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A Decline in Overutilization of Transfusion after Total Knee Arthroplasty Using Pharmacological Agents for Patient Blood Management in South Korea: An Analysis Based on the Korean National Health Insurance Claims Database from 2008 to 2019

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Background: This study aimed to evaluate the annual trends of transfusion rates and utilization of blood management agents in total knee arthroplasty (TKA) based on the operation type and to analyze the risk factors of transfusion after TKA.

Methods: Using the Korean National Insurance claims database of 797,106 primary and revision TKAs between January 2008 and October 2019, data on the patients' characteristics, comorbidities, utilization of transfusion, and blood management agents were collected. The patients were categorized into three groups based on the operation type: primary, revision, and simultaneous bilateral TKA. The transfusion rate and utilization of blood management agents (intraoperative tranexamic acid [TXA] and preoperative iron supplements) were compared, and the risk factors for transfusion were evaluated.

Results: After excluding the inaccurate data, 730,554 arthroplasties (636,292 primary, 10,540 revision, and 41,861 simultaneous bilateral TKAs) were identified. The transfusion rates of primary, revision, and simultaneous bilateral TKAs in 2019 were 64.0%, 67.7%, and 68.9%, respectively, which were significantly decreased compared with 83.2%, 88.0%, and 92.5% in 2008, respectively ($p < 0.001$). Conversely, the utilization of intraoperative TXA and preoperative iron supplements was significantly increased from 4.6% and 13.8%, respectively, in 2008 to 52.4% and 27.0%, respectively, in 2019 ($p < 0.001$). The utilization of intraoperative TXA and preoperative iron supplements significantly lowered the risk of transfusion after TKA (odds ratio [OR], 0.20; $p < 0.001$ and OR, 0.71; $p < 0.001$).

Conclusions: The transfusion rate after TKA decreased gradually from 83.5% to 64.5% between 2008 and 2019 in South Korea corresponding with the increased utilization of blood management agents. Therefore, consistent attention to patient blood management should be emphasized to reduce the transfusion rate after TKA.

Keywords: *Total knee arthroplasty, Blood transfusion, Patient blood management, Tranexamic acid, Iron supplements*

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Total knee arthroplasty (TKA) is an effective procedure to treat pain and dysfunction in patients with osteoarthritis of the knee joints.[1] Over recent decades, the incidence of TKA has increased worldwide. The advances in surgical techniques and improvements in perioperative and postoperative management have increased the survival rate and lowered the complications.[2-4] TKA is associated with substantial blood loss due to the innate nature of the surgical procedure, and an allogenic blood transfusion may be required intra- or postoperatively.[5,6] Blood transfusion after TKA increases the risk of adverse events, including superficial infection, deep infection, pulmonary embolism, and venous thrombosis.[7-9] Therefore, efforts to reduce transfusion after TKA have been emphasized and various bleeding management strategies have been introduced. These include the treatment of preoperative anemia, updating the optimal transfusion thresholds, utilization of newer pharmacologic agents, and designing devices to control bleeding.[10] In recent decades, the nationwide data of the US and Germany have shown a gradual decline in the transfusion rates after TKA.[11-13]

Among the various bleeding management strategies, the pharmacological approaches include iron supplements and erythropoietin (EPO) to control preoperative anemia and the intraoperative administration of antifibrinolytic agents, such as tranexamic acid (TXA), to reduce bleeding.[14] The efficacy of these blood management agents is well-documented.[15-17]

Although the effect of TXA administration on blood loss after TKA has been previously investigated,[15,18,19] it is unknown how often and how many centers use these agents. To date, there has been no large-scale study based on a national cohort to evaluate the annual trends of the utilization of blood management agents and to assess whether these blood management agents actually affect the decline in the transfusion rate after TKA. Therefore, this study aimed to evaluate the annual trends of transfusion rates and the utilization of blood management agents in patients with TKA by operation type in South Korea. Additionally, considering the characteristics of patients, comorbidities, and utilization of blood management agents, risk factors associated with transfusion after TKA were identified. The hypothesis was that the increased utilization of blood management agents would lead to a declining transfusion rate after TKA in Korea.

METHODS

Ethical Committee Approval

This study was reviewed and approved by the Institutional Review Board of Korea University Anam Hospital (No. 2019AN0447). Informed consent was waived because the research used anonymized data.

Database

This nationwide retrospective cohort study used data from the Korean National Health Insurance claims database. In Korea, healthcare services are covered by the National Health Insurance, which is compulsory for all Korean citizens. Medical claims are reviewed and evaluated by a public institution, the Health Insurance Review and Assessment Service (HIRA). All data are stored in the HIRA database, which primarily comprises two parts: the diagnosis code based on the International Classification of Diseases, 10th Revision (ICD-10), and the procedure code based on the Electronic Data Interchange (EDI) code. The database contains all the claims data for both inpatients and outpatients, including demographic information, diagnosis, procedure, prescribed drug information, and hospital type. HIRA provides data to researchers following approval from the official review committee.

