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Title:

Estimation of blood volume and blood loss in primary total hip and knee replacement: an analysis of formulae for perioperative calculations and their ability to predict length of stay and blood transfusion requirements

Abstract

Introduction

Blood loss continues to be a common surgical risk in total hip (THR) and knee replacements (TKR). Accurate prediction of blood loss permits appropriate counselling of risks to patients, target optimisation and forecasting future transfusion requirements. We compared blood volume formulae of Moore and Nadler, and blood loss formulae of Liu, Mercuriali, Bourke, Ward, Gross, Lisander and Meunier, to assess associations between calculated values with length of stay and transfusion requirements and determine which are useful in contemporary practice.

Methods

We retrospectively studied patients undergoing primary THR and TKR. We collected data on patient demographics, surgical interventions, pre- and postoperative haemoglobin and haematocrit values, length of stay and blood transfusion requirements. Spearman correlation tests and least squares multiple linear regression were performed.

Results

148 THRs and 91 TKRs in 239 patients were analysed over four months. There was a very strong correlation between blood volume formulae. There were multiple very strong and

strong associations between blood loss formulae. Bourke correlated significantly to length of stay, and Liu, Mercuriali, Lisander and Meunier correlated for incidence of transfusion.

Conclusion

Accurate estimation of perioperative blood loss is increasingly important as demand for joint replacement surgery increases in an ageing population. If the primary interest is the association of blood loss and length of stay, Bourke's formula should be preferred. If the primary interest is calculating risk of transfusion, the formulae of Liu or Meunier should be preferred. The formulae of Mercuriali and Lisander are becoming redundant in contemporary practice.

Keywords (MeSH)

Arthroplasty, Replacement

Blood Loss, Surgical

Length of Stay

Blood Transfusion

Hemoglobin

Orthopedic Procedures

1. Introduction

Blood loss continues to be a common surgical risk in Total Hip Replacement (THR) and Total Knee Replacement (TKR) surgery, with estimated losses of 1188-1651 millilitres (mL) in THR[1-4] and 726-1768 mL in TKR[5-9]. Within the United Kingdom (UK), it is predicted that the incidence THR or TKR for patients with osteoarthritis is set to increase by >40% by 2035 because of projected population changes in age, gender and body mass index (BMI)[10]. Many of these patients will have at least one pre-existing chronic condition. Therefore, it remains pertinent to have accurate means of predicting blood loss in this cohort to allow blood management optimisation, to appropriately counsel patients of their risks of undergoing surgery and their potential requirement for blood transfusion, to minimise risks to the patient, to monitor changes over time, and to predict future transfusion requirements.

Roughly 10% of all packed red cell transfusions occur within orthopaedics, and almost 40% of these are used in joint replacement[11]. Transfusion of allogenic blood products carries both risk to the patient and cost to the healthcare system. It is well-recognised that perioperative blood transfusions are associated with increased risk of morbidity and mortality in patients undergoing joint replacements[12-15]. Recent literature has demonstrated that patients who have been transfused with blood which has been stored for more than 14 days are at an increased risk of periprosthetic joint infection[16-18]. Reducing transfusion requirements will reduce costs to the health system from the need for a smaller supply, and also from the costs of treating the associated morbidity. Institutions should endeavour to implement rigorous blood management strategies to minimise the need for allogenic blood transfusions, utilising haemostasis, tranexamic acid, anticoagulation control, tourniquets, and red cell salvage. An essential part of these strategies is to be able to accurately measure total

blood loss. This is of particular importance to populations who cannot receive transfusions in circumstances of autoimmunity or for reasons of beliefs.

Blood loss in THR and TKR can represent 20% of a patient's blood volume. Blood losses are typically replaced with intravenous fluids and/or units of blood. A 2013 review identified numerous existing equations that permit surgeons and physicians to estimate expected blood loss for patients, to better facilitate perioperative management[19]. It was suggested that these formulae could be used for perioperative blood loss estimation and clinical research purposes. We have provided the full formulae in the Materials and Methods (section 2.) for transparency of our processes and ease of further research.

