



The influence of chronic kidney disease on the duration of hospitalisation and transfusion rate after elective hip and knee arthroplasty

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Received: 10 June 2018 / Accepted: 8 October 2018 / Published online: 15 October 2018
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Abstract

Purpose Elective hip or knee replacement is an optimal, standardised orthopaedic surgical procedure. The influence of chronic kidney disease, defined as an estimated glomerular filtration rate (eGFR) of 15–45 ml/min/1.73 m² body surface area (BSA) (KDIGO stage G3a–G4), on the duration of hospitalisation, perioperative decrease in haemoglobin (Hb) levels, and transfusion rates after orthopaedic procedures has not been fully clarified. Our study, therefore, aimed to evaluate the impact of chronic kidney disease on the previously mentioned variables.

Methods We conducted a retrospective multicentre analysis involving two orthopaedic centres. Patients who underwent elective total hip and knee replacement between 2010 and 2015 were included. We used descriptive methods and multivariate linear and binary regression analyses for our statistical evaluations.

Results We evaluated 3301 datasets (1120 men [33.9%], 2181 women [66.1%], 2043 [61.9%], and 1258 [38.1%]) elective total hip and knee replacements, respectively. The following variables were identified as risk factors for a prolonged hospital stay: patient age, admission Hb and potassium levels, perioperative Hb level decrease, year of surgery, blood transfusion, and a preoperative eGFR of 15–45 ml/min/m² BSA. Patients with an eGFR of >45 ml/min/m² BSA were discharged within 11.7 ± 3.0 days, while patients with an eGFR of 15–45 ml/min/1.73 m² BSA remained inpatient for 13.5 ± 5.0 days (*p* < 0.001). Identified risk factors for postoperative blood transfusions included age, initial Hb level, perioperative Hb decrease, prosthetic hip replacement, and the presence of allergic diathesis. Blood transfusions were performed in 7.5% of patients with an eGFR of >45 ml/min/m² BSA compared to 24.1% of patients with an eGFR of 15–45 ml/min/1.73 m² BSA (*p* < 0.001). An eGFR level of 15–45 ml/min/m² BSA was identified as a risk factor for a postoperative decrease in Hb levels.

Conclusion Chronic kidney disease, defined as an eGFR level of 15–45 ml/min/1.73 m² BSA, was a risk factor for a prolonged hospital stay after elective hip and knee arthroplasty. Further studies are necessary to better define the effect of reduced kidney function on relevant clinical and socioeconomic outcome parameters.

Keywords Joint replacement · CKD · Prolonged inpatient stay · Blood transfusion

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Introduction

Elective hip and knee replacement surgery preserve or restore mobility, especially in elderly patients. These procedures are two of the most successful standardised surgical procedures in the Western world [1]. Because of the socio-demographic development in industrialised countries, these procedures represent a significant financial burden for the national health systems of these geographical regions [2]. In Germany, hip and knee replacement procedures are among the 20 most frequently performed surgical interventions and in 2015, approximately 400,000 such surgeries were performed in German hospitals [3].

In recent years, many perioperative risk factors that could negatively affect surgical outcomes and lead to increased rates of postoperative complications have been identified. In addition to pre-existing internal conditions such as coronary artery disease, chronic obstructive pulmonary disease, high blood pressure, or diabetes mellitus [4], cognitive disorders have also been associated with postoperative complications [5]. Patients with reduced renal function often experience several other internal primary diseases [6], as well as impaired cognitive ability [7]. Furthermore, chronic kidney disease (CKD), defined as an estimated glomerular filtration rate (eGFR) of < 45 ml/min/1.73 m² body surface area (BSA), is often associated with metabolic bone disorders. The pathophysiological term for this condition is “chronic kidney disease-metabolic bone disorder” (CKD-MBD). It is caused by a broad spectrum of disorders, including disturbed acid–base homeostasis that potentially results in metabolic acidosis, and an impaired parathyroid hormone-vitamin D axis [8]. Histomorphometric studies have identified bone mineralisation disorders that display adynamic or hyperdynamic bone metabolism or a combination of both [9]. Furthermore, as renal function declines, there is an increased risk of bleeding diathesis due to uraemic thrombocytopeny [10]. Moreover, hyporegeneratory renal anaemia may also occur [11]. Therefore, we hypothesised that reduced renal function, defined as an eGFR level of 15–45 ml/min/1.73 m² BSA, could theoretically have a negative influence on postoperative complication rates that can be measured in terms of the length of hospital stay or perioperative transfusion rates after hip and knee joint arthroplasty.

