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Evaluation of the effects of two different anesthesia methods on postoperative renal functions in geriatric patients undergoing hip fracture surgery: a prospective randomized trial

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ABSTRACT

Aim: The choice of anesthesia management for hip fracture surgery is among the modifiable risk factors that can affect the outcome. This study aims to investigate the effects of two different anesthesia techniques on kidney functions with the RIFLE (Risk, Injury, Failure, Loss, and End-stage renal failure) risk score in patients who were operated on for hip fracture.

Material and Method: Serum creatinine values lower than 1.5 times (Normal value: 1.2 mg/dL) and glomerular filtration rate (GFR) below 60 mg/dl, over 65 years old, without serious comorbidity, hemoglobin (Hb) value over 9 g/dl 60 patients were included. The demographic data and biochemical parameters of the patients were recorded. The patients were randomized into two groups as spinal anesthesia (Group S) and general anesthesia (Group G). During the surgery, a urinary catheter was applied to the patients and urine output was monitored. Balance liquid electrolyte regimen was applied and after Hb control, an appropriate blood regimen was planned with Hb above 9 g/dl. Postoperatively, patients were followed at 6th, 12th, and 24th hours on the first day, and then at 24-hour intervals in the first postoperative week, and were evaluated with the RIFLE risk scores.

Results: There was no statistically significant difference between the groups in terms of demographic data, fracture type, laboratory values, and urine volumes ($p > 0.05$). In the comparison of intragroup urea values, the decrease in the 5th time interval compared to the baseline value was statistically significant in Group G. There was no statistically significant difference between the measurement times in Group S ($p > 0.05$). Preoperative creatinine values were found to be statistically significantly higher than other measurement times in the patient group in Group S ($p < 0.05$). In both groups, it was found that all measurement time urine amounts were statistically different from each other ($p < 0.05$). In comparisons between groups, There was no statistically significant difference in terms of RIFLE risk score and postoperative outcome at all measurement times ($p>0.05$).

Conclusion: There is no difference between the anesthesia method applied in hip fracture surgery and the change in renal function of patients, based on RIFLE criteria and laboratory parameters. In addition, a significant improvement in renal functions was observed in both groups, especially during the discharge period, according to preoperative values, which may indicate that the stress response to surgery can be effectively limited in both anesthesia methods.

Keywords: General anesthesia, spinal anesthesia, hip fracture, renal functions, geriatric, RIFLE criteria

INTRODUCTION

Fracture of the femur in the bone region just distal to the hip articular cartilage, up to about five centimeters below the lower border of the lesser trochanter, is referred to as "hip fracture" and these patients are generally in the advanced age group (1-3). The presence of cardiac, endocrine, renal, cerebral, and respiratory diseases increases perioperative and postoperative morbidity and mortality in geriatric patients (2,4). The choice of anesthesia management for hip fracture surgery is among the modifiable risk factors that may affectpatient mortality (4). Anesthesia used is either general anesthesia; with the airway maintained by a face mask,

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laryngeal mask airway (LMA), or endotracheal tube (ET) induction and ventilation being spontaneous or mechanical; or regional where a spinal injection of a local anesthetic or an epidural is used (5). In many studies on mortality, different results have been obtained regarding the superiority of anesthesia methods over each other, and a clear consensus has not been reached (6-8).

Acute kidney injury (AKI) is a sudden, sustained decrease of renal function, causing damage to its excretion capacity and maintenance of fluid/electrolytic homeostasis and urea and creatinine accumulation with or without urinary output reduction. This renal function decrease is observed with a reduction of the glomerular filtration rate (GFR), resulting in an elevation of serum creatinine and urea levels, which are often used to clinically evaluate the renal function (9,10). AKI is a common complication in patients undergoing major surgery (11). For this reason, fluid monitoring and stabilization of hemodynamics are very important in these patients. Studies of AKI in patients with hip fractures have reported an 8% to 24% risk of developing acute renal failure within 72 hours after surgery or during hospitalization (9,12,13). Renal failure studies were standardized by a consensus in 2004 that defined ARF based on separate criteria of creatinine and/or urinary output (14). AKI was classified, by this consensus, in three different severity categories (risk, injury, and failure) and two clinical categories (renal loss and end-stage of renal disease), and the acronym RIFLE (Risk, Injury, Failure, Loss, and End-Stage) identifies this classification as follows (9):

