ORIGINAL ARTICLE

Perioperative outcomes following a hip fracture surgery in elderly patients with heart failure with preserved ejection fraction and heart failure with a mid-range ejection fraction

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ABSTRACT

BACKGROUND: To examine the influence of heart failure (HF) with preserved ejection fraction (HFPEF) and HF with mid-range ejection fraction (HFmrEF) on perioperative cardiac and noncardiac outcomes following hip fracture surgery.

METHODS: Data of elderly patients (≥ 65 years) who underwent hip fracture surgery were retrospectively analyzed in this study. Patients with a left ventricular ejection fraction (LVEF) <40% were not included in this study. The definition of preoperative HFPEF (LVEF ≥50%) and HFmrEF (LVEF 40%–49%) was based on clinical documentation of HF in patients' medical records before surgery. The primary outcomes of this study were perioperative adverse events and mortality. The secondary outcome of interest was the length of stay in the hospital.

RESULTS: A total of 328 patients (mean age 79.2±8.7 years, and 57.3% female) were enrolled. Of the study population, 250 (76.2%) patients had no HF, 50 (15.2%) patients had HFPEF, and 28 (8.6%) patients had HFmrEF before surgery. The frequency of perioperative cardiovascular and non-cardiovascular complications was similar to a rate of 7.0%. The mean length of hospital stay was 8.1±5.8 days, and the in-hospital mortality rate was 4.6%. Patients with HFPEF and HFmrEF had a longer length of stay and were more likely to experience perioperative complications and death than the patients without HF. Multivariate analyses showed that the presence of HFPEF and HFmrEF were both associated with increased rates of perioperative complications and mortality.

CONCLUSION: Our findings suggest that the presence of HFPEF and HFmrEF may predict perioperative adverse events and mortality in elderly patients undergoing hip fracture surgery.

Keywords: HFmrEF; HFPEF; hip fracture; prognosis; surgery.

INTRODUCTION

Hip fracture has been associated with multiple comorbidities, including heart failure (HF).[1] The prevalence of hip fracture and HF is predicted to increase with the aging of the population.[2,3] Interestingly, population-based cohort studies and meta-analyses revealed that HF is associated with an increased risk of hip fracture. Thus, hip fracture and HF are two common major health problems affecting especially older people.[4,5] Although these two diseases are age-related conditions sharing common risk factors, the relationship between complications of hip fractures and HF was not well elucidated.

HF is usually categorized into the three groups according to the left ventricular ejection fraction (LVEF): HF with a reduced ejection fraction (HFrEF, LVEF <40%), HF with preserved

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ejection fraction (HFPEF, LVEF ≥50%), or HF with mid-range ejection fraction (HFmrEF, LVEF 40%–49%).[6] Current studies showed that nearly 50% of the population with HF has HFPEF and HFmrEF.[7] While many studies have focused on the incidence and effects of HFrEF in patients undergoing hip fracture surgery, it has not been thoroughly investigated whether HFPEF or HFmrEF are prevalent and predict perioperative complications.[8,9] Patients with HFPEF undergoing noncardiac surgery are at increased risk for cardiovascular complications.[9] However, there is only one study in the literature evaluating perioperative outcomes in hip fracture surgery for patients with HFPEF.[10] In this recently published database study, HFPEF was found to be a significant perioperative risk of adverse events in patients undergoing hip fracture surgery.[10] However, because of the nature of administrative databases, the value and general applicability of this study are limited.

HFmrEF is identified as a new category of HF in the 2016 European guidelines.[6] The clinical characteristics, mortality, and morbidity rates in HFmrEF are intermediate to those seen in HFrEF and HFPEF.[11–14] However, to our knowledge, there has been no study focused on the prevalence or prognostic value of HFmrEF in patients with hip fracture. We, therefore, aimed to investigate the prevalence and effects of HFmrEF and HFPEF in a real-world cohort of elderly patients undergoing hip fracture surgery.

