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Acute kidney injury following primary hip and knee arthroplasty surgery

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ABSTRACT

Acute kidney injury (AKI) is a recognised postoperative complication following primary hip/knee arthroplasty surgery. The aim of this study was to determine causative and potentially modifiable risk factors associated with postoperative AKI. Standard data were collected for 413 consecutive arthroplasty patients, both retrospectively and prospectively. Univariate and multivariate analyses were performed to identify any potential causative factors.

Eight percent of patients developed postoperative AKI. Univariate analysis found increasing age, history of previous chronic kidney disease and requirement for postoperative intravenous fluids to be risk factors for AKI. The multivariate regression analysis model identified age and volume of postoperative fluid prescription as predictive of postoperative AKI. Antibiotic regime and prescription of non-steroidal anti-inflammatory drugs had no significant effect on the risk of AKI. No patients required dialysis but length of stay increased by 50% in the AKI group.

Postoperative AKI may result in significant postoperative morbidity and increased length of stay, and may necessitate invasive therapies such as dialysis. Episodes of AKI could also predispose to future similar episodes and are associated with a long-term decrease in baseline renal function. This study has demonstrated that the identified risk factors are generally non-modifiable. Further work is suggested to determine whether targeted interventions in high risk patients would reduce the incidence of AKI.

KEYWORDS

Acute kidney injury – Arthroplasty – Knee – Hip

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The Scottish Arthroplasty Project (SAP) collects data and reports outcomes following major joint arthroplasty surgery in Scotland. These data have identified a persistent increase in prevalence of acute kidney injury (AKI) following hip and knee arthroplasty. Over the period 2004–2013, the prevalence of postoperative AKI increased from 0.47% to 0.78% following total hip arthroplasty and from 0.39% to 0.75% following total knee arthroplasty.[1]

AKI is associated with increased patient morbidity and mortality after hospital surgery and hospital admission.[2–5] Following coronary artery bypass surgery, AKI has been shown to increase 90-day mortality.[6] Ponte *et al* demonstrated that even in the absence of pre-existing renal disease, an episode of AKI was a risk factor for future renal dysfunction.[7] At ten years, 61% of such patients demonstrated some degree of chronic renal impairment.

The classification of AKI has been refined over the last decade, with the KDIGO (Kidney Disease: Improving Global Outcomes) classification being widely adopted both as a research and clinical definition. KDIGO defines AKI as: a rise in serum creatinine of ≥26.5µmol/l over 48 hours; or a rise in serum creatinine of ≥50% over ≤7 days; or a urine volume of <0.5ml/kg/h for 6 hours.[8] However, even a 25% increase in creatinine has been identified as a poor prognostic indicator. In a meta-analysis, Coca *et al* found a higher relative risk of death with an increase in serum creatinine of 25% from baseline.[9] The aims of our study were to investigate the prevalence of AKI following primary hip and knee arthroplasty, and to identify any causative factors and high risk individuals where the risk of AKI may be altered by appropriate interventions.

Methods

This study was reviewing existing care and did not involve altering patient management. As an evaluation of an existing service, it did not require ethical approval.

Data were collected from a consecutive series of patients undergoing primary hip/knee arthroplasty between October 2013 and October 2014. Patients undergoing revision procedures, unicompartmental or patellofemoral joint arthroplasty procedures were excluded. Data were obtained from hospital preoperative assessment records, medical records and the laboratory database. Preoperative renal impairment was defined as a reduced estimated glomerular filtration rate of <60ml/min/1.73m^2 or serum creatinine of >120µmol/l. Data were collected retrospectively for patients undergoing surgery between October 2013 and August 2014, and

prospectively thereafter. Data were 100% complete for both groups.

