BLOOD MANAGEMENT AND PATIENT SPECIFIC TRANSFUSION OPTIONS IN TOTAL JOINT REPLACEMENT SURGERY

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ABSTRACT

Strategies for blood management in the perioperative period of total joint replacement are changing with the better understanding of blood loss and blood replacement options in this population. The preoperative, intraoperative and postoperative options for blood management are outlined. Rationale for patient specific options are described.

INTRODUCTION

In this new millennium, the medical community in general and the orthopaedic surgeon specifically, have more scientific information available concerning the blood loss that occurs during and following total joint replacement of the lower extremity. In addition, better scientific data is available regarding the risks and benefits of various blood management options for patients. Also, newer pharmacologic and blood salvage options have been and are being developed. Finally, the medical community has obtained better data concerning the relationship of patient factors (including age, gender, comorbidities and hemoglobin levels) contributing to the blood management needs in the perioperative period. This paper will explore the various blood management options available for the orthopaedic surgeon and his or her patients when performing or undergoing total joint replacement. The preoperative planning of blood management needs will be outlined.

Blood Loss Following Total Hip or Total Knee Replacement Surgery

The blood loss associated with primary and revision total hip replacement and primary unilateral and bilateral total knee replacement has been extensively studied. In primary hip surgery the blood loss is 3.2 $\pm$ 1.3 units[141] and 4.07 $\pm$ 1.74 grams of hemoglobin.[24] Eighty seven per cent of patients lose less than 5.8 grams. In revision hip surgery the blood loss is approximately 4.0 $\pm$ 2.1 units. In primary knee replacement the blood loss ranges from 1000 to 1500 cc and averages 3.85 $\pm$ 1.4 grams of hemoglobin.[24,71,101] 87% of patients lose less than 5.25 grams of hemoglobin. Blood loss has been reported to be even higher in cementless knee replacement.[57] In the perioperative period for bilateral total knee replacement the reported blood loss is 5.42 grams $\pm$ 1.8 gram[24,71] with 87% of patients losing less than 7.22 grams. Blood loss may be greater for the second knee[21] and alterations in coagulation have been noted. Transfusion rates of 2.0 $\pm$ 1.8 units for primary total hip replacement and 2.9 $\pm$ 2.3 units for revision hip replacement have been documented.[8] The rates for knee replacement are not well studied but are estimated at 1 to 2 units for primary surgery and 3 to 4 units for revision surgery.

Several studies have documented the risk factors associated with the need for transfusion.[15,20,21,71,75,96,107,118,148] Preoperative hemoglobin level is a major predictor of the risk for transfusion following total joint replacement.[9,15,32,37,40,43,55,71] Patients with a preoperative hemoglobin of less than 10 grams have a 90% chance of needing a transfusion, those with 10 to 13.5 gram level a 40-60% chance and those with greater than 13.5 grams a 15-25% chance. Other associated risk factors include blood volume, weight, age (patients less than 65 years with a hemoglobin greater than 13.5 had 3% risk of transfusion if they didn't autodonate blood),[55] estimated blood loss, aspirin use, female sex, comorbidities, thrombocytopenia and bilateral total knee replacement.

In a study of a large number of patients (9482) undergoing total hip and knee replacement, 46% (57% hip, 39% knee) required a transfusion. The wasting rate of autologous units was 61% and 45% (highest in primary surgery and revision knee surgery.) Nine per cent of patients who autodonated blood required allogeneic transfusion (8% primary THA, 21% revision THA, 6% primary TKA, 11% revision TKA). The transfusion rate for patients with a hemoglobin of 10 to 13 (34% of all patients) was 57%. In this group, 33% of patients undergoing total hip replacement and 23% undergoing total knee replacement required allogeneic transfusion even though they donated autologous units. Predictors of allogeneic transfusion were baseline hemoglobin less

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TABLE 1.
Allogeneic Transfusion Risks

COMPLICATION	RISK PER UNIT
Minor allergic reactions	1:100
Bacterial Infection	1:2500
Viral Hepatitis	1:5000
Transfusion related lung injury	1:5000
Hemolytic Reaction	1:6000
Hepatitis B	1:63,000
Hepatitis C	1:103,000
HIV/AIDS	1:500,000
Anaphylaxis	1:500,000
Fatal Hemolytic Reaction (ABO incompatibility)	1:600,000
HTLV I/II Infection	1:641,000
GVHD	RARE
Immunomodulation	UNKNOWN

