Original Article

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Prognostic Role of Current Nutritional Indicators on Early and Late Postoperative Survival After Geriatric Hip Fracture Surgery

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Abstract

Aim: Malnutrition is reported to be related to higher mortality rates following geriatric hip fracture, and new malnutrition indicators are currently being identified. The aim of this study is to analyze prognostic nutritional index (PNI), C-reactive protein (CRP)/albumin ratio (CAR) and CRPI/PNI ratio (CPR) as prognostic factors for first-month, six-month, one-year and overall mortality following hip fracture surgery.

Methods: This study was designed as a cross-sectional study. We reviewed the medical records of patients older than 75 years with osteoporotic hip fracture surgery between January 2012 and October 2019. Preoperative serum albumin, total lymphocyte count, and CRP levels were evaluated as laboratory values. PNI, CAR, and CPR were calculated and analyzed as prognostic factors for mortality.

Results: Four hundred and thirty patients were included in the study. High American Society of Anesthesiology (ASA) score (p=0.01) and admission to the intensive care unit (ICU) (p=0.016) were found to be independently associated with worse survival in the first month. The admission to the ICU (p=0.004) was independently related to poor survival in the first six months. High ASA score (p=0.018) and admission to the ICU (p=0.016) were independently associated with a poor survival in the first year. High ASA score (p<0.001) and admission to the ICU (p<0.001) were found to be independent prognostic factors for poor overall survival.

Conclusion: PNI, CAR, and CPR were not significantly related to poor survival in the first month, six months, one year, and overall follow-up period after geriatric hip fracture surgery.

Keywords: Prognostic nutritional index, C-reactive protein/prognostic nutritional index, CRP to albumin ratio, mortality, hip fracture, elderly population

Introduction

Hip fractures in older adults are also associated with a high mortality rate, as reported by 8-37% in the literature (1), and the increased mortality risk can last for years after a hip fracture (2). Various risk factors may be related to the mortality following a surgically treated hip fracture in the geriatric population. Age, gender, high American Society of Anaesthesiologists (ASA) score, duration of hospitalization, delayed surgery, and malnutrition are some of these factors (3-5).

Malnutrition is a common clinical problem in geriatric patients who have hip fractures, and it is reported to be related to lower functional results and higher mortality rates (6). Serum albumin level and lymphocyte count, considered as serum biomarkers used to define the nutritional status of the patient, are reported as prognostic factors in osteoporotic hip fracture in geriatric patients (7). The prognostic nutritional index (PNI) is also found to be a prognostic factor in malignancies and is calculated using the formula: 10 x serum albumin (g/dL) + 0.005 x total lymphocyte count (8,9). C-reactive protein (CRP), which is

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a marker of infection and inflammation, is also reported as a prognostic factor for survival after hip fracture surgery (10). In different studies, PNI, CRP/albumin ratio (CAR), and CRP/PNI ratio (CPR) are investigated as prognostic factors for mortality after osteoporotic hip fracture surgery, but the literature has a lack of data and needs more studies on this issue (11,12).

The purpose of this study is to evaluate PNI, CAR, and CPR as prognostic factors for first-month, six-month, one-year, and overall mortality after hip fracture surgery.

Methods

Compliance with Ethical Standards

This study was approved by the University of Health Sciences Turkey, Haseki Training and Research Hospital Ethics Commitee (IRB number: 2020-221) and was conducted in accordance with the Declaration of Helsinki. Informed consent was routinely obtained from all patients before surgery.

Design of the Study

The study was designed as a cross-sectional study. We reviewed the medical records of patients older than 75 years who were diagnosed with femoral neck (FNF) and intertrochanteric femur fractures (ITFF) and underwent surgical treatment between January 2012 and October 2019. Patients' demographic and medical data were obtained from the institutional database system and phone calls. Time to surgery was determined as the time between admission to the hospital and surgery. The mortality of the patients and the date of their death were evaluated using the National Death Report System. Follow-up periods were recorded from patient files. Survivorship of the patients was assessed according to the National Population Registry System, which was checked for all patients in October 2020.

Patients with high energy or major trauma, a history of malignancy or pathological femoral fractures, subtrochanteric fractures, neglected fractures (more than four weeks), diagnosed with any systemic infection at the time of the fracture, and incomplete information on the registries were all excluded from the study. Finally, 430 patients were included in the study (Figure 1).

