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Acute kidney injury after prolonged neurosurgical operations

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ABSTRACT

Background: Acute kidney injury (AKI) is a serious condition that causes significant morbidity and mortality in medical and surgical intensive care units. In this environment, the prevalence, risk factors, and prognostic effects of this harmful disorder are well known. But there is paucity about this issue among patients with neurosurgeries. So, this work tried to detect different risk factors for the development of AKI among patients underwent prolonged neurosurgeries.

Methods: Over a two-year duration, 100 patients were recruited in the current study. Those patients were eligible for different neurosurgeries. Baseline data including demographic and laboratory in addition to perioperative data were gathered. The main end point was the development of AKI based on the Kidney Disease Improving Global Outcomes criteria

Results: Fifteen (15%) patients developed AKI; 13 (86.7%) patients had stage I; and 2 (13.3%) patients had stage II AKI. It was found that risk factors for the development of AKI were old age, operative blood loss, and operative transfusion of mannitol. Only two patients were died, and both of them developed AKI.

Conclusion: AKI is a serious complication in patients underwent prolonged neurosurgeries. It has a great effect on patient's prognosis. Early detection of different risk factors for AKI may help in new lines of therapy for those patients with subsequent improvement in their outcome.

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1. Introduction

Postoperative AKI (AKI) is a critical condition in modern medicine that is closely associated with increased risks of death and persistent renal failure. However, there are no general therapeutic or preventive measures for AKI as the clinical cause varies according to the patient's condition. Individualized approaches on the basis of appropriate risk stratification, early detection, and involvement of a specialist may be beneficial for the management of AKI [1].

AKI is a highly prevalent and prognostically important complication in various surgical settings. Patients who developed postoperative AKI are independently associated with markedly increased morbidity, mortality, and higher economic burden. A considerable amount of publications have evaluated the incidence, determinants, and consequences of AKI in patients undergoing various types of cardiac and non-cardiac surgeries [2–4].

AKI after cardiac surgery is fairly common, with some reports citing a figure close to 30% although the exact incidence varies with definition and is based on the numerous scoring systems available [5].

About 1–2% of patients develop severe renal injury requiring dialysis. AKI after cardiac surgery is associated with a substantial increase in morbidity and mortality which can exceed 60% among patients requiring dialysis. Even when there is a modest increase in serum creatinine values from baseline values, it is associated with longer hospital stay and increased costs besides adverse prognostication in outcomes [6].

Concomitant with social and economic development, the number of neurosurgical operations has increased worldwide, and great progress has been made in neurosurgery. In a multi-center prospective study, AKI occurred frequently and was associated with adverse in-hospital outcomes in neurosurgical critically ill population. Consequently, several preventive and treatment strategies have been developed [4,7].

Nevertheless, little is known about the incidence, risk factors and outcomes of postoperative AKI in neurosurgical patients and hence may lead to an unacceptable delay in initiating any therapy regimens. This work tried to solve this issue and assessed the possible risk factors for development of AKI among patients underwent prolonged (>4 h) neurosurgeries.

2. Materials and methods

The current study was prospectively performed at Assiut University Hospitals after it was approved by Local Medical Ethics Committee, Faculty of Medicine, Assiut University (approval number 17100467), and was registered in *clinicaltrials.gov* with NCT03486184. A written informed consent was obtained from all participants. The study was conducted over two years from 2018 to 2020.

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One hundred patients who were scheduled for neurosurgical operation were enrolled in the study. Exclusion criteria included history of renal transplantation, preexisting nephrectomy, presence of chronic kidney disease before neurosurgical procedure, operation less than 4 h, patients who were under 18 years old, and pregnancy.

The following data were collected from each participants: age, sex, body mass index (BMI) and baseline vital signs. Baseline laboratory data included international randomized ratio, complete blood picture, serum creatinine (sCr), and estimated glomerular filtration rate. Serum creatinine was measured 48 h postoperatively. Each of the baseline American Society of Anesthesiologists classification (ASA) and Glasgow Coma Scale (GCS) was recorded.

