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Original article

Blood transfusion and venous thromboembolism trends and risk factors in primary and aseptic revision total hip and knee arthroplasties: A nationwide investigation of 736,061 cases

Elke Jeschke[a,*], Mustafa Citak[b], Andreas M. Halder[c], Karl-Dieter Heller[d], Fritz U. Niethard[e], Peter Schräder[f], Josef Zacher[f], Hanna Leicht[g], Jürgen Malzahn[h], Christian Günster[a], Thorsten Gehrke[b]

[a] Research Institute of the Local Health Care Funds, Rosenthaler Straße 31, 10178 Berlin, Germany
[b] Department of Orthopaedic Surgery, Helios ENDO-Klinik Hamburg, Holstenstraße 2, 22767 Hamburg, Germany
[c] Department of Orthopaedic Surgery, Sana Kliniken Sommerfeld, Waldhausstraße 44, 16766 Sommerfeld/Kremmen, Germany
[d] Department of Orthopaedic Surgery, Herzogin Elisabeth Hospital, Leipziger Straße 24, 38124 Braunschweig, Germany
[e] German Society of Orthopedics and Orthopedic Surgery, Straße des 17. Juni 106-108, 10623 Berlin, Germany
[f] Department of Orthopaedic Surgery, Kreisklinik Jugenheim, Hauptstraße 30, 64342 Seeheim-Jugenheim, Germany
[g] Helios Kliniken GmbH, Friedrichstrasse 136, 10117 Berlin, Germany
[h] Federal Association of the Local Health Care Funds, Rosenthaler Straße 31, 10178 Berlin, Germany

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ABSTRACT

Background: Over the last years, new transfusion guidelines and pharmaceuticals have been introduced in primary and revision total hip and knee arthroplasty (P-THA, P-TKA, R-THA, R-TKA). In the US, a substantial decrease in transfusions has been observed in recent years. Little data exists on the subject in Europe. In this context we aimed to analyze: (1) Is there also a significant decrease in blood transfusion for these procedures in Germany? (2) Which patient and hospital related factors are associated with the risk of blood transfusion? (3) Is there a trend in complications, especially venous thromboembolism and stroke events that can be linked to tranexamic acid use?
Hypothesis: There is a significant trend in decreasing blood transfusions in hip and knee arthroplasty.
Methods: Using nationwide healthcare insurance data for inpatient hospital treatment, 736,061 cases treated between January 2011 and December 2017 were included (318,997 P-THAs, 43,780 R-THAs, 338,641 P-TKAs, 34,643 R-TKAs). Multivariable logistic regression was used to model the odds of transfusion as a function of the year of surgery. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated.
Results: In each cohort the odds of transfusion decreased over time (2017 vs. 2011 (reference): P-THA: OR 0.42 (95%CI: 0.39–0.45), P-TKA: OR 0.41 (95%CI: 0.37–0.46), R-THA: OR 0.52 (95%CI: 0.47–0.58), R-TKA: OR 0.53 (95%CI: 0.46–0.61). Patient-related risk factors for blood transfusion included older age, female gender, lower Body Mass Index, comorbidities such as renal failure, cardiac arrhythmia, congestive heart failure, valvular disease, coagulopathy, depression, and antithrombotic medication prior to surgery. Venous thromboembolism or stroke events did not increase over the study period.
Discussion: The incidence of blood transfusions in primary and revision TKA and THA decreased over the study period. This may be due to new transfusion guidelines and the introduction of novel pharmaceuticals such as tranexamic acid. A further improved patient blood management and a focus on vulnerable patient groups might lead to a further future reduction of transfusions, especially in R-THA.
Level of Evidence: III; comparative observational study.

1. Introduction

Total joint arthroplasty can be associated with substantial blood loss. It carries the risk of allogeneic blood transfusion requirement during the perioperative period [1]. Previous studies have

* Corresponding author.
E-mail address: elke.jeschke@wido.bv.aok.de (E. Jeschke).

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shown that allogeneic blood transfusion can be associated with serious complications such as surgical site and periprosthetic joint infection, postoperative deep vein thrombosis, and postoperative morbidity and mortality [2–6]. In orthopaedic operations, risk factors for transfusion include older age, female sex, comorbidities such as coagulopathy, higher American Society of Anesthesiologists (ASA) grade, lower level of preoperative hemoglobin, and increased postoperative drainage volume [7–9]. The blood transfusion rate can be lowered by means of an improved patient blood management and the administration of tranexamic acid (TXA) [10].

The reported transfusion rate varied from 3.5% to 18.5% in total knee arthroplasty and from 5.4% to 26.2% in total hip arthroplasty for hospitals in the United States from 2009 to 2011 [11]. Over the past decade, the incidence of intraoperative blood transfusion for these procedures has decreased [12,13]. A large retrospective study of more than 1,013,024 patients in the United States reported that the overall incidence of transfusion declined from 2010 to 2015 for both primary and revision total hip and knee arthroplasty [14]. Apart from these findings, there is little robust data regarding current blood transfusion trends worldwide, particularly from Europe.

In this context, we investigated a large European nationwide database to determine: 1) Is there also a significant decrease in blood transfusion for primary THA (P-THA), primary TKA (P-TKA), revision THA (R-THA) and revision TKA (R-TKA) in Germany? 2) Which patient and hospital related factors are associated with the risk of blood transfusion? 3) Is there a trend in complications, especially venous thromboembolism (VTE) and stroke events that can be linked to TXA use? We hypothesized there was a significant trend in decreasing blood transfusions for P-THA, P-TKA, R-THA and R-TKA.

2. Materials and Methods

2.1. Database Characteristics

For this observational study, we used anonymized nationwide administrative claims data of the Allgemeine Ortskrankenkasse (AOK). The AOK provides health care insurance for approximately 30 percent of the German population and is the largest nationwide provider of statutory health care insurance in Germany. We evaluated billing data for inpatient treatment, including diagnoses, procedures and length of stay, as well as patient data, including age, gender, insurance status (i.e. continued/terminated AOK membership) and survival. Diagnoses were coded according to the 10th revision of the International Classification of Diseases (ICD-10). Procedures were documented using the German version of the International Classification of Procedures in Medicine (ICPM), the "Operationen- und Prozedurenschlüssel" (OPS).

We included patients aged 20 years or older, which received P-THA, P-TKA, R-THA or R-TKA between January 2011 and December 2017 (for details, see supplement Table S1).

Patients undergoing P-THA or P-TKA were included only if they also had a primary diagnosis of osteoarthritis, osteonecrosis or rheumatoid arthritis. Cases were excluded if they had a diagnosis of tumour or post-traumatic arthritis of the joint, or if they underwent a simultaneous hip and knee arthroplasty or a bilateral one-stage procedure. Patients undergoing R-THA or R-TKA were excluded from the study if they had a septic condition, fracture, congenital deformity or tumour, or if they underwent simultaneous hip and knee arthroplasty (for details, see supplement Table S1).

