



## Risk factors for renal dysfunction after total knee joint replacement

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Renal injury and dysfunction are serious complications after major surgery, which may lead to increased morbidity and mortality. The objective of our study was to identify the possible risk factors for renal dysfunction after total knee joint replacement. A retrospective study was conducted among 702 consecutive primary knee joint replacements performed between January 2009 and December 2012 in our department. Increased postoperative serum creatinine was considered indicative of postoperative renal injury according to RIFLE criteria. Sixty three patients (9.7%) had significant moderate or severe postoperative renal dysfunction in which 8 patients (1.2%) ended with severe and permanent renal impairment. Advanced age, low intraoperative blood pressure, hypertension, general anaesthesia, and prophylactic dicloxacillin were identified as significant risk factors. Male gender and BMI were independent risk factors for postoperative increase in serum creatinine. Smoking, female gender, diabetes mellitus and duration of surgery were not identified as significant risk factors.

**Keywords :** renal injury ; renal dysfunction ; joint arthroplasty ; risk factor ; knee.

venous thrombosis, infection, increased creatinine levels and impaired renal function (1,15). These complications may in turn increase mortality and morbidity among patients who are already affected by diseases such as diabetes mellitus, hypertension, heart diseases, and obesity (3,12,19,24). The aim of this study was to identify patients with renal injury after total knee joint replacement and to detect possible risk factors and their clinical relevance in our retrospective material of 702 consecutive total knee joint replacements. In recent years, a few studies identified renal impairment as a complication to be considered after major surgery (2,8,11,14,16).

To evaluate renal function various tests may be performed such as urine dipstick test, creatinine clearance test, glomerular filtration rate (GFR) and blood urea nitrogen test. Other forms of testing include urine protein and serum creatinine. In addition, imaging techniques such as Ultrasonography and CT scan may be used as needed.

### INTRODUCTION

Total knee joint replacement for osteoarthritis and rheumatoid arthritis is considered a safe routine operation in many orthopedic departments worldwide. The procedure is however not without possible complications (4,13,17,18) ; among them are deep

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Apart from the above mentioned factors (1,3,4,12, 13,15,17,18,19,24), the surgical trauma including blood loss and blood pressure changes during and after anaesthesia may influence renal function.

Renal injury is defined as sudden and abrupt loss of renal function resulting in increased serum creatinine. Renal failure is when the kidneys fail to adequately filter waste products from the blood ; it can be acute or chronic. The term renal failure has recently been replaced by renal insufficiency when in the context of chronic kidney disease.

### MATERIALS AND METHODS

A retrospective study was performed which included a consecutive cohort of patients who underwent primary knee joint replacement performed between January 2009 and December 2012. Indications for surgery were mainly primary osteoarthritis (n = 633), post-traumatic osteoarthritis (n = 57) and rheumatoid arthritis (n = 12). A total of 678 patients with 702 total knee joint replacements were obtained from our computerized database and hospital charts. 647 out of 702 total knee joint replacement surgeries had complete data sets according to our investigation criteria (Table I). The following variables were selected (8,16) : Age, sex, body mass index (BMI), hypertension, diabetes, smoking, American Society of Anesthesiologists physical status (ASA), prophylactic antibiotics according to our protocol (one dose immediately preoperatively and 3 doses in the first postoperative day), duration of surgery, type of anaesthesia, baseline systolic and diastolic blood pressure (BP), intra-operative systolic BP, and intra-operative diastolic BP (lowest measured blood pressure intra-operatively). Dicloxacillin was the drug of choice for prophylaxis according to the accepted alternative in the Philadelphia Consensus Guidelines.

Stefánsdóttir *et al* (21) documented that Dicloxacillin is the most used prophylactic antibiotic in joint replacement surgeries in Scandinavia due to high effectiveness against 99% of the *S. aureus* strains and 80% of the coagulase-negative *Staphylococcus* (CNS) strains colonizing patients undergoing primary total joint replacements (21). Cefuroxime was the alternative for patients allergic to penicillin.