Study Population

The claims data of patients who underwent TKAs between January 2008 and October 2019 were extracted from the database using the procedure codes (EDI): N2072 and 2077 for primary TKA, and N3712, N3717, N3722, and N3727 for revision TKA. Based on the operation types, the cases were categorized into three groups: primary TKA, revisional TKA, and simultaneous bilateral TKA. The simultaneous bilateral TKA was defined as a case in which two TKA codes were entered on the same day regardless of primary or revision TKA.

Inaccurate and unclearly defined data were excluded. These included (1) patients identified with a revision TKA code prior to a primary TKA code, (2) patients claiming multiple primary or revision codes (more than three times) on the same day, and (3) patients claiming multiple hospitalizations on the same day (Fig. 1).

Patient Characteristics and Comorbidities

Patient demographics including age, sex, hospital type, and comorbidities including atrial fibrillation, liver cirrhosis, pulmonary embolism, deep vein thrombosis, angina, end-stage renal disease, chronic kidney disease, ischemic stroke, intracranial hemorrhage, hypertension, diabetes mellitus, dyslipidemia, heart failure, peripheral arterial disease, chronic obstructive pulmonary disease, cancer, and metastatic cancer were evaluated. Comorbidities within one year prior to TKA were included and were identified

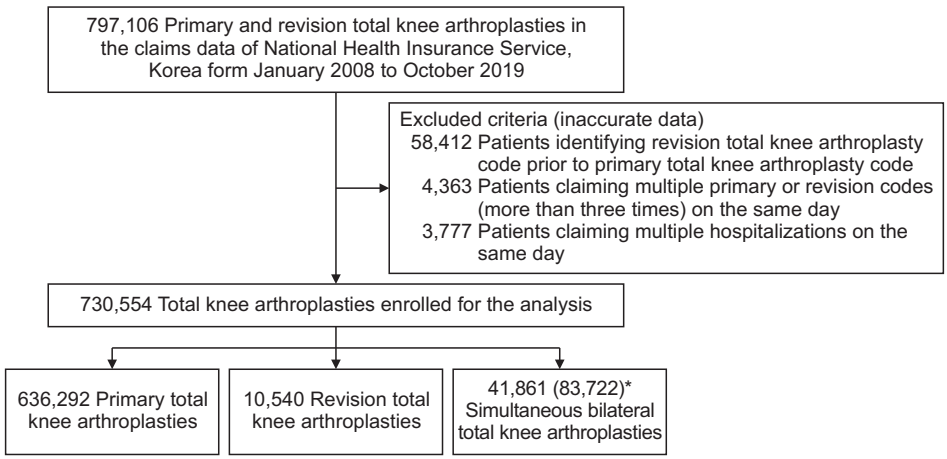

Fig. 1. Flowchart depicting data selection and categorization of the study. *Numbers in parentheses represent the number of total knee arthroplasties.

as ICD-10 and annotated using specific drug prescription codes, as described in a previous retrospective cohort study using the Korean National Health Insurance claims database.[20] A detailed definition of comorbidities is presented in Supplementary Table 1.

Blood Management Agents and Blood Transfusion

Preoperative use of anti-anemic agents, such as iron supplements and EPO, and the intraoperative administration of TXA, were assessed using the database. Utilization of preoperative iron supplements was defined as the presence of an anatomical therapeutic chemical (ATC) code for an iron supplement within 1 month prior to TKA. Likewise, the administration of EPO was identified by the presence of an ATC code for EPO within the same period. TXA administration on the day of surgery was identified by the presence of an ATC code for TXA on the same day as the procedural code for TKA. Transfusion was defined as the identification of claims codes for red blood cells (RBCs), fresh frozen platelets (FFP), and platelets (PLT) during the index hospitalization period: X2021, X2022, X2031, X2032, X2091, X2092, X2131, X2132, and X2512 for RBCs; X2041, X2042, X2051, and X2052 for FFP; X2081, X2082, X2121, X2122, X2501, X2511, X2512, and X2513 for PLT; and other codes for cryoprecipitate, white blood cells, plasma, and other components.

Statistical Analysis

Patient characteristics, comorbidities, utilization of blood management agents, and transfusion rates were compared among the three groups. The categorical variables were compared using Pearson's chi-square test, while one-way analysis of variance was employed for continuous variables. The annual trends of blood transfusion and the utilization of blood management agents were analyzed by estimating the relative risk using a log-linear Poisson regression analysis. Subgroup analyses were performed to evaluate the difference in the blood transfusion rate and utilization of blood management according to the hospital type. Multivariable logistic regression analysis with the enter method was used to identify the risk factors associated with blood transfusion after TKA. Adjusted odds ratios (OR) of risk factors were calculated using multivariable logistic regression after adjusting for age, sex, hospital type, comorbidities, operation types, and utilization of blood management agents and were presented with a 95% confidence interval (CI). All analyses were performed using SAS Enterprise software version 6.1 (SAS Institute, Cary, NC, USA). Statistical significance was set at $p < 0.05$.