TABLE 2.
Comparative Mortality Risks

One pack per day of tobacco	1:200
Influenza	1:5000
Automobile deaths	1:6000
Frequent flying academic physician	1:20,000
Leukemia	1:50,000
Birth control pills	1:50,000
Tornadoes in Midwest	1:445,000
Floods	1:455,000
Earthquakes in California	1:558,000

than 13 grams and lack of autologous blood donation. Complications of allogeneic transfusion included infection and fluid overload ($p \leq .001$) and increase in length of stay ($p \leq .01$).

Options for Blood Management in the New Millennium

Allogeneic transfusion is a potential option for blood replacement in all patients. The risks of allogeneic transfusion are listed in Table 1 and comparative mortality risks are listed in Table 2. Other risks of allogeneic transfusion include clerical error (1:20,000-24,000), bacterial contamination, infection, immunomodulation, increase length of stay, and increased cost.

The goal of a blood management program is to reduce exposure to allogeneic blood, reduce the overall need for transfusion, eliminate transfusion related complications,[5,15,18,19,25,38,39,46,69,74,81,99,123,130,142] reduce cost, and develop a global strategy for blood management which is individualized and based on risk.[24,27,46,71,77,78,104,107,125] In addition, if possible, the blood management program should improve medical and functional outcome. Along this path recent investigators have evaluated postoperative vigor[72] in relationship to facilitated recovery, shortened length of stay, improved short term and long term physical function.

Strategies have been developed to reduce transfusion and the complications of transfusion during and following total hip and knee replacement. Practice guidelines include good hemostatic technique, preoperative autologous blood donation, intraoperative and postoperative blood salvage, acute normovolemic hemodilution, unit by unit transfusion based on individual needs and pharmacologic intervention when indicated. Blood loss can be reduced[103] by preoperative, intraoperative, and postoperative measures. Preoperatively anti-platelet agents and anticoagulants should be eliminated when possible, bleeding history should be obtained, appropriate laboratory screening (CBC, platelets, coagulation studies, and bleeding time if indicated) should be performed, and a rationale approach to predonated autologous blood donation should be instituted considering preoperative risk factors and estimates of blood needs.[9,55,78,81,107] Intraoperatively blood loss can be minimized by proper anesthetic techniques, pharmacologic intervention and surgical technique. Anesthetic techniques[124,129] include hypotensive anesthesia, regional anesthesia[23,31] and euthermia.[121,122] Pharmacologic techniques include topical agents (thrombin, fibrin glue, collagen, Gelfoam, Avitene, epinephrine sponges and bone wax) and systemic antifibrinolytics (Desmopressin,[67] Aprotinin,[56,66,98,140] tranexamic acid[11-13,62,63] and E-aminocaproic acid[92]). Postoperative measures include reduced phlebotomy, careful anticoagulation, nutrition, wound compression, and potentially avoiding continuous passive motion[84,112,151] and drains.[2,10,53,64,111,116,117,119] In addition, arbitrary transfusion triggers should be avoided.[25,44,46,106,135,136] The surgeon should transfuse for symptoms instead and assess the patient for his or her physiologic risk from anemia. Hemoglobin levels as low as 8 are tolerated in the elderly without consequences[23] and between 7 and 9 even in patients in critical care units without acute cardiac disease.[60] Blood should be transfused unit by unit as needed. Patients with known cardiac disease and risk factors for morbidity from anemia[25, 83,136] should be transfused earlier. Lower hemoglobins can be accepted in women due to lower hemoglobin starting point.[46]

Specific Alternatives to Allogeneic Transfusion

Preoperative autologous blood donation continues to be the current standard alternative to accepting allogeneic transfusion during and following total joint replacement.[1,17,47,50,126,137,139,143,147-149] Typically 1 or 2 units are obtained for primary joint replacement, 3 to 5 units for bilateral total joint replacement and 4 to 6 units for revision total joint replacement. The technique is indicated for patients with a hemoglobin greater than 11 and a hematocrit greater than 33. Units are drawn at 5 to 7 day intervals with the last unit drawn at least 3 days prior to surgery. Maximizing the time between the last unit and surgery increases the starting hemoglobin. Each unit removes about 500 cc or 9% of the blood volume of the average 70 kilogram man, hence supplemental iron should be provided. Contraindications include infection, unstable cardiovascular diseases and unacceptable anemia. Risks and complications[47,81,113] include the poor endogenous erythropoietin response in patients with mild anemia leading to an increase in preoperative anemia,[68,73,82] poor tolerance in the elderly to the donation process, bacterial contamination, wastage of unused blood[9,15,33,40,47,55,75] and potential increased risk of transfusion and allogeneic blood exposure.[9,27,55,126,138]

