

Predeposited Autologous Blood Transfusion in Single-Anesthetic Bilateral Total Knee Arthroplasty with Modern Blood Conservation Strategy

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Background: This study was performed to examine the hypothesis that the rate of allogeneic blood transfusion in patients who did not predeposit an autologous blood transfusion before single-anesthetic bilateral total knee arthroplasty (TKA) would be noninferior to that in patients who did predeposit blood.

Methods: We assessed the number of allogeneic transfusions required in 338 patients undergoing single-anesthetic bilateral TKA with a preoperative hemoglobin level of ≥ 11.0 g/dL. All TKAs were performed by a single surgeon according to the same operative and postoperative protocol. All patients received a combination of intravenous and intra-articular tranexamic acid. Neither a pneumatic tourniquet nor a drain was used. The difference in the risk of allogeneic transfusion between patients without and with autologous blood predeposit was compared with a noninferiority margin of 10 percentage points.

Results: Allogeneic transfusion was required in 1 (0.5%) of 194 patients who predeposited autologous blood and 3 (2.1%) of 144 patients who did not predeposit blood. The difference in risk was -1.6 percentage points (95% confidence interval, -4.1 to 1.0 percentage points); the confidence interval did not include the noninferiority margin and included zero.

Conclusions: In single-anesthetic bilateral TKA, allogeneic transfusion requirements in patients who did not predeposit autologous blood were noninferior to those in patients who predeposited blood.

Level of Evidence: Therapeutic Level III. See Instructions for Authors for a complete description of levels of evidence.

Avoiding allogeneic blood transfusion in the perioperative period is crucial in patients undergoing total knee arthroplasty (TKA) because allogeneic transfusion is associated with the occurrence of adverse events, including periprosthetic infection, graft-versus-host disease, acute lung injury, hemolytic transfusion reaction, and deep vein thrombosis (DVT)^{1,2}. Although the majority of patients undergoing single-anesthetic bilateral TKA required allogeneic transfusion in the early 2000s³, recent advances in blood management have markedly reduced the number of patients requiring such transfusions⁴⁻⁷.

Predeposit of autologous blood, in which patients donate their own blood before surgery so that it is available for an intraoperative transfusion, is a technique used to decrease the number of patients requiring allogeneic transfusion⁸. The advantages of predeposited autologous transfusions include eliminating the risks of viral transmission and immunologically mediated hemolytic, febrile, or allergic reactions⁸. Pre-

viously, single-anesthetic bilateral TKA was considered to have good indications for predepositing blood because it had been regarded as an elective surgery with the prospect of massive blood loss³. However, the clinical impact of predepositing blood on patients undergoing single-anesthetic bilateral TKA remains to be determined in the setting of modern blood-conservation strategies. Although predepositing blood has several advantages, it also has disadvantages including cost and the risk of bacterial contamination⁸. Therefore, it is important to determine whether strategies without predepositing blood for an autologous transfusion are worse than those with predepositing in patients undergoing single-anesthetic bilateral TKA with modern blood-conservation strategies.

This study was performed to compare the rate of allogeneic transfusion required in the perioperative period between patients undergoing single-anesthetic bilateral TKA with and without predepositing blood. We hypothesized that

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJSOA/A459>).

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forgoing the use of predeposited blood would be noninferior to depositing an autologous blood transfusion before surgery with respect to the rate of postoperative allogeneic transfusion.

Materials and Methods

This study was performed following institutional review board approval. We retrospectively identified patients undergoing single-anesthetic bilateral TKA between January 2017 and December 2021 performed by a single surgeon (S.T.) in the Adult Reconstruction and Joint Replacement Department at 2 different hospitals (Hokusuikai Kinen Hospital, Mito, Japan, and Nekoyama Miyao Hospital, Niigata, Japan).