RESULTS

A total of 797,106 arthroplasties were identified in the database from January 2008 to October 2019 in Korea. After excluding inaccurate data, 730,554 arthroplasties were enrolled. Among these, 636,292 primary TKAs, 10,540 revision TKAs, and 83,722 arthroplasties in 41,861 cases of simultaneous bilateral TKAs were identified. The patient characteristics and comorbidities by operation type are presented in Table 1.

The overall transfusion rate after TKA decreased from 83.5% in 2008 to 64.5% in 2019. The annual relative risk of transfusion after TKA was 0.98 (95% CI, 0.97–0.98; $p < 0.001$), indicating a significant gradual decline during the study period. Specifically, the transfusion rates of primary, revision, and simultaneous bilateral TKAs in 2019 were significantly lower than those in 2008 (64.0%, 67.7%, and 68.9% vs. 83.2%, 88.0%, and 92.5%, respectively, $p < 0.001$) (Table 2, Fig. 2). The mean transfusion rate after primary TKA during the study period was significantly

Table 1. Baseline Characteristics of Patients with TKA by the Operation Type in Korea from 2008 to 2019

Characteristics	Total (n = 688,693)	Primary TKA (n = 636,292)	Revision TKA (n = 10,540)	Simultaneous bilateral TKA (n = 41,861)	*p*-value
Age (yr)	70.6 ± 7.1	70.5 ± 7.1	70.6 ± 9.1	71.5 ± 7.2	< 0.001
Age distribution					-
< 60 yr	45,113 (6.6)	42,051 (6.6)	944 (9.0)	2,118 (5.1)	
60–69 yr	240,634 (34.9)	224,446 (35.3)	3,211 (30.5)	12,977 (31.0)	
70–79 yr	338,867 (49.2)	311,827 (49.0)	5,082 (48.2)	21,958 (52.5)	
≥ 80 yr	64,079 (9.3)	57,968 (9.1)	1,303 (12.4)	4,808 (11.5)	
Sex					< 0.001
Male	94,940 (13.8)	87,282 (13.7)	2,184 (20.7)	5,474 (13.1)	
Female	593,753 (86.2)	549,010 (86.3)	8,356 (79.3)	36,387 (86.9)	
Hospital type					< 0.001
Clinic	21,908 (3.2)	21,040 (3.3)	193 (1.8)	675 (1.61)	
Hospital, general hospital	581,925 (84.5)	538,490 (84.6)	7,142 (67.8)	36,293 (86.7)	
Tertiary hospital	84,860 (12.3)	76,762 (12.1)	3,205 (30.4)	4,893 (11.7)	
Comorbidity					
Atrial fibrillation	16,807 (2.4)	14,990 (2.4)	494 (4.7)	1,323 (3.2)	< 0.001
Liver cirrhosis	5,328 (0.8)	4,759 (0.8)	200 (1.9)	369 (0.9)	< 0.001
Pulmonary embolism	3,749 (0.5)	3,375 (0.5)	146 (1.4)	228 (0.5)	< 0.001
Deep vein thrombosis	15,029 (2.2)	13,834 (2.2)	384 (3.6)	811 (1.9)	< 0.001
Angina	14,415 (2.1)	13,409 (2.1)	334 (3.2)	672 (1.6)	< 0.001
End stage renal disease	592 (0.1)	494 (0.1)	47 (0.5)	51 (0.1)	< 0.001
Chronic kidney disease	12,067 (1.8)	10,601 (1.7)	519 (4.9)	947 (2.3)	< 0.001
Ischemic stroke	55,603 (8.1)	50,968 (8.0)	1,241 (11.8)	3,394 (8.1)	< 0.001
Intracranial hemorrhage	1,326 (0.2)	1,210 (0.2)	40 (0.4)	76 (0.2)	< 0.001
Hypertension	451,257 (65.5)	415,426 (65.3)	7,462 (70.8)	28,369 (67.8)	< 0.001
Diabetes mellitus	165,510 (24.0)	151,477 (23.8)	3,358 (31.9)	10,675 (25.5)	< 0.001
Dyslipidemia	462,321 (67.1)	426,773 (67.1)	7,110 (67.5)	28,438 (67.9)	0.001
Heart failure	46,278 (6.7)	41,807 (6.6)	1,236 (11.7)	3,235 (7.7)	< 0.001
Peripheral artery disease	168,290 (24.4)	154,907 (24.4)	3,186 (30.2)	10,197 (24.4)	< 0.001
Chronic obstructive pulmonary disease	138,521 (20.1)	126,711 (19.9)	3,193 (30.3)	8,617 (20.6)	< 0.001
Cancer	36,245 (5.3)	32,843 (5.2)	953 (9.0)	2,449 (5.9)	< 0.001
Metastatic cancer	1,846 (0.3)	1,627 (0.3)	87 (0.8)	132 (0.3)	< 0.001
Antianemic and antifibrinolytic agents					
Iron supplements	148,811 (21.6)	135,294 (21.3)	2,592 (24.6)	10,925 (26.1)	< 0.001
Tranexamic acid	151,330 (22.0)	136,806 (21.5)	2,188 (20.8)	12,336 (29.5)	< 0.001
Erythropoietin	2,877 (0.4)	2,671 (0.4)	80 (0.8)	126 (0.3)	< 0.001

Values are presented as mean ± standard deviation or number (%).
TKA: total knee arthroplasty.