2.2. Outcome measures

The primary outcome was an allogenic or autologous transfusion procedure (OPS 8-800.X) from the day of the initial surgery until discharge from hospital. A subgroup analysis was conducted for patients who received six or more units. We also evaluated cases with a diagnosis of venous thromboembolism (deep vein thrombosis: ICD-10 I80.1, I80.2, I80.3, I82.2; pulmonary embolism: I26) or stroke (I63, I64) within 90 days of index surgery.

2.3. Statistical analysis

Descriptive statistics including medians, inter-quartile ranges (IQRs), and proportions were used to describe the study sample. Baseline patient characteristics were compared using Pearson's Chi^2 test for categorical variables and the Mann-Whitney U test for continuous measures. The Cochrane-Armitage test was used to evaluate the significance of time trends within cohorts.

Multivariable logistic regression was used to model the odds of transfusion as a function of the year of surgery. Adjusted odds ratios (OR) and 95% confidence intervals (CI) were calculated. Patient age, gender, Body Mass Index (BMI), implantation vs. revision of a component, previous joint replacement (revision of the same joint within 2 years of index surgery), antithrombotic medication prior to surgery and comorbidities were included as independent patient-related variables. Comorbidities were defined using the Elixhauser conditions [15]. These include 31 acute and chronic diseases which we implemented using the coding algorithm by Quan et al. [16]. In addition, osteoporosis and dementia were included as independent variables. All comorbidities were entered as separate dichotomous variables. Patient age was entered as a continuous variable.

Additionally, hospital size, university hospital status and hospital volume of the index procedure (P-THA, P-TKA, R-THA, and R-TKA) were introduced in the regression models as hospital characteristics. Hospital size was defined as small (< 300), medium (300–499) or large (> 500) based on number of beds. Hospital volume was categorized into quintiles. Patients were assigned to volume categories based on the number of procedures performed at their respective hospitals during the year of surgery. Furthermore, the length of stay was included as an additional predictor in the regression models. All analyses were performed using STATA 16.0 (StataCorp LP, College Station, Texas). A p-value < 0.05 was considered statistically significant.

3. Results

3.1. Study population and outcome

We included a total of 736,061 cases in the analysis: 318,997 P-THAs, 43,780 R-THAs, 338,641 P-TKAs, and 34,643 R-TKAs. A flowchart detailing patient selection is shown in Fig. 1. Tables 1 and 2 provide a detailed overview of patient characteristics undergoing primary or revision total hip and knee arthroplasty. The patient comorbidity burden was lower for knee cohorts, especially for P-TKA. Transfusion rates were 48,350/318,997 (15.2%), 16,545/43,780 (37.8%), 28,094/338,641 (8.3%), and 5,726/34,643 (16.5%) for P-THA, R-THA, P-TKA and R-TKA patients, respectively.

The proportions of patients aged more than 70 years, female patients, antithrombotic medication prior to surgery and most comorbidities were higher among patients with blood transfusions in all cohorts. Regarding hospital characteristics there was a higher proportion of transfusions in large hospitals, hospitals with low volume of the respective procedure and university hospitals in all cohorts (Fig. 2).

3.2. Trends

During the study period, the occurrence of blood transfusion after surgery declined significantly. Comparing transfusion rates in 2017 to 2011, the rate after P-THA had dropped by 52.8%, and the

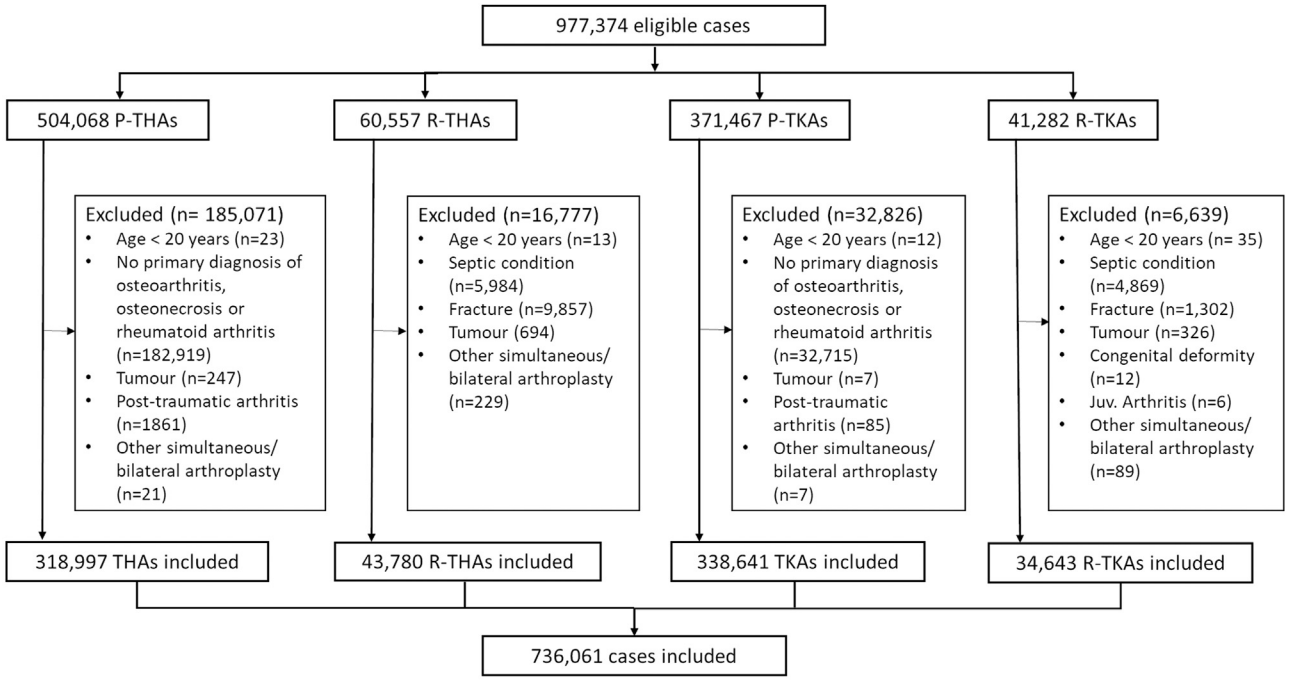

Fig. 1. Flowchart of patient selection (P-THA, primary total hip arthroplasties; P-TKA, primary total knee arthroplasties; R-THA, revision total hip arthroplasties; R-TKA, revision total knee arthroplasties).