MATERIALS AND METHODS

Study Participants and Data Collection

Approval for this study was granted by the Faculty ethics committee. This is a single-center and retrospective study conducted in the Medical Faculty hospital, which is a tertiary hospital. This study included elderly patients (≥65 years) who underwent surgery for acute hip fracture. The medical records of patients with femoral neck, intertrochanteric, or subtrochanteric hip fracture undergoing surgery (internal fixation, hemiarthroplasty, or total hip arthroplasty) from June 2016 to June 2019 were retrospectively analyzed. The definition of preoperative HFPEF and HFmrEF was based on clinical documentation of HF in patients' medical records in our hospital before the surgery. However, patients were not included if the medical records and echocardiographic examination reports did not have adequate information about the parameters related to HFPEF and HFmrEF, such as left ventricular hypertrophy, diastolic functions, and LVEF. In our institution, patients were defined as HFmrEF or HFPEF according to current European guidelines; patients who had at least one sign and symptom of heart failure, elevated natriuretic peptide levels, and at least one additional echocardiographic criterion was defined as HFmrEF or HFPEF according to the LVEF; HFmrEF patients had an LVEF of 40%–49%, and HFPEF patients had an LVEF ≥50%.[6] Patients who had an LVEF <40%, patients with prosthetic valves, and patients with congenital heart diseases were excluded from the study. Patients with multiple trauma, and/or accidents, patients treated non-surgically, and patients with missing information on outcome were also excluded from this study. Data for demographic information, including age, gender, comorbid diseases, body mass index, and all medications, were collected. Laboratory data on admission and American Society of Anesthesiologists (ASA) physical status before surgery were recorded.

Study Endpoints

The primary study endpoint was perioperative cardiovascular and non-cardiovascular complications and in-hospital mortality. The secondary outcome of interest was the length of stay in the hospital. Cardiovascular complications were defined as an acute coronary syndrome, nonfatal cardiac arrest, severe arrhythmias, acute heart failure, pulmonary embolism, and cardioembolic stroke. Non-cardiovascular complications were lobar pneumonia, delirium, respiratory failure, bacteremia, and acute renal failure.

Statistical Analysis

Data were analyzed using SPSS for Windows (version 24; SPSS Inc, Chicago, IL). Comparison of the patients' characteristics in three groups (patients with HFmrEF, Patients with HFPEF, and patients with no heart failure) was made using the Chi-square test. Multivariate logistic regression analyses were used to identify predictors of perioperative complications and mortality.

RESULTS

A total of 430 elderly patients underwent hip fracture surgery in our institution during the study period. Thirty-six were excluded from this study due to missing or incomplete information about preoperative echocardiography and medical records, and 14 patients were excluded from this study due to prosthetic heart valve or multiple trauma. Data of the remaining 380 patients were analyzed, and 52 patients were also excluded from this study due to an LVEF <40%. Therefore, 328 patients (mean age 79.2±8.7 years and 57.3% female) were included in this study. Of the patients, 280 had surgery at 48 hours postadmission and 48 had surgery >48 hours postadmission.

The definition of preoperative HFPEF and HFmrEF was based on patients' medical records in 182 patients. However, 98 of the patients had a new diagnosis of HFPEF or HFmrEF after preoperative echocardiography. Time to surgery for patients who underwent preoperative echocardiography was not different from the patients who did not undergo preoperative echocardiography (32.4±12.5 hours vs 33.4±11.9 hours, respectively; p=0.32).

Comparison of the Baseline Demographics and Surgical Characteristics

Among participants, 250 (76.2%) patients had no HF, 50 (15.2%) patients had HFPEF and 28 (8.6%) patients had

HFmrEF preoperatively. Comparison of baseline demographic and surgical characteristics of hip fracture patients with HFmrEF, HFPEF and without HF is presented in Table 1. There were no significant differences about the type of fracture, type of surgical procedure, anesthetic techniques, the prevalence of hypertension, chronic kidney disease and, cerebrovascular disease between three groups. However, age, gender, ASA physical status, body mass index and the prevalence of comorbidities were significantly different among groups. Patients with HFmrEF were predominantly (71.4%) male, whereas 70% of the HFPEF patients and 58% of the patients without HF were female. The prevalence of coronary artery disease was highest in HFmrEF patients, but the prevalence of diabetes mellitus and atrial fibrillation was highest in HFPEF patients. Compared to the other two groups, patients with HFPEF were older and had higher body mass indexes.

Comparison of the Outcomes

The incidence of perioperative cardiovascular and non-cardiovascular complications was similar to a rate of 7.0%. The mean length of hospital stay was 8.1±5.8 days, and the in-hospital mortality rate was 4.6%.