The inclusion criterion for this study was a preoperative hemoglobin level of ≥ 11.0 g/dL, because different allogeneic transfusion criteria were used in patients with preoperative hemoglobin levels above and below the cutoff value of 11.0 g/dL at the 2 hospitals where the study was performed^{9,10}. For patients with a preoperative hemoglobin level of ≥ 11.0 g/dL, we planned to perform allogeneic transfusion if they had a postoperative hemoglobin level of < 7.0 g/dL or if they had a postoperative hemoglobin level of < 10.0 g/dL and symptoms related to anemia. For patients with a preoperative hemoglobin level of < 11.0 g/dL, anemia was treated more actively because anemic patients would have a higher rate of complications after TKA¹¹. The exclusion criterion was treatment without combined intravenous and intra-articular tranexamic acid (TXA) administration.

The surgical technique and blood-conservation strategy were similar at the 2 hospitals in which this study was performed^{9,10}. All single-anesthetic bilateral TKAs were performed under the same session of anesthesia; the operation on the second side began following completion of wound closure on the first side. A pneumatic tourniquet was not used in any patients, and no drainage system was placed. Intraoperatively, patients received 1 g of TXA intravenously plus 1 g of intra-articular TXA in each knee. An additional 1-g dose of TXA was administered intravenously 6 hours after the initial administration. We did not administer TXA to patients having a known allergic reaction to TXA or severe renal dysfunction. Neither intraoperative nor postoperative blood salvage was used. We applied a bilateral intermittent foot-pump system for the prevention of DVT before the patient began walking.

The decision whether to predeposit an autologous blood transfusion was made by the patient after being informed by the surgeon of both the advantages and disadvantages of autologous transfusion in TKA, with 1 exception: we encouraged all patients to donate autologous blood before surgery at 1 of the institutions between February 2017 and January 2019 according to the protocol of a randomized controlled study performed in that time period¹⁰. Patients predeposited 800 or 400 mL of blood. For patients who predeposited 800 mL of autologous blood, we routinely returned half (400 mL) of the predeposit to the patient on the day of the single-anesthetic bilateral TKA and returned the remaining 400 mL on the day

after the TKA. For patients who predeposited 400 mL of blood, we returned all 400 mL on the day of the single-anesthetic bilateral TKA.

The primary outcome was the proportion of patients undergoing single-anesthetic bilateral TKA who required allogeneic transfusion during the perioperative period. Secondary outcomes were the hemoglobin level measured at 1, 3, and 7 days after TKA and perioperative complications, with special reference to bleeding-related and thrombotic events according to the Lassen criteria¹². We routinely screened patients for the presence of DVT using ultrasonography at 1 day after surgery. Additionally, patients were screened for DVT with use of the Wells score at 7 days after surgery¹³, and patients with a score of ≥ 3 were again tested using ultrasonography.

Statistical Analysis

This retrospective comparative noninferiority study was designed to test the hypothesis that patients undergoing single-anesthetic bilateral TKA without use of a predeposited autologous transfusion would have a perioperative allogeneic transfusion rate that was noninferior to that of patients with a predeposited autologous transfusion. Prior to data collection, a sample size of 117 participants per group was calculated based on a noninferiority margin of 10 percentage points, 4% of patients with a predeposit requiring allogeneic transfusion, 6% of patients without a predeposit requiring allogeneic transfusion, a 1-sided alpha level of 0.025, and 80% power. We determined the noninferiority margin and the expected allogeneic transfusion rate for each group based on a consensus among a panel of researchers who reviewed studies assessing the allogeneic transfusion rate during the perioperative period in patients undergoing single-anesthetic bilateral TKA^{3,5-7,14}. Two previous studies including patients who underwent single-anesthetic bilateral TKA had differences in allogeneic transfusion rates between patients without and with predeposited autologous blood transfusion of 39%³ and 31% to 71%¹⁴. However, we considered that applying those rates of allogeneic transfusion to the calculation of the noninferiority margin was inappropriate because the blood-conservation strategies used in those studies did not include TXA administration^{3,14}. Recent studies including a routine TXA administration regimen had rates of allogeneic transfusion ranging from 0% to 29% even in patients without a predeposited autologous blood transfusion³⁻⁵. We organized a focus group discussion to define the appropriate estimate for the noninferiority margin in our study, and concluded that a 10-percentage-point difference in the rate of postoperative allogeneic transfusion was the largest clinically acceptable difference between patients forgoing predeposit of an autologous transfusion and those depositing autologous blood before surgery.