•Risk: increase of 1.5 times of serum creatinine concerning basal creatine and/or urinary debt of 0.5 mL · kg−1 h−1 for six hours;

•Injury: increase of two times of serum creatinine to basal creatinine and/or urinary debt of 0.5 mL · kg−1 h−1 for 12 hours;

•Failure: increase of three times of serum creatinine in relation to basal creatinine and/or urinary debt of 0.3 mL · kg−1 h−1 for 24 hours (oliguria), 12 hours (anuria), or when the creatinine values are above 4.0 mg · dL−1;

•Renal loss: acute renal failure for more than four weeks; and

•End-stage: renal failure for more than three months.

In this study, we hypothesized that spinal anesthesia applied in geriatric patients undergoing hip surgery may be a more protective technique than general anesthesia in the early postoperative period in terms of acute renal failure. This study, it is aimed to evaluate this effect by using the RIFLE criteria. The primary outcome of this study is to investigate the effects of two different anesthesia techniques on kidney functions by using the RIFLE criteria in patients who will be operated on for hip fracture. The secondary outcome, on the other hand, is to investigate the mortality and morbidity of patients through the early detection of renal dysfunction using RIFLE criteria.

MATERIAL AND METHOD

This study was planned as prospective, randomized, controlled, and double-blind. After the approval of the Ankara Numune Training and Research Hospital Clinical Researches Ethics Committee (ID: E.Kurul-E-16-1025, Date: 10.08.20016). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. It was planned for geriatric patients who applied to the orthopedics clinic of the high volume tertiary medical center with hip fracture between September 2016 and September 2017. Those who were less than 1.5 times the normal serum creatinine values according to the hospital reference values (Normal value: 1.2 mg/dL) and GFR below 60 mg/dl, over 65 years of age, without a previous history of liver, kidney and heart failure, were included in the study. Sixty patients with hemoglobin (Hb) values over 9 g/dl were included. The patients were randomized using the random.org method and divided into two groups as spinal anesthesia (Group S) and general anesthesia (Group G). Allocation was done by the closed envelope method.

Those with liver, kidney, and heart failure, unregulated hypertension and diabetes mellitus, those with a history of regular non-steroidal anti-inflammatory drug use in the last 6 months, and those with a history of drug use affecting kidney functions were excluded from the study.

Demographic data and biochemical parameters (Hb, serum creatinine, and blood urea nitrogen (BUN)) values of the patients who were preoperatively prepared were recorded. Isolyte S (balanced solution) infusion at 10 ml/kg/h was given to the patients. In Group S, a unilateral spinal block was applied to the patients using 1.5 ml 0.5% Heavy Bupivacaine with a 25 G spinal needle (Egemen, 11 cm, Quince 25G) with the patient lying on their side through the L 4-5 intervertebral space. Balance anesthesia induction 0.3 mg/kg midazolam, 0.25-0.50 µg/kg remifentanil, 2% propofol 1.5-2 mg/kg, 0.6 mg/kg rocuronium intravenous (iv) bolus was administered to the patients in Group G and appropriate endotracheal (7-8.0 cuffed) tube was intubated. Sevoflurane 1.0-1.2 MAC, and 0.5 µg/kg/h remifentanil infusion were administered for anesthesia maintenance. During the surgery, urine output was monitored by applying a urinary catheter to the patients, and recording was started when the urine in the first bag was emptied and the bladder was empty. After the balance fluid electrolyte regimen and Hb

control, an appropriate blood regimen was planned with Hb above 9 g/dl. The urinary catheter was removed after the first 48 hours in the patients. Following the removal of the urinary catheter, the patient's urine was collected in a measurable urine cup and a 24-hour follow-up was performed. Postoperatively, patients were followed up at 6th, 12th, and 24th hours on the first day, and then at 24-hour intervals in the first postoperative week and were evaluated with a RIFLE risk score. Patients from the risk group were consulted to the nephrology clinic.