Patients' data concerning age, gender, type of fracture, the type of anesthesia, implant type used in the surgery, ASA classification, time of surgery, delay to surgery, duration of hospital stay, and history of intensive care unit (ICU) admission were collected. An ASA score was used to determine the preoperative general health status of the patients according to their comorbidities. The preoperative ASA classification was determined by the anesthesiologists' preoperative evaluation. The patients' ASA scores were categorized as low (ASA 1-2) or high (ASA 3-4) (13).

Preoperative serum albumin, total lymphocyte count, and CRP levels were evaluated as laboratory values. PNI, CAR, and CPR were calculated and analyzed as prognostic factors for mortality. Laboratory values obtained on the first admission to the hospital were used for preoperative evaluation to get an idea about the long-term health status of the patients.

Operation Data

All the patients included in the study were treated in a single, fully equipped training and research hospital. All the patients with FNF were operated on using hemiarthroplasty (HA), while patients with ITFF were treated using HA, intramedullary nailing, and dynamic hip screws. All patients were operated on as soon as possible upon completion of the preoperative preparations.

Outcome Measurements

The primary outcome was survival, determined as the time from the surgery to death or the end of the study. The

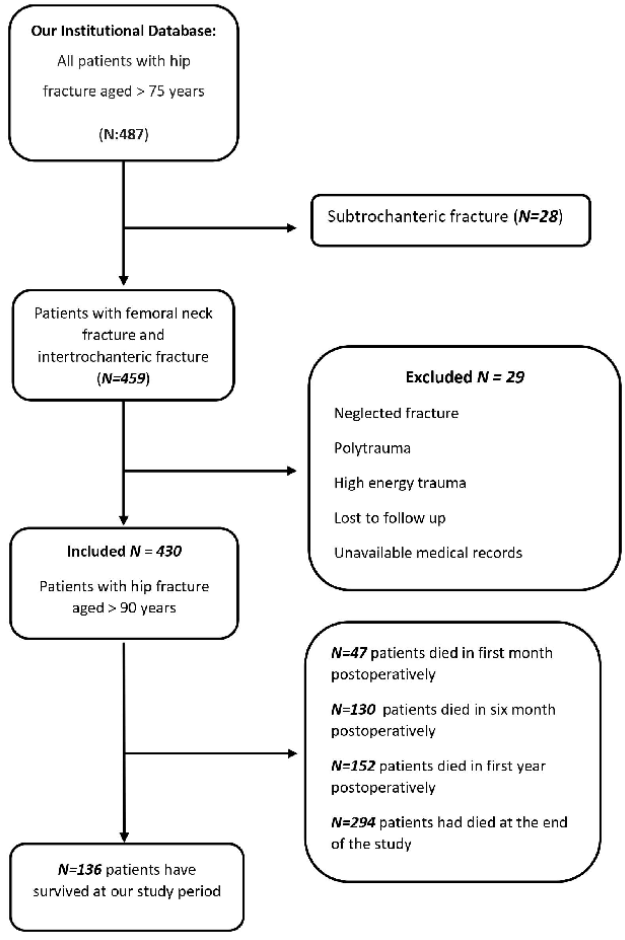

Figure 1. Flowchart of our study

patients' survival was evaluated in four different periods according to survival time: in the first month, six months, the first year, and overall survival. Demographic and laboratory values were analyzed for validity as prognostic factors for mortality following geriatric hip fracture surgery in each period.

Statistical Analysis

SPSS (for Microsoft, v. 22.0, SPSS Inc., Chicago, IL, USA) was used as a statistical software. The survival of the patients was evaluated using Kaplan-Meier survival analysis. Furthermore, univariate Cox regression analysis was used to determine potential prognostic factors for the survival of the patients. The prognostic factors with p-values (two-sided) ≤0.05 were chosen for inclusion in the multivariate Cox proportional hazard model to identify independent variables in a stepwise fashion. Variables with p-values of 0.05 or less in multivariate analysis were retained as independent risk factors. A p-value <0.05 was set as statistically significant.

Results

The mean age of the patients was 84.3±7 years. Two-hundred eighty-two patients were female (65.5%), and 148 patients were male (35.5%). Two-hundred seventy-four patients (%63.7) had ITFF, while 156 patients (36.3%) had FNF. The mean follow-up period was 25.6±23.4 months. The mean delay to surgery was 5.8±3.6 days. The average length of hospital stay was 12.2±8.4 days. One-hundred thirty-two patients (30.6%) had postoperative ICU admissions.