Table 2. Annual Trends of Transfusion Rates of Patients with TKA by the Operation Type in Korea between 2008 and 2019

Variable	Transfusion	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*	*p*-value†
Total		42,817	48,222	52,892	53,406	55,851	54,797	54,898	59,777	67,874	68,190	69,745	60,224	
	Yes	35,734 (83.5)	40,542 (84.1)	44,409 (84.0)	45,851 (85.9)	48,074 (86.1)	46,935 (85.7)	45,853 (83.5)	48,192 (80.6)	51,596 (76.2)	48,559 (71.2)	47,419 (70.0)	38,871 (64.5)	< 0.001
Operation type														
Primary TKA		41,127	46,637	51,057	51,194	52,757	50,939	50,389	54,458	61,806	60,999	62,091	52,838	
	Yes	34,202 (83.2)	39,146 (83.9)	42,833 (83.9)	43,972 (85.9)	45,366 (86.0)	43,519 (85.4)	41,903 (83.2)	43,683 (80.2)	46,647 (75.5)	43,035 (70.6)	41,822 (67.4)	33,791 (64.0)	< 0.001
Revision TKA		702	635	736	867	924	878	870	1,002	969	1,006	1,038	913	
	Yes	618 (88.0)	561 (88.3)	663 (90.1)	757 (87.3)	795 (86.0)	755 (86.0)	745 (85.6)	808 (80.6)	755 (77.9)	737 (73.3)	744 (71.7)	618 (67.7)	< 0.001
Simultaneous bilateral TKA		988	950	1,099	1,345	2,170	2,980	3,639	4,317	5,099	6,185	6,616	6,473	
	Yes	914 (92.5)	835 (87.9)	913 (83.1)	1,122 (83.4)	1,913 (88.2)	2,661 (89.3)	3,205 (88.1)	3,701 (85.7)	4,194 (82.3)	4,787 (77.4)	4,853 (73.4)	4,462 (68.9)	< 0.001

Values are presented as number (%).
TKA: total knee arthroplasty.
*The data were collected from January to October 2019. †*p*-value by Poisson regression for linear trend.