Statistical Analysis

Analysis of the data was done using IBM SPSS 25.0 statistical package program. While evaluating the study data, the Chi-Square ($\chi 2$) test was used to compare the qualitative data as well as descriptive statistical methods (frequency, percentage, mean, standard deviation, median, min-max). The suitability of the data to the normal distribution was evaluated with Kolmogorov-Smirnow and Shapiro-Wilk tests. The Mann-Whitney U test was used for the intergroup comparisons of the data that did not show normal distribution, and the Friedman test was used for the intragroup comparisons. Dunn's post-hoc test was used to find the source of the difference in cases where there was a difference in group comparisons. Values with a probability (P) less than $\alpha=0.05$ were accepted as significant and there was a difference between groups, values with a higher probability were considered as insignificant and there was no difference between groups.

Sample Size And Power Analysis

The sample size was calculated using G*Power© software version 3.1.9.2 (Institute of Experimental Psychology, Heinrich Heine University, Dusseldorf, Germany). The sample size was calculated for the Mann Whitney U-test, which was used for testing the main hypothesis of (RIFLE score for 24 hours) the present study. Depending on previous research results with two-sided (two tails) type I error 0.05 and power of 80% ($1-\beta=0.8$), effect size (d) factor 0.5, should involve ≥ 112 subjects.

Power analysis was done with the G*Power 3.1.9.2 statistical package program; n1=49, n2=56, $\alpha=0.05$, Effect Size d=0.65; Power $(1-\beta)=0.90$.

RESULTS

Our study included 157 patients who applied to the orthopedics clinic of our hospital between September 2016 and September 2017. 112 of these patients who met the criteria agreed to participate in the study. Afterward, 7 patients in the general anesthesia group were excluded from the study before the operation because they wanted to drop out of the study. The operations of the patients were planned with general anesthesia and one of the spinal anesthesia methods. In the spinal anesthesia group, all 56 patients were included in the study. The study was completed by 49 patients in the general anesthesia group and 56 patients in the spinal anesthesia group (**Figure 1**).

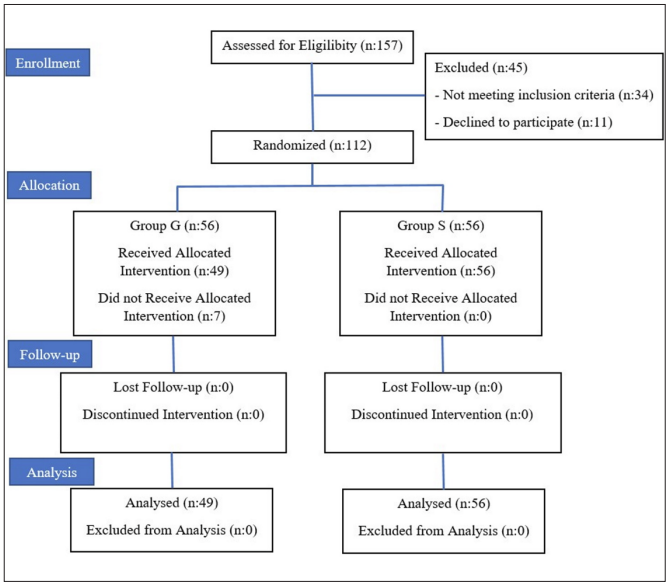

Figure 1. Flowchart of patients. Group G: general anesthesia, Group S: spinal anesthesia.

