The effect of spinal anesthesia on blood transfusion rate in total joint arthroplasty

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Background: Total joint arthroplasty (TJA) patients often receive allogeneic blood transfusion. The use of regional anesthesia (RA) is thought to protect against the need for blood transfusion, but many randomized trials of RA in TJA have not reached this conclusion unanimously. We sought to describe the effect of RA on allogeneic transfusion in a large retrospective TJA series. **Methods:** We examined data from all TJAs performed in Edmonton, Alberta, in the year 2000 (n = 1875) and used logistic regression modelling to determine the relation between the use of RA and allogeneic transfusion. **Results:** Twenty-eight percent of TJA subjects received an allogeneic transfusion. Transfusion was independently associated with increasing age, decreasing body mass, decreasing preoperative hemoglobin, female sex, increased comorbidity and prolonged operative time. After controlling for these factors, we found that the use of RA (in the form of spinal anesthesia) compared with general anesthesia reduced the odds ratio (OR) for transfusion to 0.729 (95% confidence interval [CI] 0.559–0.949). This represents the combination of a strong relation between RA and transfusion prevention in hip arthroplasty (OR 0.646, 95% CI 0.443–0.944) and a nonsignificant relation in knee arthroplasty (OR 0.825, 95% CI 0.564–1.208). **Conclusion:** The use of spinal anesthesia protects against allogeneic transfusion in arthroplasty of the hip but not the knee. This is consistent with what is known about the hemodynamic consequences of spinal anesthesia.

Contexte : Les patients qui subissent une arthroplastie totale (AT) reçoivent souvent une transfusion de sang allogène. On croit que l'anesthésie régionale (AR) protège contre le besoin de transfusion sanguine, mais beaucoup d'études randomisées portant sur l'AR dans les cas d'AT n'ont pas atteint cette conclusion à l'unanimité. Nous voulions décrire l'effet d'une AR sur la transfusion de sang allogène dans le contexte d'une importante série rétrospective d'AT. **Méthodes :** Nous avons analysé des données provenant de toutes les AT pratiquées à Edmonton (Alberta) en 2000 (n = 1875) et nous avons utilisé la modélisation par régression logistique pour déterminer le lien entre l'utilisation de l'AR et la transfusion de sang allogène. **Résultats :** Vingt-huit pour cent des patients qui ont subi une AT ont reçu une transfusion de sang allogène. On a établi un lien indépendant entre la transfusion et l'âge croissant, la baisse de la masse corporelle, la diminution du taux d'hémoglobine préopératoire, le sexe féminin, une comorbidité accrue et la durée prolongée de l'opération. Compte tenu de ces facteurs, nous avons constaté que le recours à l'AR (sous forme d'anesthésie rachidienne) comparativement à l'anesthésie générale a réduit le coefficient de probabilité (CP) de transfusion à 0,729 (intervalle de confiance à 95 % [IC], 0,559–0,949). Le résultat représente la combinaison d'un lien solide entre l'AR et la prévention de la transfusion dans des cas d'arthroplastie de la hanche (CP 0,646, IC à 95 %, 0,443–0,944) et d'un lien non significatif dans les cas d'arthroplastie du genou (CP 0,825, IC à 95 %, 0,564–1,208). **Conclusion :** L'anesthésie rachidienne protège contre la transfusion de sang allogène dans les cas d'arthroplastie de la hanche mais non du genou. Le résultat est conforme avec ce que l'on sait des conséquences hémodynamiques de l'anesthésie rachidienne.