Surgical data including type of surgical procedure, duration of anesthesia, intraoperative estimated blood loss, hemodynamics during anesthesia, anesthetic agents (sevoflurane and propofol), amount and type of intraoperative fluids administered (crystalloid and colloid), intraoperative use of mannitol and furosemide, transfusions (red blood cells, platelets, and plasma), and urine output were recorded.

The primary outcome was the development of AKI. AKI was defined based on the KDIGO criteria for AKI within 1 week after surgery as any of the following: increase in sCr by ≥0.3 mg/dl (≥26.5 µmol/l) within 48 h or increase in sCr to ≥1.5 times baseline within 1 week or urine output <0.5 ml/kg/h for 6 h [8].

AKI is staged according to the following: stage 1: increase of sCr to 1.5–1.9 times from baseline, or ≥0.3 mg/dl (≥26.5 µmol/l) increase of sCr, or urine output <0.5 ml/kg/h for 6–12 h. Stage 2: increase of sCr to 2.0–2.9 times from baseline or urine output <0.5 ml/kg/h for ≥12 h. Stage 3: 3 times increase of sCr from baseline or ≥4.0 mg/dl (≥353.6 µmol/l) increase of sCr or initiation of RRT or urine output <0.3 ml/kg/h for ≥24 h or anuria for ≥12 h [8].

Secondary outcomes included: hospital stay, reintubation, renal replacement therapy (RRT), and mortality.

3. Sample size

For sample size, statistical calculation was based on a power of 80% and 95% confidence interval, and the MedCalc ® version 123.0.0 software was used with α-error 5%; according to a previous report, AKI among patients underwent non-cardiac surgeries ranged between 7.5% and 24% [4], and a minimum sample size of 106 cases was required. Assuming a drop-out ratio of 5%, the sample size was 100 cases.

4. Statistical analysis

Continuous variables were expressed as mean ± SD and compared by Student *t*-test, while categorical variables were expressed as number (percentage) and compared by Chi^2 test. The clinical perioperative variables with $P < 0.10$ in univariate analysis were included in multivariate analysis. Logistic multivariate forward stepwise regression was then used to determine the most efficient predictors of AKI. All the tests were two-tailed, and $P < 0.05$ was considered as statistically significant. SPSS version 20 was used.

5. Results

5.1. Baseline data among enrolled patients based on development of AKI (Table 1, Figure 1)

Out of enrolled patients, 15 (15%) patients developed AKI. Both groups of patients based on the development of AKI had insignificant differences as regards baseline with the exception of significantly higher mean age among patients with AKI (46.98 ± 12.34 vs. 40.10 ± 9.34 (years); $P = 0.01$). Other baseline data are summarized in Table 1.

5.2. Diagnosis among enrolled patients (Table 2)

Table 1. Baseline data of enrolled patients based on development of AKI.

	AKI ($n = 15$)	Non-AKI ($n = 85$)	*P*-value
Age (years)	46.98 ± 12.34	40.10 ± 9.34	**0.01**
Sex	5 (33.3%)	41 (48.2%)	0.28
Male	10 (66.7%)	44 (51.8%)	
Female			
Body mass index (kg/m^2)	23.56 ± 2.34	24.01 ± 2.01	0.43
Diabetes mellitus	3 (20%)	12 (14.1%)	0.55
Hypertension	4 (26.7%)	13 (15.3%)	0.27
Ischaemic heart disease	1 (6.7%)	3 (3.5%)	0.56
Prior neurosurgeries	2 (13.3%)	4 (4.7%)	0.19
Hemoglobin (mg/dl)	12.22 ± 2.22	11.89 ± 1.98	0.56
Platelets (10^3/µl)	234.05 ± 44.58	246.09 ± 34.56	0.23
Leucocytes (10^3/µl)	7.87 ± 2.34	8.08 ± 1.23	0.60
INR	± 0.03	1.01 ± 0.04	0.35
Creatinine (mg/dl)	1.01 ± 0.10	1.08 ± 0.11	0.51
eGFR (ml/minute/1.73 m^2)	97.56 ± 4.50	99.34 ± 2.97	0.05
Heart rate (b/minute)	87.78 ± 12.76	85.44 ± 10.10	0.42
SBP (mmHg)	122.22 ± 10.87	121.23 ± 9.34	0.71
DBP (mmHg)	77.09 ± 7.77	76.66 ± 5.55	0.79
ASA class I	15 (100%)	85 (100%)	– -
Type of procedure	1 (6.7%)	2 (2.4%)	0.36
Evacuation	14 (93.3%)	83 (97.6%)	
Extraction			