Preoperative autologous donation decreases hemoglobin by 1.2 – 1.5 grams/dl. The advantages of this technique include the reduction in perioperative allogeneic blood exposure[6,15,126] hence eliminating the risks of allogeneic blood transfusion.[19,58] Recent studies have also demonstrated a potential reduction in the risk of postoperative deep venous thrombosis in total knee[3] and total hip procedures.[8]

An alternative or adjunct to preoperative autologous blood donation is perioperative blood salvage. Intraoperative blood salvage has been shown to be beneficial in cases involving more than 1000 cc of blood loss.[42,80,92,122,124,132,144] Sixty per cent of intraoperative blood loss[124] can be salvaged and 400 to 500 cc of salvaged blood is required for reinfusion. The blood cells that are salvaged are altered (by irrigation, air, cement) and careful washing is important to avoid coagulopathy.[88,100,143] It is not cost effective in primary arthroplasty if preoperative autologous donation is used. Postoperative salvage and reinfusion drainage systems are also available using washed or unwashed and filtered cells.[14,22,26,28,29,36,41,51,54,59,61,76,86,87,127,128,131,145,146,148,150] Postoperative wound drainage is collected and reinfused. Complications of unwashed reinfusion have included hypertension, hyperthermia, upper airway edema, coagulopathy[100,133], febrile reaction, transfusion of byproducts of hemolysis and intraoperative contaminants[133] and even death. Blood can only be collected for 4 to 6 hours thus limiting reinfusion to 500 to 1000 cc. The advantages of this technique are that significant amounts of blood can be retrieved and reinfused. Postoperative blood salvage can reduce allogeneic blood transfusion exposure if no autologous blood is available,[7,75,105] and further reduce allogeneic exposure when autologous blood is available.[150]

Another option for avoiding allogeneic blood transfusion is normovolemic or hypervolemic hemodilution.[30,47,93,95,109,110,122] With acute normovolemic hemodilution blood is collected immediately preoperatively by the anesthesiologists and stored for reinfusion postoperatively. The volume removed is repleted with crystalloid and colloid. Hypervolemic hemodilution is performed without phlebotomy only using crystalloid. The rationale for this approach is that blood that is lost at surgery will have a lower hematocrit and that the cells and blood that is retransfused is healthier. Indications, as with the other described techniques, are in cases with expected significant blood loss (such as total joint replacement). The patient must be healthy enough to tolerate acute anemia. Risks include the time consuming nature of the procedure and the procedure is contraindicated in patients with coronary artery, renal, pulmonary and hepatic disease.[30] The advantages of this technique[24,47,122] include reduction in perioperative allogeneic blood exposure[110] (particularly if combined with other autologous blood use strategies[109]), reduced cost (no inventory or testing costs, no patient costs associated with procurement), and the reduced risk of clerical error (blood never leaves the room).

The other option in blood management is to increase hematopoiesis with pharmaceutical intervention. This has routinely been done by administering iron to those patients donating blood. However a much more effective way to increase hematopoiesis is the administration of erythropoietin alpha, a recombinant human erythoropoietin.[16,32,34,35,43,45,49,52,65,79,89-92,94,120,134,138] Erythropoietin stimulates the differentiation of progenitor cells to become dedicated to the red blood cell line. The recombinant form mimics the physiologic action of endogenous erythropoietin glycoprotein hormone. In this technique, weekly injections (600 units/Kg) are given preoperatively on day 21, 14, and 7 as well as on the day of surgery. Alternately, the drug can be given daily for 10 days (300 units/Kg) followed by 4 days postoperatively. Adequate levels of iron must be maintained.[34,48] The technique is presently indicated for patients with hemoglobin levels of 10 to 13, those unable or unwilling to undergo preoperative autologous blood deposit, bilateral and revision cases and patients that are Jehovah's Witnesses.[102,134] The advantages of this approach are that it augments the number and quality of preoperative autologous deposited units[45,108,114,115,] and