The aims of this paper are four-fold: 1) to compare the methods of Moore and Nadler at estimating a patient's *blood volume* in patients undergoing THR and TKR; 2) to compare the aforementioned seven formulae at estimating *blood loss* in patients undergoing THR and TKR; 3) to assess the strength of associations between calculated blood loss values and outcomes (length of stay; transfusion requirements); and 4) to assess the feasibility of using these formulae in modern clinical practice.

2. Material and Methods

This paper is reported as per the STROBE checklist[20]. A retrospective cohort study was performed in a tertiary elective orthopaedic centre in the UK. Inclusion criteria for participants were any patient undergoing a unilateral primary THR or TKR as an elective procedure. Patients were excluded if they were undergoing complex primary surgery, revision surgery, or synchronous bilateral primary surgery.

Consecutive data were retrospectively collected over four months from December 2018 to April 2019. Data parameters collected included: admission time and date, discharge time and date, gender, operation and laterality, height, weight, body mass index, grade of operating surgeon, surgical time (minutes), haematocrit, haemoglobin, volumes of transfused blood (mL), and length of stay (days). Haematocrit values sought were preoperative, days 3 and 5 postoperatively, and the last value before discharge. Haemoglobin values sought were preoperative and day 1 postoperative. These were defined *a priori* based on the data required to calculate the previously defined blood loss formulae. A minimum allowable haematocrit value of 0.33 was set.

A data extraction table containing the required data and the blood volume/loss formulae was piloted. Once proven to be accurate, the data parameters listed above were collected retrospectively. Three researchers (RLD, EL, IJ) extracted the data parameters listed above. Any disputes were settled through discussion until consensus was reached.

The common theme among all formulae is the necessity to first estimate a patient's *blood volume* (BV). The calculations of Moore[21] and Nadler[22] are the most commonly used, as described in Figure 1.

After this, the *blood loss* formulae utilise variables such as haematocrit (Hct), haemoglobin (Hb), and volumes of transfused blood. The individual blood loss formulae of Liu[23], Mercuriali[24], Bourke[25], Ward[26], Gross[27], Lisander[28] and Meunier[29] are also summarised in Figure 1, with the addition of which blood volume calculations their formulae are derived from. All of these equations have similar foundations.

Data generated from the *blood volume* formulae of Moore and Nadler and the *blood loss* formulae of Liu, Mercuriali, Bourke, Ward, Gross, Lisander and Meunier were analysed to determine the data distribution. D'Agostino and Pearson omnibus normality tests indicated that the data was non-parametric.

All blood volumes were converted to total volume in mL, and blood loss as mL of blood lost. Spearman correlation tests were performed to determine the correlation of the calculation of blood volume per patient and the calculation of blood loss according to the formulae, given the non-parametric data distribution. The thresholds described by Evans[30] were used to determine the strength of positive correlations with an r of 1.0 to 0.8 being very strong; 0.79 to 0.6 being strong; 0.59 to 0.4 being moderate; 0.39 to 0.2 being weak; and 0.19 to 0 being very weak.

Least squares multiple linear regression was then performed for the dependent outcomes of length of stay in days and the incidence of receiving a postoperative blood transfusion. Due to collinearity (r^2 greater than 0.75) separate models were run for each of the *blood loss* formulae.

In these models, the independent variables included were side of operation, type of operation (THR or TKR), gender (male or female), body mass index, preoperative haematocrit,

preoperative haemoglobin, last recorded postoperative haematocrit during inpatient stay, and day 1 postoperative haemoglobin.

Our local transfusion policy for managing postoperative anaemia is to transfuse a single unit of allogenic blood to patients with a Hb <70g/L (or <80g/L in patients with known cardiovascular disease or displaying symptomatic anaemia), and Hb levels must be checked post-transfusion before determining if further transfusions are indicated. Supplementation with oral or intravenous iron in patients with postoperative anaemia is also considered.