As the primary outcome, we estimated the difference in risk between the groups with and without predeposited blood. We determined that noninferiority of a strategy without a predeposit would be shown if the lower boundary of the 95% confidence interval was greater than -10 percentage points. The significance of the difference between the allogeneic transfusion rates was also assessed using the Fisher exact test. Secondary

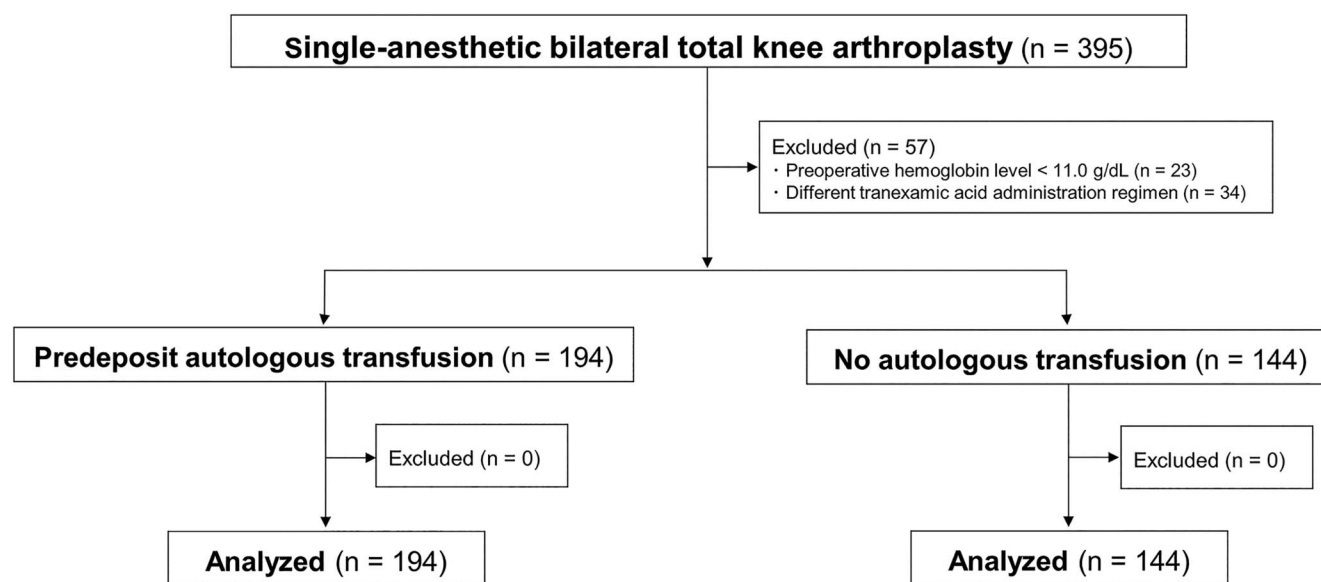


Fig. 1
Patient flow diagram.

outcomes and baseline characteristics were compared using the Student t test for continuous measures and the Fisher exact test for dichotomous data. Tests were 2-sided, and the level of significance was set at $p < 0.05$.

Source of Funding

No external funding was received for this investigation.

Results

Of 395 patients undergoing single-anesthetic bilateral TKA during the study period, 338 were included in the analysis (Fig. 1). Table I summarizes the demographic characteristics of the patients.

Allogeneic transfusion was required for 1 (0.5%) of 194 patients who predeposited an autologous transfusion and 3 (2.1%) of 144 patients who did not predeposit it. The difference in risk between the 2 groups was -1.6 percentage points (95% confidence interval, -4.1 to 1.0 percentage points). This indicated that the no-predeposit group was noninferior because the confidence interval did not include the predefined inferiority margin of -10 percentage points (Fig. 2). The Fisher exact test showed that there was no significant difference between the 2 groups ($p = 0.32$).

