



Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2019.87
2019;22 (2):140-149

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Received: 06/03/2019
Accepted: 27/05/2019

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RESEARCH

SYNERGISTIC EFFECT OF FRAILTY AND MALNUTRITION ON POSTOPERATIVE FIRST-MONTH MORTALITY AND DELIRIUM STATUS AMONG GERIATRIC AGE GROUP PATIENTS WITH HIP FRACTURES

ABSTRACT

Introduction: We aimed to determine the effect of preoperative frailty status and malnutrition on delirium and first-month mortality during the early postoperative period in patients aged >65 years with hip fractures.

Materials and Method: In total, 56 (44 female and 12 male) patients operated for hip fractures were prospectively analyzed. Clinical frailty scale was used to determine the preoperative frailty status. Nutritional Risk Screening 2002 scores were measured to examine the risk of malnutrition status. The 4 "AT" test was conducted for the diagnosis of delirium. Mortality rates were determined in the postoperative month 1.

Results: Of the total, 29 (51.8%) patients were found to be frail, 22 (39.3%) were found to be prefrail, and 5 (8.9%) were found to be nonfrail. Further, 34 (60.8%) patients were at the risk of malnutrition. Additionally, 38 (67.8%) patients had delirium and 8 (14%) patients died during the postoperative month 1. Although Nutritional Risk Screening 2002 scores positively correlated with first-month mortality, no correlation was found between malnutrition and delirium status. A positive correlation was found between clinical frailty scale score and delirium; however, there was no correlation between clinical frailty scale score and first-month mortality. Positive predictive values of malnutrition and frailty together for first-month mortality increased up to 54.5% from 17.6% and 13.6% and that of delirium increased to 80.2% from 54.5% and 72.4%, respectively.

Conclusion: Morbidity and mortality rates can be reduced after hip fractures by detecting frailty and malnutrition together and taking necessary preoperative precautions in the elderly.

Keywords: Geriatrics; Age determination by skeleton; Forensic medicine

ARAŞTIRMA

KIRILGANLIK VE MALNÜTRİSYON BİRLİKTELİĞİNİN KALÇA KIRIĞI OLAN GERİATRİ YAŞ GRUBU HASTALARIN BİR-AYLIK MORTALİTE VE DELİRİUM DURUMLARINA ETKİSİ

Öz

Giriş: Kalça kırıklarında mortalite ve morbiditeyle sonuçlanan faktörler halen tartışılmaktadır. Bu çalışmanın amacı preoperatif kırılabilirlik ve malnutrisyon durumunun; kalça kırığı gelişen 65 yaş üzerindeki kişilerde, delirium ve bir aylık mortalite üzerine etkisini belirlemektir.

Gereç ve Yöntem: Kalça kırığı nedeniyle opere edilmiş, ortalama yaşı 79.4 (aralık 65-95 yıl) olan 56 (44 Kadın/12 Erkek) hasta prospektif olarak incelendi. Preoperatif kırılabilirlik durumunun tespiti için klinik kırılabilirlik skalası kullanıldı. Malnutrisyon durumunu anlamak amacıyla Nutrisyonel Risk Taraması-2002 skorları hesaplandı. Delirium tespiti için 4AT testi uygulandı. Mortalite yüzdeleri postoperatif birinci ayda belirlendi.

Bulgular: Klinik kırılabilirlik skalasına göre 29 (51.8%) hasta kırılabilir, 22 (39.3%) hasta kırılabilir-öncesinde ve 5 (8.9%) hasta kırılabilir değildi. Nutrisyonel Risk Taraması-2002 skoruna göre 34 (60.8%) hasta malnutrisyon riski altındaydı. 4 AT testine göre 38 (67.8%) hastada delirium gözlemlendi. Postoperatif 1. ayda mortalite 14% (8 patients) idi. Nutrisyonel Risk Taraması-2002 skoru ile bir aylık mortalite ile pozitif korelasyon varken, delirium ile malnutrisyon arasında ilişki bulunamamıştır (p=0.49). Klinik kırılabilirlik skalası ile delirium arasında pozitif korelasyon bulunmuşken (r= 0.46, p=0.018); bir aylık mortalite ile ilişkisi tespit edilememiştir (p=0.59). Malnutrisyon ve kırılabilirlik birlikte değerlendirildiğinde pozitif prediktif değeri bir aylık mortalite için sırasıyla %17.6 ve %13.6'dan %54.5'e yükselmiştir; delirium içinde pozitif prediktif değer 54.5 ve 72.4%'den %80.2'ye artmıştır.