3. Results

3.1 Participant demographics and data

Retrospective consecutive data was collected from 239 patients undergoing a primary THR or TKR between 10/12/2018 and 18/04/2019 in our centre. 148 THRs and 91 TKRs were performed during this period. 150 participants were female and 89 were male. Further breakdown of participant demographics is provided in Table 1.

With the exceptions of the formulae of Mercuriali and Ward, all other blood volume and blood loss formulae were able to utilise data from 98-100% of our participants, which could only utilise 33% and 24% of data respectively.

3.2 Blood volume

There was a very strong correlation between the blood volume formulae as calculated with the formulae of Moore and Nadler ($r=0.955$, 95% CI 0.942 to 0.965).

3.3 Blood loss

The strongest associations between the blood loss calculated by the formulae were found to be between Ward and Lisander ($r=0.993$), Ward and Bourke ($r=0.972$), Mercuriali and Lisander ($r=0.969$), Meunier and Ward ($r=0.948$), Lisander and Liu ($r=0.906$) and Mercuriali and Liu ($r=0.849$). Strong correlations (r 0.79 to 0.6) were also observed between the formulae of Lisander and Meunier ($r=0.645$), Liu and Meunier ($r=0.632$) and Meunier and

Mercuriali ($r=0.611$). The remaining correlations were all of moderate (3), weak (5) or very weak (2) association.

Due to similar values or missing data, correlation could not be calculated between the formula of Ward and those of Liu and Mercuriali. The full Spearman correlation matrix for comparison of blood loss estimate formulae can be found in Table 2.

3.4 Length of stay

In the multiple regression models, for the dependent outcome of length of stay (days), the blood loss formula of Bourke ($p=0.0002$) was the only one which contributed significantly in the model to length of stay; the others did not ($p=0.152$ to 0.994). The full multiple linear regression model estimates, 95% CI and p values for the predictive value of blood loss formulae calculations on length of stay can be found in Table 3.

3.5 Transfusion

For the incidence of transfusion, the blood loss formulae of Liu ($p<0.0001$), Mercuriali ($p<0.0001$), Lisander ($p<0.0001$) and Meunier ($p<0.0001$) correlated, but the others did not ($p=0.099$ to 0.840) and it could not be calculated for Ward due to collinearity. The full multiple linear regression model estimates, 95% CI and p values for the predictive value of blood loss formulae calculations on incidence of transfusion can be found in Table 3.

4. Discussion

Our study retrospectively collected consecutive data on 239 patients who underwent a total of 148 primary THR and 91 primary TKR between December 2018 and April 2019 in our centre. Blood volume and/or blood loss estimates were calculated using the formulae of Moore, Nadler, Liu, Mercuriali, Bourke, Ward, Gross, Lisander and Meunier. Correlation between blood loss formulae was possible for all equations except that of Ward with those of Liu and Mercuriali due to similar values or missing data. Multiple regression models for the dependent outcomes of length of stay (in days) and the incidence of receiving a postoperative blood transfusion was possible for all blood loss formulae, except for the formula of Ward and the incidence of receiving a postoperative blood transfusion.

4.1 Blood volume

Very strong correlation between the blood volume formulae of Moore and Nadler was observed in our study. Therefore, we recommend that either of these two formulae can be utilised to estimate blood volumes in men and women. Whilst the seven individual blood loss formulae assessed in this paper state which of the two blood volume calculations are utilised in their equations, these findings suggest that either Moore's or Nadler's formulae may be used for this purpose. Whilst this study has deemed the two blood volume formulae comparable, we have not assessed their degree of accuracy. Our literature review did not yield any previous comparisons of these two blood volume equations in perioperative patients.

