

## Acute kidney injury following hip fracture

## **Abstract**

**Background:** Hip fracture causes disability and excess mortality in the aging population. Acute kidney injury (AKI), is known to diminish survival of critically ill and trauma patients. AKI is also a common perioperative complication among surgical patients. We examined the effect of AKI on the survival of hip fracture patients in a Finnish hip fracture population and the risk factors for AKI in a prospective study.

**Methods:** The study cohort constituted of 486 consecutive low-energy trauma hip fracture patients referred to Satakunta Central Hospital (Pori, Finland) and Turku University Hospital (Turku, Finland). The patients underwent standard diagnostics and treatment in the emergency department (ER) and were operated according to the local treatment protocol. Serum creatinine (sCr) was analyzed daily pre- and post-operatively during the hospital stay. Patients were divided into groups; AKI and non-AKI based on Kidney Disease: Improving Global Outcomes (KDIGO) criteria.

**Results:** The incidence of AKI in the study cohort was 8.4 % (40/475). Eleven patients were excluded due to missing sCr data. The baseline characteristics of AKI and non-AKI groups differed significantly concerning baseline sCr but were otherwise similar. At 90-day follow-up, the overall mortality was 14.4 %. Patients with AKI had a significantly higher mortality (35.0 %) than those with no AKI (12.7 %) ( $p < 0.001$ ). Dementia, preoperative sCr and any stage of AKI were independent predictors for mortality. Dementia and preoperative sCr were independently associated with post-operative AKI.

**Conclusion:** In this study AKI was a significant factor associated with a 3 -fold mortality during the first three months after surgery for low-energy trauma hip fracture.

**Keywords:** hip fracture, acute kidney injury, AKI, mortality, incidence

## **Introduction**

Hip fracture is a major challenge in the aging population [1,2] causing disability and excess mortality [3,4]. Despite its declining incidence during recent years, survival after hip fracture has not shown any improvement [5]. While the excess mortality following hip fracture is well described in the literature [1,6] its reasons, however, remain largely unclear.

Acute kidney injury (AKI), previously called acute renal failure, has been broadly studied among critically ill [7–9] and trauma patients [10–13] and it is known to diminish survival significantly. Acute kidney injury is also a common perioperative complication in surgical patients [14–16]. While acute kidney injury has been well studied in elective orthopaedic patients [17–20] there are only few small studies concerning low-energy hip fracture patients [21–24].

In 2012, the Kidney Disease: Improving Global Outcomes (KDIGO) completed international, clinical practice guideline for AKI, which covers AKI definitions, risk assessment, evaluation, prevention, and treatment. The serum creatinine criteria for the onset of AKI are a serum creatinine (sCr) rise of  $26\mu\text{mol/L}$  or more in 48 hours or a rise in sCr levels to 1,5-fold from baseline in a week (Table 1) [25].

We aimed to determine the effect of AKI on the survival of hip fracture patients in a Finnish hip fracture population in a prospective study. We assumed that patients developing AKI will do worse than patients without AKI. Secondary outcomes were the incidence of AKI and possible predictive factors for AKI.

## **Materials and Methods**

A cohort of consecutive low-trauma hip fracture patients referred to Satakunta Central Hospital (Pori Finland) during a period from February 2017 to January 2018 and to Turku University Hospital during a period from June 2017 to December 2018 was formed. All patients presenting in the emergency departments with hip fractures underwent standard diagnostics and treatment in the ER and were operated according to the local treatment protocol for different types of hip fractures under spinal anesthesia or general anesthesia. The only exception to the normal treatment protocols was that sCr was

analyzed more frequently during hospital stay. Exclusion criteria from the statistical analyses was missing pre- or post-operative serum creatinine data.

Demographic and medical history data were collected from electronic medical records. All relevant medical co-morbidities were recorded. These were categorized as heart and peripheral vascular disease (which included ischaemic heart disease, and vascular disease), cerebral vascular disease, diabetes mellitus, hypertension and dementia. A mentioning of an existing disease in the records was determined as a sufficient definition and used in the calculation of Charlson comorbidity index. sCr was recorded up till six days post-operatively or as long as patient stayed at medical centers. Using sCr we determined the occurrence of AKI using the KDIGO criteria and according to that, patients were divided into AKI and non-AKI groups. To determine risk factors for developing AKI, we recorded the mechanism of the trauma, type of the femoral fracture (collum, intertrochanteric or sub-trochanteric), operative treatment method, perioperative blood loss, duration of the operation, pre-operative serum sodium, potassium, hemoglobin, hematocrit, cardiac troponin, creatinine and post-operative serum hemoglobin, cardiac troponin and creatinine. All patients were followed up to three months and the three-month post-operative mortality was recorded.