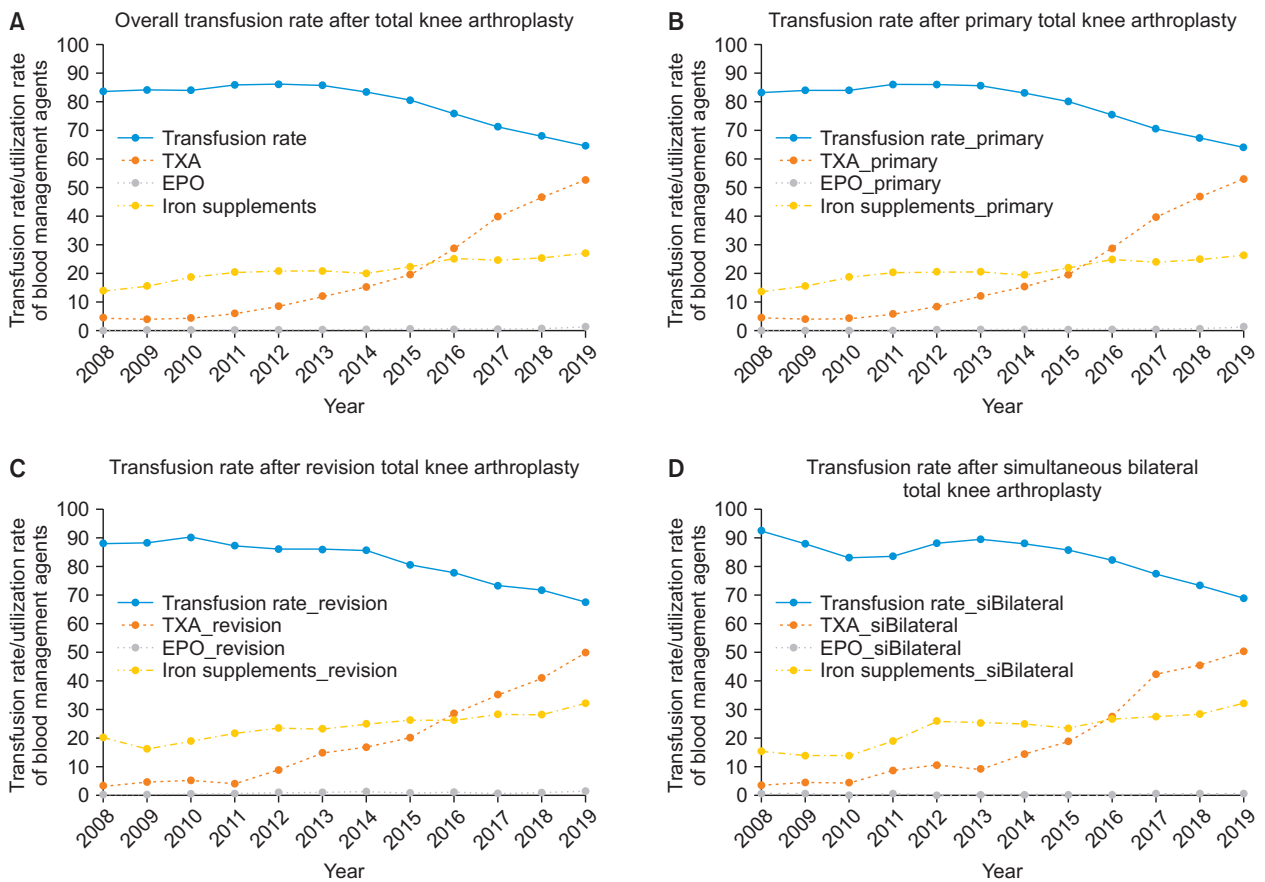

Fig. 2. Transfusion rate and utilization of blood management agents after total knee arthroplasty from 2008 to 2019 in South Korea. The overall transfusion rate (A), as well as the transfusion rates after primary total knee arthroplasty (B), revision total knee arthroplasty (C), and simultaneous bilateral total knee arthroplasty (D), are presented. TXA: tranexamic acid, EPO: erythropoietin, si: simultaneous.

lower than that after revision and simultaneous bilateral TKAs ($p < 0.001$). The mean transfusion rate during the same period between revision and simultaneous bilateral TKAs was significantly different ($p < 0.02$). However, the difference was minimal at 1%. Among all transfusions, the most common feature was RBC alone (97.5%), followed by the combination of RBC and PLT (1.2%).

In contrast, the utilization of intraoperative TXA and preoperative iron supplements in all cases significantly increased from 4.6% and 13.8%, respectively, in 2008 to 52.4% and 27.0%, respectively, in 2019 ($p < 0.001$) (Table 3, Fig. 2). Following subgroup analysis according to the hospital type, intraoperative TXA and preoperative iron supplements were used more frequently in tertiary hospitals. Despite higher comorbidities in the tertiary hospitals, the overall transfusion rate was significantly lower in the tertiary hospitals (59.1%) as compared to that in the clinics (79.9%) and in hospitals and general hospitals (81.5%) ($p < 0.001$) (Table 4, Supplementary Table 2).

The multivariable logistic regression analysis revealed that the utilization of intraoperative TXA and preoperative iron supplements significantly lowered the transfusion risk after TKA (OR, 0.21; $p < 0.001$ and OR, 0.71; $p < 0.001$). Among the comorbidities, liver disease, deep

Table 3. Annual Trends of the Use of Antianemic and Antifibrinolytic Agents Combined with TKA by the Operation Type in Korea between 2008 and 2019

