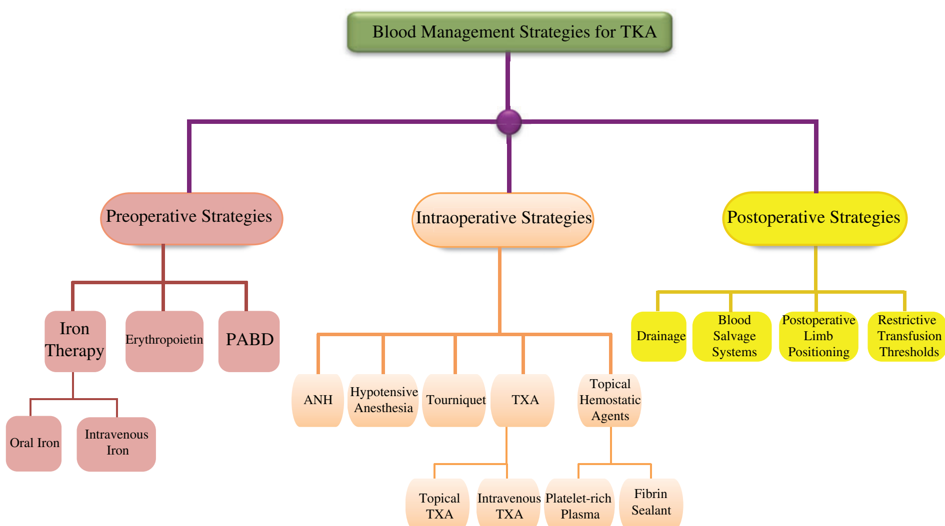

Fig. 2 Flow chart showing perioperative blood management strategies for total knee arthroplasty.

authors found that compared with liberal transfusion strategies, a restrictive transfusion strategy (Hb level, 7–8 g/dL) resulted in a 43% decrease in transfusion rates and was not associated with a higher risk of 30-day mortality or other complications, including myocardial infarction, stroke, pneumonia, infection, and mortality[98]. Another meta-analysis suggests that the implementation of restrictive transfusion thresholds for non-cardiac surgery in patients with cardiovascular disease increases the risk of acute coronary syndromes (*RR*, 1.78; $P = 0.01$; $I^2 = 0\%$)[99]. The present study supports the application of a more liberal transfusion threshold (Hb level > 8 g/dL) for patients with acute or chronic cardiovascular disease. Thus, we recommend adhering to restrictive transfusion thresholds in TKA (Hb level, 7–8 g/dL), but for patients with cardiovascular disease, utilizing more liberal transfusion thresholds (Hb level > 8 g/dL).

Summary

Perioperative blood management strategies for TKA aim to reduce allogeneic blood transfusion rates and associated risks, while reducing associated healthcare costs (Fig. 2). Although various blood management strategies are available, the efficacy and cost–benefit of commonly used methods are debatable and further research is required. For PABD and tourniquet, current evidence does not support their routine use in TKA. The most common strategies used in hospitals is treating iron-deficiency anemia with intravenous iron preoperatively and tranexamic acid intraoperatively, and implementing restrictive transfusion standards postoperatively. There are many factors that, when managed appropriately, help reduce the rates of allogenic transfusions in TKA. Therefore, it is possible to establish a highly efficient, safe, and cost-effective blood management protocol eliminating the need for blood transfusions in TKA. Building a blood management algorithm founded on evidence-based medicine is the ideal direction for improving perioperative blood management for the future.

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