We, therefore, conducted a multicentre analysis of the influence of a reduced renal function of 15–45 ml/min/1.73 m² BSA on the length of inpatient stay, perioperative decrease in haemoglobin (Hb) levels, and transfusion rates. We evaluated these parameters in a cohort of 3301 patients who underwent an elective hip or knee replacement between 2010 and 2015.

Study approval

The study was approved by the local ethics committee (16-7259-BO). Data were coded in a manner ensuring that subjects could not be identified either directly or through linked identifiers. Since this study involved a retrospective review of existing data, specific informed consent from the patients was not required.

Materials and methods

The medical records of patients who underwent elective hip or knee replacement surgery in one of two centres (Universitätsklinikum Essen, Evangelisches Krankenhaus Essen-Werden) between early 2010 and late 2015 comprised the data for review. During this period, 3354 surgeries were performed. As complete data were unavailable for 53 of the patients (1.6%), a total of 3301 patients were included in the analysis (Fig. 1). The cohort was divided by eGFR levels into two groups: group A with eGFR levels above 45 ml/min/1.73 m² BSA (National Kidney Foundation stages 1, 2, and 3a) and group B with eGFR levels between 15 and 45 ml/min/1.73 m² BSA (National Kidney Foundation stages 3b and 4). This classification was chosen to (i) better compare our patient cohort with previous cohorts described in the literature and (ii) as these patients are more likely to be affected by bleeding problems, hyperkalemia, and anaemia than patients with eGFR levels in the range of 45–60 ml/min/1.73 m² BSA. Patients with severely reduced renal function (< 15 ml/min/1.73 m² BSA, National Kidney Foundation stage 5) and patients on dialysis were excluded from the analysis due to the complex interplay between the application of erythropoietin, intravenous iron, and intermittent anticoagulation during dialysis on the outcome parameters. Patients who were transferred postoperatively to another department or hospital were also excluded from the study.

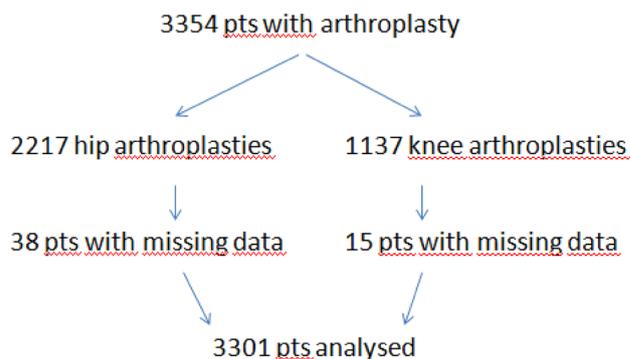


Fig. 1 Patient flow-chart

All patients were examined before admission according to a standardised preoperative procedure. This included recording the patient's medical histories, the performance of physical examinations by an orthopaedic specialist and an anaesthetist, and preoperative laboratory diagnostic testing preoperatively (haematology with full blood count, C-reactive protein, coagulation with partial prothrombin time [Quick], prothrombin time, international normalised ratio, fibrinogen, electrolytes such as sodium, potassium, and calcium, and kidney function tests with creatinine, eGFR, and urea).

The indication for a perioperative transfusion of two units of blood was based exclusively on a standardised set of criteria: Hb < 7 mg/dl (all patients) or Hb 7–8 mg/dl in patients with clinical symptoms such as buzzing in the ears, dizziness, and angina pectoris or already diagnosed high-grade coronary artery disease.