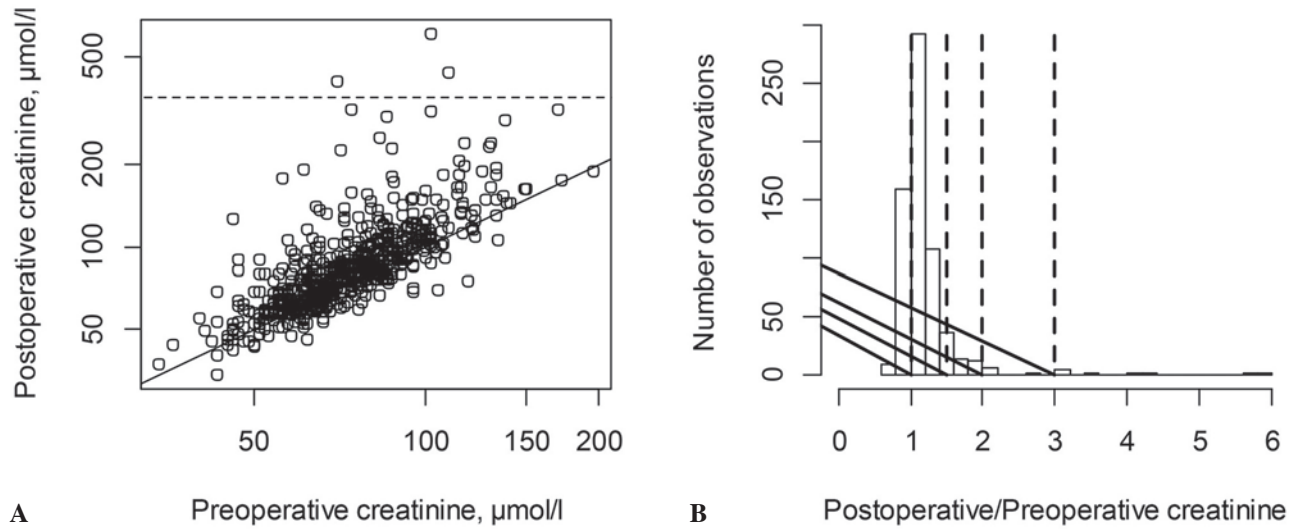
The following patients were not included due to missing data : 36 patients were missing intra-operative systolic and diastolic BP, 19 patients were missing postoperative serum creatinine measurements, 16 patients were missing BMI, two patients were missing baseline systolic and diastolic BP. However, they did not differ from the included patients regarding age, sex, preoperative creatinine, diabetes mellitus, hypertension, ASA scores, type of anaesthesia, prophylactic antibiotics and duration of surgery. In addition, two patients who were known to have severe renal dysfunction and were in hemodialysis were excluded as any new renal injury could not have been detected.

The protocol in our department for elective total knee joint replacement surgery includes measuring serum creatinine ; once preoperatively and three consecutive days postoperatively. In cases of an increase in postoperative serum creatinine, serum creatinine was controlled daily until it subsided or patients were referred to the nephrology department. The highest serum creatinine during the first postoperative week was chosen as a sign for maximum renal injury.

We used RIFLE classification proposed by the Acute Dialysis Quality Initiative Group to identify patients with renal impairment (2,11,14). The patients were divided accordingly into two groups ; those with RIFLE < 1.5 times increase in serum creatinine where renal impairment is absent or mild, and those with RIFLE ≥ 1.5 times increase in serum creatinine indicating moderate or severe

Table I. — Variables examined as risk factors for renal dysfunction after total knee joint replacement

1. Age	10. Smoking
2. Gender	11. Prophylactic antibiotics (Dicloxacillin)
3. ASA score	12. Prophylactic antibiotics (cefuroxime)
4. BMI	13. Preoperative S. Creatinine or preexisting renal dysfunction
5. Duration of surgery	14. Postoperative S. Creatinine
6. Hypertension	15. Baseline systolic blood pressure
7. Diabetes mellitus	16. Baseline diastolic blood pressure
8. Type of anaesthesia (Universal)	17. Intra-operative systolic blood pressure
9. Type of anaesthesia (Spinal)	18. Intra-operative diastolic blood pressure



**Fig. 1.** — **A** : XY plot of preoperative versus postoperative serum creatinine. The patients had a mean increase in postoperative serum creatinine of 8  $\mu\text{mol/l}$  (0.0-15.4, 95% confidence interval on the difference,  $p = 0.05$  paired T-test). The diagonal line depicts no change. The broken line is set at the limit of 355  $\mu\text{mol/l}$  (see table II). The normal range for women is 50-90  $\mu\text{mol/l}$  and for men 60-105  $\mu\text{mol/l}$ . **B** : Histogram of relative change in serum creatinine. The mean relative change was 1.2. The vertical broken lines depict 1 = no change, 1.5, 2 and 3 according to the RIFLE classification.