The postoperative hemoglobin level was significantly higher in the predeposit group than in the no-predeposit group at 1, 3, and 7 days after TKA (Table II).

TABLE I Patient Demographic and Baseline Clinical Characteristics

	Predeposited Autologous Transfusion (N = 194)*	No Predeposited Autologous Transfusion (N = 144)*	P Value
Age (yr)	75 ± 6	76 ± 7	0.33†
Sex, female/male	158/36	119/25	0.89‡
Height (cm)	151 ± 8	151 ± 7	0.90†
Weight (kg)	61.9 ± 10.2	62.2 ± 11.3	0.75†
Body mass index (kg/m ²)	27.0 ± 3.7	27.1 ± 4.2	0.80†
Diagnosis, osteoarthritis/rheumatoid arthritis	191/3	142/2	>0.99‡
Receiving chronic antithrombotic therapy, yes/no	28/166	16/128	0.42‡
History of diabetes mellitus, yes/no	31/163	31/113	0.20‡
Preoperative hemoglobin (g/dL)	13.2 ± 1.1	13.2 ± 1.2	0.71†
Operative time for 1 knee (min)	83 ± 13	82 ± 11	0.52†
Intraoperative total blood loss (mL)	145 ± 77	146 ± 85	0.92†

*The values are given as the mean ± standard deviation or as the count. †Student t test. ‡Fisher exact test.

The Risk Difference of the Primary Outcome

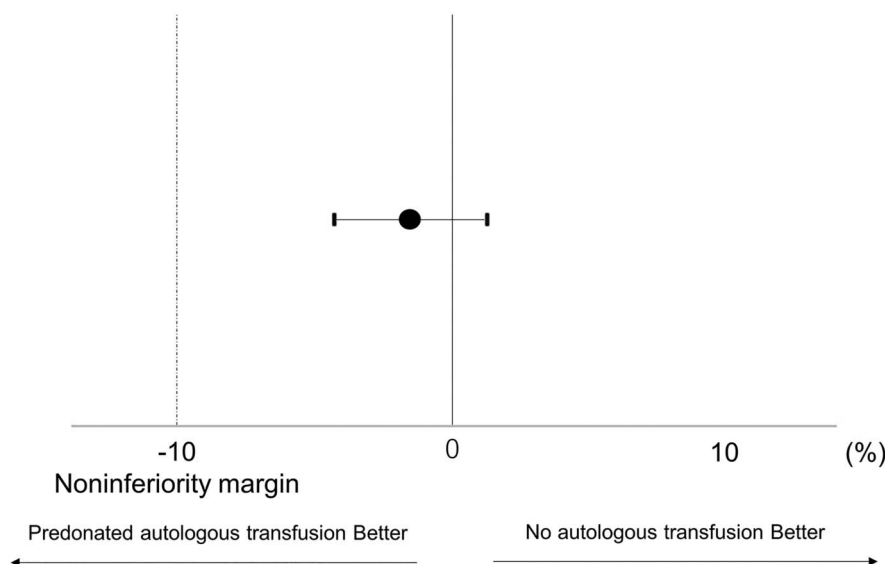


Fig. 2 Interpretation of the rate of allogeneic transfusion by comparison of the confidence interval with the noninferiority margin. Given that the confidence interval does not cross the noninferiority margin and includes zero, the interpretation is that the no-predeposit strategy was noninferior to the strategy of predepositing an autologous transfusion. The error bars indicate the 2-sided 95% confidence interval. The dashed vertical line indicates the noninferiority margin.

DVTs were detected in 6 (3.1%) of 194 patients in the predeposit group and 2 (1.4%) of 144 patients in the no-predeposit group. No pulmonary embolism was detected in either group. One (0.5%) of 194 patients in the predeposit group experienced an acute myocardial infarction. The rate of thrombotic events did not differ between the 2 groups ($p = 0.31$). No bleeding-related events other than postoperative anemia occurred in any of the patients.

Discussion

This study evaluated patients undergoing single-anesthetic bilateral TKA with combined intravenous and intra-articular TXA administration, without use of a pneumatic tourniquet or placement of a drain. The rate of requiring an allogeneic transfusion in patients who did not predeposit an autologous blood transfusion was not worse than the rate in those who made a predeposit, based on a 10-percentage-point noninferiority margin.