There was no statistically significant difference between the groups in terms of gender, age, and fracture type ($p > 0.05$) (**Table 1**).

Table 1. Comparison of patient characteristics between groups

		Group G (n=49)	Group S (n=56)	P
Gender	Female	29 (% 59.2)	40 (% 71.4)	0.266 a
	Male	20 (% 40.8)	16 (% 28.6)	
Age, (year)	80 (65-96)	79 (65-100)	0.969 b	
Fracture type	Femur neck	11 (% 22.4)	22 (% 39.3)	0.103 a
	Intertrochanteric	30 (% 61.2)	30 (% 53.6)	
	Subtrochanteric	8 (% 16.3)	4 (% 7.1)	
Operation	Endoprothesis	12 (% 24.5)	18 (% 32.1)	0.103 a
	Proximal Femoral Nail	37 (% 75.5)	38 (% 67.9)	

Continuous variables are expressed as either the mean±standard deviation (SD) or median (Q1-Q3) and categorical variables are expressed as either frequency (percentage). a: Chi-Square Test, b: Mann-Whitney U Test. Group G: general anesthesia, Group S: spinal anesthesia.

In comparison between groups, there was no statistically significant difference between the groups in terms of urea, serum creatinine, GFR, and urine values at all measurement times ($p > 0.05$).

In group comparisons; in the comparison of urea values, the decrease in the 5th time interval compared to the baseline value in the general patient group was statistically significant. In the spinal patient group, there was no statistically significant difference between the measurement times ($p > 0.05$). In the comparison of serum creatinine values, it was observed that there

was no statistically significant difference between the measurement times in the general patient group in terms of serum creatinine values ($p > 0.05$). In the spinal patient group, preoperative serum creatinine values were found to be statistically significantly higher than the other measurement times ($p < 0.05$). In the comparison of GFR values, it was observed that there was no statistically significant difference between the measurement times in both general and spinal patient groups ($p > 0.05$). In the comparison of urine volumes, a statistically significant difference was observed between the measurement times in both general and spinal patients ($p < 0.05$). In both groups, it was found that the urine volumes at all measurement times were statistically different from each other ($p < 0.05$) (**Table 2**) (**Figure 2**).

Table 2. Comparison of renal function tests between groups

		Group G (n=49)	Group S (n=56)	P a
Urea (mg/dL)	Preoperative1	58.2±28.2	57.0±27.1	0.946
	PO 6. hour2	55.1±26.6	54.9±26.6	0.944
	PO 24. hour 3	55.9±27.8	57.2±25.0	0.738
	PO 48. hour 4	56.9±31.4	58.5±28.1	0.761
	Discharge5	43.3±21.5	52.1±30.3	0.119
	P b	0,000	0,166	
	Difference	1 with 5	--	
Creatinin (mg/dL)	Preoperative1	1.1±0.5	1.2±0.6	0.772
	PO 6. hour 2	1.1±0.6	1.0±0.5	0,169
	PO 24. hour 3	1.1±0.6	1.1±0.6	0.977
	PO 48. hour 4	1.1±0.8	1.1±0.5	0.644
	Discharge5	0.9±0.4	1.0±0.7	0.606
	P b	0.002	0.048	
	Difference	1 with 5	1 with 5	
GFR (ml/min)	Preoperative1	61.8±23.6	58.2±21.5	0.383
	PO 6. hour 2	63.7±24.8	63.3±21.1	0.944
	PO 24. hour 3	65.3±24.9	61.4±19.9	0.458
	PO 48. hour 4	80.6±36.2	69.6±31.7	0.115
	Discharge5	91.1±33.9	78.1±31.5	0.091
	P b	0.000	0.000	
	Difference	1 with 4-5	1 with 4-5	
Urine volumes (mL)	PO 6. hour	669.4±211.6	594.6±187.2	0.068
	PO 12. hour	1333.7±356.5	1293.8±377.2	0.505
	PO 24. hour	1878.6±493.9	1885.7±514.0	0.870
	P b	0.000	0.000	
	Difference	All	All	

Continuous variables are expressed as the mean±standard deviation (SD).
a: Mann-Whitney U Test, b: Chi-Square Test, c: FriedmanTest
Group G: general anesthesia, Group S: spinal anesthesia, GFR: Glomerular filtration rate; PO: Postoperative.