Comparison of perioperative complications, mortality, and length of hospital stay are presented in Table 2. Compared to patients without heart failure, the incidence of perioperative cardiovascular and non-cardiovascular complications, and in-hospital mortality rates were higher, and length of hospital stay was longer in patients with HFmrEF and HFPEF. Patients with HFPEF and HFmrEF also had a higher incidence of intensive care unit discharge after surgery.

When HFPEF and HFmrEF patients were compared, there were no significant differences between the two groups con-

Table 1. Comparison of the demographic and surgical characteristics of hip fracture patients with HFmrEF, HFPEF and without heart failure

	Patients with no HF (n=250)	Patients with HFmrEF (n=28)	Patients with HFPEF (n=50)	p-value		
				HFmrEF vs. No HF	HFPEF vs. No HF	HFmrEF vs. HFPEF
Age, years	78.9±8.3	77.2±7.5	81.2±9.4	NS	0.001	<0.001
Female sex	145 (58.0)	8 (28.6)	35 (70.0)	<0.001	0.032	<0.001
Body mass index (kg/m^2)	28.4±6.9	27.5±5.8	30.4±7.7	NS	0.003	0.012
ASA physical status	3 (1–5)	4 (1–5)	4 (1–5)	0.005	0.016	NS
Comorbidities						
Atrial fibrillation	21 (8.4)	5 (17.9)	19 (38.0)	0.001	<0.001	0.040
Hypertension	195 (78.0)	22 (78.6)	39 (78.0)	NS	NS	NS
Diabetes mellitus	65 (26.0)	8 (28.6)	16 (32.0)	NS	0.023	0.045
Chronic kidney disease	25 (10.0)	3 (10.7)	6 (12.0)	NS	NS	NS
Coronary artery disease	35 (14.0)	15 (53.6)	15 (30.0)	<0.001	0.035	0.013
Cerebrovascular disease	15 (6.0)	3 (10.7)	4 (8.0)	NS	NS	NS
Type of Fracture						
Femoral neck	128 (51.2)	13 (46.4)	26 (52.0)	NS	NS	NS
Intertrochanteric	102 (40.8)	13 (46.4)	21 (42.0)	NS	NS	NS
Subtrochanteric	20 (8.0)	2 (7.1)	3 (6.0)	NS	NS	NS
Surgical Procedure						
Internal fixation	103 (41.2)	11 (39.3)	24 (48.0)	NS	NS	NS
Hemiarthroplasty	135 (54.0)	15 (53.6)	23 (46.0)	NS	NS	NS
Total hip arthroplasty	12 (4.8)	2 (7.1)	3 (6.0)	NS	NS	NS
Type of anesthesia						
General anesthesia	88 (35.2)	10 (35.7)	21 (42.0)	NS	NS	NS
Regional anesthesia	162 (64.8)	18 (64.3)	29 (58.0)	NS	NS	NS

Data were presented as mean±standard deviation, median (minimum–maximum) or number (%). ASA: American Society of Anesthesiologists; HF: Heart failure; HFmrEF: Heart failure with a mid-range ejection fraction; HFPEF: Heart failure with a preserved ejection fraction; NS Non-significant.

Table 2. Perioperative complications, mortality and length of the in-hospital stay

	Patients with no HF (n=250)	Patients with HFmrEF (n=28)	Patients with HFPEF (n=50)	p-value		
				HFmrEF vs. No HF	HFPEF vs. No HF	HFmrEF vs. HFPEF
Cardiovascular complications	12 (4.8)	5 (17.9)	6 (12.0)	<0.001	0.001	0.010
Non-cardiovascular complications	11 (4.4)	4 (14.3)	8 (16.0)	<0.001	<0.001	NS
Death	5 (2.0)	4 (14.3)	6 (12.0)	<0.001	<0.001	NS
Length of Stay (days)	7.5±5.3	9.5±8.7	9.6±8.3	0.023	0.032	NS
Discharge to ward	228 (91.2)	23 (82.1)	40 (80.0)	0.041	0.030	NS
Discharge to the intensive care unit	22 (8.8)	5 (17.9)	10 (20.0)	0.012	0.001	NS

Data are presented as mean ± standard deviation or number (%). HF: Heart failure; HFmrEF: Heart failure with a mid-range ejection fraction; HFPEF: Heart failure with a preserved ejection fraction; NS Non-significant.

cerning non-cardiovascular complications, length of stay, or mortality rates. However, patients with HFmrEF were more likely to experience cardiovascular complications compared to the patients with HFPEF (17.9 vs. 12%, respectively; p=0.001).