Allogeneic blood transfusion is often given in total joint arthroplasty (TJA) of the hip and knee. There is widespread interest in reducing the frequency of these transfusions.[1–3]

A recent meta-analysis concluded that regional anesthesia (RA) reduces perioperative bleeding and transfu-

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sion in general.[4] However, regarding the more specific question of whether RA reduces blood loss or transfusion rates in TJA, the literature is inconclusive. We identified 26 English-language randomized controlled trials (RCTs) in which TJA patients were randomized to either RA or general anesthesia and in which blood loss or transfusion rates were stated (Table 1). In 11 trials, RA reduced bleeding or transfusion rates; in 14 trials, there was no difference, and in 1 trial, RA resulted in more bleeding than general anesthesia. In general, the largest and most recent trials have shown no difference in transfusion rates between regional and general anesthesia. Most trials compared general anesthesia with continuous epidural anesthesia. The use of newer perioperative anticoagulants in TJA has made continuous epidural anesthesia less popular because of concerns about epidural hemorrhage.[30] The RA technique used in the overwhelming majority of TJAs in our region is single-shot spinal anesthesia.

Thus we undertook this observational study to address whether RA, as administered in our region, compared with general anesthesia affects the rate of exposure to allogeneic blood in TJA.

Methods

We obtained approval from the Health Research Ethics Board of the University of Alberta. We performed a retrospective analysis of transfusion rates and the use of RA, using data collected for a previous study.[31] To create the database, we extracted the following data from the records of all patients undergoing TJA in our health region in the year 2000: age, weight, height, preoperative hemoglobin, ASA class (as a measure of medical comorbidity), anesthetic type, operation performed, surgeon's name, surgery duration, postoperative hemoglobin, length of hospital stay and transfusions given. The data set was imported into SAS for Windows Version 8. We performed univariate analysis to look for associations between receiving allogeneic red cells (in any amount) and each of the predictor variables in the database. Predictor variables were compared in the transfused and nontransfused series by Student's t test or chi-square test, as appropriate. Predictor variables that showed a statistically significant relation ($p < 0.05$) with the risk of transfusion on univariate testing were considered for inclusion in the development of a logistic regression model.

Logistic regression modelling seeks to apply a curve to the distribution of variables in a data set, fitting the curve as closely as possible to the data set. The output generated is a coefficient that is transformed into an odds ratio (OR) for each increment in that variable, resulting in the outcome modelled. In this study, for example, the model gives the OR of a woman receiving allogeneic transfusion, compared with a man, after all the other factors were taken into account. The ORs for continuous variables such as age and hemoglobin are interpreted as the increase or decrease in odds of allogeneic transfusion per increase in year of age or g/dl of hemoglobin. ORs greater than 1.0 suggest that the outcome is more likely than in the comparator group, whereas ORs of less than 1.0 indicate that the outcome is less likely. The model was constructed

Table 1

Randomized trials of regional anesthesia (RA) versus general anaesthesia in total joint arthroplasty of the lower limb reporting blood loss or blood transfusion requirements

Trial	Year	Joint studied	Regional anesthesia arm technique	*N*	Outcome
Keith[5]	1977	Hip	Epidural	27	RA better
Hole et al[6]	1980	Hip	Epidural	60	ND
Modig et al[7]	1980	Hip	Epidural	16	RA better
Thorburn et al[8]	1980	Hip	Spinal	85	RA better
Hole et al[9]	1982	Hip	Epidural	18	ND
Chin et al[10]	1982	Hip	Epidural	42	RA better
Bonnet et al[11]	1982	Hip	Epidural	19	ND
Riis et al[12]	1983	Hip	Epidural	30	ND
Modig et al[13]	1983	Hip	Epidural	30	RA better
Hole[14]	1984	Hip	Epidural	20	ND
Hedenstierna and Lofstrom[15]	1985	Both	Spinal	16	RA better
Modig et al[16]	1986	Hip	Epidural	94	RA better
Jakobsen et al[17]	1986	Hip	Epidural	30	ND
Fredin and Rosberg[18]	1986	Hip	Epidural	60	ND
Modig and Karlstrom[19]	1987	Hip	Epidural	38	RA better
Davis et al[20]	1987	Hip	Spinal	101	RA better
Donadoni et al[21]	1989	Hip	Epidural	80	ND
Neilson et al[22]	1990	Knee	Spinal	64	ND
Salo and Nissila[23]	1990	Hip	Spinal	22	RA worse
Jones et al[24]	1990	Both	Spinal	146	ND
Planes et al[25]	1991	Hip	Spinal	188	ND
Jorgensen et al[26]	1991	Knee	Epidural	39	ND
Dauphin et al[27]	1997	Hip	Epidural	37	RA better
Kohro et al[28]	1998	Knee	Epidural	22	ND
Borghi et al[29]	2002	Hip	Epidural	210	ND