Forty-seven patients (10.9%) died in the first month after surgery. One hundred thirteen patients (26.3%) were dead in six months, while one hundred fifty-two patients (35.3%) were dead in the first year following surgery. The overall mortality rate was 68.4% (Figure 2). According to the Kaplan-Meier analysis, the mean survival period was 37.7 months and the survival rate was 11.2% at the end of the study (Figure 3).

The average preoperative CRP value was 68.6±62.2 mg/dL. The mean PNI was 42.4±8.4. The mean CPR was 1.72±1.67. The mean CAR was 20.8±2.4. Baseline demographic data of the patients included in the study are presented in Table 1.

Analysis for first-month survival

In the first month, PNI, CPR, and CAR were not significantly associated with worse survival in the first month. The other analyzed items are shown in Table 2.

Analysis for six-month survival

PNI, CPR, and CAR were not significantly associated with poorer survival in the first six months. The other analyzed items are shown in Table 3.

Analysis for first-year survival

In the first year, PNI, CPR, and CAR were not significantly associated with worse survival in the first year. The other analyzed items are shown in Table 4.

Analysis for overall survival

PNI, CPR and CAR was not found to be independent prognostic factors for overall survival. The other analyzed items are shown in Table 5.

Discussion

The incidence of hip fractures will gradually increase with the increase in life expectancy. The 1-year mortality rate in hip fractures in patients over 65 years of age has been reported to be between 8% and 35% in the literature (1,14). It was reported in the literature that patients' postoperative mortality and morbidity were affected by their age, higher ASA score, comorbid diseases, and preoperative nutritional status (11,12,15-17).

Table 1. Demographic data of the all patients

	Patients with hip fracture aged more than 75 years (n: 430)	
	Mean ± SD	Min.-Max.
Age, years	84.3±7	75-104
Gender, female/male	282/148	
Side, Right/Left	229/201	
Fracture type, Int./C	274/156	
Treatment method IMN/HA/DHS	188/189/53	
Survive, months	25.6±23.4	0.1-113.4
Delay to surgery, day	5.8±3.6	1-20
Hospital stay, day	12.2 ± 8.4	2-108
History of intensive care unit, n (%)	132 (30.6%)	
Type of anesthesia G, R	65/365	
ASA score		
Low (1-2), n (%)	237 (55.1%)	
High (3-4), n (%)	193 (44.9%)	
Mortality		
In first months, n (%)	47 (10.9%)	
In six months, n (%)	113 (26.3%)	
In first years, n (%)	152 (35.3%)	
Overall, n (%)	294 (68.4%)	
C-reactive protein, mg/dL	68.6±62.2	0.01-272
Preoperative prognostic nutritional index (PNI)	42.4±8.4	22.5-90
CRP/PNI ratio	1.72±1.67	0.1-11.4
CRP/albumin ratio	20.8±2.4	0.1-137

SD: Standard deviation, Min.: Minimum, Max.: Maximum, Int.: Intertrochanteric fracture, C: Collum fracture, IMN: Intramedullary nailing, HA: Hemiarthroplasty, DHS: Dynamic hip screws, G: General, R: Regional, ASA: American Society of Anesthesiology, CRP: C-reactive protein, PNI: Prognostic nutritional index

Table 2. Univariate and multivariate Cox regression analysis for patients who died in first month after surgery			
Factors		**Hazard ratio and the 95% CI**	**p-value**
Univariate Cox regression analysis			
Age		**1.025 (0.986-1.066)**	**0.211**
Sex			
	Female	Reference	Reference
	Male	1.424 (0.799-2.539)	0.231
ASA Score	Low	Reference	Reference
	High	2.479 (1.356-4.532)	0.033*
Side	Right	Reference	Reference
	Left	0.831 (0.466-1.482)	0.532
Delay to surgery		1.156 (0.980-1.133)	0.156
Hospital stay		1.018 (0.997-1.039)	0.09
Intensive care	No	Reference	Reference
	Yes	3.864 (1.529-9.767)	0.004*
Type of anesthesia	Spinal	Reference	Reference
	General	0.975 (0.437-2.177)	0.951
Type of fracture	Intertrochanteric	Reference	Reference
	Collum	1.098 (0.610-1.977)	0.756
Preoperative C-reactive protein		1.004 (1.000-1.008)	0.041*
Prognostic nutritional index		0.966 (0.928-1.005)	0.088
CRP/PNI Ratio		1.185 (1.038-1.352)	0.012*
CRP/Albumin ratio		1.014 (1.003-1.025)	0.014*
Multivariate Cox regression analysis			
ASA Score	Low	Reference	Reference
	High	2.275 (1.219-4.245)	0.010**
Intensive care		3.163 (1.239-8.075)	0.016**
Preoperative C-reactive protein		0.993 (0.976-1.010)	0.417
CRP/PNI ratio		1.260 (0.477-3.329)	0.641
CRP/Albumin ratio		1.012 (0.931-1.101)	0.773