The recorded patient-specific data were age, sex, type of joint arthroplasty (hip or knee), side of prosthesis implantation (right or left), length of hospital stay, preoperative potassium level in mmol/l, Hb level in g/dl, the difference between the Hb levels on admission and on discharge in g/dl, and the presence of diabetes mellitus or allergic diathesis. If the patient had a previous blood transfusion, the patient's symptoms, year of surgery, and renal function (eGFR < or > 45 ml/min/1.73 m² BSA) were also recorded.

The multivariate linear and binary logistic (backwards procedure) regression analyses were conducted after adjustments for the following variables: patient age in years, Hb level on admission, perioperative difference in Hb levels, potassium level on admission, year of surgery, sex, type of joint replacement (hip or knee), side of prosthesis implantation (right or left), blood transfusions (yes/no), presence of diabetes mellitus (yes/no), presence of a history of allergic diathesis (yes/no), and an eGFR of 15–45 versus > 45 ml/min/1.73 m² BSA. The selection of the variables for the corresponding regression models followed after clinical assessment with regard to their potential significance for the respective outcome parameter and whether they had been documented as completely as possible in the dataset.

Statistical analyses

The differences between the patient groups with eGFR < or > 45 ml/min/1.73 m² BSA are presented using descriptive methods. eGFR was provided automatically by the laboratory according to the CKD-EPI formula [12]. The influence of the target parameter, eGFR < or > 45 ml/min/1.73 m² BSA, on the dependent variables *length of inpatient stay and need for blood transfusion*, was analysed using adjusted linear and binary logistic regression. All categorical variables were dichotomised. A logarithmic transformation of

metric variables was not performed. The patient groups are presented via descriptive statistical methods, with averages and standard deviations for continuous variables, and absolute figures and percentages for categorical variables. A *p* value < 0.05 was considered significant. Statistical analyses were performed using SPSS version 22.0 (IBM Corp., Armonk, NY).

Results

The databases comprised patient data recorded between 1 January 2010 and 31 December 2015. A total of 3301 datasets were evaluated. The patient cohort included 2181 women (66.1%). Hip replacement surgery was performed in 2043 (61.9%) cases. Surgeries were performed on the right side in 1732 (52.5%) patients. Diabetes mellitus was recorded in 402 (12.2%) patients and 372 (11.3%) had allergic diathesis. Perioperative blood transfusions were performed in 276 (8.4%) patients. Major patient characteristics of patients with eGFR levels of 15–45 ml/min/1.73 m² BSA and greater are shown in Table 1.

Influence of renal function on the length of hospital stay

The results of the linear regression analysis are shown in detail in Table 2. On average, patients with an eGFR of > 45 ml/min/1.73 m² BSA remained inpatient for 11.7 ± 3.0 days, and patients with an eGFR of 15–45 ml/min/1.73 m² BSA remained inpatient for 13.5 ± 5.0 days (*p* < 0.001).

Influence of renal function on the rate of blood transfusion

The results of the binary regression analysis are shown in detail in Table 3. The target parameter, an eGFR of 15–45 ml/min/1.73 m² BSA, narrowly missed the a priori determined significance level with a *p* value of 0.09. Blood transfusion was necessary for 24.1% of patients with an eGFR of 15–45 ml/min/1.73 m² BSA but only for 7.5% of patients with an eGFR > 45 ml/min/1.73 m² BSA (*p* < 0.001). On average, patients with an eGFR of 15–45 ml/min/1.73 m² BSA received 0.53 ± 0.08 transfusions, whereas patients with a higher eGFR > 45 ml/min/1.73 m² BSA received only 0.17 ± 0.01 transfusions (*p* < 0.001).

Influence of renal function on perioperative fall in haemoglobin levels

The results of the linear regression analysis are shown in detail in Table 4. On average, patients with an eGFR of > 45 ml/min/1.73 m² BSA experienced a perioperative

Table 1 Overview of the characteristics for patients with an eGFR of > 45 ml/min/m² respectively 15–45 ml/min/m² BS