All primary total knee replacements were performed using cemented implants (Vanguard®, Biomet, Warsaw, IN, US; and PFC®, DePuy, Warsaw, IN, US) with a tourniquet. Tranexamic acid (1g) was given routinely. For primary total hip arthroplasty, the standard implant was the cemented Exeter™ stem (Stryker, Kalamazoo, MI, US) using Refobacin® cement (Biomet; 1g gentamicin per 40g mix) for patients with cemented/uncemented acetabular components depending on age and pathology. Two differing antibiotic regimens were in use at the surgeon's discretion: teicoplanin 400mg/gentamicin 3mg/kg ideal body weight as a single bolus dose following induction or cefuroxime 1.5g as a single bolus dose on induction.

In recent years, there has been a move towards enhanced recovery after surgery (ERAS), which is now standard practice following arthroplasty for all elective orthopaedic hospitals in Scotland. One of the tenets of ERAS protocols is early mobilisation and the commencement of oral fluid intake as soon as possible following surgery, which has led to reduced use of intravenous fluid administration.

Spinal anaesthesia was the preferred anaesthetic technique, with general anaesthesia with/without a regional block being the alternative in cases of failed or contraindicated spinal anaesthesia. The ERAS protocol involves admitting patients on the day of surgery, minimising postoperative medical intervention and encouraging early mobilisation. For this reason, urethral catheterisation is not used routinely and is only performed for cases of urinary retention or for monitoring of urine output in high risk patients.

For the purposes of this study, AKI was defined as a rise in serum creatinine of >50% from baseline.[8] The KDIGO classification's criterion of an increment of ≥26.5µmol/l over 48 hours was not used as part of the definition since this may be misleading in the perioperative period owing to the dilutional effects of crystalloid infusions. Urine volumes were not documented reliably and so were not used to identify AKI. This is a consequence of not routinely catheterising patients in the immediate postoperative period.

Baseline serum creatinine was defined as the most recent value prior to surgery and was always measured within 21 days of the operation at the preoperative assessment clinic. The peak value was defined as the highest serum creatinine within seven days following surgery. Creatinine was assayed using the Jaffe method with Roche Modular P units (Roche Diagnostics, Basel, Switzerland) and calibrated to the UK National External Quality Assessment Service adjustment for isotope dilution mass spectrometry traceability.

Statistical analysis

Univariate analysis was performed with t-tests for interval level data and chi-squared tests for categorical data. Multivariate logistic regression was carried out using a model with backward elimination, with AKI as the dependent variable, and all the pre and postoperative variables that were significant in the univariate analysis as predictors. Both inclusion and removal criteria were set using a p-value of 0.05.

Results

A total of 413 patients were included in the study. The cohort demographic and characteristics are presented in Table 1. Postoperative AKI (rise in serum creatinine of >50% from baseline) affected 34 patients (8.2%). Ninety-six patients (23.2%) had an increase in creatinine of >25% from baseline.

Univariate analysis of a number of previously reported preoperative risk factors[10,11] for AKI (Table 2) identified a significantly higher mean age for patients who developed AKI compared with those who did not (71 vs 66 years, p=0.009). In those patients who had biochemical evidence of pre-existing renal impairment prior to surgery (n=52, 12.6%), a higher prevalence of postoperative AKI was observed (9/52 [17.3%] vs 25/361 [6.9%]). There was no statistically significant difference with regard to the other preoperative risk factors analysed, which comprised patient sex, diabetes mellitus, angiotensin converting enzyme inhibitor (ACEi)/angiotensin receptor blocker (ARB) use, non-steroidal anti-inflammatory drugs (NSAIDs) and diuretic use.

The results for the univariate analysis of intra and postoperative risk factors are summarised in Table 3. In terms of intravenous fluid use in the first 24 hours following surgery,

Table 1 Preoperative characteristics of patients undergoing primary arthroplasty (n=413)

Characteristics		n
Mean age in years: 66.5 (SD: 10.8, range: 21–89)		
Sex	Male	166 (40.7%)
	Female	245 (59.3%)
Procedure	Hip replacement	187 (45.3%)
	Knee replacement	226 (54.7%)
Preoperative renal impairment	Total	52 (12.6%)
	eGFR <60ml/min/1.73m^2	39 (9.4%)
	Creatinine >120µmol/l	13 (3.1%)
Diabetes mellitus		58 (14.0%)
ACEis/ARBs		150 (36.3%)
NSAIDs		136 (32.9%)
Diuretics	Total	95 (23.0%)
	Loop	35 (8.5%)
	Thiazide	56 (13.6%)
	Potassium sparing	4 (1.0%)