Better = less bleeding or transfusion; ND = no difference; RA = regional anesthesia; worse = more bleeding or transfusion.

with the maximum likelihood function. The probability modelled was that the subject received allogeneic red cell products, in any amount, as a binary variable. Nominal variables were used in binary format. One ordinal variable was used (ASA classification), and this was dichotomized into high (ASA III–V) and low (ASA I–II) categories. Continuous variables were entered without manipulation. Indicator variables were constructed depending on whether the surgeon concerned had performed less than 25, between 25 and 50, between 50 and 100, or more than 100 TJAs in the year of study. Subjects were considered to have received RA if a combined regional/general anesthetic technique was used.

We performed forward and backward stepwise logistic regression modelling. We compared the 2 models and made additional adjustments by hand. The goal of this iterative process was to exclude as far as possible any covariates that might confound the association between anesthesia type and transfusion. Finally, we applied the derived model to subsets of hip and knee joint TJA subjects, respectively.

Results

A total of 1875 subjects underwent TJA during the study period. They are described in Table 2. A total of 517 subjects (28%) underwent transfusion with allogeneic blood. The mean amount used was 2.36 units per transfused case, resulting in a mean donor unit exposure for the whole series of 0.67 units per case. Fewer than 3% of autologous units were given intraoperatively, whereas 38% of units were given during the first 24 postoperative hours and 44% during the next 24 hours.

Anesthetic techniques were chosen by the attending anesthesiologist, and hemodynamic goals for the intraoperative period were determined individually. The RA technique used in more than 98% of cases was single-shot spinal anesthesia, administered by injection of 1.2–4 mL of 0.5% or 0.75% isobaric or hyperbaric bupivacaine, with or without fentanyl, into the lumbar cistern. Preservative-free morphine, 0.1–0.5 mg, was usually added for postoperative analgesia. Fentanyl, midazolam, propofol or some combination of these were most often used for adjunctive sedation. General anesthesia comprised propofol infusion or inhaled isoflurane, sevoflurane or desflurane with or without nitrous oxide, supplemental opioids and muscle relaxants. Both positive pressure ventilation and spontaneous breathing techniques were used. We grouped all spinal and all general anesthetic subjects together, irrespective of the specific technique used. Seventeen

Table 2

Demographic characteristics of the subject group

Characteristics	Group; mean (and standard deviation)* Transfused (*n* = 517)	Not transfused (*n* = 1358)	*p*
Age, yr	71 (12)	66 (11)	< 0.0001
Male, total %	36	46	< 0.0001
Weight, kg	77 (18)	89 (19)	< 0.0001
Height, cm	164 (11)	168 (11)	< 0.0001
ASA ≥ III, total %	45	37	0.0003
Admission hemoglobin, g/dl	131 (14)	140 (13)	< 0.0001
Hip, total %	51	48	NS
Knee, total %	49	52	NS
Revision procedure, total %	20	9	< 0.0001
Regional anesthesia used, total %	68	73	0.049
Operative time, min	98 (58)	75 (28)	< 0.0001
Autologous blood recipients, total %	0.6	3.3	NS

NS = not significant.
*Unless otherwise indicated.