In comparisons between groups; There was no statistically significant difference between the groups in terms of GFR values at all measurement times ($p > 0.05$).

In group comparisons; In the comparison of GFR values, it was observed that there was no statistically significant difference in terms of GFR values between the measurement times in both the general and spinal patient groups ($p > 0.05$).

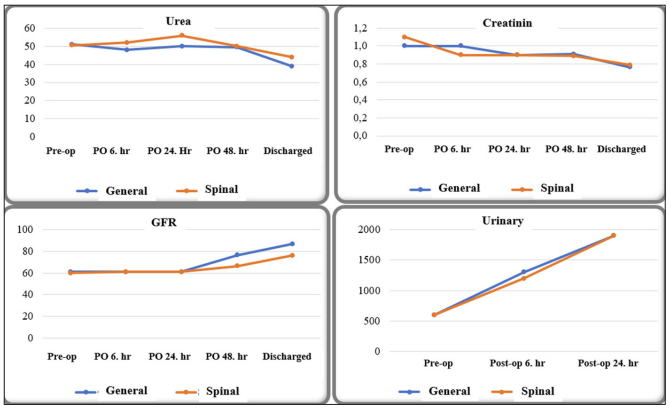

Figure 2. Comparison of renal function tests between groups. GFR: Glomerular filtration rate; Pre-op: Preoperative; PO: Postoperative

In comparisons between groups; It was found that there was no statistically significant difference between the groups in terms of RIFLE values at all measurement times ($p > 0.05$) (**Table 3**) (**Figure 3**).

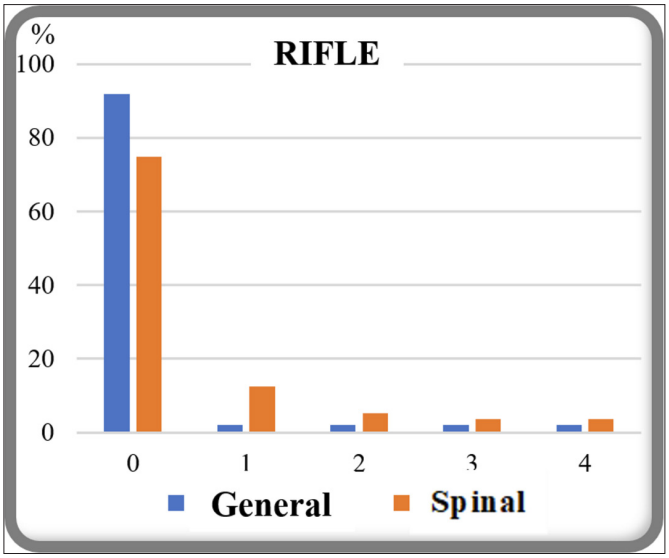

Figure 3. Comparison of RIFLE scores and groups. RIFLE: Risk, Injury, Failure, Loss, and End-stage renal failure.

Table 3. Comparison of RIFLE scores and groups

		Group G (n=49)	Group S (n=56)	P a
RIFLE	0	45(%91.8)	42(%75.0)	0.212
	1	1(%2.0)	7(%12.5)	
	2	1(%2.0)	3(%5.4)	
	3	1(%2.0)	2(%3.6)	
	4	1(%2.0)	2(%3.6)	
Complication	Yes	5(%10.2)	8(%14.3)	0.736

Continuous variables are expressed as either the mean±standard deviation (SD) or median (Q1-Q3) and categorical variables are expressed as either frequency (percentage). a: Chi-Square Test. Group G: general anesthesia, Group S: spinal anesthesia, RIFLE: Risk, Injury, Failure, Loss, and End-stage renal failure.