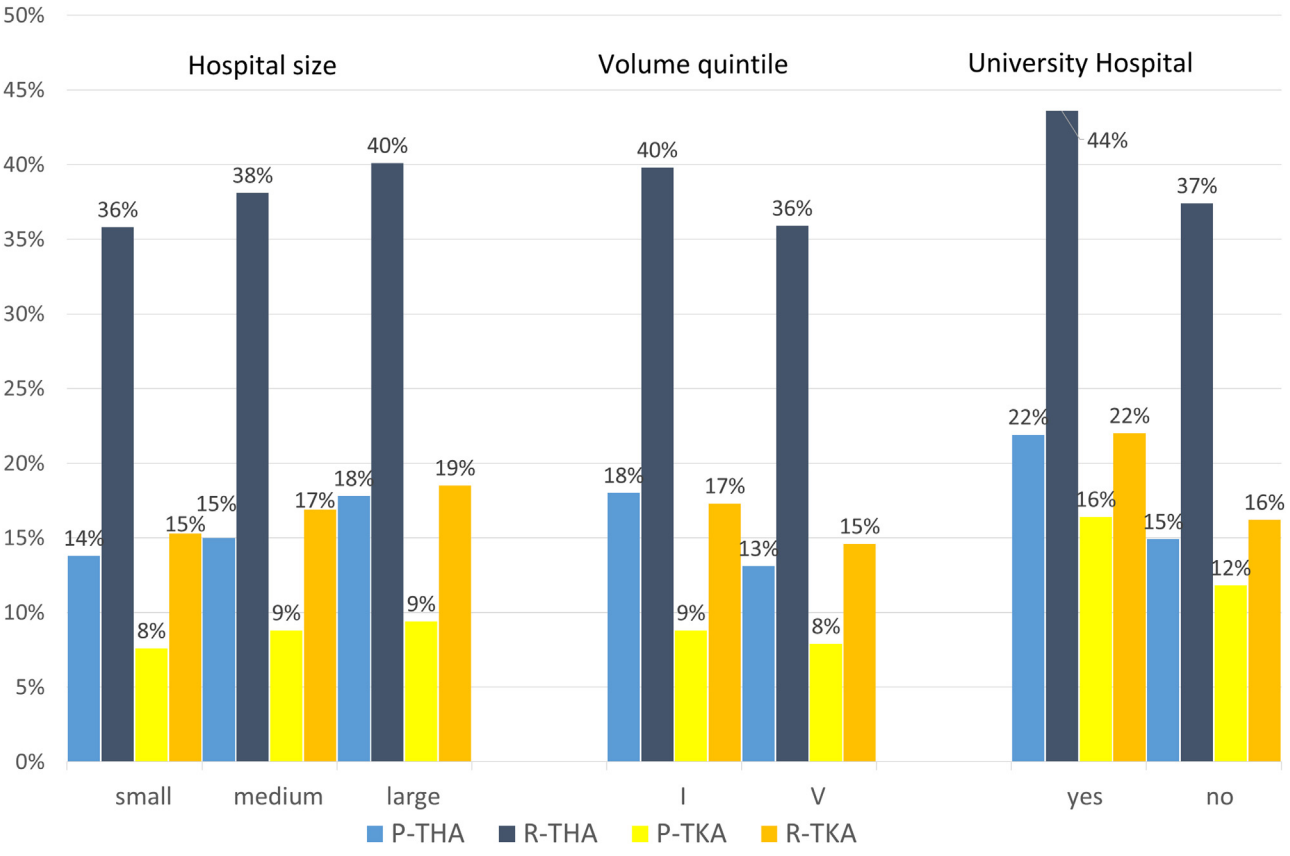

Fig. 2. Transfusions rate by hospital characteristics (P-THA, primary total hip arthroplasties; P-TKA, primary total knee arthroplasties; R-THA, revision total hip arthroplasties; R-TKA, revision total knee arthroplasties).

Table 1
Demographic characteristics of patients undergoing primary and revision total hip arthroplasty by transfusion.

Demographics	P-THA			R-THA		
	Not Transfused	Transfused	*p*-value	Not Transfused	Transfused	*p*-value
Total, *n*	270,647	48,350		27,235	16,545	
Length of stay (days), median (IQR)	11 (9–13)	13 (11–17)	< 0.001	13 (11–22)	19 (13–32)	< 0.001
Age (y), median (IQR)	70 (61–77)	76 (71–81)	< 0.001	73 (63–79)	77 (71–82)	< 0.001
Age (y), *n* (%)			< 0.001			< 0.001
< 50	9,397 (5.9)	473 (2.1)		1,503 (5.5)	307 (1.9)	
50–59	44,147 (16.3)	2,851 (5.9)		3,470 (12.7)	977 (5.9)	
60–69	68,062 (25.2)	6,630 (13.7)		5,418 (19.9)	2,237 (13.5)	
70–79	104,768 (38.7)	21,890 (45.3)		11,112 (40.8)	6,976 (42.2)	
80–89	36,310 (13.4)	15,198 (31.4)		5,352 (19.7)	5,505 (33.3)	
≥ 90	846 (0.3)	742 (1.5)		380 (1.4)	543 (3.3)	
Female gender, *n* (%)	156,336 (57.8)	35,738 (73.9)	< 0.001	15,583 (57.2)	11,098 (67.1)	< 0.001
BMI (kg/m^2), *n* (%)			< 0.001			< 0.001
< 30	223,659 (82.6)	41,673 (86.2)		22,863 (83.9)	14,217 (85.9)	
30-34	24,776 (9.2)	3,604 (7.5)		2,313 (8.5)	1,196 (7.2)	
35-39	13,973 (5.2)	1,932 (4.0)		1,310 (4.8)	672 (4.1)	
≥ 40	8,239 (3.0)	1,141 (2.4)		749 (2.8)	460 (2.8)	
Prosthesis implanted, *n* (%)			< 0.001			
THA	250,621 (92.6)	47,080 (97.4)				
Hip Resurfacing	1,340 (0.5)	45 (0.1)				
Short-Stem THA	18,686 (6.9)	1,225 (2.5)				
Component revised, *n* (%)						< 0.001
Liner/head				6,813 (25.0)	2,308 (13.9)	
Cup				9,805 (36.0)	5,784 (35.0)	
Femur				4,665 (17.1)	2,332 (14.1)	
Femur and cup				5,952 (21.9)	6,121 (37.0)	
Previous joint replacement, *n* (%)				2,694 (9.9)	2,086 (12.6)	< 0.001
Comorbidities [a], *n* (%)						
Hypertension						
Uncomplicated	161,602 (59.7)	33,398 (69.1)	< 0.001	16,852 (61.9)	11,447 (69.2)	< 0.001
Complicated	7,450 (2.8)	3,081 (6.4)	< 0.001	1,218 (4.5)	1,277 (7.7)	< 0.001
Fluid and electrolyte disorders	23,873 (8.8)	10,153 (21.0)	< 0.001	4,336 (15.9)	5,270 (31.9)	< 0.001
Diabetes mellitus						
Uncomplicated	40,067 (14.8)	8,628 (17.8)	< 0.001	4,359 (16.0)	3,025 (18.3)	< 0.001
Complicated	4,643 (1.7)	1,938 (4.0)	< 0.001	843 (3.1)	834 (5.0)	< 0.001
Hypothyroidism	38,291 (14.1)	7,739 (16.0)	< 0.001	3,939 (14.5)	2,636 (15.9)	< 0.001
Cardiac arrhythmia	26,724 (9.9)	9,500 (19.6)	< 0.001	3,973 (14.6)	3,946 (23.9)	< 0.001
Renal failure	18,524 (6.8)	8,550 (17.7)	< 0.001	3,013 (11.1)	3,506 (21.2)	< 0.001
Chronic pulmonary disease	20,672 (7.6)	4,465 (9.2)	< 0.001	2,494 (9.2)	1,754 (10.6)	< 0.001
Congestive heart failure	14,847 (5.5)	6,667 (13.8)	< 0.001	2,821 (10.4)	3,256 (19.7)	< 0.001
Depression	11,105 (4.1)	3,263 (6.7)	< 0.001	1,606 (5.9)	1,408 (8.5)	< 0.001
Osteoporosis	9,751 (3.6)	3,764 (7.8)	< 0.001	1,957 (7.2)	2,009 (12.1)	< 0.001
Peripheral vascular disorders	7,230 (2.7)	2,416 (5.0)	< 0.001	991 (3.6)	1,028 (6.2)	< 0.001
Rheumatism	6,424 (2.4)	1,634 (3.4)	< 0.001	942 (3.5)	591 (3.6)	0.532
Valvular disease	5,434 (2.0)	2,863 (5.9)	< 0.001	890 (3.3)	1,142 (6.9)	< 0.001
Coagulopathy	3,402 (1.3)	2,763 (5.7)	< 0.001	1,184 (4.3)	2,344 (14.2)	< 0.001
Neurological disorders	4,340 (1.6)	1,674 (3.5)	< 0.001	879 (3.2)	900 (5.4)	< 0.001
Deficiency anemia	3,199 (1.2)	908 (1.9)	< 0.001	526 (1.9)	445 (2.7)	< 0.001
Dementia	1,690 (0.6)	1,136 (2.3)	< 0.001	800 (2.9)	1,059 (6.4)	< 0.001
Antithrombotic medication prior to surgery, *n* (%)	40,207 (14.9)	12,290 (25.4)	< 0.001	5,806 (21.3)	4,778 (28.9)	< 0.001