Sonuç: Yaşlı hastalarda kalça kırığı durumunda preoperatif kırılabilirlik ve malnutrisyonun birlikte tespiti ve gerekli önlemlerin alınması ile morbidite ve mortalite yüzdeleri düşürülebilir.

Anahtar sözcükler: Kırılabilirlik; Malnutrisyon; Mortalite; Delirium



INTRODUCTION

The annual rate of increase in hip fractures varies from 1% to 3% with an incidence of 1.6 million/year, which is estimated to be 6.3 million/year by 2050. In operated hip fractures, the mortality rate is 30% during year 1, whereas in nonoperated hip fractures, it is 90%. One-year mortality is doubled in patients who are rehospitalized for any reason within the first 30 days. In the last 10 years, there was a 41.2% increase in the number of rehospitalizations during postoperative month 1 after hip fractures. Hip fractures are one of the most common causes of hospitalization in the geriatric population (1).

The prevalence of malnutrition is high (between 30% and 60%) in hospitalized geriatric patients (2). Malnutrition in surgical patients is associated with increased complications, poor outcomes, and increased mortality. Visvanathan et al. found an association between malnutrition and muscle dysfunction, cognitive dysfunction, increased fall risk, prolonged hospitalization, morbidity, and mortality (3). Similarly, Norman et al. also found a close association between malnutrition and morbidity and mortality and prolonged recovery time in patients with hip fractures (4). Preoperative albumin levels, total lymphocyte counts, Mini Nutritional Assessment, and Nutritional Risk Screening can be used to determine the nutritional status. Nutritional risk screening is recommended in patients undergoing surgery (5).

Frailty is a common geriatric syndrome that is clinically recognized and characterized by a decline in physiological reserves and function across multiple organ systems. This condition makes the elderly more vulnerable to adverse health issues. Chen et al. stated that frailty can be used for the risk assessment of patients scheduled to be operated (6). Johnson et al. argued that determining the frailty index is an important clinical marker prior to deciding for surgery (7). Modified frailty index, Fried frailty index, and clinical frailty scale (CFS) have been frequently used indices to determine the frailty status (7). Although there is a correlation

between frailty and malnutrition, this association is not fully understood in cases of hip fractures.

The increase in the survival rates results in advancement in the incidence of hip fractures. Advances in living standards, surgical techniques, and implant technologies have increased patient expectations. However, clarification of the predictive causes of morbidity and mortality in hip fractures may help to meet increased patient demands. In this study, we aimed to determine the preoperative frailty and nutritional status in geriatric patients with hip fractures and to study the effects of these two conditions on postoperative first-month mortality, delirium, and other complications.

MATERIALS AND METHOD

Ethical approval was obtained from the local ethical committee (Decision number IDF: 2337/18). This prospective study included the patients in the geriatric age group (>65 years) who were admitted to orthopedic clinics with the diagnosis of intracapsular or extracapsular hip fracture and had undergone surgical intervention between January 2017 and October 2017. Patients with multiple and pathological fractures were excluded. The patients who were previously diagnosed with dementia were also excluded from the study after consultation with the patient and their relatives. Demographic characteristics [age, sex, and body mass index (BMI)], comorbidities (hypertension, diabetes, coronary heart diseases, renal failure, and chronic obstructive pulmonary diseases), dominant extremity, polypharmacy status, mechanism and site of fracture, and ambulatory status were preoperatively determined. The handgrip strength of each patient was measured by the same physician thrice using a dynamometer (Baseline® hydraulic hand dynamometers), and the average value was considered. The American Society of Anesthesiologist scoring, type of anesthesia, operation time, implant used, blood transfusion requirement, and complications were

intraoperatively recorded. In the postoperative period, the length of hospital stay and postoperative first-month mortality and morbidity were determined. In addition, renal markers [glomerular filtration rate (GFR)] and hemoglobin levels were recorded preoperatively and at 24 and 72 h of the postoperative period.