Variable	Agent		2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019*	*p*-value†
Total			42,817	48,222	52,892	53,406	55,851	54,797	54,898	59,777	67,874	68,190	69,745	60,224	
	Iron supplements	Yes	5,910 (13.8)	7,511 (15.6)	9,868 (18.7)	10,810 (20.2)	11,597 (20.8)	11,429 (20.9)	10,949 (19.9)	13,217 (22.1)	17,020 (25.1)	16,646 (24.4)	17,613 (25.3)	16,241 (27.0)	< 0.001
	Erythropoietin	Yes	36 (0.1)	52 (0.1)	51 (0.1)	53 (0.1)	154 (0.3)	237 (0.4)	202 (0.4)	358 (0.6)	321 (0.5)	288 (0.4)	456 (0.7)	669 (1.1)	< 0.001
	Tranexamic acid	Yes	1,949 (4.6)	1,941 (4.0)	2,280 (4.3)	3,155 (5.9)	4,758 (8.5)	6,548 (11.9)	8,380 (15.3)	11,662 (19.5)	19,483 (28.7)	27,154 (39.8)	32,441 (46.5)	31,579 (52.4)	< 0.001
Operation type															
Primary TKA			41,127	46,637	51,057	51,194	52,757	50,939	50,389	54,458	61,806	60,999	62,091	52,838	
	Iron supplements	Yes	5,616 (13.7)	7,278 (15.6)	9,577 (18.8)	10,368 (20.3)	10,821 (20.5)	10,471 (20.6)	9,829 (19.5)	11,942 (21.9)	15,406 (24.9)	14,668 (24.0)	15,448 (24.9)	13,870 (26.3)	< 0.001
	Erythropoietin	Yes	30 (0.1)	48 (0.1)	48 (0.1)	45 (0.1)	146 (0.3)	224 (0.4)	184 (0.4)	342 (0.6)	297 (0.5)	259 (0.4)	418 (0.7)	630 (1.2)	< 0.001
	Tranexamic acid	Yes	1,893 (4.6)	1,870 (4.0)	2,193 (4.3)	3,004 (5.9)	4,452 (8.4)	6,139 (12.1)	7,712 (15.3)	10,656 (19.6)	17,808 (28.8)	24,183 (39.6)	29,019 (46.7)	27,877 (52.8)	< 0.001
Revision TKA			702	635	736	867	924	878	870	1,002	969	1,006	1,038	913	
	Iron supplements	Yes	142 (20.2)	102 (16.1)	139 (18.9)	188 (21.7)	216 (23.4)	203 (23.1)	217 (24.9)	263 (26.2)	254 (26.2)	285 (28.3)	292 (28.1)	291 (31.9)	< 0.001
	Erythropoietin	Yes	1 (0.1)	1 (0.2)	3 (0.4)	5 (0.6)	8 (0.9)	9 (1.0)	11 (1.3)	7 (0.7)	10 (1.0)	4 (0.4)	9 (0.9)	12 (1.3)	0.009
	Tranexamic acid	Yes	22 (3.1)	28 (4.4)	38 (5.2)	34 (3.9)	80 (8.7)	131 (14.9)	145 (16.7)	201 (20.1)	277 (28.6)	354 (35.2)	424 (40.8)	454 (49.7)	< 0.001
Simultaneous bilateral TKA			988	950	1,099	1,345	2,170	2,980	3,639	4,317	5,099	6,185	6,616	6,473	
	Iron supplements	Yes	152 (15.4)	131 (13.8)	152 (13.8)	254 (18.9)	560 (25.8)	755 (25.3)	903 (24.8)	1,012 (23.4)	1,360 (26.7)	1,693 (27.4)	1,873 (28.3)	2,080 (32.1)	< 0.001
	Erythropoietin	Yes	5 (0.5)	3 (0.3)	0	3 (0.2)	0	4 (0.1)	7 (0.2)	9 (0.2)	14 (0.3)	25 (0.4)	29 (0.4)	27 (0.4)	0.001
	Tranexamic acid	Yes	34 (3.4)	43 (4.5)	49 (4.5)	117 (8.7)	226 (10.4)	278 (9.3)	523 (14.4)	805 (18.6)	1,398 (27.4)	2,617 (42.3)	2,998 (45.3)	3,248 (50.2)	< 0.001

Values are presented as number (%).
TKA: total knee arthroplasty.
*The data were collected from January to October 2019. †*p*-value by Poisson regression for linear trend.

Table 4. Comparison of Transfusion Rates and Use of Antianemic and Antifibrinolytic Agents during TKA by the Hospital Type

Variable	Total				Primary TKA				Revision TKA				Simultaneous bilateral TKA			
	Clinic	Hospital, general hospital	Tertiary hospital	*p*-value	Clinic	Hospital, General hospital	Tertiary hospital	*p*-value	Clinic	Hospital, General hospital	Tertiary hospital	*p*-value	Clinic	Hospital, General hospital	Tertiary hospital	*p*-value
Cases	21,908	581,925	84,860		21,040	538,490	76,762		193	7,142	3,205		675	36,293	4,893	
Transfusion	17,515 (79.9)	474,378 (81.5)	50,142 (59.1)	< 0.001	17,000 (80.8)	438,221 (81.4)	44,698 (58.2)	< 0.001	156 (80.8)	6,081 (85.1)	2,319 (72.4)	< 0.001	359 (53.2)	30,076 (82.9)	3,125 (63.9)	< 0.001
Agents																
Iron supplements	1,953 (8.9)	127,741 (22.0)	19,117 (22.5)	< 0.001	1,722 (8.2)	116,511 (21.6)	17,061 (22.2)	< 0.001	10 (5.2)	1,847 (25.9)	735 (22.9)	< 0.001	221 (32.7)	9,383 (25.9)	1,321 (27.0)	< 0.001
Erythropoietin	4 (0.0)	2,522 (0.4)	351 (0.4)	< 0.001	4	2,370 (0.4)	297 (0.4)	< 0.001	0	46 (0.6)	34 (1.1)	< 0.001	0	106 (0.3)	20 (0.4)	0.0368
Tranexamic acid	3,137 (14.3)	14.3 (20.4)	118,603 (34.9)	< 0.001	2,792 (13.3)	107,618 (20.0)	26,396 (34.4)	< 0.001	8 (4.2)	1,200 (16.8)	980 (30.6)	< 0.001	337 (49.9)	9,785 (27.0)	2,214 (45.3)	< 0.001

Values are presented as number (%).
TKA: total knee arthroplasty.

vein thrombosis, angina, end-stage renal disease, chronic kidney disease, ischemic stroke, hypertension, diabetes mellitus, peripheral arterial disease, chronic obstructive pulmonary disease, and cancer were significantly correlated with blood transfusion after TKA. Moreover, older age, female sex, hospital type (clinic, hospital, and general hospital), and operation type (revision and simultaneous bilateral TKAs) were identified as significant risk factors for transfusion after TKA. The detailed ORs are presented in Table 5.