P-THA, primary total hip arthroplasties; R-THA, revision total hip arthroplasties. Significance defined as $p < 0.0019$ after Bonferroni correction.

[a] Double entries are possible; sorted by descending frequency; other comorbidities included in the analysis but with a frequency < 2.0% in the whole cohort are not shown (pulmonary circulation disorders, liver disease, blood loss anemia, peptic ulcer disease excluding bleeding, paralysis, alcohol abuse, drug abuse, psychoses, AIDS/HIV, weight loss).

corresponding decreases in transfusion rates after P-TKA, R-THA and R-TKA were 60.9%, 28.1% and 37.5%, respectively (Fig. 3). Across cohorts, significantly decreased odds of transfusion as compared to 2011 were first observed for 2013. The odds of transfusion continued to decline in subsequent years up to 2017 (Table 3). There was also a significant decline of blood transfusion of six or more units in the R-THA cohort (2011: 498/7,046 (7.1%), 2017: 166/5,588 (3.0%) ($p < 0.001$)) and R-TKA cohort (2011: 70/5,146 (1.4%), 2017: 26/4,905 (0.5%) ($p < 0.001$)).

At the same time, the proportions of patients aged 80 years and older, male gender, patients with antithrombotic medication prior to surgery, and specific diagnoses like renal failure increased (Fig. 4). Between 2011 and 2017 the length of stay decreased in all cohorts (median (interquartile range, IQR): P-THA: 12 days (10-14) in 2011 to 10 days (8-12) in 2017; P-TKA: 12 days (10-14) to 10 days (8-12); R-THA: 15 days (12-23) to 14 days (10-24); R-TKA: 13 days (11-15) to 11 days (9-14)).

3.3. Risk factors for transfusion

Table 3 shows the results of the multiple logistic regression analysis. In each cohort, the odds of transfusion decreased over time (2017 vs. 2011 (reference): P-THA: OR 0.42 (95%CI: 0.39–0.45), P-TKA: 0.41 (95%CI: 0.37–0.46), R-THA: 0.52 (95%CI: 0.47–0.58), R-TKA: 0.53 (95%CI: 0.46–0.61); all cohorts: $p < 0.001$). Across cohorts, patient-related risk factors for blood transfusion included older age (P-THA: OR 1.05 (95%CI: 1.04–1.05), P-TKA: 1.06 (95%CI: 1.06–1.06), R-THA: 1.03 (95%CI: 1.03–1.03), R-TKA: 1.05 (95%CI: 1.05–1.06); all cohorts: $p < 0.001$), female gender (P-THA: OR 1.86 (95%CI: 1.80–1.92), P-TKA: 1.59 (95%CI: 1.53–1.66), R-THA: 1.47

Table 2
Demographic characteristics of patients undergoing primary and revision total knee arthroplasty by transfusion.