The status of delirium and cognitive functions of patients were also recorded during the hospital stay using the 4 "AT" test, which is an assessment test for delirium (8). This test comprises the following parameters: alertness (0–4 point), abbreviated mental test 4 (0–2 point), attention (0–2 point), and acute change or fluctuating course (0–4 point). The test was applied to the patients preoperatively and on postoperative days 1, 3, and 7, if they were not discharged from the hospital. Accordingly, patients with a score of ≥ 4 have possible delirium \pm cognitive impairment, those with a score of 1–3 have possible cognitive impairment, and those with a score of 0 have no delirium.

Nutritional Risk Screening 2002 (NRS-2002) analysis was performed at the hospital to determine the status of nutrition. The test starts with an initial screening. If the answer to any of the four questions asked in the initial screening test is yes, then the final screening is performed. After the addition of 1 point for patients aged ≥ 70 years, patients who scored ≥ 3 in the final screening were considered to be at a risk of malnutrition. Patients who did not undergo the final screening or scored < 3 points, including the final screening score, were not accepted as at the risk of malnutrition. Turkish version of this test was validated (9). Evaluation of this test was made within the first 24 hours after admission.

CFS was used to determine the frailty status of patients (10, 11). Face-to-face evaluations were performed with patients and their family members. CFS was determined on a scale of 1 (very fit)–9 (terminally ill), wherein the patient should be in one category, and is focused on clinical judgment. Each point on this scale concurs with a written description of frailty, complemented by a visual chart to identify

the classification of frailty. Category 2 refers to "well" for people who have no active disease symptom but are less fit than category 1. Category 3 refers to "managing well" for people whose medical problems are well controlled and are not regularly active beyond routine walking. Category 4 refers to "vulnerable" people who do not need daily help; however, symptoms often limit their activities. Category 5 refers to "mildly frail" people who often have more evident slowing and need help in daily livings. Category 6 refers to "moderately frail" people who need help with all outside activities. Category 7 refers to "severely frail" people who are completely dependent for personal care. Category 8 refers to "very severely frail" people completely dependent for personal care and approaching the end of life. The patients who met the first three criteria were termed as nonfrail, those who met the fourth criterion were termed as prefrail, and those who met the fifth–ninth criteria were termed as frail. Assessments took place within 24 hours of the admission, and the Turkish version of this test was validated (12).

All the patients were evaluated by the same physician. He also performed all of these three tests that were designed to be used by any health professional at first contact with the patient and convenient for use in daily clinical practice. These tests are practical and simple to conduct and no special training is required.

Statistical analysis was performed using the SPSS software 21.0 (IBM, Illinois, USA). The variables were investigated using visual and analytical methods to determine if they were normally distributed or not. Frailty, malnutrition, and delirium test results were not normally distributed; therefore, nonparametric tests were conducted to compare these parameters. Mann–Whitney U-test was used to compare results between these parameters, and the correlation coefficients and their significance were calculated using the Spearman test. For multivariate analysis, possible factors identified with univariate analyses were further entered into the logistic regression



analysis to determine independent predictors. A 5% type-I error level was used to infer statistical significance. Power analysis was performed where a sample size of 52 patients would provide 80% power with a 95% confidence interval (CI) on any differences between study groups.

RESULTS

A total of 56 patients (44 female and 12 male) were operated for isolated hip fracture, and the mean age was 79.4 years (range, 65–95 years). Fracture was detected in the right hip in 22 (39.2%) patients and left hip in 34 (60.8%) patients. The mean BMI was 25.2 kg/m² (range, 13–40 kg/m²). Smoking was detected in 9 (16%) patients. The reason for trauma was ground level fall in majority of patients [44 (78.5%) patients], and most of the patients [32 (57.1%) patients] could be mobilized without any support. The mean handgrip strength was 15 (range, 5–30) (Table 1). The mean preoperative hemoglobin (Hb) values were 11.8 [8.8–15.6, standard deviation (sd)=2.3], and the mean postoperative Hb values were 10.1 (8.1–13.3, sd=1.9) ($p=0.426$). The mean preoperative GFR was 56 (7–105, sd=12.3), and the mean postoperative GFR was 42 (6–84, sd=14.8) ($p=0.064$). At least 1 out of 26 postoperative complications were seen in 18 (32%) patients. Complications are summarized in Table 2. Postoperative first-month mortality rate was 14% (8 patients). According to the 4 "AT" test, 38 (67.8%) patients had delirium, 11 (19.7%) patients had cognitive impairment, and 7 (12.5%) patients showed no delirium. The median time for duration of delirium was 1.3 (range, 0–3 days) days.