### *Statistical analysis*

Between groups differences were assessed with Chi square test or Fisher's exact test for proportions and an independent samples T-test for continuous variables. Categorical variables are presented as count and percentage and continuous variables as mean +/- standard deviation or median and interquartile range. Univariate binary logistic regression was used to identify factors associated with postoperative AKI and mortality. Variables with a p-value under 0.10 were evaluated with logistic regression. Variables with a  $p < 0.10$  were then entered into the multivariable models.

A multivariable binary logistic regression model was built with backward selection (Wald) including pre- and intraoperative variables to identify independent predictors of AKI and another model including also postoperative variables to identify independent predictors of mortality. A p-value of  $< 0.1$  was

used for removal from the models. P-values of <0.05 were considered statistically significant for all analyses.

## Results

499 patients were enrolled, 11 were excluded from the analysis because of missing sCr data and 13 were excluded from the analysis due to high energy trauma mechanism. The demographics of patients with acute kidney injury (AKI group) and those without acute kidney injury (non-AKI group) are shown in Table 2. The groups did not differ significantly on baseline values except concerning baseline sCr ( $p=0.004$ ) and eGFR ( $p=0.002$ ) which were significantly higher in the AKI group. The mechanisms of trauma, fracture types and operation types are shown in Table 3. The groups did not differ concerning any of these variables. Operation time was not available in several patients so it was excluded from the analyses.

Diagnostic elevation of sCr as a sign of AKI was detected in 40 patients and the incidence of AKI was 8.4 % in the study population. The 40 patients were staged after KDIGO criteria to AKI stage 1 (28/40, 70.0 %), stage 2 (9/40, 22.5 %) and stage 3 (3/40, 7.5 %). Survival was not significantly different between stages.

In logistic regression analysis, dementia (RR 1.97,  $p=0.05$ ) and preoperative sCr (1.01,  $p<0.001$ ) were independent and significant predictors of AKI (Table 4). Diabetes mellitus also seemed predictive (RR 1.93) but was not statistically significant in our study population ( $p=0.10$ ). The type of the fracture or the type of the operation did not predict the development of AKI.

At 90-day follow-up, the overall cumulative mortality was 14.4%. The patients with any level of AKI had a significantly higher mortality of 35.0 % than those without AKI (12.7 %,  $p<0.001$ ) (Figure1). In binary regression analysis dementia (RR 2.41,  $p=0.001$ ), preoperative sCr (RR 1.008,  $p=0.01$ ) and any stage of AKI (RR 3.72,  $p<0.001$ ) were independent predictors for mortality (Table 5).

## Discussion

In high energy trauma patient population the incidence of acute kidney injury is reported to be 15 – 40 % [11–13]. According to the few published studies, the incidence of AKI in hip fracture patients is 15 - 24 % [21–23]. In our study the incidence was lower, 8.4 %. Our standard of care protocol is to start fluid transfusions in the ER and discontinue nephrotoxic medications. The lower incidence of AKI in our study cohort may at least partly be explained by differences in standards of care and patient populations.

The reported risk factors for AKI in hip fracture patients are male sex, vascular diseases, hypertension, diabetes, chronic kidney disease and pre-morbid use of nephrotoxic medications [21] but the evidence on this matter is scarce. Contrasting previous reports, in our population, vascular diseases was not associated with an increased risk for AKI nor was gender. However, our results do support the finding that diabetes mellitus is a possible risk factor (RR 1.93,  $p=0.10$ ), which is logical since diabetes is the most prevalent etiology for chronic kidney failure in the Finnish population i.e. diabetic nephropathy [26–28].