Variables	eGFR > 45 ml/min/m ² BS (n = 3135)				eGFR 15–45 ml/min/m ² BS (n = 166)				p-Wert
	Mean + STD	95% CI	Median	Range	Mean + STD	95% CI	Median	Range	
Age (years)	68.3 ± 11.4	67.9/68.7	70.3	85.9	76.1 ± 9.0	74.7/77.5	76.2	69.7	<0.000
Hospital stay (days)	11.7 ± 3.0	11.6/11.8	11.0	43	13.5 ± 5.1	12.8/14.3	12.0	40	<0.000
Potassium (mmol/l)	4.5 ± 0.4	4.4/4.5	4.5	3.3	4.6 ± 0.5	4.5/4.7	4.6	2.4	<0.000
Creatinine (mg/dl)	0.8 ± 0.2	0.7/0.8	0.7	1.5	1.6 ± 0.5	1.6/1.7	1.5	2.6	<0.000
eGFR (ml/min/m ² BS)	86 ± 17	85/87	87	121	36 ± 7	35/37	37	30	<0.000
Haemoglobin on admission (g/dl)	13.7 ± 1.3	13.6/13.7	13.8	10.3	12.5 ± 1.7	12.3/12.7	12.4	8.1	<0.000
Difference haemoglobin (g/dl) ^a	− 3.3 ± 1.3	− 3.3/− 3.2	− 3.3	10.2	− 2.9 ± 1.5	− 3.2/− 2.7	− 3.0	8.8	0.004
Transfusions (%)	236 (7.5)	–	–	–	40 (24.1)	–	–	–	<0.000
Diabetes mellitus (%)	362 (11.5)	–	–	–	40 (24.1)	–	–	–	<0.000
Allergic diathesis (%)	359 (11.4)	–	–	–	13 (7.8)	–	–	–	Ns
Women (%)	2075 (66.2)	–	–	–	106 (63.9)	–	–	–	Ns
Hip THR (%)	1939 (61.9)	–	–	–	104 (62.7)	–	–	–	Ns
Right side THR (%)	1644 (52.4)	–	–	–	88 (53.0)	–	–	–	Ns

THR total hip replacement

^aThe difference between the haemoglobin value at the time of admission and the time of discharge was calculated in g/dl. 276 patients who received blood transfusions perioperatively were excluded. Metric variables were evaluated using the Mann–Whitney *U* test und categorical variables using the chi-square test

Table 2 Results of the linear regression model to search for risk factors for prolonged hospitalisation

Variables	Beta coefficient	Regression coefficient	p-level
Age (years)	+0.094	+0.026	0.000
Haemoglobin on admission (g/dl)	− 0.046	− 0.107	0.031
Difference in haemoglobin (g/dl)	+0.085	+0.203	0.000
Potassium on admission (mmol/l)	− 0.061	− 0.459	0.000
Year of operation	− 0.238	− 0.433	0.000
Sex (m/f)	− 0.014	− 0.095	0.428
Type of joint replacement (knee/hip)	− 0.031	− 0.202	0.060
Anatomical side (right/left)	+0.002	− 0.015	0.885
Blood transfusion (yes/no)	+0.147	+1.685	0.000
Diabetes mellitus (yes/no)	+0.001	+0.012	0.942
Allergic diathesis (yes/no)	+0.001	+0.008	0.963
eGFR 15–45 versus > 45 ^a	+0.076	+1.103	0.000

^aeGFR according to the CKD-EPI formula was automatically reported by the laboratory

decrease in Hb levels of -3.3 ± 1.3 g/dl, whereas patients with CKD stage G3a-G4 showed a fall of -2.9 ± 1.5 g/dl ($p=0.004$). Nevertheless, these results have to be interpreted cautiously as patients who had received blood transfusion were excluded from this analysis.

Discussion

Our analysis showed that patients with chronic kidney disease (CKD) have a markedly longer hospital stay than patients with normal renal function. The average hospital

stay for patients with reduced renal function was almost 2 days longer than that for patients with normal renal function. The transfusion rate of 24.1% was also markedly higher than the 7.5% rate in patients without CKD, although the multivariate regression analysis narrowly missed the pre-determined significance level.