DISCUSSION

The primary findings of the present study were that the transfusion rate after TKAs gradually decreased, and conversely, the utilization of blood management agents increased during the study period regardless of operation types in Korea. The use of blood management agents, such as preoperative anti-anemic agents and TXA, significantly lowered the transfusion risk after TKA. These agents were more frequently used in tertiary hospitals where the transfusion rate after TKA was also lower compared to other types of hospitals.

Similar to the present study, recent nationwide cohort studies showed a gradual decline in the transfusion rate after TKA.[11,12] In a large retrospective cohort study that included 1,013,024 patients in the United States, the overall incidence of transfusion after TKA declined from 18.1% in 2010 to 3.2% in 2015.[12] A similar trend was reported in a nationwide investigation of 736,061 cases of total hip and knee arthroplasty in Germany;[11] wherein the transfusion rates after primary TKA and revision TKA decreased from 11.5% and 19.7%, respectively, in 2011 to 4.5% and 12.1%, respectively, in 2017. However, the present study showed that the transfusion rate after TKA in Korea was substantially higher than that in these countries. Even considering that the differences in race and healthcare system may contribute to the difference in transfusion rate after TKA, this indicates that transfusion after TKA is overutilized in Korea. Similar findings were observed in a study evaluating the transfusion rate after total hip arthroplasty (THR) from 2007 to 2015 in Korea.[21] Although the transfusion rate after primary THR decreased from 78.7% in 2007 to 71.5% in 2015, the absolute transfusion rates were higher than those reported from other countries.[12]

These results showing overutilization of transfusion might originate from the different insurance systems and the relative lack of effort in patient blood management in TKA, rather than surgical technique-related issues; these have significant implications for orthopedic surgeons and

Table 5. Risk Factors Analysis for Transfusion after TKA

Variable	Unadjusted odds ratio	95% CI	*p*-value	Adjusted odds ratio	95% CI	*p*-value
Operation type			< 0.001			< 0.001
Primary TKA	Reference			Reference		
Revision TKA	1.18	1.12–1.24	< 0.001	1.50	1.43–1.59	< 0.001
Simultaneous bilateral TKA	1.10	1.08–1.13	< 0.001	1.30	1.27–1.34	< 0.001
Age			< 0.001			< 0.001
< 60 yr	Reference			Reference		
60–69 yr	1.00	0.98–1.03	0.90	1.05	1.02–1.08	0.001
70–79 yr	1.20	1.18–1.23	< 0.001	1.31	1.27–1.34	< 0.001
≥ 80 yr	1.37	1.33–1.41	< 0.001	1.67	1.62–1.73	< 0.001
Sex						
Male	Reference			Reference		
Female	1.43	1.41–1.46	< 0.001	1.50	1.47–1.52	< 0.001
Hospital type			< 0.001			
Clinic	2.76	2.66–2.86	< 0.001	2.11	2..4–2.20	< 0.001
Hospital, general hospital	3.05	3.01–3.10	< 0.001	2.71	2.67–2.76	< 0.001
Tertiary hospital	Reference			Reference		
Comorbidity						
Atrial fibrillation	0.80	0.70–0.83	< 0.001	0.98	0.94–1.02	0.24
Liver cirrhosis	1.08	1.01–1.15	0.03	1.42	1.32–1.53	< 0.001
Pulmonary embolism	0.91	0.84–0.98	0.02	1.05	0.97–1.14	0.23
Deep vein thrombosis	0.70	0.68–0.72	< 0.001	0.77	0.74–0.79	< 0.001
Angina	0.94	0.93–0.96	< 0.001	0.95	0.94–0.97	< 0.001
End stage renal disease	0.89	0.73–1.07	0.22	1.55	1.24–1.94	0.001
Chronic kidney disease	1.01	0.96–1.05	0.83	1.35	1.28–1.42	< 0.001
Ischemic stroke	1.13	1.11–1.16	< 0.001	1.04	1.01–1.06	0.001
Intracranial hemorrhage	0.96	0.84–1.10	0.56	1.01	0.88–1.16	0.89
Hypertension	1.13	1.12–1.14	< 0.001	1.08	1.07–1.10	< 0.001
Diabetes mellitus	1.04	1.04–1.06	< 0.001	1.03	1.02–1.05	0.001
Dyslipidemia	0.90	0.89–0.92	< 0.001	1.01	1.00–1.03	0.08
Heart failure	1.01	0.99–1.04	0.35	1.02	0.99–1.05	0.13
Peripheral artery disease	1.26	1.24–1.27	< 0.001	1.17	1.16–1.19	< 0.001
Chronic obstructive pulmonary disease	0.94	0.93–0.96	< 0.001	0.94	0.93–0.96	< 0.001
Cancer	0.78	0.76–0.80	< 0.001	0.91	0.89–0.94	< 0.001
Metastatic cancer	0.85	0.77–0.95	0.001	1.11	0.98–1.24	0.10
Antianemic and antifibrinolytic agents						
Iron supplements	0.69	0.68–0.70	< 0.001	0.71	0.70–0.73	< 0.001
Tranexamic acid	0.20	0.20–0.20	< 0.001	0.21	0.20–0.21	< 0.001
Erythropoietin	0.43	0.40–0.46	< 0.001	0.79	0.72–0.86	< 0.001