4.2 Blood loss

The strongest associations between the blood loss formulae were found to be between Ward and Lisander, Ward and Bourke, Mercuriali and Lisander, Meunier and Ward, Lisander and Liu, and Mercuriali and Liu. Of these correlations, the formulae of Mercuriali, Lisander and Liu all strongly associated as a triple. Yet it remains that there is no gold standard to accurately and reliably quantify blood loss[31-33]. This echoes Jaramillo *et al* in 2018 who performed a comparison of the blood loss formulae of Ward, Bourke and Gross (referenced against direct measurements of blood loss) in patients undergoing elective laparoscopic urological surgery and found poor agreement between the equations and the direct measurements, citing substantial overestimations of blood losses by the equations[34]. Similarly, in 2015, Gao *et al* compared four blood loss equations in patients who had undergone TKR and also demonstrated large differences among the calculations[35]. Nonetheless, the demand to estimate losses in the perioperative period remains important due to imprecision of direct measurement techniques which are liable to inaccuracy due to losses that are either hidden or difficult to measure, and these may account for up to 60% of the total blood losses[23, 32, 33]. The literature on this topic remains sparse and very few studies have examined and compared these blood loss formulae in detail. Of the studies that have done so, many have been limited by small sample sizes and low volumes of blood loss.

The aforementioned strongly associated formulae were generally also observed to be the formulae that most correlated with the incidence of blood transfusion: Liu, Mercuriali, Lisander, and Meunier. The exception to this was the formula of Ward which could not be calculated due to collinearity. The remaining formulae did not show significant correlation with the incidence of blood transfusion.

The only blood loss formula contributed significantly in the multiple regression models to length of stay was that of Bourke. The other formulae did not show significant correlation with length of stay. It is worth considering that the median length of stay amongst our participants was 4.4 days, and this is in a centre that will often operate on patients of higher BMI, higher ASA and with multiple co-morbidities[36]. In contrast, many Enhanced Recovery Protocols across the UK aim for a typical inpatient stay of two days for THRs and three days for TKRs. Further to this, there is also an increasing trend in developed countries to move towards day-case joint replacements in selected patients[35, 37]. Given this, it would appear that some blood loss equations are more applicable to modern practices than others: for example, Mercuriali's formula necessitates a haematocrit level of the fifth postoperative day to make its calculation, but if the majority of patients have been discharged by this stage it may be more meaningful to use alternative formulae. As surgical techniques continue to advance, the value of certain blood loss formulae may fall, and the window of those that retain utility will narrow. Interestingly, it was Mercuriali's formula that Gibon[19] recommended as the "most suitable formula for comparable studies regarding blood loss in surgery."

4.3 Limitations

This was a retrospective data analysis performed in a single centre. No controls were in place for variables such as age, BMI, surgeon grade, use of tranexamic acid or other haemostatic controls, co-morbidities including antiplatelets and anticoagulants, and postoperative venous thromboembolism prophylaxis choice. Typically, our patients have antiplatelets and anticoagulants stopped preoperatively as per national recommendations and receive

perioperative tranexamic acid. Our centre will often operate on patients of higher BMI, higher ASA and with multiple co-morbidities[36].

5. Conclusions

The need for THR and TKR will continue to increase, among a population that is ageing and suffering from more chronic diseases. Concurrently, surgical advances are trending towards reducing the typical length of stay. This combination increases the importance of being able to accurately estimate perioperative blood loss, and numerous equations exist for this purpose. There was wide variation in the degree of agreement between the different formulae we assessed. If the primary interest is the association of blood loss and length of stay, the formula of Bourke should be preferred. As this formula allows any postoperative haematocrit value to be used, it remains applicable even with reduced length of stay. If the primary interest is calculating the risk of transfusion, the formulae of Liu, Mercuriali, Lisander or Meunier should be preferred; however, the median length of stay being less than five days makes Mercuriali redundant, and Lisander requires blood tests at the end of the hospital stay, which are often not performed, therefore we recommend the formulae of Liu or Meunier.

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