Demographics	P-TKA			R-TKA		
	Not Transfused	Transfused	*p*-value	Not Transfused	Transfused	*p*-value
Total, *n*	310,547	28,094		28,917	5,726	
Length of stay (days), median (IQR)	11 (9–13)	13 (11–15)	<0.001	11 (9–14)	15 (12–23)	<0.001
Age (y), median (IQR)	70 (62–76)	76 (71–80)	<0.001	69 (60–76)	75 (69–80)	<0.001
Age (y), *n* (%)			<0.001			<0.001
<50	5,299 (2.9)	74 (0.6)		1,365 (4.7)	83 (1.5)	
50–59	50,927 (16.4)	1,345 (4.8)		5,382 (18.6)	394 (6.9)	
60–69	90,418 (29.1)	4,399 (15.7)		7,914 (27.4)	1,049 (18.3)	
70–79	125,248 (40.3)	14,051 (50.0)		10,879 (37.6)	2,595 (45.3)	
80–89	34,642 (11.2)	7,887 (28.1)		3,284 (11.4)	1,534 (26.8)	
≥90	417 (0.1)	212 (0.8)		93 (0.3)	71 (1.2)	
Female gender, *n* (%)	202,662 (65.3)	21,313 (75.9)	<0.001	18,953 (65.5)	4,209 (73.5)	<0.001
BMI (kg/m^2), *n* (%)			<0.001			<0.001
<30	230,834 (74.3)	22,465 (80.0)		21,442 (74.2)	4,371 (76.3)	
30–34	35,356 (11.4)	2,825 (10.1)		3,360 (11.6)	626 (10.9)	
35–39	25,352 (8.2)	1,684 (6.0)		2,343 (8.1)	399 (7.0)	
≥40	19,005 (6.1)	1,120 (4.0)		1,772 (6.1)	330 (5.8)	
Prosthesis implanted, *n* (%)			<0.001			
Unicondylar	31,833 (10.3)	157 (0.6)				
Bicondylar surface	247,763 (79.8)	25,040 (89.1)				
Bicompartimental knee prosthesis	452 (0.2)	45 (0.2)				
Endoprothesis with extended flexion mobility	30,499 (9.8)	2,852 (10.2)				
Component revised, *n* (%)						<0.001
Patella/onlay				9,043 (31.3)	737 (12.9)	
Unicondylar				4,539 (15.7)	552 (9.6)	
Bicondylar				13,211 (45.7)	3,859 (67.4)	
Stemmed				920 (3.2)	229 (4.0)	
Other				1,204 (4.2)	349 (6.1)	
Previous joint replacement, *n* (%)				2,099 (7.3)	507 (8.9)	<0.001
Comorbidities [a], %						
Hypertension						
Uncomplicated	204,180 (65.7)	20,514 (73.0)	<0.001	18,687 (64.6)	4,080 (71.3)	<0.001
Complicated	8,733 (2.8)	1,830 (6.5)	<0.001	1,011 (3.5)	422 (7.4)	<0.001
Fluid and electrolyte disorders	24,638 (7.9)	5,389 (19.2)	<0.001	2,820 (9.8)	1,391 (24.3)	<0.001
Diabetes mellitus						
Uncomplicated	59,045 (19.0)	6,020 (21.4)	<0.001	5,605 (19.4)	1,234 (21.6)	<0.001
Complicated	6,289 (2.0)	1,337 (4.8)	<0.001	792 (2.7)	319 (5.6)	<0.001
Hypothyroidism	51,682 (16.4)	4,811 (17.1)	<0.001	5,082 (17.6)	1,128 (19.7)	<0.001
Cardiac arrhythmia	29,527 (9.5)	5,337 (19.0)	<0.001	3,143 (10.9)	1,269 (22.2)	<0.001
Renal failure	20,247 (6.5)	5,130 (18.3)	<0.001	2,291 (7.9)	1,148 (20.0)	<0.001
Chronic pulmonary disease	24,695 (8.0)	2,687 (9.6)	<0.001	2,783 (9.6)	620 (10.8)	<0.001
Congestive heart failure	17,256 (5.6)	3,831 (13.6)	<0.001	2,120 (7.3)	967 (16.9)	<0.001
Depression	15,561 (5.0)	2,024 (7.2)	<0.001	1,936 (6.7)	478 (8.3)	<0.001
Osteoporosis	9,171 (3,0)	1,916 (6.8)	<0.001	1,413 (4.9)	604 (10.5)	<0.001
Peripheral vascular disorders	6,725 (2.2)	1,259 (4.5)	<0.001	780 (2.7)	263 (4.6)	<0.001
Rheumatism	7,887 (2.5)	1,187 (4.2)	<0.001	860 (3.0)	228 (4.0)	<0.001
Valvular disease	5,609 (1.8)	1,486 (5.3)	<0.001	656 (2.3)	365 (6.4)	<0.001
Coagulopathy	3,705 (1.2)	1,291 (4.6)	<0.001	538 (1.9)	446 (7.8)	<0.001
Neurological disorders	5,361 (1.7)	1,111 (4.0)	<0.001	722 (2.5)	246 (4.3)	<0.001
Deficiency anemia	2,928 (0.9)	487 (1.7)	<0.001	328 (1.1)	98 (1.7)	<0.001
Dementia	1,420 (0.5)	531 (1.9)	<0.001	201 (0.7)	178 (3.1)	<0.001
Antithrombotic medication prior to surgery, *n* (%)	47,619 (15.3)	7,088 (25.3)	<0.001	5,626 (19.5)	1,767 (30.9)	<0.001

P-TKA, primary total knee arthroplasties; R-TKA, revision total knee arthroplasties. Significance defined as $p < 0.0019$ after Bonferroni correction.

[a] Double entries are possible; sorted by descending frequency; other comorbidities included in the analysis but with a frequency < 2.0% in the whole cohort are not shown (pulmonary circulation disorders, liver disease, blood loss anemia, peptic ulcer disease excluding bleeding, paralysis, alcohol abuse, drug abuse, psychoses, AIDS/HIV, weight loss).

(95%CI: 1.40–1.55), R-TKA: 1.41 (95%CI: 1.32–1.52); all cohorts: $p < 0.001$), antithrombotic medication prior to surgery (P-THA: OR 1.26 (95%CI: 1.21–1.31), P-TKA: 1.19 (95%CI: 1.13–1.26), R-THA: 1.12 (95%CI: 1.06–1.18), R-TKA: 1.20 (95%CI: 1.11–1.30); all cohorts: $p < 0.001$) as well as lower BMI and different comorbidities (for details, see Table 3).

Previous joint replacement was a risk factor for blood transfusion in R-THA and R-TKA patients (R-THA: OR 1.35 (95%CI: 1.25–1.46), $p < 0.001$, R-TKA: 1.50 (95%CI: 1.34–1.69) ($p < 0.001$)). Additionally, university hospital status was an independent risk factor for blood transfusion in all cohorts except R-THA (P-THA: OR 1.71 (95%CI: 1.29–2.26) ($p < 0.001$), P-TKA 1.44 (95%CI: 1.12–1.86) ($p = 0.005$), R-TKA 1.44 (95%CI: 1.09–1.91) ($p = 0.01$)). The predictive accuracy of the fully adjusted models as expressed by the C-statistic was 0.77 (P-THA), 0.78 (P-TKA), 0.73 (R-THA) and 0.75 (R-TKA).

3.4. Thrombogenic events

Over the study period, there was no increase of VTE or stroke events (Table 4). Conversely, we observed a significant decrease of VTE after P-THA (from 457/47,040 (1.0%) in 2011 to 303/45,825 (0.7%) in 2017) and after P-TKA (from 748/51,565 (1.5%) in 2011 to 549/50,744 (1.1%) in 2017).