Table II. — The RIFLE Classification

	GFR Criteria	Urine Output Criteria
Risk	SCr increased 1.5 times	0.5 mL (kg h) for 6 h
Injury	SCr increased 2.0 times	0.5 mL (kg h) for 12 h
Failure	SCr increased 3.0 times or creatinine = 355 $\mu\text{mol/L}$ when there was an acute rise of > 44 $\mu\text{mol/L}$	0.3 mL (kg h) for 24 h or anuria for 12 h
Loss	Persistent ARF ; complete loss of kidney function for > 4 wk	
End-stage renal disease	End-stage renal disease for > 3 months	

renal impairment (Table II). Pre-renal failure is defined as sudden loss of blood flow to the kidneys resulting in kidney hypo-perfusion without tissue damage in the kidney itself. When there is tissue damage in the kidneys this will lead to either acute or chronic renal failure. It is not possible to distinguish whether the changes in the kidneys were caused by pre-renal factors or renal tissue damage using serum creatinine, as done in this study.

For statistical analysis, the R software was used (www.r-project.org). For the continuous variables the Welch two-sample t-test was used and for the categorical variables the Pearson's Chi-squared test with Yates' correction or Fisher's Exact test for Count Data was used. The paired T-test was used as indicated – multivariate linear regression modeling was performed and stepwise

model reduction was done using an automated algorithm minimizing the AIC Value (Akaike's Information Criterion).

## RESULTS

During the study period, 63 out of 647 patients had significant moderate or severe renal impairment resulting in an overall incidence of 9.7% (RIFLE  $\geq 1.5$ ) (Table III).

Fifty patients (7.7%) had RIFLE 1.5-2, 8 patients (1.23%) had RIFLE 2-3, and 10 patients (1.54%) had RIFLE  $\geq 3$ . Out of these 63 patients, 55 improved but 8 patients ended with severe and

Table III. — The variables advanced age, systolic hypotension intra-operatively, pre-operative hypertension treatment, higher ASA scores and prophylactic intravenous Dicloxacillin revealed significant postoperative renal dysfunction. Patients not receiving Dicloxacillin pre-operatively were given cefuroxime

Variables	Rifle < 1.5 n = 584	Rifle ≥ 1.5 n = 63	p-value	Test
Mean age	69 (Range 37-93)	73 (Range 49-91)	0.002*	T
Mean BMI	29 (Range 17-48)	29 (Range 20-41)	0.56	T
Duration of Surgery (minutes)	81 (Range 43-180)	77 (Range 45-180)	0.17	T
Baseline systolic BP	150 (Range 90-225)	153 (Range 111-200)	0.39	T
Baseline diastolic BP	86 (Range 46-114)	85 (Range 59-114)	0.30	T
Intra-operative systolic BP	95 (Range 60-150)	91 (Range 65-130)	0.03*	T
Intra-operative diastolic BP	54 (Range 30-90)	52 (Range 35-75)	0.17	T
General anaesthesia	381 yes/50 no	50 yes/13 no	0.03*	C
Gender	242M/342F	28M/35F	0.7	C
Smoking	486 No/98 Yes	48 No/15 Yes	0.2	C
Hypertensive patients	362	49	0.02*	C
Normotensive patients	219	14		
Diabetes Mellitus	527 No/57 Yes	53 No/10 Yes	0.19	C
ASA score 1	111	8	0.02*	C
ASA score 2	410	42		
ASA score 3	63	13		
Dicloxacillin	40 No/ 544 Yes	0 No/63 Yes	0.03*	F

T = Welch two sample test, C = Chi square test, F = Fisher exact test.

permanent renal impairment (i.e. in dialysis) with an incidence of 1.2%. These 63 patients were followed for at least one year postoperatively.

As shown in table III, advanced age, low intra-operative systolic BP, hypertension, high ASA scores and choosing prophylactic Dicloxacillin were significant risk factors for renal impairment after total knee joint replacement on univariate analysis.

Generalized multivariate modeling was performed using the relative changes in serum creatinine as a dependent variable. It confirmed that advanced age, hypertension, general anaesthesia, low intra-operative BP and prophylactic Dicloxacillin were significant risk factors. In addition, male gender and BMI were significant independent risk factors for a rise in serum creatinine.

Smoking, female gender, diabetes mellitus and duration of surgery were not significant risk factors.

## DISCUSSION

Acute postoperative renal dysfunction may increase hospital stay, morbidity, mortality and cost (5). To date, preventative strategies are the only effective measures to reduce morbidity in cases of postoperative renal dysfunction (5). In order to influence our guidelines, it is vital to detect significant risk factors for the development of renal dysfunction after total knee joint replacement.

Our study has some limitations worth mentioning. Firstly, the study design is retrospective using data as registered in the medical records. Secondly, we had no record of the actual fluid input and output which could have potential influence on renal function. Lastly, data was incomplete in 53 patients and they therefore were excluded from the study. Theoretically, this could have influenced our results.

In accordance with Abelha *et al* (1), Mantilla *et al* (13), Nergelius *et al* (15) and Parvizi *et al* (17) we found increased age as an independent risk factor for renal dysfunction after major surgery. However, Sharrock *et al* (19) was not able to confirm the age factor in this regard, may be due to the relatively small number of patients included in the study.