ACEis = angiotensin converting enzyme inhibitors; ARBs = angiotensin receptor blockers; eGFR = estimated glomerular filtration rate; NSAIDs = non-steroidal anti-inflammatory drugs; SD = standard deviation

Table 2 Univariate analysis of preoperative risk factors

Characteristics	With AKI (*n*=34)	AKI prevalence	*p*-value	Mean difference / odds ratio (95% CI)
Mean age in years With AKI (*n*=34): 71.1 (SD: 10.4) No AKI (*n*=379): 66.1 (SD: 10.8)			**0.009***	0.5 (0.1–0.9)
Sex	Male (15/168)	8.9%	0.67**	
	Female (19/245)	7.8%		
Preoperative renal impairment	No (25/361)	6.9%	**0.025*****	2.8 (1.2–6.4)
	Yes (9/52)	17.3%		
Diabetes mellitus	No (29/355)	8.2%	0.80***	
	Yes (5/58)	8.6%		
ACEis/ARBs	No (19/263)	7.2%	0.32**	
	Yes (15/150)	10.0%		
NSAIDs	No (22/276)	8.0%	0.78**	
	Yes (12/137)	8.8%		
Diuretics	No (26/318)	8.2%	0.99**	
	Loop (3/35)	8.6%		
	Thiazide / potassium sparing (5/60)	8.3%		

ACEis = angiotensin converting enzyme inhibitor; AKI = acute kidney injury; ARBs = angiotensin receptor blocker; CI = confidence interval; NSAIDs = non-steroidal anti-inflammatory drugs; SD = standard deviation
*t-test; **chi-squared test; ***Fisher's exact test

those patients who received a small amount (<1l) were less likely to develop AKI than those who received more than a litre (22/339 [6.5%] vs 12/74 [16.2%], p=0.006). The remaining risk factors analysed (type of procedure [hip/knee], intraoperative fluid volume, NSAIDs, antibiotics, tranexamic acid and transfusion) did not appear to have a significant effect on the risk of AKI.

A multivariate logistic model (Table 4) identified that age (in decades) and the requirement for more than a litre of postoperative fluids were significant predictors of postoperative AKI. Every extra decade in age increased the odds ratio of postoperative AKI by 1.62. The use of more than a litre of postoperative fluids increased the odds of AKI by 2.71. However, the fit of this model was poor (Nagelkerke R^2=0.07).

The median length of stay increased by 50% (4 days [range: 2–20 days] vs 6 days [range: 3–12 days]) for those patients who developed AKI (50% increase in creatinine from baseline) (p<0.001). For those patients who experienced a rise of 25% from baseline, the median length of stay increased from 4 to 5 days.

Discussion

In this observational study of AKI following primary hip/knee arthroplasty at a single centre, a substantially higher rate of AKI has been demonstrated than that reported by SAP (8.2% vs 0.8%).[1] SAP identifies AKI cases based on diagnostic coding (International Classification of Diseases codes N17 or N19). The data are therefore open to errors arising from the methods used to identify and code for instances of renal impairment. This suggests that significant underreporting and a lack of awareness may exist regarding the prevalence of AKI following arthroplasty.

It is important in terms of informed consent that all major complications of surgery are discussed. If the results of this study are consistent with those from other units throughout the UK, then the risk of AKI and its future implications should be considered at the time of the patient giving consent as it may be the single most common complication following arthroplasty.

Our study was based on laboratory data and will therefore be more accurate than data from SAP. Our findings suggest marked underascertainment in the SAP audit. SAP has reported an increasing incidence of AKI following arthroplasty from 2004 to 2013.[1] Given our data, this may be explained in part by ascertainment bias and illustrates the importance of using laboratory-based case finding in future audits.