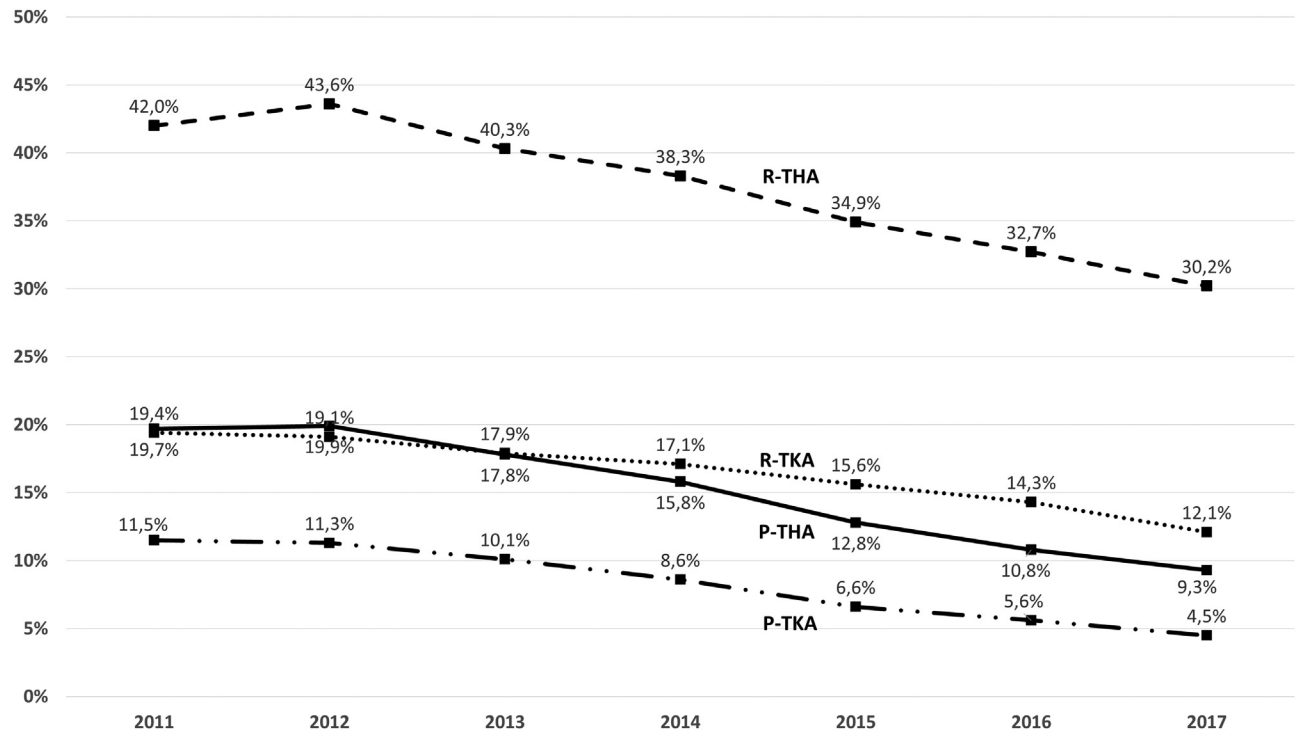

Fig. 3. Trends in transfusion after primary and revision hip and knee arthroplasty (P-THA, primary total hip arthroplasties; P-TKA, primary total knee arthroplasties; R-THA, revision total hip arthroplasties; R-TKA, revision total knee arthroplasties).

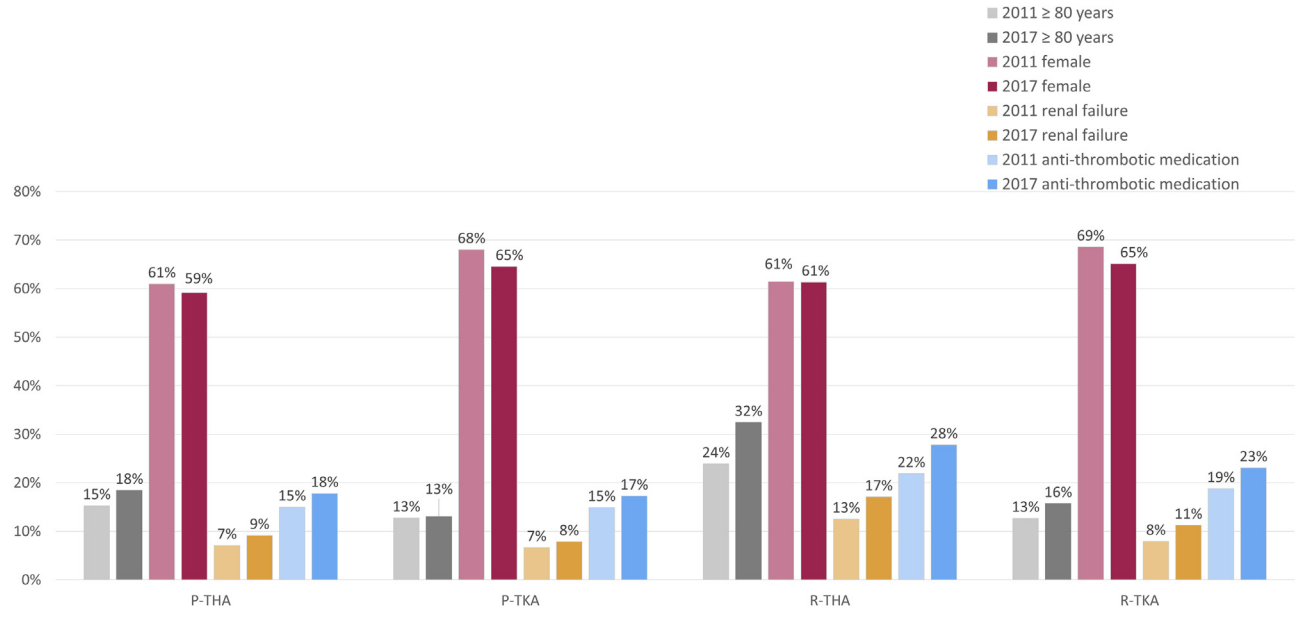

Fig. 4. Patient characteristics for primary and revision hip and knee arthroplasty in 2011 and 2017 (P-THA, primary total hip arthroplasties; P-TKA, primary total knee arthroplasties; R-THA, revision total hip arthroplasties; R-TKA, revision total knee arthroplasties).

4. Discussion

In our study, we analyzed trends and risk factors for blood transfusion in Germany. The most important finding is that blood transfusions after primary and revision total hip and knee arthroplasty decreased significantly over the study period. Between 2011 and 2017 the blood transfusion rate decreased from 19.7% to 9.3% for P-THA, from 11.5% to 4.5% for P-TKA, from 42.0% to 30.2% for R-THA and from 19.7% to 9.3% for R-TKA. After controlling for patient- and hospital-related factors the odds of transfusion decreased by about fifty percent for primary arthroplasty cases and over sixty percent for revision procedures (P-THA: 58%, P-TKA: 59% > R-THA: 48%, R-TKA: 47%) over the study period. There was also a significant decline of blood transfusion of six or more units for R-THA (7.1% to 3.0%) and R-TKA (1.4% to 0.5%).

This result is comparable with a large retrospective study of 1,013,024 patients in the USA where the overall incidence of transfusion declined from 2010 to 2015 (P-THA: 22.1% to 7.1%; P-TKA: 18.1% to 3.2%; R-THA: 30.6% to 18.5%; R-TKA: 19.8% to 9.8%) [14]. However, we found that risk factors such as older age and

Table 3
Results of multivariable logistic regression analysis for independent risk factors for transfusion after primary and revision hip and knee arthroplasty.