To our knowledge, this is the first study to examine the effectiveness of predeposited autologous blood in patients undergoing single-anesthetic bilateral TKA in the setting of modern blood-conservation strategies. Predepositing blood was previously reported to significantly reduce the rate of allogeneic transfusion in patients undergoing single-anesthetic bilateral TKA^{3,14}. In a retrospective single-center study, 84% of patients who did not donate their own blood before single-anesthetic bilateral TKA between 1997 and 2001 required an allogeneic transfusion, compared with 45% of patients who predeposited blood³. In another retrospective single-center study of patients undergoing single-anesthetic bilateral TKA between 1995 and 2000, 98% of patients with no predeposited blood received an allogeneic transfusion, compared with 67% of the patients with 1 unit of autologous blood, 51% of patients with 2 units, 29% of patients with 3 units, and 27% of patients with 4 units¹⁴. It is notable that these rates of allogeneic transfusion were unacceptably high in both

TABLE II Postoperative Hemoglobin Levels*

	Predeposited Autologous Transfusion (N = 194)†	No Predeposited Autologous Transfusion (N = 144)†	Difference (95% CI)	P Value‡
POD 1	12.1 ± 1.2	11.5 ± 1.3	0.6 (0.3 to 0.9)	<0.001
POD 3	11.4 ± 1.3	10.1 ± 1.2	1.3 (1.0 to 1.5)	<0.001
POD 7	10.8 ± 1.3	9.7 ± 1.2	1.1 (0.8 to 1.4)	<0.001

*CI = confidence interval, and POD = postoperative day. †The values are given as the mean ± standard deviation, in mg/dL. ‡Student t test.

studies compared with recent studies despite using predeposit autologous transfusions^{3,14}. Recent studies in which perioperative routine TXA use has become common have not had such high rates of allogeneic blood transfusion⁵⁻⁷. A retrospective multi-center study had an allogeneic transfusion rate of 29% in single-anesthetic bilateral TKA performed from 2013 to 2016 and showed that both the use of a drain and the use of a pneumatic tourniquet were independent risk factors for transfusion⁵. In a retrospective single-center study in 475 patients undergoing single-anesthetic bilateral TKA from 2016 to 2019 with routine TXA administration, 22% of patients without a predeposit required an allogeneic transfusion⁶. Another retrospective single-center study had an allogeneic blood transfusion rate of 0% in 125 patients undergoing single-anesthetic bilateral TKA from 2015 to 2021 who routinely received TXA and had a preoperative hemoglobin level of >11.0 g/dL⁷. The results of our retrospective single-surgeon study add information about the clinical impact of predepositing autologous blood in patients undergoing single-anesthetic bilateral TKA in the setting of modern blood-conservation strategies.

The postoperative hemoglobin level was slightly but significantly higher in the patients in the present study who received a predeposited autologous transfusion. The mean differences in the level of hemoglobin were 0.6, 1.3, and 1.1 g/dL on postoperative days 1, 3, and 7, respectively. These results suggest that predepositing blood may be an option for select patients at higher risk for requiring allogeneic transfusion than the patients included in this study, such as those with a preoperative hemoglobin level of <11.0 g/dL, to avoid the need for allogeneic transfusion. Because

the blood donation itself can be a risk for patients with severe anemia, few such patients would be suitable for depositing blood prior to single-anesthetic bilateral TKA with modern blood-conservation strategies. We speculate that predepositing blood may be indicated for patients with a hemoglobin level between 10.0 and 11.0 g/dL.

This study had several limitations, the most important of which was its retrospective nature. In addition, all TKAs were performed by a single surgeon. Although this would reduce the degree of variation in blood loss due to the surgical technique, it could also reduce the generalizability of the study.

In conclusion, this retrospective comparative study showed that the requirement for allogeneic transfusion in patients who had not predeposited an autologous transfusion was noninferior to that in patients who had predeposited blood. ■

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