In this study, the three-month mortality in a low-energy trauma hip fracture cohort was significantly higher among patients with any level of AKI than in patients with no AKI. This finding is in line with reports on high energy trauma and critically ill patients where AKI is one of the most frequent organ dysfunctions and has an adverse effect on the prognosis [7,8,29]. The mortality in these patient populations is substantial (17.5 – 57 %) compared to patients without acute kidney injury (2.3 – 5.8 %) [11,12,30]. According to literature, the risk of death after hip fracture surgery is highest precisely during the first three months but the difference compared to age-matched controls persists over years [31,32]. In our population AKI seems to be one of the factors explaining this excess mortality.

The early AKI within 2 days post-injury is known to outperform hepatic, cardiac, or pulmonary dysfunction as a predictor of multi organ failure (MOF) and death in severely injured patients (8). MOF is likely to explain the increased mortality in this patient population. AKI has not been the center of interest in hip fracture studies for long and the existence of AKI also in this population has only recently become evident. Hence the reason for excess mortality in hip fracture patients developing AKI is not

researched. It is likely that the same organ failure mechanisms that explain mortality among other critically ill patient populations also explain mortality in hip fracture patients.

To define actions for preventing AKI and the associating increased mortality, more research is needed on the exact mechanisms leading to death of AKI patients. For earlier detection and possible prevention of developing AKI in hip fracture patients, the sCr should be routinely analyzed every day and at least two days post-operatively. If changes in sCr levels were to be detected, there should be immediate actions to protect the kidneys.

We acknowledge that our study has limitations. The demographic data on the patients was gathered from electronic medical records where some information might be erroneously coded or missing. Also we might have missed some patients in the enrollment. The three months follow-up time is quite short and hence we have no insight on the long-term survival of our patients. On the other hand, our study represents, to our knowledge, the largest prospectively gathered cohort of low-energy hip fracture patients focusing on the incidence and consequences of AKI.

## **Conclusion**

In Finnish hip fracture patient population the incidence of AKI was 8.4 %. In our study AKI was a significant factor associated with a 3 -fold mortality during the first three months after hip fracture surgery. The mortality in the AKI patient population was 35.0 %.

## **Declaration of Competing Interest**

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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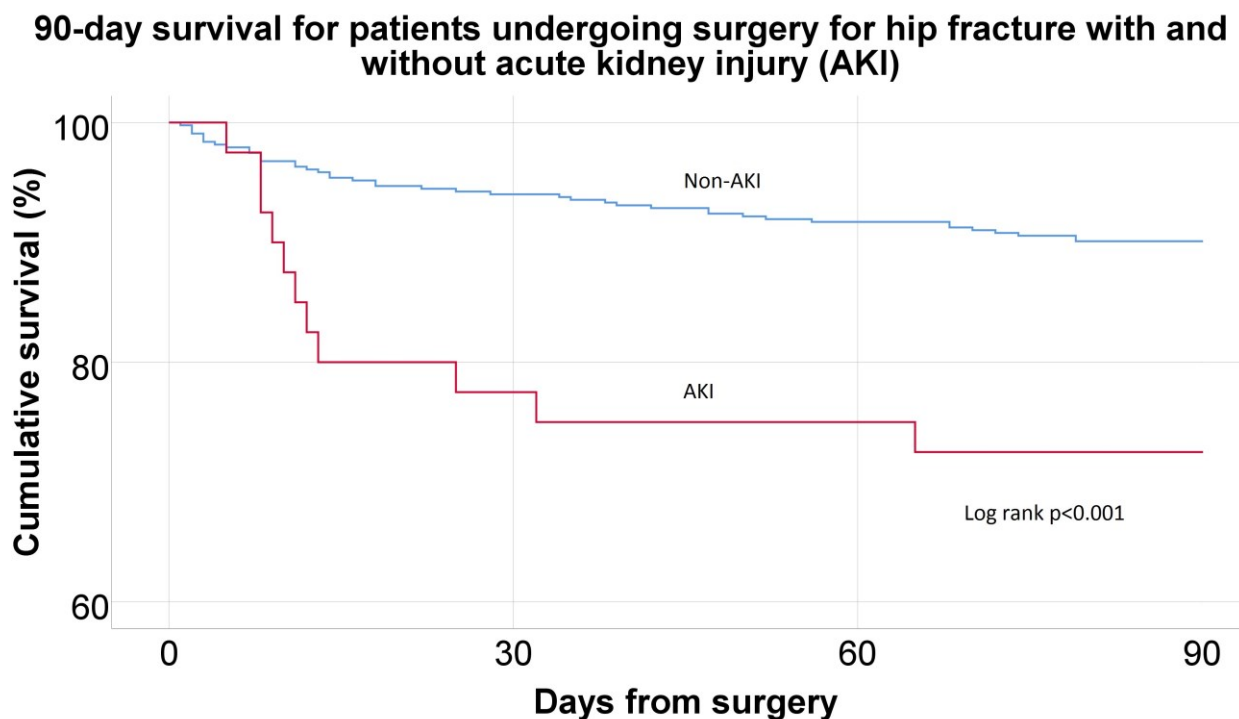
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**Table 1. KDIGO staging for AKI**