Table 3

Final logistic regression model

Parameter	Comparator	All subjects (*n* = 1875) Beta	SE	*p*	ORT	95%CI	Hips only (*n* = 918) ORT	95%CI	Knees only (*n* = 957) ORT	95%CI
Intercept		3.7325	1.5273	0.0145						
Age	per yr	0.0344	0.0056	< 0.0001	1.035	1.024–1.046	1.036	1.021–1.052	1.031	1.013–1.048
Female sex	v. males	0.3489	0.1676	0.0373	1.418	1.021–1.969	1.169	0.731–1.870	1.681	1.052–2.684
Weight	per kg	–0.0304	0.00402	< 0.0001	0.970	0.962–0.978	0.972	0.961–0.983	0.965	0.954–0.976
Preoperative Hgb	per g/dl	–0.0502	0.00510	< 0.0001	0.951	0.942–0.961	0.959	0.945–0.973	0.945	0.932–0.958
Regional anesthesia	v. GA	–0.3166	0.1350	0.0190	0.729	0.559–0.949	0.646	0.443–0.944	0.825	0.564–1.208
Surgery time	per min	0.0166	0.0018	< 0.0001	1.017	1.013–1.020	1.020	1.014–1.025	1.014	1.009–1.020
Revision surgery	v. primary	0.1235	0.1972	0.5311	1.132	0.769–1.666	1.073	0.608–1.895	1.080	0.630–1.853

CI = confidence interval; GA = general anesthesia; ORT = odds ratio for transfusion; SE = standard error.

percent of subjects received combined spinal and general anesthetics; we classified these subjects as "spinals." Postoperative analgesia was given with intravenous patient-controlled analgesia with opioids.

We found positive associations between transfusion risk and increasing age, female sex, low body weight, short stature, preexisting anemia, surgical time, use of only general anesthesia, ASA class greater than II and revision surgery. There was no difference in transfusion rate between hip or knee arthroplasty. Individual surgeons performed a median of 58 arthroplasties during the year (range 1–185), but there was no correlation between surgical volume and transfusion rate ($p > 0.05$).

Surgeons and anesthetists decided when to transfuse blood on a patient-specific basis. A hemoglobin measurement was recorded less than 12 hours before the commencement of blood transfusion in 471 of the 505 subjects who underwent transfusion. The mean (and standard deviation [SD]) hemoglobin at the time of transfusion was 81 g/dl (SD 8 g/dl). Eighty percent of subjects who underwent transfusion had a pretransfusion hemoglobin between 71 and 89 g/dl. The mean (and SD) discharge hemoglobin was 103 g/dl (SD 12 g/dl) in the group who did not undergo transfusion and 100 g/dl (SD 10 g/dl) in the group who did (p = NS). There was no difference in the risk of transfusion between the 2 hospital sites at which TJA was performed ($p > 0.05$)

The final regression model is shown in Table 3. The association between RA and lowered odds of transfusion in TJA overall is statistically significant. Subset modelling of hip and knee joints separately shows that the use of RA is highly protective against transfusion in hip arthroplasty, but that it is not protective in knee arthroplasty. Revision surgery did not retain statistical significance as an independent predictor of transfusion risk, indicating that the increased risk of transfusion in revision surgery is explicable by the other factors in the model. Operative time was significantly greater in revision than in primary cases (118 v. 74 min).

Discussion

Our principal finding is that the use of RA reduces the risk of blood transfusion in hip but not knee arthroplasty. The effect size is large. Hip arthroplasty subjects receiving RA had an OR of transfusion of 0.646, compared with those receiving only general anesthesia, after we adjusted for other factors that are known to affect the transfusion rate.

This finding is biologically plausible. RA is thought to reduce bleeding in orthopedic surgery by lowering pressure on both the arterial and venous sides of the circulation. In a study of 38 subjects undergoing total hip arthroplasty, Modig and Karlstrom[32] showed that the use of epidural anesthesia, compared with general anesthesia, was associated with reductions in mean arterial pressure, pulmonary artery pressure and right atrial pressure of 13%, 21% and 44%, respectively. They also transduced the pressure wave from a peripheral vein within the surgical incision and recorded values close to 20 mm Hg during the procedure in the epidural group, compared with 30 mm Hg in those given general anesthesia with mechanical ventilation. In hip arthroplasty, the hemodynamic effect of single-shot spinal anesthetic with bupivacaine coincides with the intraoperative period, where most of the bleeding takes place. However, in knee arthroplasty, which is performed under tourniquet in our centre, most of the bleeding occurs after the period of anesthetic effect, into surgical drains. A further possibility is that RA does actually reduce blood loss in knee arthroplasty but that our analysis did not detect it. Since we analyzed almost 1000 knee procedures, we contend that, if such an effect exists, it is probably small.