	OR [95%-CI]			
	P-THA	R-THA	P-TKA	R-TKA
Year				
2011	Ref.	Ref.	Ref.	Ref.
2012	1.01 (0.96–1.06)	1.07 (0.98–1.15)	1.01 (0.96–1.06)	0.97 (0.87–1.08)
2013	0.88 (0.83–0.93)	0.90 (0.82–0.98)	0.90 (0.85–0.95)	0.89 (0.79–0.99)
2014	0.76 (0.71–0.80)	0.81 (0.74–0.89)	0.77 (0.72–0.82)	0.81 (0.72–0.92)
2015	0.59 (0.55–0.63)	0.69 (0.62–0.76)	0.59 (0.54–0.64)	0.70 (0.62–0.80)
2016	0.49 (0.45–0.52)	0.63 (0.58–0.70)	0.50 (0.45–0.55)	0.65 (0.57–0.74)
2017	0.42 (0.39–0.45)	0.52 (0.47–0.58)	0.41 (0.37–0.46)	0.53 (0.46–0.61)
Age (years)	1.05 (1.04–1.05)	1.03 (1.03–1.03)	1.06 (1.06–1.06)	1.05 (1.05–1.06)
Female gender	1.86 (1.80–1.92)	1.47 (1.40–1.55)	1.59 (1.53–1.66)	1.41 (1.32–1.52)
Body mass index (kg/m^2)				
< 30	Ref.	Ref.	Ref.	Ref.
30–34	0.79 (0.72–0.87)	0.85 (0.76–0.95)	0.86 (0.77–0.95)	0.93 (0.83–1.05)
35–39	0.74 (0.68–0.80)	0.86 (0.77–0.96)	0.76 (0.69–0.84)	0.83 (0.73–0.94)
≥ 40	0.72 (0.66–0.78)	1.10 (0.96–1.27)	0.74 (0.68–0.80)	0.95 (0.82–1.10)
Prosthesis implanted [a]				
P-THA, Hip Resurfacing	0.57 (0.37–0.89)	–	–	–
P-TKA, Unicondylar	–	–	0.09 (0.08–0.11)	–
Component revised [a]				
R-THA, Femur and cup	–	2.14 (2.02–2.27)	–	–
R-TKA, Unicondylar	–	–	–	0.78 (0.70–0.87)
Comorbidities				
Hypertension, uncomplicated	1.09 (1.06–1.13)	1.09 (1.04–1.14)	1.12 (1.07–1.18)	–
Hypertension, complicated	1.13 (1.03–1.24)	–	1.15 (1.04–1.28)	–
Fluid and electrolyte disorders	1.57 (1.46–1.67)	1.59 (1.48–1.71)	1.65 (1.53–1.77)	1.69 (1.54–1.86)
Diabetes, uncomplicated	1.05 (1.02–1.08)	–	1.05 (1.02–1.09)	–
Diabetes, complicated [b]	1.12 (1.03–1.21)	–	1.20 (1.10–1.32)	–
Hypothyroidism	0.94 (0.91–0.98)	–	0.93 (0.89–0.97)	–
Cardiac arrhythmia	1.16 (1.12–1.20)	1.07 (1.01–1.14)	1.18 (1.13–1.23)	1.21 (1.10–1.33)
Renal failure	1.57 (1.49–1.65)	1.31 (1.22–1.41)	1.72 (1.62–1.82)	1.57 (1.43–1.73)
Chronic pulmonary disease	–	–	–	–
Congestive heart failure	1.15 (1.08–1.21)	1.15 (1.07–1.24)	1.15 (1.07–1.24)	1.16 (1.04–1.29)
Depression	1.30 (1.24–1.37)	1.14 (1.04–1.25)	1.23 (1.16–1.31)	–
Osteoporosis	1.28 (1.21–1.35)	1.27 (1.17–1.39)	1.36 (1.26–1.46)	–
Peripheral vascular disorders	1.28 (1.21–1.36)	1.27 (1.15–1.41)	1.37 (1.24–1.51)	–
Rheumatism	1.23 (1.14–1.32)	–	1.49 (1.36–1.63)	–
Valvular disease	1.47 (1.38–1.57)	1.31 (1.15–1.49)	1.43 (1.33–1.55)	1.29 (1.10–1.50)
Coagulopathy	2.67 (2.45–2.92)	2.40 (2.15–2.68)	2.12 (1.94–2.32)	2.30 (1.94–2.72)
Neurological disorders	1.59 (1.48–1.71)	1.35 (1.20–1.51)	1.74 (1.61–1.88)	1.28 (1.07–1.52)
Dementia	1.38 (1.25–1.53)	1.22 (1.08–1.37)	1.58 (1.39–1.80)	–
Weight loss	1.50 (1.06–2.11)	–	–	–
Alcohol abuse	2.10 (1.91–2.43)	1.79 (1.45–2.20)	2.61 (2.11–3.23)	2.54 (1.63–3.95)
Drug abuse	1.92 (1.63–2.26)	1.36 (1.07–1.73)	2.02 (1.69–2.42)	1.86 (1.17–2.92)
Psychoses	1.44 (1.19–1.75)	1.62 (1.23–2.13)	2.35 (1.90–2.91)	4.55 (2.88–7.19)
Paralysis	1.50 (1.34–1.69)	1.41 (1.18–1.69)	1.41 (1.13–1.26)	–
Liver disease	1.58 (1.40–1.78)	–	1.63 (1.41–1.89)	–
Peptic ulcer disease excluding bleeding	1.51 (1.07–2.14)	–	1.75 (1.18–2.62)	–
Pulmonary circulation disorders	1.23 (1.10–1.38)	–	1.45 (1.27–1.64)	1.37 (1.04–1.81)
Previous joint replacement [c]	–	1.35 (1.25–1.46)	–	1.50 (1.34–1.69)
Antithrombotic medication prior to surgery	1.26 (1.21–1.31)	1.12 (1.06–1.18)	1.19 (1.13–1.26)	1.20 (1.11–1.30)
Length of stay (days)	1.05 (1.05–1.05)	1.01 (1.01–1.01)	1.05 (1.04–1.06)	1.03 (1.02–1.03)
University hospital	1.71 (1.29–2.26)	–	1.44 (1.12–1.86)	1.44 (1.09–1.91)

P-THA, primary total hip arthroplasties; P-TKA, primary total knee arthroplasties; R-THA, revision total hip arthroplasties; R-TKA, revision total knee arthroplasties. Models were adjusted for patient age, gender, body mass index (BMI), component implanted or revised, previous joint replacement, comorbidities, antithrombotic medication prior to surgery, and hospital characteristics (hospital size, hospital procedure volume, University hospital). Only significant results are shown.

[a] Reference other procedures according to Table 1 and Table 2.

[b] i.e. coma, ketoacidosis, vascular disease.

[c] Revision of the same joint in less than 10 years before the index surgery.

comorbities increased over the period of study. Potential reasons for the decrease in blood transfusions include new transfusion guidelines, and the introduction of novel pharmaceuticals and devices for bleeding control and blood management [12,13]. The introduction of an enhanced recovery program in Germany may also have contributed to the decrease of blood transfusions. This program includes optimized pre-, intra- and postoperative protocols. For instance, patients with anemia are detected preoperatively and are optimized e.g. with iron supplements prior to elective surgery. Discontinuing the use of tourniquets during [17,18] knee arthroplasty and the use of suction drainages [17,19] are also potentially beneficial factors.

As expected, we found a higher rate of transfusion in revision arthroplasty compared to primary total joint arthroplasty, with the highest rate of transfusions in R-THA (R-THA: 37.8% > R-TKA: 16.5% > P-THA: 15.2% > P-TKA: 8.3%, mean rates of transfusion 2011–2017). This finding has also been reported in previous studies [14,20]. However, the incidence of transfusion in our study was higher in all cohorts except P-TKA compared to recent findings from the United States [14,21,22]. For example, the transfusion rates for

Table 4
Trends in venous thromboembolism and stroke after primary and revision hip and knee arthroplasty.