Stage	Serum creatinine (sCr)
<b>1</b>	1.5 – 1.9 time baseline or ≥ 0.3 mg/dl (26.5µmol/l) increase
<b>2</b>	2.0 – 2.9 times baseline
<b>3</b>	3 times baseline or ≥ 4.0 mg/dl (353.6 µmol/l) increase or initiation of RRT or in patients <18 years a decrease in eGFR <35 ml/min/1.73 m <sup>2</sup>

AKI=acute kidney injury; RRT=renal replacement therapy

**Table 2. Baseline characteristics**

Variable	Non-AKI (n=435)	AKI (n=40)	P value
<b>Female</b>	288 (66.2%)	23 (57.5%)	0.27
<b>Age (years)</b>	81.8 ± 9.1	81.2 ± 11.0	0.66
<b>CCI -score</b>	5.1 ± 1.8	5.4 ± 2.0	0.26
<b>Smoking</b>	36 (8.3%)	2 (5.0%)	0.47
<b>Alcohol abuse</b>	12 (2.8%)	0	0.29
<b>Cardiovascular disease</b>	193 (44.4%)	22 (55.0%)	0.20
<b>Hypertension</b>	269 (61.8%)	21 (52.5%)	0.25

<b>Diabetes</b>	79 (18.2%)	12 (30.0%)	0.07
<b>History of stroke/TIA</b>	63 (14.5%)	7 (17.5%)	0.61
<b>Dementia</b>	158 (36.3%)	9 (22.5%)	0.08
<b>Preoperative Hb</b>	123 ± 17	119 ± 15	0.16
<b>Preoperative sCr</b>	83 ± 33	112 ± 58	0.004
<b>eGFR under 60 ml/min/m<sup>2</sup></b>	171 (36.0%)	26 (65.0%)	0.002
<b>Operation time (min)</b>	61.5 ± 30.0	62.0 ± 19.0	0.95
<b>Intraoperative bloodloss (ml)</b>	282 ± 235	305 ± 280	0.59

AKI=acute kidney injury; CCI=Charlson comorbidity index; TIA=transient ischaemic attack; Hb=haemoglobin; sCr=serum creatinine; eGFR=estimated glomerular filtration rate

**Table 4. Predictors of post-operative AKI in hip fracture patients**

Variable	Univariate			Multivariate		
	RR	95% Ci	P value	RR	95% Ci	P value
<b>Diabetes</b>	1.93	0.94 – 3.96	0.07	-	-	0.10
<b>Dementia</b>	1.97	0.91 – 4.23	0.09	2.37	1.00 – 4.98	0.05
<b>Preoperative sCr (per unit)</b>	1.01	1.01 – 1.02	<0.001	1.01	1.01 – 1.02	<0.001

AKI=acute kidney injury; RR=risk ratio; Ci=confidence interval; sCr=serum creatinine

**Table 5. Binary regression for predictors of 90-day mortality in hip fracture patients with and without post-operative AKI**

Variable	Univariate			Multivariate		
	RR	95% Ci	p-value	RR	95% Ci	p-value
<b>AKI</b>	3.72	1.83-7.56	<0.001	3.95	1.82 – 8.59	<0.001
<b>Dementia</b>	2.41	1.45-4.03	0.001	2.75	1.60 – 4.73	<0.001
<b>Preoperative sCr (per unit)</b>	1.008	1.002-1.01	0.01	-	-	0.16
<b>Diabetes</b>	1.41	0.78-2.57	0.26	-	-	0.68

AKI=acute kidney injury; RR=risk ratio; Ci=confidence interval; sCr=serum creatinine