TKA: total knee arthroplasty, CI: confidence interval.

for health policymakers in Korea. The overutilization of transfusion may be related to several correctable factors. First, blood management strategies to reduce transfusion after TKA might not have been actively implemented in many centers in Korea, especially in small-sized hospitals. As shown in the present study, the transfusion rate decreased concurrently with the increased utilization of blood management agents. The efficacy of TXA and iron supplements on transfusion after TKA has been reported in numerous studies, suggesting the importance of patient blood management strategies to reduce the transfusion rate.[14-16] Practically, the blood management agents were more utilized in the tertiary hospital; hence, the transfusion rate in these hospitals was lower than that in other hospital types, despite that the patients in the tertiary hospital had multiple comorbidities than others. Second, the relatively sufficient blood supply and low cost of blood products might have contributed to the overutilization of transfusion in Korea. The report of global need and availability of blood products in 2019 showed that Korea is one of the five countries with over 5000 red cell products available for transfusion per 100,000 population.[22] Moreover, the ratio of blood product demand versus supply was < 1, indicating relatively sufficient availability of blood products in the country. Additionally, the cost of RBC transfusion in Korea is approximately $100, which is lower than $200 in the United States.[21,23] Third, the blood transfusion guidelines have not been well observed in Korea, especially by orthopedic surgeons. Although efforts have been made to establish blood transfusion guidelines updated by the Korean Society of Blood Transfusion, a survey in 2016 reported that only 13.9% of the orthopedic surgeons were aware of these updates.[24] The threshold for transfusion has moved toward more restrictive values over time. Recently, the American Association of Blood Banks (AABB) suggested hemoglobin levels of 7 and 8 g/dL for hemodynamically stable and unstable patients, respectively, as the thresholds for RBC transfusion.[25] Corresponding with the 2016 AABB recommendations, the Korean guidelines were updated with the restricted threshold.[26] However, in Korea, it could be inferred that transfusion after TKA was still utilized on a routine basis or according to the previous liberal threshold, under a hemoglobin level of 10 g/dL.[25]

The present study has several limitations. First, this is a retrospective cohort study based on claims codes. Therefore, inherent potential bias could exist due to the retrospective design, errors in claims, and data acquisition. However, previous studies have validated the accuracy of the HIRA coding system to be 70% to 90%, indicating an acceptable level of accuracy for analyses.[27,28] Moreover, the exclusion of inaccurate data could lead to selection bias. However, the exclusion portion was 7.9% of the entire cohort, which was not a considerable portion. Second, the claims data-based analysis could not identify wasted blood products; after being prepared, blood products might have been left unused and then discarded. Thus, the transfusion rate after TKA might have been overestimated. Third, the method of administration and dosage of iron supplements and TXA were not evaluated in the present study. Iron supplements can be administered orally and intravenously at various timings and durations. These different methods and dosages could show different efficacies in the correction of hemoglobin levels. A recent systematic review showed that intravenous administration was more effective than oral administration.[29] However, the optimal timing and dose of iron supplements were not determined. Although TXA can be administered orally, intravenously, or topically (intra-articular),[18,19,30] the recommendations for dosage and route of administration remain controversial. The recent guidelines of the American Association of Hip and Knee Surgeons in 2018 stated that TXA showed an equivalent effect in reducing blood loss regardless of the administration route and that its superiority was not determined.[30] Lastly, among the bilateral TKAs, the intervals between two TKAs were not identified, except for simultaneous bilateral TKAs. Therefore, the staged bilateral TKA was included in the primary TKA group, and the transfusion rate might have been overestimated.

Despite these limitations, the present large-scale retrospective cohort study based on nationwide data clearly showed that utilization of blood management agents, such as the preoperative iron supplements and the intraoperative administration of TXA in TKA, practically decreased the transfusion rates after TKA. Among the factors affecting the transfusion rate, unlike the patients' comorbidities, preoperative anemia and perioperative bleeding were correctable factors by patient blood management. Therefore, our findings suggest the need for interest in patient blood management, including the use of blood management agents, to reduce the transfusion rate after TKA among orthopedic surgeons and healthcare policymakers.

In conclusion, the transfusion rate after TKA gradually decreased from 83.5% to 64.5% between 2008 and 2019 in Korea corresponding with the increased use of blood management agents. Therefore, consistent attention to patient blood management should be emphasized to reduce the transfusion rate after TKA.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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SUPPLEMENTARY MATERIAL

Supplementary material is available in the electronic version of this paper at the CiOS website, www.ecios.org

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