In univariate analysis, the risk factors associated with higher rates of postoperative AKI were age, pre-existing chronic kidney disease and administration of more than a litre of postoperative intravenous fluids. There was no increase in incidence of AKI with the use of gentamicin/teicoplanin prophylaxis when compared with cefuroxime. Furthermore, the use of preoperative or postoperative NSAIDs was not shown to be significantly higher in the AKI group. After multivariate analysis, only age and volume of postoperative fluids remained as significant predictors of AKI.

Table 3 Univariate analysis of intra/postoperative risk factors

Characteristics	With AKI (*n*=34)	AKI prevalence	*p*-value	Odds ratio (95% CI)
Procedure	Hip (20/187)	10.7%	0.10*	1.8 (0.9–3.7)
	Knee (14/226)	6.2%		
Intraoperative fluids	<1l (20/211)	9.5%	0.54*	
	1–2l (9/145)	6.2%		
	>2l (5/57)	8.8%		
Intraoperative NSAIDs	No (33/370)	8.9%	0.24**	
	Yes (1/43)	2.3%		
Antibiotics	Teicoplanin/gentamicin or other (19/202)	9.4%	0.40*	
	Cefuroxime (15/211)	7.1%		
Tranexamic acid	No (3/28)	10.7%	0.62*	
	Yes (31/385)	8.1%		
Transfusion	No (32/387)	8.3%	0.92*	
	Yes (2/26)	7.7%		
Postoperative fluids	No / <1l (22/339)	6.5%	**0.006***	2.8 (1.3–5.9)
	>1l (12/74)	16.2%		
Postoperative NSAIDs	No / stopped preoperatively (23/263)	8.7%	0.54**	
	Yes (continued preoperative NSAID) (6/82)	7.3%		
	Yes (commenced new NSAID) (3/56)	5.4%		
	Yes (continued preoperative NSAID + commenced new NSAID) (2/12)	16.7%		

AKI = acute kidney injury; CI = confidence interval; NSAID = non-steroidal anti-inflammatory drug
*chi-squared test; **Fisher's exact test

Table 4 Multivariate regression analysis

	B	*p*-value	Exp(B) (95% CI)
Age in decades	0.48 ±0.19	**0.012**	1.62 (1.11–2.35)
>1l postoperative fluids	1.00 ±0.39	**0.011**	2.71 (1.26–5.82)
Constant	–5.95 ±1.37	0.000	0.003

CI = confidence interval

This study was observational and so it is only possible to demonstrate association rather than causation. For example, the patients who received more than a litre of postoperative fluids had an AKI rate of 16.2% compared with 6.5% for the group receiving a smaller amount. This possibly reflects treatment bias with patients who were thought more likely to develop AKI (from a history of pre-existing disease) receiving more intravenous fluids postoperatively. Treatment bias may also explain the lack of association of ACEi/ARB use and NSAIDs with the development of AKI. Pharmacodynamic arguments would suggest caution in the co-prescription of both ACEis/ARBs and NSAIDs as this profoundly inhibits the kidneys' ability to respond to hypotension or hypoperfusion. In the majority of cases, ACEi/ARB use would be stopped prior to surgery and NSAIDs avoided where possible if a risk of renal impairment was considered likely.

A number of case-controlled[10–16] and observational cohort studies[17–19] have previously examined risk factors for AKI following arthroplasty surgery. These include older age,[17] male sex,[18] higher body mass index,[10–12,19] increased weight,[13] preoperative renal impairment,[10,17] chronic obstructive pulmonary disease,[10] liver disease,[10,16] cardiac disease,[10,19] solid organ transplantation,[13] hypertension[10] or number of hypertension medications,[11] diabetes mellitus,[11] cerebrovascular or peripheral vascular disease,[11] ACEi/ARB

use[18,19] and use of postoperative NSAIDs.[17] Others have also noted associations with general anaesthesia,[11] blood transfusion,[11,20] antibiotic irrigation,[20] antibiotic spacers[21] and antibiotic cement.[22]

A variety of treatment related factors have been identified as being associated with AKI. Antimicrobial stewardship guidance led many departments to move away from cephalosporins because of the increased risk of *Clostridium difficile* infection. However, it has been shown that some alternative regimens such as flucloxacillin and gentamicin are associated with increased incidence of AKI[18,23–25] as a result of interstitial nephritis. In our study, there was no increased incidence of AKI with gentamicin/teicoplanin compared with cefuroxime.