Predictors of the Outcomes

Twenty-three patients (7%) had cardiovascular complications following surgery. These complications were acute coronary syndrome in nine patients, acute HF in eight patients, nonfatal cardiac arrest two patients, severe arrhythmias in two patients, pulmonary embolism in two patients, and cardioembolic stroke in one patient. Multivariate analysis showed that increased age, atrial fibrillation, coronary artery disease, HFPEF, HFmREF and preoperative ASA status were independent predictors of perioperative cardiovascular complications (Table 3).

Twenty-three patients (7%) had non-cardiovascular complications. The most common complication was delirium in eight patients, followed by acute renal failure in five patients, pneumonia in four patients, respiratory failure in four patients, and bacteremia in two patients. Older age, ASA status, diabetes mellitus, HFPEF and HFmrEF were identified as significant predictors of non-cardiovascular complications in multivariate analysis (Table 4).

A total of 15 (4.6%) patients died. Age, ASA status, HFPEF and HFmrEF were predictors of in-hospital mortality in multivariate analysis (Table 5).

Table 3. Multivariate analysis for the prediction of the perioperative cardiovascular complications

	Odds Ratio	95% CI	p
Age (per 1 y)	3.188	2.023–5.034	<0.001
Atrial fibrillation	1.345	1.123–3.435	0.020
Coronary artery disease	2.134	1.185–3.854	0.012
HFmrEF	2.567	1.734–4.453	<0.001
HFPEF	1.867	1.134–2.789	0.001
ASA status	1.568	1.236–4.675	0.015

ASA: American Society of Anesthesiologists; HFmrEF: Heart failure with a mid-range ejection fraction; HFPEF: Heart failure with a preserved ejection fraction; CI: Confidence interval.

Table 4. Multivariate analysis for the prediction of perioperative non-cardiovascular complications

	Odds Ratio	95% CI	p
Age (per 1 y)	1.768	1.119–3.315	0.003
ASA status	2.453	1.102–5.954	<0.001
Diabetes mellitus	3.245	1.586–4.789	<0.001
HFmrEF	1.326	1.096–3.564	0.023
HFPEF	2.563	1.091–4.654	<0.001

ASA: American Society of Anesthesiologists; HFmrEF: Heart failure with a mid-range ejection fraction; HFPEF: Heart failure with a preserved ejection fraction; CI: Confidence interval.

Table 5. Multivariate analysis for the prediction mortality

	Odds Ratio	95% CI	p
Age (per 1 y)	3.456	1.105–6.256	<0.001
ASA status	2.052	1.103–3.786	<0.001
HFmrEF	1.758	1.035–6.689	0.004
HFPEF	1.523	1.028–5.361	0.005

ASA: American Society of Anesthesiologists; HFmrEF: Heart failure with a mid-range ejection fraction; HFPEF: Heart failure with a preserved ejection fraction; CI: Confidence interval.

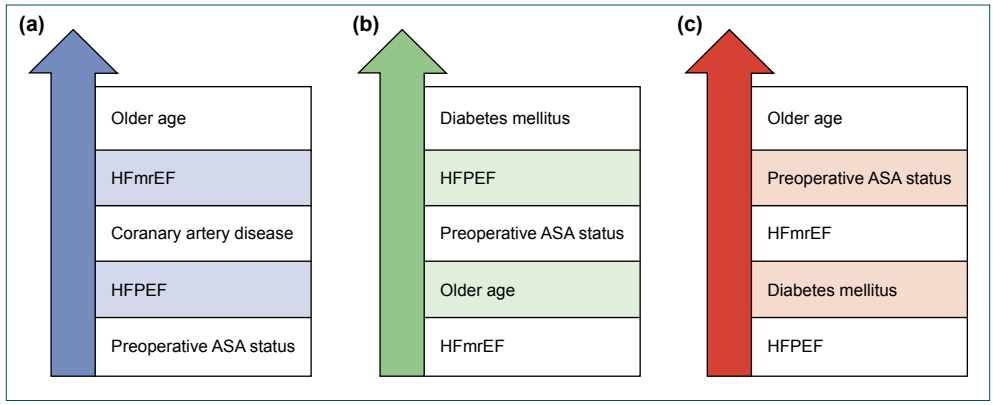

Figure 1. Predictors of the cardiovascular complications **(a)**, non-cardiovascular complications **(b)**, and mortality following hip fracture surgery in individuals aged 65 and older **(c)**.