In comparisons between groups; It was found that there was no statistically significant difference between the groups in terms of hospitalization time, hospitalization time after surgery, postoperative anesthesia care unit (PACU) requirement, time in PACU, time in hospital ward, intensive care unit (ICU) requirement and time in ICU values ($p > 0.05$) (**Table 4**).

Table 4. Comparison of time and requirements between groups			
	Group G (n=49)	**Group S (n=56)**	**P**
Hospitalization time (day)	11.5±6.2	10.0±4.7	0.376 a
Hospitalization time after surgery (day)	3.3±3.0	3.3±3.4	0.858 a
PACU requirement	30 (% 61.2)	38 (% 67.9)	0.614 b
Time in PACU (day)	0.7±0.6	0.7±0.6	0.442 a
Time in hospital ward (day)	8.4±4.8	7.9±4.0	0.644 a
ICU requirement	13 (% 26.5)	18 (% 32.1)	0.678 b
Time in ICU (day)	2.4±5.8	1.3±2.7	0.792 a

a: Mann-Whitney U Test, b: Friedman test. Group G: general anesthesia, Group S: spinal anesthesia, PACU: postoperative anesthesia care unit, ICU: intensive care unit

In both groups; It was found that the relations between RIFLE variables and PACU need, PACU time, ICU need and ICU time values were not statistically significant (p>0.05) (**Table 5**).

Table 5. Comparison of groups with correlation test in terms of time and needs								
	PACU Need		**PACU Time**		**ICU Need**		**ICU Time**	
	r	Pa	r	Pa	r	Pa	r	Pa
GA RIFLE	0.212	0.144	0.212	0.143	0.172	0.237	0.218	0.132
SA RIFLE	-0.134	0.325	-0.153	0.259	0.234	0.083	0.226	0.095

a: Spearman's Rho Correlation Test. PACU: postoperative anesthesia care unit, GA: General anesthesia, SA: Spinal anesthesia, ICU: intensive care unit, RIFLE: Risk, Injury, Failure, Loss, and End-stage renal failure.

DISCUSSION

The results of this study showed that there was no difference between the anesthesia method applied in patients who were operated on for hip fracture and the change in renal functions of the patients, based on RIFLE criteria and laboratory parameters. In addition, a significant improvement in renal functions was observed in both groups, especially during the discharge period, according to preoperative values.

Hip fractures have serious consequences, especially in frail elderly individuals, and are associated with decreased quality of life and increased morbidity and mortality (15-17). The most important of these complications is AKI, which is defined as a sudden decrease in kidney function, which is a common postoperative complication. AKI is a comprehensive clinical syndrome involving intrarenal and extrarenal pathologies. Postoperative AKI is associated with a longer hospital stay, increased hospital costs, and a significantly high rate of morbidity and mortality (18-20).

The relationship between anesthesia technique and mortality in surgeries performed after hip fractures has been evaluated (21,22). However, studies on the effect of anesthesia type on AKI are limited (23,24). Weingarten et al. (24) reported that general anesthesia was an independent risk factor for the development of postoperative renal failure in patients who underwent joint arthroplasty. Regional anesthesia techniques can be associated with avoidance of airway management, reduced blood loss, potentially reduced risk of deep vein thrombosis, and improved postoperative analgesia. Conversely, it may be associated with a more stable hemodynamic condition in general anesthesia, unlike regional anesthesia (3,25). Considering these effects of general and regional anesthesia, the stable hemodynamics provided in general anesthesia and the limited blood loss provided by regional anesthesia may limit the deterioration of renal functions by keeping the pre-renal blood flow stable, which has a serious effect on renal functions (26). This situation is especially important in fragile geriatric patients. In this study, limited changes and similarities in RIFLE and renal function parameters in both groups show that both anesthesia methods can be used safely in hip fracture surgery in patients.