According to CFS, 5 (8.9%) patients were nonfrail, 29 (51.8%) were frail, and 22 (39.3%) were prefrail. The mean NRS-2002 score was determined as 4.2 (range, 0–7) with 22 (39.2%) patients scoring <3 points and 34 (60.8%) patients at a risk of malnutrition. There was a positive correlation between frailty and malnutrition ($\rho=0.36$, $p=0.026$). The mean NRS-2002 score was 1.9 for nonfrail patients and 4.8 for frail patients ($p=0.018$) (Table 3).

Postoperative complications were found to be higher in patients with NRS-2002 score >3 points in multivariate logistic regression analysis, even when performed considering age, sex, weight, and smoking parameters [odds ratio (OR), 3.89, 95% CI, 1.92–7]. At the same time patients in the group of risk of malnutrition, according to the NRS-2002 score, positively correlated with the first-month mortality ($\rho=0.064$, $p=0.035$). The positive correlation was found between length of hospital stay and NRS-2002 score ($\rho=0.18$, $p=0.038$). There was no correlation between malnutrition and preoperative and postoperative delirium ($p=0.49$). Although a positive correlation was found between CFS score and postoperative complications ($\rho=0.12$, $p=0.021$), length of hospital stay ($\rho=0.73$, $p=0.028$), and postoperative 4 "AT" test ($\rho=0.46$, $p=0.018$), there was no correlation with mortality ($p=0.59$) (Table 4).

The positive predictive values (PPVs) of malnutrition and frailty for mortality were 17.6% and 13.6%, respectively; however, when patients with scores of NRS-2002 > 3 and CFS > 4 were taken into consideration, PPV for mortality increased to 54.5%. Moreover, PPV for delirium increased to 80.2%, showing the combination of malnutrition (52.6%) and frailty (72.4%) (Table 5).

DISCUSSION

Hip fractures are associated with increased morbidity and mortality in the geriatric population. Although the effects of preoperative malnutrition and frailty status of patients on morbidity and mortality were separately evaluated, to our knowledge, there is no information about the effects of the association of both factors on postoperative first-month mortality and delirium.

Frailty is closely related to mortality and clinical functions in patients with hip fractures. Different tests have been used in previous studies to determine the frailty index. In their prospective study of 179 geriatric patients, Gregorovic et al. found that

increased frailty with respect to CFS was associated with increased mortality and decreased functional results for 3 months (13). Similarly, Basic et al. found a positive correlation between the frailty status of geriatric patients hospitalized due to an acute disease determined using CFS and the predicted in-hospital mortality [OR=2.97 (2.11–4.17)], new nursing home placement [OR=1.60 (1.14–2.24)], and length of hospital stay [hazard ratio=0.87 (0.81–0.93)] (14). Kua et al. compared two frailty scoring systems modified Fried criteria and reported Edmonton frail scale (REFS) in their study that comprised 100 geriatric patients with hip fractures. They declared that REFS was a good predictor of postoperative results and also for 6 months of basic activities of daily living (15). In our study, postoperative morbidity and length of hospital stay positively correlated with frailty; conversely, there was no correlation with first-month mortality. The reasons for this might be that CFS was used for determining frailty status and only first-month mortality rates were investigated. Long-term mortality rates or various frailty scoring systems may result in different outcomes.