Increased age was associated with the highest risk for cardiovascular complications (odds ratio 3.19), and mortality (odds ratio 3.46). The presence of diabetes mellitus was associated with the highest risk for non-cardiovascular complications (odds ratio 3.25) (Fig. 1). The odds ratio for HFmrEF was higher than the HFPEF for cardiovascular complications and mortality, while HFPEF had a higher odds ratio than the HFmrEF for the prediction of non-cardiovascular complications.

DISCUSSION

To our knowledge, this is the first study in the literature investigating the prevalence and prognostic value of HFPEF and HFmrEF in patients undergoing hip fracture surgery. We found that 15.2% of the elderly patients with hip fractures had HFPEF, and 8.6% of these patients had HFmrEF at presentation. The incidence of perioperative adverse events was higher, and length of hospital stay was prolonged in patients with HFPEF and HFmrEF than that of those without HF. Moreover, compared to patients with HFPEF, patients with HFmrEF were more likely to experience cardiovascular complications following surgery.

Previous studies showed that several clinical and laboratory variables, such as advanced age, male gender, higher preoperative natriuretic peptide levels, high preoperative ASA classification, history of HF predict hospital readmission, mortality, and morbidity in patients undergoing hip fracture surgery.[15–19] However, only a few studies specifically investigated the prevalence and effects of HF in patients undergoing surgery for hip fracture, and most of these studies included only patients with HFrEF. In a population-based study, the prevalence of preoperative HF was found in 27% of the 1212 patients undergoing hip surgery.[8] Patients with preoperative HF were older, heavier, and more likely male. They also had a longer length of stay, and higher in-hospital mortality compared to patients without HF.[8] However, this study did not separately analyze patients as HFrEF and HFPEF. In a prospective study, 1050 patients with hip fractures who were aged 65 years or older were included.[20] The prevalence of the congestive HF was 6.1% at the time of the hip fracture and patients with a history of congestive HF were at a 40% higher risk of mortality.[20] The only study in the literature examining the prevalence and effects of HFPEF in hip fracture patients has recently been published.[10] In this study, Bohsali et al.[10] identified patients aged 50 years and older with hip fractures undergoing surgery using the Nationwide Inpatient Sample. Among patients, 1.53% was identified with HFPEF and 1.10% with HFrEF. Compared with patients without HF, patients with HFPEF and HFrEF were more likely to be older and had a higher burden of comorbidities. Patients with HFPEF were more likely to be female, whereas patients with HFrEF were less likely to be females. The results of their study revealed that perioperative risk for the acute coronary syndrome, stroke, and death was comparable and similarly elevated in HFrEF and HFPEF patients.[10] Similar to the study that was conducted by Bohsali et al., our study showed that patients with preoperative HFPEF were older, heavier, more likely to be female, and had a higher burden of comorbidities compared to patients without HF. However, we found no differences in age and body mass index between patients with HFmrEF and patients without HF. Compared to patients without HF, patients with HFmrEF were more likely to be male and had a higher burden of comorbidities, including coronary artery disease and atrial fibrillation. Our study results also showed that the presence of HFPEF and HFmREF were predictors of perioperative cardiovascular and non-cardiovascular complications, mortality, and prolonged length of stay in elderly patients undergoing hip fracture surgery. Interestingly, we found that HFmrEF is a better predictor for cardiovascular complications compared to HFPEF, whereas HFPEF is a better predictor for non-cardiovascular complications compared to HFmrEF.