		Year of procedure							
	Total	2011	2012	2013	2014	2015	2016	2017	*P for Trend*
P-THA									
Total, *n*	318,997	47,486	45,758	43,415	44,956	45,347	45,803	46,232	
VTE, %	0.8	1.0	0.9	0.8	0.7	0.7	0.7	0.7	< 0.001
Stroke, %	0.3	0.3	0.4	0.2	0.3	0.3	0.3	0.3	0.0789
P-TKA									
Total, *n*	338,641	51,897	49,533	44,721	45,265	46,657	49,556	51,012	
VTE, %	1.2	1.5	1.3	1.3	1.2	1.2	1.1	1.1	< 0.001
Stroke, %	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.0173
R-THA									
Total, *n*	43,780	7046	6997	6376	6125	5961	5687	5588	
VTE, %	1.4	1.5	1.2	1,7	1.5	1.4	1.1	1.4	0.4575
Stroke, %	0.6	0.6	0.5	0.6	0.6	0.7	0.8	0.7	0.1408
R-TKA									
Total, *n*	34,643	5146	5156	4806	4690	4981	4959	4905	
VTE, %	1.3	1.5	1.2	1.2	1.2	1.2	1.3	1.2	0.4329
Stroke, %	0.3	0.3	0.3	0.3	0.3	0.2	0.3	0.4	0.6236

VTE: venous thromboembolism; P-THA: primary total hip arthroplasties; P-TKA: primary total knee arthroplasties; R-THA: revision total hip arthroplasties; R-TKA: revision total knee arthroplasties.

2015 in our study were 12.8% for P-THA compared to 7.1% [14] and 8.7% [21], and 34.9% for R-THA compared to 18.5% [14] and 10.3% [22], respectively. Factors such as improved blood management and a focus on vulnerable patients may produce a further future reduction of transfusions, especially in R-THA.

Patient-related risk factors for blood transfusion in our study included older age, female gender, previous joint replacement, lower BMI, and comorbidities such as renal failure, cardiac arrhythmia, congestive heart failure, valvular disease, coagulopathy, depression, neurological disorders, and antithrombotic medication before surgery. These findings correspond to previous reports of higher age as a risk factor for transfusion [9,14]. In accordance with our results other studies also found female gender, lower BMI, and comorbidities like preoperative anemia, cardiac disease and depression to be associated with a higher risk of blood transfusion [7–9,20,23,24].

Our findings suggest that university hospital status is an independent risk factor for blood transfusion in all cohorts except R-THA. Hospital size and hospital volume were not found to be risk factors. This may reflect that specialized high-volume centres or university hospitals are more likely to have complex cases. Kimball et al. [14] demonstrated recently that smaller hospitals in the United States were associated with higher odds of transfusion compared to large hospitals in all four cohorts, and that academic hospitals were associated with higher odds of transfusion compared to community facilities in three of four cohorts. The authors cited access to internal blood bank resources and a higher burden of complex cases in academic centres as possible explanations for the higher odds in academic hospitals.

The efficacy of TXA has been well described and it can decrease bleeding intraoperatively, but might increase the incidence of VTE and stroke events. Therefore, another study focus was to determine complications with a focus on VTE and stroke events that can be associated with TXA use. We observed a significant decrease in VTE after P-THA and after P-TKA. These results suggest that TXA have a benefit in reducing the blood transfusion rate without an increase in VTE and stroke events, and are consistent with recent reports [25–27]. In a study by Qiu et al. [28], topical application of TXA was effective in reducing blood loss in total hip arthroplasty patients receiving continuous aspirin for prevention of cardiovascular or cerebrovascular diseases without increasing the 90-day complication rate. However, in a randomized controlled trial by King et al. [29], the utilization of oral TXA regimen was non-inferior to a topical/IV/oral regimen in total knee arthroplasty with regard to efficacy and safety. In our study, the use and dosage of TXA is not reported in detail, which is a limitation of our database.

Our study also has further limitations. (1) First, although it is based on nationwide data of the largest healthcare insurance in Germany, there may be variations in terms of age, gender, social status, and morbidity between patients insured by different German healthcare providers [30]. For instance, comparing AOK cases to all German patients with R-THA in 2017, there are slight differences to our study population (female gender 61.3% [AOK] vs 59.0% [Germany], age ≥ 70 years 67.2% [AOK] vs 67.7% [Germany]) [31]). Even though our analysis was risk-adjusted for age, gender and comorbidities, we may not have been able to capture all relevant factors. (2) Second, data were generated as routine data for billing, and coding inaccuracies cannot be ruled out. However, billing data are regularly checked for correctness. (3) Third, the German insurance database does not provide information on preoperative or intraoperative hemoglobin levels or other reasons for transfusion. (4) Finally, detailed surgical information regarding the complexity of the procedures, such as a bone defect classification for revision procedures, the approach used for THA and the information about patients with extended trochanteric osteotomy are lacking in the dataset. Furthermore, we were unable to use the ASA score for risk adjustment, since it relies on information, which is not available in our database. Instead, we used the Elixhauser classification of comorbidities, which was specifically developed for use with routine data. It has previously been used by Ondeck et al. [32], for instance, who were able to show that the discriminative ability of Elixhauser's comorbidity measure is superior to other comorbidity scores for inpatient adverse outcomes after total hip arthroplasty.

5. Conclusion

In summary, this is the largest study, which has blood transfusion rates and trends from 2011 to 2017 in Germany. As hypothesized there is a significant trend in decreasing blood transfusion for both primary and revision total hip and knee arthroplasty, which may be due to new transfusion guidelines and the introduction of novel pharmaceuticals such as TXA. We found no increase of VTE and stroke events. Also, our results suggest that factors such as improved patient blood management and a focus on vulnerable patient groups may still reduce transfusions further in the future, especially in R-THA.

Ethics approval

This study is based on data provided by hospitals for health insurance billing. The recommendations for good practice in secondary data analysis developed by the German Working Group on the Collection and Use of Secondary Data were applied in full. Therefore, no formal ethical committee approval was needed.

Disclosure of interest

Dr. Citak reports other from Waldemar Link, outside the submitted work. Dr. Gehrke reports other from Waldemar Link, other from Zimmer Biomet, other from Ceramtec and other from Heraeus, outside the submitted work. Dr. Halder reports personal fees from Zimmer Biomet, personal fees from DePuy and personal fees from Lima, outside the submitted work. Dr. Heller reports grants and personal fees from Zimmer Biomet, grants and personal fees from Asculap AG, personal fees from Smith & Nephew, other from Johnson & Johnson and other from Conformis, outside the submitted work. Dr. Malzahn reports personal fees from Zimmer Biomet, personal fees from AAA Implantate and personal fees from DePuy, outside the submitted work. Mr. Günster, Dr. Jeschke, Dr. Leicht, Dr. Niethard, Dr. Schräder and Dr. Zacher declare that they have no competing interest.

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Authors' contributions

Elke Jeschke and Mustafa Citak contributed equally to the writing of the article. All authors were involved in the conception of the research and decided on the research question and study design. EJ, CG, HL, JM, TG were involved in data acquisition. EJ, MC, AH, TG provided the analysis of data. AH, KH, FUN, PS, JF, TG supported the clinical interpretation of the study results. EJ and MC wrote the manuscript. All co-authors proofread the manuscript critically and approved its final version.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.otsr.2021.102987.

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