Naik *et al* (14) and Nergelius *et al* (15) confirmed our finding that patients with hypertensive disease (under treatment) had a significant increase in risk for renal impairment.

Our patients received either general anaesthesia (n = 455) or spinal anaesthesia (n = 228). General anaesthesia was an independent risk factor for the development of renal dysfunction postoperatively. The type of anaesthesia was chosen at the discretion of the attending anesthesiologist after individual clinical assessment of the patient. Thus, this observation could have been due to confounding by indication. Jafari *et al* (8) could not confirm this finding – perhaps due to inadequate data regarding the number of patients who received general anaesthesia or other forms of anaesthesia.

Low intraoperative blood pressure was encountered under general and spinal anaesthesia as expected resulting in a decrease of renal blood flow, thus was considered as a significant risk factor (Table III) for pre-renal failure (8).

Several authors (3,8,17,24) have shown high BMI as an independent risk factor following joint replacement surgery. In our study, a p value of 0.049

was found (Table IV) which confirmed the earlier findings. Abelha *et al* (1) could not identify BMI as an independent risk factor. This conclusion was perhaps due to the included population having a lower BMI of 22-28 than our patients with a BMI of 17-48.

Our patients received prophylactic antibiotics in the form of either Dicloxacillin (n = 652) or cefuroxime (n = 41). Those receiving the former had a significant increased risk of renal impairment. Isacson and Collert (7), Solgaard *et al* (20) concluded the same results in their respective studies. This may warrant a change in the use of Dicloxacillin as a prophylactic antibiotic. Dicloxacillin was chosen as the routine drug of choice according to the local spectrum of bacteria. Cefuroxime was considered to have a higher risk of inducing bacterial resistance and possibly more prone to induce intestinal infection with *Clostridium difficile* (23,25).

The ASA score was an independently significant risk factor for the development of renal impairment (Table III), which corresponds to the findings of Abelha *et al* (1), Belmont *et al* (3), Jafari *et al* (8) and Parvizi *et al* (17).

Male gender was found to be an independent increased risk for renal impairment. Male patients were analysed and found to be older with an increased rate of smoking compared to the female gender. The males required longer surgery time whereas the females required a relatively shorter surgery time. Additionally, the male gender had a

Table IV. — Model output after stepwise reduction. The dependent variable was the relative change in serum creatinine defined as post-operative creatinine/pre-operative creatinine (data shown in figure 1)

	Estimate	Std. error	P-value
Intercept	0.3747324	0.2258781	0.098
Age	0.0051939	0.0019364	0.00750**
Gender male	0.0767590	0.0348524	0.02799*
BMI	0.0077107	0.0039147	0.04930*
Smoking	0.0672324	0.0466922	0.15038
Hypertension	0.1062243	0.0363956	0.00364**
General anaesthesia	0.1028394	0.0360408	0.00446**
Dicloxacillin	0.1716705	0.0707266	0.01549*
Duration of surgery	-0.0014397	0.0009004	0.11032

higher degree of diabetes mellitus and hypertensive disease to which may have increased their risk for renal impairment. Jepsen *et al* (10) discussed confounding factors which may be associated with the outcome of being at a higher risk. It has been shown in several epidemiological studies that men tend to seek medical assistance at a later stage than women (6,9,22).

This study was conducted on a group of patients who underwent total knee joint replacement after exhausting the conservative treatment options. Joint replacement surgery entails well documented complications ; some of which may be serious but preventable such as renal dysfunction. The guidelines for performing this kind of surgery should be improved including a meticulous control of blood pressure before and during surgery, a good preoperative assessment by the anaesthesiologist, and choosing the safest possible prophylactic antibiotic according to individual assessment of the patient's risk factors.

In accordance with this study, risk of renal dysfunction after knee replacement surgery is a serious complication that should be taken into consideration when informing the patients preoperatively and when choosing antibiotic prophylaxis. In addition, meticulous blood pressure control during surgery will optimize pre-renal blood flow and kidney function. In patients with renal impairment preoperatively, the optimal choice of antibiotics and other necessary medication is vital for maximum renal protection.

### CONCLUSION

Our study, in accordance with other studies confirms increased risk of renal injury after total knee joint replacement surgery. These findings may warrant a change in the protocol for informed consent as well as preoperative preparation protocols. Risk of renal impairment may have to be included in the preoperative information given to patients intended for total knee joint replacement. High-risk patients (advanced age, high BMI, hypertensive disease and high ASA scores) should possibly be identified early for further optimization pre-and intra-operatively.

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