* These p -values were less than 0.05 (Univariate analysis)
** These p -values were less than 0.05 (Multivariate analysis)
CI: Confidence interval, ASA: American Society of Anesthesiology, CRP: C-reactive protein, PNI: Prognostic nutritional index

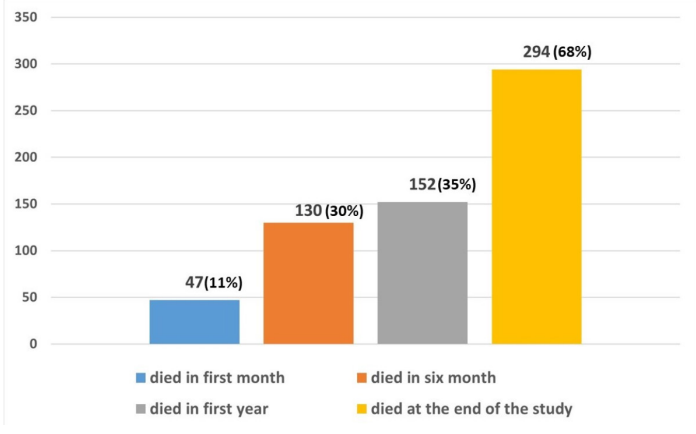

Figure 2. Illustration of the number of died patients in the study

Table 3. Univariate and multivariate Cox regression analysis for patients who died in six months after surgery			
Factors		**Hazard ratio and the 95% CI**	**p-value**
Univariate Cox regression analysis			
Age		1.012 (0.987-1.037)	0.367
Sex			
	Female	Reference	Reference
	Male	1.437 (0.989-2.089)	0.06
ASA Score	Low	Reference	Reference
	High	1.864 (1.283-2.708)	0.001*
Side	Right	Reference	Reference
	Left	1.176 (0.813-1.701)	0.389
Delay to surgery		1.024 (0.975-1.076)	0.349
Hospital stay		1.018 (1.004-1.032)	0.01*
Intensive care	No	Reference	Reference
	Yes	2.348 (1.448-3.809)	<0.001*
Type of anesthesia	Spinal	Reference	Reference
	General	1.256 (0.775-2.037)	0.355
Type of fracture	Intertrochanteric	Reference	Reference
	Collum	1.192 (0.818-1.737)	0.361
Preoperative C-reactive protein		1.006 (1.003-1.008)	<0.001*
Prognostic nutritional index		0.973 (0.948-0.998)	0.036*
CRP/PNI ratio		1.257 (1.154-1.369)	<0.001*
CRP/Albumin ratio		1.019 (1.012-1.026)	<0.014*
Multivariate Cox regression analysis			
ASA Score	Low	Reference	Reference
	High	1.701 (1.160-2.494)	0.07
Hospital stay		1.013 (0.996-1.031)	0.144
Intensive care		2.060 (1.262-3.362)	0.004**
Preoperative C-reactive protein		0.993 (0.981-1.005)	0.269
Prognostic nutritional index		1.005 (0.973-1.037)	0.781
CRP/PNI ratio		1.312 (0.652-1.071)	0.446
CRP/Albumin ratio		1.015 (0.963-1.071)	0.568

* These p -values were less than 0.05 (Univariate analysis)
** These p -values were less than 0.05 (Multivariate analysis)
CI: Confidence interval, ASA: American Society of Anesthesiology, CRP: C-reactive protein, PNI: Prognostic nutritional index