Elective hip or knee replacement is one of the most standardised surgical procedures in orthopaedic surgery, with established protocols for the pre- and perioperative management of patients. Cost calculations for hospitals are therefore based on the average values for specific parameters. The costs associated with inpatient lengths of stay and the

Table 3 Results of the binary logistic regression model (backwards procedure) to search for risk factors for perioperative blood transfusions

Variables	<i>p</i> -level	Risk ratio	95% CI
Age (years)	0.000	1.036	1.022–1.049
Haemoglobin on admission (g/dl)	0.000	0.501	0.439–0.573
Difference in haemoglobin (g/dl)	0.003	1.215	1.067–1.384
Potassium on admission (mmol/l)	0.193	0.814	0.597–1.109
Year of operation	0.264	0.956	0.992–1.035
Sex (m/f)	0.062	1.350	0.985–1.850
Type of joint replacement (hip/knee)	0.000	1.766	1.307–2.385
Anatomical side (right/left)	0.130	1.233	0.940–1.619
Diabetes mellitus (yes/no)	0.195	1.330	0.864–2.046
Allergic diathesis (yes/no)	0.029	1.838	1.065–3.171
^a eGFR 15–45 versus > 45	0.090	0.685	0.442–1.061

^aeGFR according to the CKD-EPI formula was automatically reported by the laboratory

possible need for blood transfusions are important data for hospital administration. It is therefore increasingly important to identify the modifiable risk factors to minimise the burdens on patients due to their illness and minimise financial burdens on health systems.

Many variables influencing the peri- and postoperative course after joint replacement surgery have been described. These include social and demographic factors as well as concomitant medical conditions and surgical techniques [13]. CKD is associated with many of these factors. Indeed, a higher incidence of joint arthroplasty procedures has been noted in patients with kidney failure on renal replacement therapy or after kidney transplantation in comparison with the general population [14, 15]. However, the influence of an eGFR between 15 and 45 ml/min/m² BSA and the length of hospital stay and perioperative transfusion rates

or perioperative complications has not been conclusively investigated.

Other studies of elective hip or knee arthroplasty have reported comparable results. Ackland et al. found a higher rate of complications and that inpatient stays were prolonged by four additional days for patients with an eGFR of < 50 ml/min/1.73 m² BSA after elective hip or knee arthroplasty. However, all the patients in this group were over 50 years of age [16]. Another study comparing patients with stage-3 CKD to patients with normal renal function after hip and knee replacement showed that the patients with CKD not only had higher rates of infection but also higher mortality rates. However, this increase in mortality rate was only demonstrable for patients who had undergone hip arthroplasty [17]. A study by Miric et al. evaluated a large sample of more than 20,000 patients after hip arthroplasty, and their findings did not reveal any increase in mortality for patients with CKD. However, they reported an increased rate of hospital re-admissions [18]. A large register study of more than 74,000 hip and knee arthroplasty patients revealed an increase in the rate of complications and mortality, depending on the stage of CKD (stages 1–5) [19]. Another register study concerning complication rates during inpatient stays that was based on more than one million datasets (38,308 CKD/ESRD patients versus 978,378 non-CKD/ESRD patients), indicated that CKD was associated with wound infection, transfusions, deep vein thrombosis, and mortality [20]. Further, the same study reported higher rates of wound infections, transfusions, and higher mortality rates in dialysis patients than in renal transplant patients [20].

Chronic kidney disease is associated with both lower Hb levels and elevated risks of bleeding. In our group of patients with reduced renal function, the Hb level was 1.4 g/dl lower than that of the control group. However, the average preoperative level of 12.3 g/dl was primarily within the non-critical range. Although the multivariate regression

Table 4 Results of the linear regression model to search for risk factors for an increased perioperative fall in haemoglobin level

Variables	Beta coefficient	Regression coefficient	<i>p</i> -level
Age (years)	−0.042	−0.005	0.012
Haemoglobin on admission (g/dl)	−0.483	−0.477	0.000
Potassium on admission (mmol/l)	−0.056	−0.171	0.001
Year of operation	−0.039	−0.028	0.017
Sex (m/f)	−0.055	−0.146	0.002
Type of joint replacement (knee/hip)	+0.029	+0.076	0.071
Anatomical side (right/left)	−0.006	−0.015	0.709
Diabetes mellitus (yes/no)	+0.005	+0.020	0.750
Allergic diathesis (yes/no)	+0.015	0.057	0.373
eGFR 15–45 versus > 45 ^a	−0.016	−0.062	0.557