In their study on 215 geriatric patients operated for hip fractures, Koren-Hakim et al. advocated that the Mini Nutritional Assessment-Short Form (MNA-SF), Malnutrition Universal Screening Tool, and NRS-2002 test can be used for the diagnosis of malnutrition (16). However, they argued that only MNA-SF can be used to predict mortality and readmission. Although the Mini Nutritional Assessment is often used to evaluate malnutrition, it is time-consuming and not recommended for patients with mental status. For this reason, the European Society for Clinical Nutrition and Metabolism developed the NRS-2002 evaluation test. In their studies, Anthony and Kondrup et al. recommended NRS-2002 for predicting mortality in hospitalized patients (5,10). In addition, Ozkalkanli et al. found that NRS-2002 was superior to the subjective global assessment in terms of predicting complications in patients undergoing orthopedic surgery (17). We used NRS-2002 as a marker of nutritional status in our study.

Although mortality, postoperative morbidity, and hospital stay correlated with malnutrition, there was no correlation with both preoperative and postoperative delirium. Similarly, Ozbilgin et al. found a positive correlation between mortality and NRS-2002, which was used as a nutritional assessment tool in a postoperative intensive care unit, but could not detect a correlation with delirium (18). Ringaitien et al. found that patients undergoing coronary artery bypass surgery with the risk of malnutrition status, according to NRS-2002, were more likely to have postoperative delirium ($p < 0.0191$) (19). The difference in patient population and surgical intervention might have affected the outcome of our study. At the same time, the use of the Confusion Assessment Method for Intensive Care Unit for the detection of postoperative delirium may explain different results from our study.

Although there was a correlation between malnutrition and first-month mortality, we could not find any correlation between frailty and first-month mortality. In case of delirium, the opposite results were true; there was a positive correlation with frailty but not with malnutrition. However, when examined together, they synergistically act to create a powerful index for the prediction of both mortality and delirium. Patients who were both frail and had the risk of malnutrition showed a 54.5% chance of postoperative first-month mortality and 80.2% had the possibility of delirium. Therefore, detection of frailty and malnutrition together may give clearer results for predicting delirium and first-month mortality.

Low handgrip strength (<27 kg for men and <16 kg for women) is a component of sarcopenia that was defined according to the consensus of the European Working Group on Sarcopenia in Older People (20). In addition to low handgrip strength, polypharmacy has also been shown as a contributing factor for sarcopenia. Kimura et al. found that polypharmacy is significantly common among patients with sarcopenia compared to those without sarcopenia ($p=0.004$) (21). Polypharmacy



increases with aging and it is reported to be among the causes of sarcopenia, as well as malnutrition (22). Although 32.1% of our patients have polypharmacy, and low mean handgrip strength was observed among female patients. sarcopenia screening was not performed in our cohort, and this can be considered as a limitation of the study because sarcopenia is a contributor to the development of frailty. Although frailty is a geriatric syndrome that displays significant overlap with sarcopenia, it represents a much broader concept than sarcopenia.

The relatively lower number of patients in our study may be considered as a limitation. However, prospective and long-term follow-ups of geriatric patients are extremely difficult in daily practice. In geriatric patients with hip fractures, several parameters affect morbidity and mortality, which may have affected the results. However, in our prospectively designed study, these parameters were attempted to be standardized as much as possible. A questionnaire filled by the physician was used to determine the malnutrition status. The study could be improved by adding laboratory parameters, such as albumin levels and total lymphocyte counts, and anthropometric data. However, questionnaire is the frequently used nutrition survey for the detection of malnutrition

in daily practice in hospitalized patients, which was validated by various studies. Postoperative surgical complications, such as implant failure, nonunion, and malunion, were not analyzed. Our study was planned for the postoperative first-month period. Therefore, previously mentioned complications, which were considered long-term, were not followed so as to minimize variables that would affect the results in the early period. Although it is among the most widely used clinical test for delirium internationally, the Turkish version of 4"AT" test was not validated yet, which was also another limitation of the study. Although cognitive impairment was determined by the 4"AT" test, general cognitive status assessment was not studied.

In conclusion, because the predetermination of hip fractures is not possible in daily practice, it is important to determine the preoperative nutritional and frailty status of patients in terms of postoperative outcomes. The treatment of hip fractures with a multidisciplinary approach and treatment of malnutrition and frailty together in perioperative period will decrease postoperative complications and early mortality. At the same time, examining preoperative risk factors in patients with hip fractures may permit doctors to predict possible outcomes and inform their relatives in advance.