Malnutrition is linked to lower postoperative survival, delayed bone healing, increased surgical site infection, and higher rates of postoperative complications (18). Recently, PNI, CAR, and CPR have been investigated to assess patients' nutritional status. To our knowledge, this is the first study to examine these three items as a prognostic factor for mortality following surgically treated osteoporotic hip fractures in elderly patients. Ren et al. found that PNI was not associated with poorer survival, but the CPR was an independent predictor for 1-year mortality in their study (11). Capkin et al. (12) concluded that preoperative CAR can be used as a prognostic factor for 1-year mortality in patients over 65 years old who had a hip fracture. Belangero et al. (19) showed low preoperative albumin levels and high preoperative CRP levels were related to significantly higher mortality rates following surgically treated ITFF. But the results of our study were incompatible with the results in the current literature. This may be because the lower age limits of the patient groups evaluated in the studies were different, and the postoperative rehabilitation and follow-up protocols used in the studies were different as well.

Several studies studied mortality rates in different time periods after geriatric hip fracture surgery. Foss and Kehlet (20) showed a 13% mortality rate in the first month postoperatively after hip fracture surgery. The six-month mortality rates of elderly patients with hip fractures were reported to be 19.5% in the study by Zaki et al. (21) and

Table 4. Univariate and multivariate Cox regression analysis for patients who died in first year after surgery

Factors		Hazard ratio and the 95% CI	p-value
Univariate Cox regression analysis			
Age		1.002 (0.981-1.024)	0.857
Sex			
	Female	Reference	Reference
	Male	1.234 (0.888-1.713)	0.210
ASA Score	Low	Reference	Reference
	High	1.606 (1.167-2.209)	0.004*
Side	Right	Reference	Reference
	Left	1.049 (0.763-1.442)	0.770
Delay to surgery		1.034 (0.992-1.078)	0.117
Hospital stay		1.016 (1.003-1.030)	0.014*
Intensive care	No	Reference	Reference
	Yes	1.895 (1.288-2.788)	0.002*
Type of anesthesia	Spinal	Reference	Reference
	General	1.217 (0.798-1.856)	0.363
Type of fracture	Intertrochanteric	Reference	Reference
	Collum	1.158 (0.610-1.605)	0.377
Preoperative C-reactive protein		1.005 (1.003-1.007)	<0.001*
Prognostic nutritional index		0.985 (0.964-1.007)	0.170
CRP/PNI ratio		1.234 (1.139-1.337)	<0.001*
CRP/Albumin ratio		1.017 (1.010-1.024)	<0.001*
Multivariate Cox regression analysis			
ASA Score	Low	Reference	Reference
	High	1.482 (1.069-2.054)	0.018**
Intensive care		1.631 (1.096-2.429)	0.016**
Hospital stay		1.012 (0.996-1.028)	0.136
Preoperative C-reactive protein		0.993 (0.983-1.028)	0.135
CRP/PNI Ratio		1.231 (0.743-2.038)	0.420
CRP/Albumin ratio		1.020 (0.975-1.068)	0.392

* These p-values were less than 0.05 (Univariate analysis)
** These p-values were less than 0.05 (Multivariate analysis)
CI: Confidence interval, ASA: American Society of Anesthesiology, CRP: C-reactive protein, PNI: Prognostic nutritional index

Table 5. Univariate and multivariate Cox regression analysis for overall survival of the patients after surgery

Factors		Hazard ratio and the 95% CI	p-value
Univariate Cox regression analysis			
Age		1.016 (1.001-1.031)	0.040*
Sex			
	Female	Reference	Reference
	Male	1.200 (0.945-1.523)	0.135
ASA Score	Low	Reference	Reference
	High	1.584 (1.258-1.994)	<0.001*
Side	Right	Reference	Reference
	Left	1.029 (0.819-1.295)	0.804
Delay to surgery		1.033 (1.003-1.064)	0.033*
Hospital stay		1.018 (1.007-1.030)	0.002*
Intensive care	No	Reference	Reference
	Yes	1.088 (1.401-2.375)	<0.001*
Type of anesthesia	Spinal	Reference	Reference
	General	1.159 (0.842-1.594)	0.365
Type of fracture	Intertrochanteric	Reference	Reference
	Collum	1.065 (0.840-1.351)	0.602
Preoperative C-reactive protein		1.004 (1.002-1.005)	<0.001*
Prognostic nutritional index		0.986 (0.970-1.003)	0.101
CRP/PNI ratio		1.167 (1.091-1.248)	<0.001*
CRP/Albumin ratio		1.012 (1.007-1.018)	<0.001*
Multivariate Cox regression analysis			
Age		1.005 (0.989-1.022)	0.528
ASA Score	Low	Reference	Reference
	High	1.520 (1.191-1.940)	<0.001**
Intensive care		1.590 (1.212-2.085)	<0.001**
Delay to surgery		1.015 (0.982-1.050)	0.382
Hospital stay		1.012 (0.997-1.027)	0.128
Preoperative C-reactive protein		0.994 (0.986-1.003)	0.199
CRP/PNI ratio		1.238 (0.814-1.884)	0.318
CRP/Albumin ratio		1.520 (1.191-1.940)	0.555