In our unit, an enhanced recovery programme is employed for patients undergoing elective lower limb arthroplasty. The purpose is to encourage mobilisation as early as possible. Consequently, patients currently receive less intravenous fluid than prior to the adoption of this technique. One concern would be that this may be associated with an increased risk of postoperative AKI. In this study, 72% of patients received no intravenous fluids postoperatively. Patients with low volumes of intravenous fluids (<1l) had a lower rate of AKI than those who received more (>1l) as well as those who received no fluids. Although the number of patients was small, this warrants further investigation.

Development of AKI is a known risk factor for future renal disease. Ponte *et al* performed a retrospective follow-up review of over 180 patients who had developed AKI during their hospital stay.[7] Only 46% had recovered their previous levels of renal function at ten years. Ishani *et al* demonstrated that an episode of AKI in elderly patients is a risk factor for future end stage renal failure.[26] AKI has immediate consequences in terms of morbidity and increased in length of hospital stay. In addition, it also has long-term repercussions with regard to future renal disease.

The development of AKI was associated with a 50% increase in the length of stay following arthroplasty surgery. In Scotland, over 14,000 primary hip and knee arthroplasties are undertaken annually. In 2013 the mean length of stay for these procedures was 5 days, and the rate of renal failure was 0.8% for both hip and knee replacements.[1] This equates to almost 120 patients each year whose length of stay may have been increased as a consequence of AKI. Preventing AKI could result in significant savings for the National Health Service by reducing potentially avoidable inpatient days.

Conclusions

In our representative cohort of primary hip/knee arthroplasty patients, 8.2% developed AKI in the perioperative period. The most significant factor predicting AKI was age. It appears that SAP, which records complications following arthroplasty surgery, significantly underreports the incidence of AKI as a postoperative complication. It is essential that future national audits use laboratory-based case finding of AKI rather than coded reporting. This has important implications regarding informed consent of patients who choose to undergo primary hip/knee replacement surgery. AKI is a multifactorial pathology. Further study is required to identify how addressing multiple risk factors proactively may limit the prevalence of this condition.