Data were expressed as frequency (percentage) or mean (SD). *P* value was significant if <0.05. AKI: acute kidney injury; INR: international randomized ratio; eGFR: estimated glomerular filtration rate; ASA: American Society of Anesthesiologists Classification; SBP: systolic blood pressure.

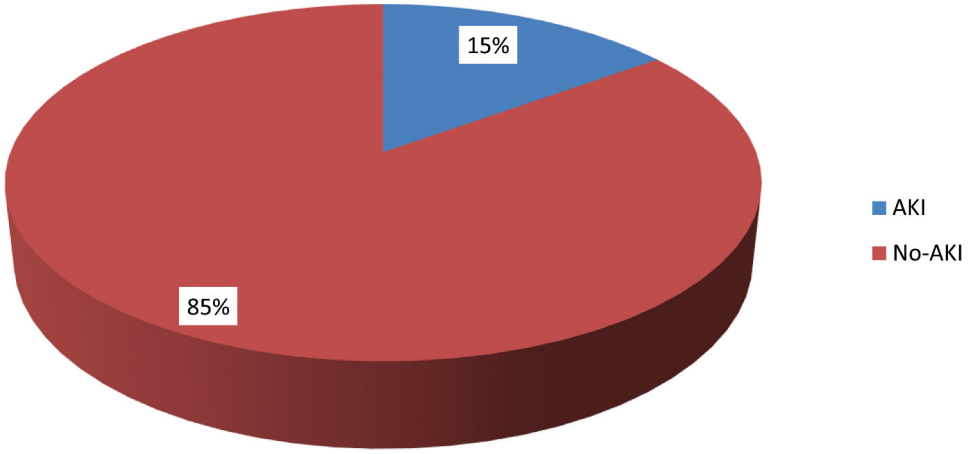

Figure 1. Frequency of acute kidney injury among enrolled patients.

Table 2. Diagnosis among enrolled patients.

Diagnosis	*N* = 100
Meningioma	52 (52%)
Glioma	29 (29%)
Pituitary adenoma	6 (6%)
High parietal granuloma	4 (4%)
Brain abscess	3 (3%)
Epidermoid	3 (3%)
Cerebellar tumor	2 (2%)
Neoplastic intraventricular mass	1 (1%)

Data were expressed as frequency (percentage). N: number.

Table 3. Intraoperative data of enrolled patients based on development of AKI.

	AKI (*n* = 15)	Non-AKI (*n* = 85)	*P*-value
Anesthesia duration (h)	5.89 ± 0.23	5.81 ± 0.19	0.14
Intraoperative fluid (l)	3.45 ± 0.21	3.39 ± 0.20	0.31
Mannitol infusion	5 (33.3%)	3 (3.5%)	**<0.001**
RBCs transfusion	2 (13.3%)	10 (11.8%)	0.86
FFP transfusion	1 (6.7%)	3 (3.5%)	0.56
Blood loss (l)	1.89 ± 0.25	1.24 ± 0.31	**<0.001**
Minimum MAP (mmHg)	72.45 ± 4.56	73.50 ± 5.65	0.49
Urine output (ml)	2287.45 ± 267.98	2290.23 ± 268.11	0.97

Data were expressed as frequency (percentage) or mean (SD). *P* value was significant if <0.05. AKI: acute kidney injury; RBCs: red blood corpuscles; FFP: fresh frozen plasma; MAP: mean arterial pressure.