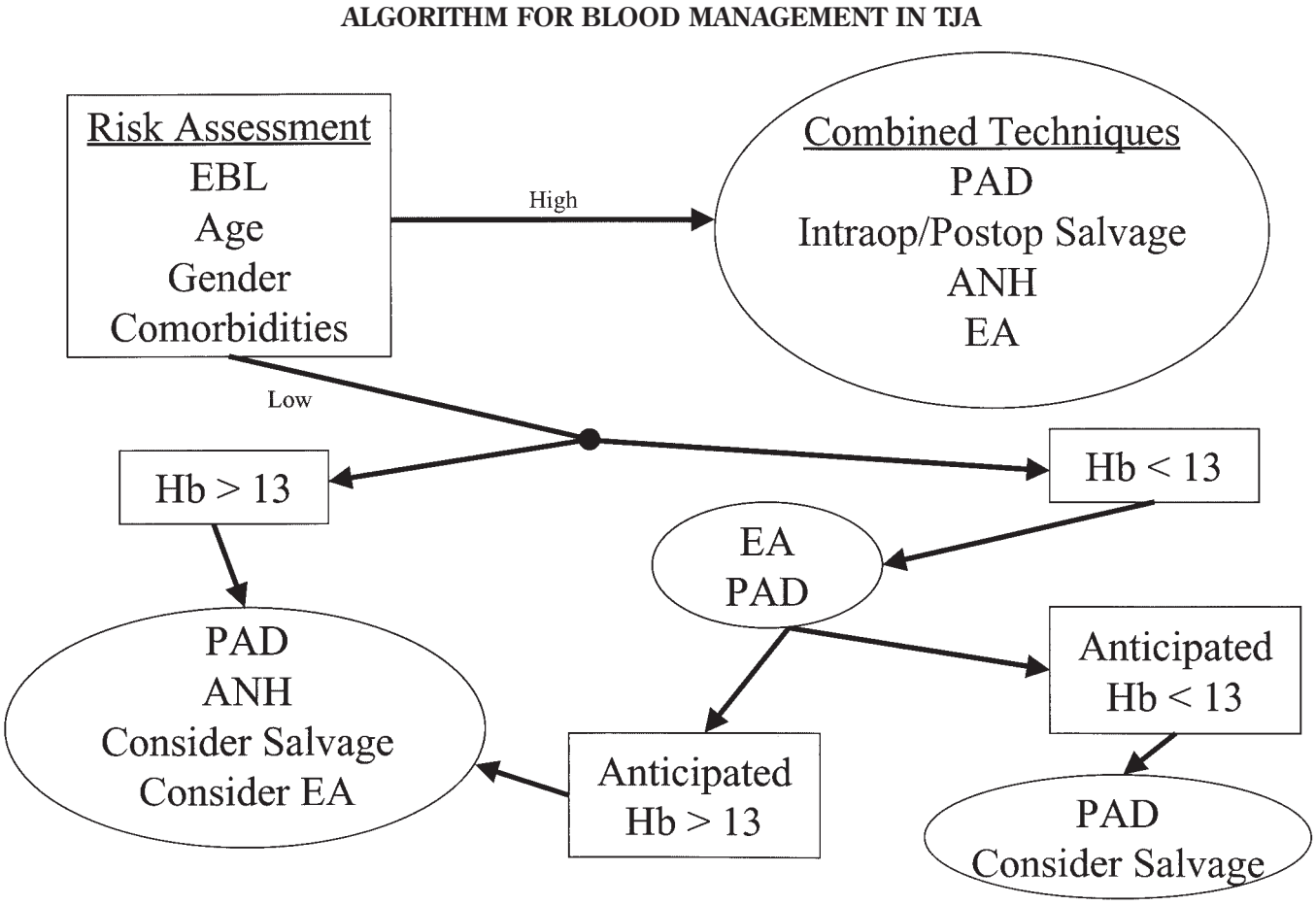

Figure 1. Proposed algorithm for blood management in total joint replacement. (Estimated Blood Loss, EBL; Preoperative Autologous Donation, PAD; Acute Normovolemic Hemodilution, ANH; Erythropoietin alpha, EA; Hemoglobin (gm/dl), Hb)