Previous studies showed that perioperative diastolic dysfunction and/or HFPEF was associated with perioperative adverse events and mortality in patients undergoing noncardiac surgery.[21–23] However, to our knowledge, no prior study used LVEF in the stratification of patients with hip fractures who underwent surgery. Due to the aging of the population, the incidence of HFPEF/HFmrEF and hip fracture is grow-

ing in the general population. Theoretically, HFPEF/HFmrEF and osteoporosis/osteoporotic fractures may have common pathophysiological components, such as hyperaldosteronism, up-regulation of cytokines, and increased inflammatory mediators.[24–27] Therefore, the prevalence of HFPEF and HFmrEF may be higher in hip fracture patients than in the general population. Although it may be challenging to identify patients with HFPEF and HFmrEF for anesthesiologists and surgeons, our study showed that preoperative determination of these two conditions is essential for proper perioperative risk stratification. Thus, future larger and prospective studies are needed to verify whether preoperative HFPEF and HFmrEF increase perioperative complications.

Study Limitations

The results of the present study are based on a retrospective registry, and we did not have follow-up data after discharge. This study was carried out in a single center and included only elderly patients undergoing surgery for hip fracture, and the definition of HFPEF and HFmrEF in the present study was based on medical records.

Conclusion

To our knowledge, the present study is the first study that has analyze the prevalence and impact of HFPEF and HFmrEF in patients undergoing surgery for hip fracture. We found that the prevalence of HFPEF was 15.2%, and the prevalence of HFmrEF was 8.6% in this cohort; and compared to participants without HF, HFmrEF and HFPEF patients with hip fractures had a higher burden of comorbidities, a longer length of hospital stay, and higher rates of perioperative complications. Although preoperative identification of patients with HFPEF and HFmrEF is important in clinical practice, further prospective studies are needed to clarify the prognostic implications of this growing HF population in patients with hip fracture.

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ORİJİNAL ÇALIŞMA - *ÖZET*

Korunmuş ejeksiyon fraksiyonu ile kalp yetersizlikli ve sınırda ejeksiyon fraksiyonu ile kalp yetersizlikli yaşlı hastalarda kalça kırığı cerrahisi sonrası perioperatif sonuçlar

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AMAÇ: Korunmuş ejeksiyon fraksiyonu (KEF-KY) ile kalp yetersizliğinin (KY) ve sınırda ejeksiyon fraksiyonu (SEF-KY) ile KY'nin kalça kırığı cerrahisini takiben perioperatif kardiyak ve kardiyak olmayan sonuçlar üzerindeki etkisini incelemek.
GEREÇ VE YÖNTEM: Kalça kırığı ameliyatı geçiren yaşlı hastaların (≥65 yaş) verileri geriye dönük olarak incelendi. Sol ventrikül ejeksiyon fraksiyonu (SVEF) <%40 olan hastalar çalışmaya dahil edilmedi. Ameliyat öncesi KEF-KY (SVEF ≥%50) ve SEF-KY (SVEF %40–49) tanımı, hastaların ameliyat öncesi tıbbi kayıtlarında KY'nin klinik dokümantasyonuna dayanmaktadır. Çalışmanın birincil sonuçları perioperatif olumsuz olaylar ve mortaliteydi. İlgilenilen ikincil sonuç hastanede kalış süresiydi.
BULGULAR: Toplam 328 hasta (ort. yaş 79.2±8.7 yıl ve %57.3 kadın) çalışmaya dahil edildi. Çalışma popülasyonunun 250'sinde (%76.2) KY yoktu, 50'sinde (%15.2) KEF-KY ve 28'inde (% 8.6) SEF-KY vardı. Perioperatif kardiyovasküler ve kardiyovasküler olmayan komplikasyonların sıklığı %7.0 ile benzerdi. Ortalama hastanede kalış süresi 8.1±5.8 gündü ve hastane içi mortalite oranı %4.6 idi. KEF-KY ve SEF-KY hastalarının kalış süresi daha uzundu ve KY olmayan hastalara göre perioperatif komplikasyon ve ölüm yaşama olasılığı daha yüksekti. Çok değişkenli analizler, KEF-KY ve SEF-KY varlığının her ikisinin de artmış perioperatif komplikasyonlar ve mortalite ile ilişkili olduğunu göstermiştir.
TARTIŞMA: Çalışmamız, KEF-KY ve SEF-KY varlığının kalça kırığı ameliyatı geçiren yaşlı hastalarda perioperatif olumsuz olayları ve mortaliteyi tahmin edebileceğini göstermiştir.
Anahtar sözcükler: Cerrahi; HFmrEF; HFPEF; kalça kırığı; prognoz.

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