Table 4. Postoperative data and outcome of patients based on development of AKI.

	AKI (*n* = 15)	Non-AKI (*n* = 85)	*P*-value
48-h creatinine (mg/dl)	2.34 ± 0.78	0.76 ± 0.22	**<0.001**
ICU stay (day)	2.50 ± 0.25	1.50 ± 0.15	**0.04**
Hospital stay (day)	12.34 ± 2.45	9.98 ± 1.30	**<0.001**
Renal replacement therapy	5 (33.3%)	0	**<0.001**
Stage of AKI	13 (86.7%)		
Stage I	2 (13.3%)		
Stage II			
Mortality	2 (13.3%)	0	**0.02**

Data were expressed as frequency (percentage) or mean (SD). *P* value was significant if <0.05. AKI: acute kidney injury; ICU: intensive care unit.

The most frequent diagnosis among enrolled patients was meningioma (52%) followed by glioma (29%), pituitary adenoma (6%), and high parietal granuloma (4%). Each of brain abscess and epidermoid was presented in 3 (3%) patients. Two patients had cerebellar tumor, and another patient had neoplastic intraventricular mass.

Table 5. Multivariate regression analysis for prediction of AKI.

	Odd's ratio	95% confidence interval	*P*-value
Age (years)	1.56	1.11–2.98	0.04
Intraoperative blood loss (ml)	2.11	1.98–3.09	<0.001
Intraoperative mannitol infusion	2.22	2.01–3.98	<0.001

AKI: acute kidney injury. *P* value was significant if <0.05.

5.3. Intraoperative data among enrolled patients based on development of AKI (Table 3)

Both groups had insignificant differences as regards intraoperative data with exception to significantly higher estimated blood loss among patients with AKI (1.89 ± 0.25 vs. 1.24 ± 0.31 (liter); $P < 0.001$). Also, patients who developed AKI had significantly higher frequency of intraoperative mannitol infusion (5 (33.3%) vs. 3 (3.5%); $P < 0.001$).

5.4. Postoperative data and outcome among enrolled data based on development of AKI (Table 4)

Patients who developed AKI had a significantly higher 48-h creatinine, ICU stay, and hospital stay. Also, 5 (33.3%) patients with AKI required RRT. Stage I and II AKI is presented in 13 (86.7%) and 2 (13.3%) patients, respectively. Only two patients died, and both of them developed AKI.

5.5. Multivariate regression analysis for prediction of AKI (Table 5)

Based on the current study, predictors of AKI among patients underwent prolonged neurosurgeries were age, intraoperative blood loss, and intraoperative mannitol infusion.

6. Discussion

AKI during hospitalization after major surgical procedures is a risk factor for short-term mortality. Although several studies have reported a higher prevalence of AKI in various patient populations underwent various surgeries and confirmed the association of less severe AKI with short-term mortality, few studies have focused on AKI in the cohort of neurosurgical patients [9].

An unfavorable prognosis is often linked with neurocritical disease. One of the newest disciplines of intensive care medicine, specialized neurocritical care, has emerged from neurosurgical postoperative observation and treatment. The introduction of neurocritical treatment resulted in a significant reduction in death and an increased prognosis for the neurocritically ill patients. As a result, the prognosis for this patient population is favorable [9].

As a result, non-neurological disorders are largely determining the prognosis of this patient population, rather than the underlying neurologic or neurosurgical conditions. AKI is an independent risk factor for death following traumatic brain injury, ischemic stroke, and sub-arachnoid hemorrhage in these non-neurologic complications [10,11].

Here, in the current study, we enrolled patients underwent different prolonged neurosurgeries (>4 h) over a two-year duration. Out of the enrolled patients, 15 (15%) patients developed AKI. Five (33.3%) patients with AKI required RRT. In line with the current study, AKI was reported in 13.5% in patients undergoing neurological surgery within the first 7 days [4].