276 patients who received blood transfusions perioperatively were excluded

^aeGFR according to the CKD-EPI formula was automatically reported by the laboratory

analysis provided data that remained just below the significance level, a markedly higher rate of transfusions was still required for patients with reduced eGFRs. Graves et al. reported an increased transfusion rate and prolonged inpatient stays for a small group of 86 patients with an eGFR of > 30 ml/min/1.73 m² BSA and anaemia [21], which are comparable to our results. A study by Augustin et al. involving 90 patients compared the transfusion rates of patients with an eGFR of < 30 ml/min/1.73 m² BSA to a cohort of patients with normal renal function matched according to age, sex, and type of joint replacement. They also identified an increased risk of blood transfusion in patients with reduced renal function [22]. The influence of an eGFR of < 60 ml/min/1.73 m² BSA was also investigated in patients undergoing minimally invasive knee arthroplasty. Here, CKD proved to be an independent risk factor for blood transfusion, cardiovascular complications, and hospital re-admission within 30 days after discharge [23]. The specific influence of renal dysfunction in other areas of orthopaedic surgery is also being increasingly recognised and evaluated [24].

The results of our analysis are consistent with those of the aforementioned authors in that they presented evidence of a negative influence on the inpatient lengths of stay and transfusion rates. However, there are some relevant differences in their study designs that must be considered. To our knowledge, our analysis is the first multicentre study on this topic in Germany. Furthermore, we investigated a patient population with an eGFR of 15–45 ml/min/1.73 m² BSA, a range that has not yet been studied in detail for its effect on these factors. The other studies focussed on CKD, which was often defined as an eGFR < 60 ml/min/m² BSA [16, 20, 23] or an eGFR of < 30 ml/min/1.73 m² BSA [19, 22]. Our study design provided some significant advantages. First, the management of blood transfusions in our study population was performed according to a defined procedure, thus excluding the possibility of distorted results due to iatrogenic factors. Second, with an exclusion rate of only 1.6%, an almost complete dataset from two supra-regional clinics was available for evaluation. A third important point is that the patients were selected according to a relatively narrow set of criteria, i.e. only patients who were expected to have an overall low-risk profile were included. Therefore, the study cohort comprised only patients who had undergone elective joint replacement surgery followed by inpatient or, in a few cases, outpatient rehabilitation therapy. We excluded any patient who experienced postoperative complications requiring transfer to another department or hospital. If we had included patients with more severely reduced renal function or patients who had been transferred to other departments, we assume that the influence of CKD on the target parameters would have been much greater.

As with all retrospective analyses, our study has limitations. The risk analysis was based only on the parameters

available in our database and, therefore, we could not take many other known variables into consideration [13]. The patient's hospital length of stay in the hospital is, at best, a surrogate parameter indicating postoperative complications after elective joint replacement surgery. It does not necessarily provide any information about the individual factors that might have contributed to the prolonged stay. An elevated transfusion rate is certainly only one of many risk factors. Furthermore, at this point, we cannot provide any data about the long-term results of these surgeries or the patient outcomes. This information will be presented in future studies.

Conclusions

Reduced kidney function with an eGFR between 15 and 45 ml/min/1.73 m² BSA was identified as an independent risk factor for prolonged hospitalisation after elective total hip or knee replacement surgery. The data also suggest an elevated rate of blood transfusions in patients with reduced kidney function. In the future, these factors should be considered during pre- and perioperative medical care and in administrative planning.

Author Contributions CK collected the data and helped in drafting the manuscript. FPT designed the study, performed the statistical analyses, and drafted the manuscript. IL performed the data acquisition and conceived the study. SL conceived the study and helped in drafting the manuscript. MJ designed and conceived the study, and helped in drafting the manuscript. All authors have read and approved the final manuscript. The authors CK and FPT contributed equally to the manuscript.

Compliance with Ethical Standards

Conflict of interest All of the authors declare that they have no conflict of interest.

Ethical approval All of the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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