Stress response to surgery and trauma is an important problem in patients. If this situation cannot be controlled well, it causes acceleration of the catabolic process in patients and deterioration in organ functions with long-term hospitalization (27-29). As a result, this condition is associated with increased morbidity and mortality (29). It has been reported that regional anesthesia limits the stress response more with its central blocking effect. However, it has been reported that this stress response suppressive effect is more limited in general anesthesia (29). This catabolic process is more pronounced, especially in situations that significantly increase the stress response, such as a hip fracture (30). When the fragile geriatric population of this patient group is added to the stress response caused by pain, malnutrition, and trauma, the already borderline organ functions may deteriorate further. Limiting the time to surgery and effective perioperative management may limit this deterioration in these patients. In this study, the higher preoperative renal functions in both groups and the return of these values to more normal levels, especially during discharge, can be explained by the fact that the two anesthetic methods are used to reduce the surgical stress in these patients. As a result, general and spinal anesthesia can be considered as the anesthetic methods preferred in these patients and do not have superiority over each other.

In previous studies, advanced age, low preoperative GFR, emergency surgery, liver disease, obesity, high-risk surgery, and peripheral vascular occlusive disease were accepted as preoperative predictors of AKI in noncardiac surgeries (13,31,32). Intraoperative problems such as bleeding due to anesthesia and hypovolemia have also

been shown to be risk factors for postoperative AKI (33). In addition, hypotension is a common condition during hip surgery, but it has been suggested that this may also lead to AKI. In this study, patients in both groups had similar characteristics in terms of demographic data and comorbidities. In addition, in order to limit the negative effects of possible perioperative hypotension on renal functions, a balance liquid electrolyte regimen was applied to the patients and an appropriate blood regimen was planned with Hb above 9 g/dl after Hb control.

Postoperative complications are more important especially in major surgeries such as hip surgery. This situation may adversely affect the outcome of the patients and may also cause deterioration of renal functions. Various studies have been conducted to determine whether regional anesthesia provides benefits over general anesthesia for surgeries in general, but the evidence remains conflicting (34). Meta-analyses of randomized clinical trials comparing regional anesthesia versus general anesthesia for hip fracture surgery have found borderline significant results on reductions in the risk of short-term complications and mortality associated with regional anesthesia, whereas there is no evidence of a reduction in risk at three months postoperatively (25). In this study, complications developed at a similar rate in both groups, while an intraoperative patient developed death, while 2 patients in the spinal anesthesia group and 1 patient in the general anesthesia group needed dialysis.

There are some limitations to this study. Initially, the study was designed as a single center. This may cause limitations in the evaluation of the general population. Therefore, multicenter prospective and large series studies may be more useful in evaluating the difference of anesthetic methods. Secondly, the use of only RIFLE criteria in addition to the parameters that evaluate renal function in the study may limit objective results. Finally, the relationship of these two anesthesia types with long-term mortality and complications could not be demonstrated, since long-term postoperative follow-up of the patients could not be performed.

CONCLUSION

In conclusion, there is no difference between the anesthesia method applied in patients who were operated on for hip fracture and the change in renal functions of the patients, based on RIFLE criteria and laboratory parameters. In addition, a significant improvement in renal functions was observed in both groups, especially during the discharge period, according to preoperative values, which may indicate that the stress response to surgery can be effectively limited in both anesthesia methods. The effects of the type of anesthesia applied in the patients in terms of postoperative complications and dialysis needs are similar. Large series of prospective randomized studies on this subject will contribute to the emergence of clearer results on the effects of anesthesia methods on renal functions and AKI development.

ETHICAL DECLARATION

Ethics Committee Approval: The study was initiated with the approval of the Ankara Numune Training and Research Hospital Clinical Researches Ethics Committee (ID: E.Kurul-E-16-1025, Date: 10.08.2016).

Informed Consent: All patients were informed about the application and their informed consent was obtained.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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