Table 1. Characteristics of the patients.

Variable	n (%)
Gender*	
Male	12 (21.5)
Female	44 (78.5)
Age	79.4 (range, 65-95)
Body Mass Index (mean,sd), kg/m²	25.2 (range 13-40)
Mechanism of injury	
Ground level fall	44 (78.5%)
Fall from height	7 (12.5%)
Traffic accident	3 (5.3%)
Other	2 (3.7%)
Pre-injury functional status*	
No assistive device	32 (57.2%)
Cane	10 (17.8%)
Rolling Walker	8 (14.3%)
Wheelchair	5 (8.9%)
Transfers only	1 (1.7%)
Handgrip (kg)	
Female	10 (range, 5-25)
Male	30 (range, 10-60)
Polypharmacy*	
≤4	38 (67.9%)
>4	18 (32.1%)
Type of fracture*	
Intracapsular	30 (53.6%)
Extracapsular	26 (46.4%)
Length of hospital stay (day)	8.2 (range, 3-26)
ASA score	
2	6 (10.7%)
3	34 (60.7%)
4	16 (28.6%)

*Number of patients; ASA: the American society of anesthesiologist scoring



Table 2. Analysis of postoperative complications.

Variable	n (%)
Acute kidney injury	8 (14.6)
Myocardial infarction	2 (3.5)
Acute Respiratory Distress Syndrome	1 (1.7)
Stroke	1 (1.7)
Pneumonia	2 (3.5)
30-day readmission	3 (5.3)
Deep vein thrombosis-pulmonary embolism	6 (10.6)
Surgical site infection	3 (5.3)

Table 3. Comparison of frailty phenotypes with certain variables.

Variable	CFS			p
	Non-frail	Pre-Frail	Frail	
Number of patients	5 (8.9%)	22 (39.3%)	29 (51.8%)	0.025
NRS-2002 score	1.9	4.2	4.8	0.008
4-AT test score	2.3	3.8	7.6	0.017
Mortality rate (number)	3 (5.3%)	2 (3.5%)	3 (5.3%)	0.542
Handgrip (kg)	22	18	12	0.043
Polypharmacy (>4 drug use)	5	5	8	0.086
Type of fracture				
Intracapsular	13 (23.2%)	7 (12.5%)	10 (17.8%)	0.436
Extracapsular	6 (10.7%)	12 (21.4%)	8 (14.2%)	0.074

CFS: clinical frailty scale; NRS-2002 score: nutritional risk screening-2002 score; 4-AT test: assessment test for delirium

Table 4. Comparison of malnutrition with certain variables.

Variable	NRS-2002		
	<3	3 and more	p
Number of patients	22 (39.2%)	34 (60.8%)	0.041
CFS score	2.8	5.2	0.008
4-AT test	2.4	3.1	0.245
Mortality rate (number)	2	6	0.012
Handgrip (kg)	17	14	0.209
Polypharmacy (>4 drug use)	10	8	0.455
Type of fracture			
Intracapsular	12	18	0.024
Extracapsular	11	15	0.37

NRS-2002 score: nutritional risk screening-2002 score, CFS: clinical frailty scale, 4-AT test: assessment test for delirium

Table 5. Comparison of malnutrition with certain variables.

Variable				
Variable	Sensitivity (%)	Spesificity (%)	Pozitive Predictive Value (%)	Negative Predictive Value (%)
NRS-2002>3	75	41.6	17.6	90.9
CFS>4 (Frail)	37.5	60.4	13.6	85.2
NRS-2002 >3 and CFS>4	75	89.5	54.5	95.5
Delirium				
Variable	Sensitivity (%)	Spesificity (%)	Pozitive Predictive Value (%)	Negative Predictive Value (%)
NRS-2002 >3	47.7	11	52.6	9
CFS>4 (Frail)	42.4	66.5	72.4	35.4
NRS-2002 >3 and CFS>4	44.2	77.8	80.2	40

NRS-2002 score: nutritional risk screening-2002 score; CFS: clinical frailty scale



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