*These p-values were less than 0.05 (Univariate analysis)
**These p-values were less than 0.05 (Multivariate analysis)
CI: Confidence interval, ASA: American Society of Anesthesiology, CRP: C-reactive protein, PNI: Prognostic nutritional index

25.0% in the study by Prodovic et al. (22). In their study, Bilsel et al. (15) reported a 35% 1-year mortality rate following hip fracture surgery. The mortality rates found in this study for the first month, six months, and one year following geriatric hip fracture surgery, were consistent with the literature.

Quach et al. (23) reported that the ASA score was independently associated with one-year mortality following hip fracture surgery. Paksima et al. (24) found that patients with a higher ASA score had a higher mortality rate following hip fracture. Bilsel et al. (15) showed that patients with high 3 or 4 ASA status had a significantly increased risk of mortality. We found a high ASA (3-4) score was independently related to poor survival in the first month, six months, one year, and overall follow-up period. Hasan et al. (25) found that the mortality rate of patients

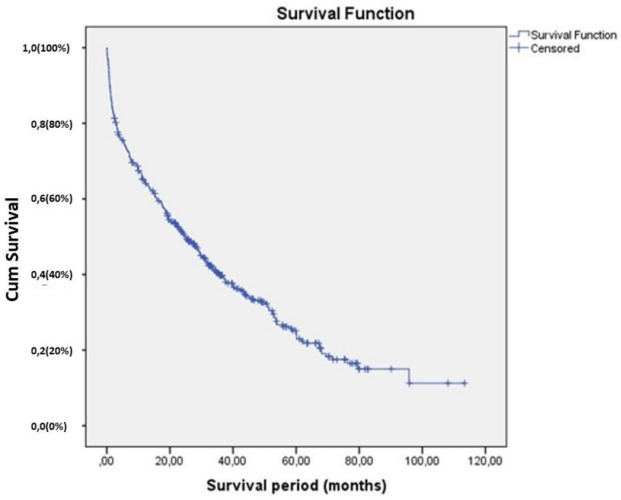

Figure 3. Kaplan-Meier survival curve of the patients included in the study

with postoperative ICU admission was significantly higher than those without admission to the ICU. Our findings were compatible with the current literature.

Study Limitations

There are some limitations in the study. Firstly, our study includes a small number of patients. Secondly, there are several factors affecting mortality rates, such as dementia, dialysis, and preoperative mobilization status of the patient. They were not investigated in our study. Thirdly, we could not also assess the postoperative complications in detail because of the retrospective nature of our study. However, the nutritional indicators examined in our study have recently started to be used in clinical practice, and they are not frequently used in clinical orthopedic practice. The evaluation of these three new markers is the most important strength of our study. Because each of these indicators has been evaluated separately in the literature.

Conclusion

Our results suggest that PNI, CAR, and CPR were not associated with poor survival in the first month, six months, one-year, and overall follow-up period following geriatric hip fracture surgery. Patients with a high ASA (3-4) score and those admitted to the postoperative ICU, on the other hand, should be closely monitored because they are more likely to die.

Ethics

Ethics Committee Approval: This study was approved by the University of Health Sciences Turkey, Haseki Training and Research Hospital Ethics Commitee (IRB number: 2020-221).

Informed Consent: Informed consent was routinely obtained from all patients before surgery.

Authorship Contributions

Concept: M.E., S.B., Design: M.E., S.B., E.G., M.Er., Data Collection and/or Processing: M.E., S.B., E.G., K.A.C., S.O.S., Analysis and/or Interpretation: M.E., S.B., M.Y., Literature Research: M.E., S.B., E.G., K.A.C., M.Er., Writing: M.E., S.B., M.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

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