References

1. Scottish Arthroplasty Project. *Biennial Report 2014*. Edinburgh: NHS National Services Scotland; 2014.
2. Levy EM, Viscoli CM, Horwitz RI. The effect of acute renal failure on mortality. A cohort analysis. *JAMA* 1996; **275**: 1,489–1,494.
3. Chertow GM, Burdick E, Honour M *et al*. Acute kidney injury, mortality, length of stay, and costs in hospitalized patients. *J Am Soc Nephrol* 2005; **16**: 3,365–3,370.
4. Thakar CV, Christianson A, Freyberg R *et al*. Incidence and outcomes of acute kidney injury in intensive care units: a Veterans Administration study. *Crit Care Med* 2009; **37**: 2,552–2,558.
5. Joannidis M, Metnitz B, Bauer P *et al*. Acute kidney injury in critically ill patients classified by AKIN versus RIFLE using the SAPS 3 database. *Intensive Care Med* 2009; **35**: 1,692–1,702.
6. Brown JR, Cochran RP, Dacey LJ *et al*. Perioperative increases in serum creatinine are predictive of increased 90-day mortality after coronary artery bypass graft surgery. *Circulation* 2006; **114(1 Suppl)**: I-409–I-413.
7. Ponte B, Felipe C, Muriel A *et al*. Long-term functional evolution after an acute kidney injury: a 10-year study. *Nephrol Dial Transplant* 2008; **23**: 3,859–3,866.
8. Kidney Disease: Improving Global Outcomes. Section 2: AKI definition. *Kidney Int Suppl* 2012; **2**: 19–36.
9. Coca SG, Peixoto AJ, Garg AX *et al*. The prognostic importance of a small acute decrement in kidney function in hospitalized patients: a systematic review and meta-analysis. *Am J Kidney Dis* 2007; **50**: 712–720.
10. Jafari SM, Huang R, Joshi A *et al*. Renal impairment following total joint arthroplasty: who is at risk? *J Arthroplasty* 2010; **25(6 Suppl)**: 49–53.
11. Weingarten TN, Gurrieri C, Jarett PD *et al*. Acute kidney injury following total joint arthroplasty: retrospective analysis. *Can J Anaesth* 2012; **59**: 1,111–1,118.
12. Kelz RR, Reinke CE, Zubizarreta JR *et al*. Acute kidney injury, renal function, and the elderly obese surgical patient: a matched case-control study. *Ann Surg* 2013; **258**: 359–363.
13. Li X, Guo D, Shi G *et al*. Role of total hip replacement arthroplasty between transplantation and acute kidney injury. *Ren Fail* 2014; **36**: 899–903.
14. Luo X, Jiang L, Du B *et al*. A comparison of different diagnostic criteria of acute kidney injury in critically ill patients. *Crit Care* 2014; **18**: R144.
15. Fujii T, Uchino S, Takinami M, Bellomo R. Validation of the Kidney Disease: Improving Global Outcomes criteria for AKI and comparison of three criteria in hospitalized patients. *Clin J Am Soc Nephrol* 2014; **9**: 848–854.
16. Deleuran T, Vilstrup H, Overgaard S, Jepsen P. Cirrhosis patients have increased risk of complications after hip or knee arthroplasty. *Acta Orthop* 2015; **86**: 108–113.
17. Aveline C, Leroux A, Vautier P *et al*. Risk factors for renal dysfunction after total hip arthroplasty. *Ann Fr Anesth Reanim* 2009; **28**: 728–734.
18. Challagundla SR, Knox D, Hawkins A *et al*. Renal impairment after high-dose flucloxacillin and single-dose gentamicin prophylaxis in patients undergoing elective hip and knee replacement. *Nephrol Dial Transplant* 2013; **28**: 612–619.
19. Nielson E, Hennrikus E, Lehman E, Mets B. Angiotensin axis blockade, hypotension, and acute kidney injury in elective major orthopedic surgery. *J Hosp Med* 2014; **9**: 283–288.
20. Gelman ML, Frazier CH, Chandler HP. Acute renal failure after total hip replacement. *J Bone Joint Surg Am* 1979; **61**: 657–660.
21. Luu A, Syed F, Raman G *et al*. Two-stage arthroplasty for prosthetic joint infection: a systematic review of acute kidney injury, systemic toxicity and infection control. *J Arthroplasty* 2013; **28**: 1,490–1,498.
22. Lau BP, Kumar VP. Acute kidney injury (AKI) with the use of antibiotic-impregnated bone cement in primary total knee arthroplasty. *Ann Acad Med Singapore* 2013; **42**: 692–695.
23. Ross AD, Boscainos PJ, Malhas A, Wigderowitz C. Peri-operative renal morbidity secondary to gentamicin and flucloxacillin chemoprophylaxis for hip and knee arthroplasty. *Scott Med J* 2013; **58**: 209–212.

24. Bailey O, Torkington MS, Anthony I *et al*. Antibiotic-related acute kidney injury in patients undergoing elective joint replacement. *Bone Joint J* 2014; **96**: 395–398.
25. Craxford S, Bayley E, Needoff M. Antibiotic-associated complications following lower limb arthroplasty: a comparison of two prophylactic regimes. *Eur J Orthop Surg Traumatol* 2014; **24**: 539–543.
26. Ishani A, Xue JL, Himmelfarb J *et al*. Acute kidney injury increases risk of ESRD among elderly. *J Am Soc Nephrol* 2009; **20**: 223–228.