The incidence of AKI in our study is similar to those reported among several non-cardiac surgery cohorts, which varied from 7.5% to 24% but lower than those in cardiac surgery. Although several studies had reported the incidence of AKI in traumatic brain injury cohorts, ranging from 8% to 25%, the postoperative AKI incidence of entire neurosurgical critically ill cohort has not been well described [12–15].

However, depending on the study population and the definition of AKI, the incidence of AKI in critical care reaches up to 70%. Concerning the incidence of dialysis-dependent AKI, it was found that an incidence of RRT among patients who developed AKI reached 12% [9,16].

In the current study, predictors of AKI among patients underwent prolonged neurosurgeries were age, intraoperative blood loss, and intraoperative mannitol infusion. In accordance with the current results, in previous studies, development of AKI was significantly related to the estimated blood loss during operation [4,17,18].

On the one hand, severe bleeding can result in hemodynamic compromise and hemoglobin deficiency. Anemia, induced by a substantial decrease in hemoglobin, may limit renal oxygen supply, stimulate oxidative stress, and inhibit hemostasis, both of which lead to the development of AKI. Excessive bleeding, on the other hand, can necessitate RBC (red blood cell) transfusions.

Transfused stored RBCs can degrade tissue oxygen delivery, promote a pro-inflammatory state, and intensify tissue oxidative stress, all of which are correlated with AKI. Intraoperative hypovolemia caused by intraoperative blood loss or insufficient fluid therapy can lead to AKI production [19,20].

Age, GFR, ischemic heart disease, chronic heart failure, and type of stroke were all independent predictors of AKI in the aforementioned Covic et al. report [21]. Patients with AKI after a traumatic brain injury were older, had lower Glasgow Coma Scale rates, greater seriousness of disease scores, and higher serum creatinine and blood urea nitrogen levels.

It was reported that reoperation was a risk factor for development of AKI in patients underwent neurosurgeries. Although the mechanisms of AKI caused by reoperation have not been fully clarified, the logical assumption is that they involve exacerbation of many of the factors, such as hemodynamic compromise, bleeding, and operative trauma, which are related to AKI occurrence [4,20].

Since several previous studies have found a connection between mannitol and kidney damage, we investigated the link between this drug and AKI. The use of mannitol during surgery was found to be an independent risk factor for postoperative AKI in our research. Since the processes by which mannitol usage is linked to the frequency of AKI are not well understood, the possibility exists [22,23].

Aside from the toxic effect on the kidney, the connection between AKI and intraoperative mannitol use can also be due to illness seriousness, such as high intracranial pressure or cerebral edema. In general, intraoperative mannitol use indicates more severe neuropathophysiological insults associated with a high risk of AKI [24].

It is becoming abundantly clear that even minor kidney damage is associated with an increased risk of morbidity and mortality. In contrast to non-AKI patients, we discovered that AKI patients had a considerably higher rate of in-hospital and ICU death, as well as other poor outcome, which was reported with previous researches [4].

Despite the lack of effective treatment regimens at the moment, assessing modifiable risk factors for AKI may lead to the development of novel strategies for preventing postoperative AKI in neurosurgical critically ill patients. As a result, we attempted to identify modifiable predictor factors that predispose to AKI. It is worth noting that all of the risk factors found in our analysis are potentially modifiable. Before we can translate our findings into clinical practice, we need to do further intervention studies to demonstrate the efficacy of these modifiable risk factors.

The main limitations of the current study included the following: (1) lack of longer duration of follow-up after hospital discharge and (2) the variables selected as potential risk factors are based on existing literature and investigator hypotheses, as with all observational studies, but the impact of residual or unmeasured confounders on the reported correlations between the risk factors and AKI cannot be ruled out.

In conclusion, the frequency of AKI in patients underwent prolonged neurosurgeries was fairly common (15%). The main risk factors included old age, operative blood loss, and operative mannitol transfusion. Development of AKI would affect the outcome of those patients.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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