maximizes perioperative hemoglobin,[138] particularly in comparison to matched populations of autologous donors. Preoperatively, postoperatively, and at discharge, hemoglobin levels were higher in the erythropoietin alpha group compared to the preoperative autologous donation group. Recently, it has been shown to improve postoperative vigor.[72] Especially in patients with preoperative hemoglobin levels of 10 to 13 grams it significantly reduced transfusion risk (16 versus 45%). In this study hemoglobin level was directly proportional to readiness to resume activities of daily living and muscle strength. Improved hemoglobin enhanced the postoperative recuperative power (vigor and functional ability) and ability to participate in early intensive rehabilitation, thereby minimizing length of stay.[97] Other advantages of erythropoietin alpha are that it stimulates an accelerated response to anemia[4] and significantly reduces allogeneic blood exposure even in revision and bilateral surgery. The disadvantages of the drug are that it is injectable and expensive.

Patient Specific Transfusion Options

With all of the data available today concerning the blood loss associated with primary and revision total joint replacement, as well as the costs, benefits, and risks associated with the various blood management options and a better understanding of patient specific factors (such as the individual's blood volume and preoperative hemoglobin status), orthopaedic surgeons can better outline and implement blood management strategies for their patients. Although costs of allogeneic blood and autologous donation are hospital specific, autologous blood donation is considered more expensive and is bundled into the DRG of the procedure (Medicare part A) without additional reimbursement.[152] In addition, wastage has been documented in up to 80 percent of cases.[9,15,33,40,55,75]

When developing a cost effective strategy for blood management it should be based on patient risk. The goal should be to minimize morbidity to the patient including minimization of preoperative and postoperative

anemia, transmission of disease from transfusion and avoiding other morbidities from allogeneic or autologous transfusion. In addition, maximum functional outcome and postoperative vigor should be maintained and cost should be minimized. Waste and inappropriate use of technology should be avoided. Utilization of resources should be tailored to the documented needs of the patients.

Individual patient risk of transfusion should be assessed. Transfusion trigger should be determined based on the minimum hemoglobin that is acceptable given the patient's health, age and risk factors. The estimated blood loss should be determined (and this is probably surgeon and anesthesia dependent). The acceptable blood loss which will avoid transfusion trigger should be determined. Starting hemoglobin and patient weight and blood volume (males 65 to 70 cc blood/kg lean body weight, females 55 to 65 cc blood/kg lean body weight) are the important factors in this determination. An acceptable risk of allogeneic exposure should be chosen.

Algorithms for blood management in total joint replacement (Figure 1) have been developed.[9,24,27,40,47,55,71,77,78,81,85,104,107,125] The goal is to minimize transfusion by instituting institutional guidelines for transfusion,[6,44,69,70] reducing transfusion triggers, utilizing aggressive strategies to reduce blood exposure and blood loss, and using marrow stimulants such as erythropoietin. Patients are categorized as high risk for transfusion (i.e. difficult revision surgery) or low risk (i.e. routine primary hip or knee replacement). If a patient is low risk and has a hemoglobin above 13 grams, he or she and the surgeon may decide on predeposit autologous donation, normovolemic hemodilution, intraoperative and postoperative salvage or erythropoietin alpha. If the patient is low risk with a preoperative hemoglobin less than 13, the options include erythropoietin alpha or autologous donation (if the patient's hemoglobin is greater than 11). Since the need for transfusion in patients with a hemoglobin of 10 to 13 grams is high even with predeposit autologous blood we consider erythropoietin alpha (33% for primary hips and 23% primary knees). If following this therapy the anticipated hemoglobin is still less than 13, intraoperative salvage or additional autologous blood donation (if the hemoglobin is above 11) can be considered.

SUMMARY

In summary, total joint arthroplasty results in significant blood loss. Patients undergoing total joint replacement are at significant risk for transfusion. There has been a paradigm shift to reducing the need for its inevitability and to improving perioperative blood management to maximize hemoglobin and positively impact early and long term outcome. This requires preoperative risk assessment, preoperative preparation, optimizing operative technique, and proper postoperative management as outlined in this manuscript.

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