Direct comparisons between the present study and previous investigations are made difficult by several factors. Most trials have compared continuous epidural anesthesia delivered via an indwelling catheter with general anesthesia. This design permits the epidural infusion to continue for 24 hours or more, in contrast to the general anesthetic, which wears off much more quickly. General anesthesia has also changed since the earlier studies were performed. Many of these used opioid/butyrophenone neuroleptanalgesia or nitrous oxide/opioid/muscle relaxant combinations in the general anesthetic arm — techniques that are rarely used today. Some studies recorded actual blood loss in the perioperative period, whereas others recorded the volume or number of blood transfusions given. In some studies, blood loss was automatically replaced by allogeneic transfusion once the loss had reached a certain volume (e.g., 500 mL); in other studies, transfusions were given according to clinical criteria or for unstated reasons. Thus transfusion rates vary across these studies from 0% to 100%.

The overall effect of autologous blood donation in our series was negligible because only 57 of our 1877 subjects underwent it.

One limitation of our study is that our data were collected retrospectively from sources not specifically intended for research. The data on blood product use, however, were drawn from the computerized blood product inventory management system and were confirmed by manually reviewing the patients' records. We did not specifically record the use of intraoperative cell salvage and reinfusion, because this technique is rarely used in our region.

Statistical modelling methods cannot correct for confounding factors that are not recorded in the data set. The most relevant example of this shortcoming in our current study relates to the use of medications that affect blood coagulation, such as ASA

and warfarin. In our region, the clinical practice is for these medications to be discontinued prior to surgery and for coagulation parameters to be documented to have returned to normal (in the case of warfarin) before proceeding with the case, but we did not record whether this had in fact been done. A possible source of bias is that, in subjects with known or suspected imperfect coagulation, RA was avoided. However, preliminary data from a separate investigation (currently being conducted in our region) indicate that this may not be a significant concern: of 197 TJA subjects in that series, 31 were taking ASA when surgery was scheduled, but 24 of them went on to receive spinal anesthesia. An additional 5 were taking warfarin at scheduling, but 4 received spinal anesthesia.

It may seem surprising to those who perform the procedure that revision surgery does not appear as an independent predictor of transfusion risk in the final model. This is because revision procedures took much longer than did the primary cases, and the model was better able to capture the difference in blood transfusion rates by using the duration of surgery, which is a continuous variable expressed in minutes, rather than revision status, which is a binary variable.

We divided subjects into 2 groups by severity of comorbid illness, using the ASA grade. The ability of this simple clinical score to discriminate well between those at high and those at low risk of perioperative complications has been clearly documented.[33]

The decision to transfuse in any given subject was made by the individual clinician, but there was a high degree of uniformity in transfusion practice nonetheless: Each of the 28 surgeons in our study individually initiated postoperative transfusion at a mean hemoglobin in the range 76–86 g/dl (the mean for the entire series was 81 g/dl).

An RCT can answer clinical practice questions and would be the best way of determining the overall effect of RA on outcomes such as mortality and major morbidity, because the randomization process would divide known and unknown confounding factors evenly between the groups. The value of an observational study such as this in an area that has already been the subject of many RCTs may therefore be questioned. When all relevant trials are examined together, it is impossible to definitively answer whether RA protects against transfusion in TJA or not. Although a meta-analysis of the existing trials might overcome some of the limitations of these individual RCTs, this is not currently available. Our analysis, based on a large unselected consecutive series of nonexperimental cases, may better reflect the clinical reality.

RA in the form of single-shot spinal anesthesia is strongly protective against allogeneic transfusion in total hip arthroplasty.

Competing interests: None declared.

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