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Prediction of the Mortality with Comorbidity – Polypharmacy Score in the Osteoporotic Hip Fractures

Predikce mortality pomocí CPS – komorbidity-polyfarmakoterapie skóre u osteoporotických zlomenin kyčle

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ABSTRACT

PURPOSE OF THE STUDY

Osteoporotic hip fractures commonly associated with comorbid diseases and use of multiple drugs. Polypharmacy status and the comorbidity-polypharmacy score (CPS) are the most common two grading system to predict mortality risk for the trauma patients older than 45 years. The purpose of the study was to determine whether the CPS or polypharmacy can predict the mortality risk in the older patients had a surgery due to an osteoporotic hip fracture.

MATERIAL AND METHODS

Consecutive patients aged > 65 years had an osteoporotic hip fracture due to a simple trauma were enrolled in the study. Detailed data were collected included comorbid conditions, medications, T-scores and additional fractures. Patients were divided into four groups according to CPS classification and polypharmacy status was indicated in case of using five or more drugs before admission. Overall mortality was assessed using Kaplan-Meier survival testing. Factors influencing 1-year, 2-year and 5-year mortality were evaluated using a multivariate logistic regression model with adjusted odds ratios (AORs) and a threshold significance at $p < 0.05$.

RESULTS

A total of 109 patients (65% women) with a mean age 80 ± 8.06 were included in the study. The mean time to death from the surgery was 42.06 ± 34.9 months. The Kaplan-Meier survival curves showed a significant difference in mortality among CPS groups. (Log-Rank test < 0.001). CPS presented a significant prediction in 1-year (AOR: 4.2; $p < 0.05$) and 2-year mortality (AOR: 2.9; $p < 0.05$) after adjustment for several covariates (including age, gender, surgical procedure) whereas 5-year mortality did not reveal a significant prediction ($p = 0.46$) Polypharmacy existence did not independently predict both overall or year-based mortality ($p > 0.05$) .

CONCLUSIONS

CPS is a better predictor for mortality risk than polypharmacy existence in the first two years in the patients underwent surgery for an osteoporotic hip fracture.

Key words: osteoporotic hip fracture, mortality, polypharmacy, comorbidity.

INTRODUCTION

The individuals aged more than 65 years have been expected to reach 20% of the population by 2030 (14). The geriatric patients with osteoporotic hip fractures associated with multiple comorbidities combined with polypharmacy and trauma surgeons face to manage the complications corresponding the comorbidity beside the hip fracture surgery. In the US, the patients take five or more medications raised from 12.8% to 39% between 1988 and 2010 (1). Mortality following the hip fracture surgery may be linked to complications of the fracture or individual characteristics of the patient such as comorbid hypertension or low-bone density (15, 17).

Polypharmacy refers to the use of multiple medications by the same individual, however, no consensus has been agreed regarding a threshold number. Polypharmacy can be defined as a continuous or dichotomous variable. While some studies determined the association between mortality and polypharmacy among older adults, (1, 3, 13) a recent systematic review did not find a significant relation (4). The Comorbidity-Polypharmacy Score (CPS) has been defined to predict the morbidity and mortality in elderly such that a sum of the number of drugs and comorbid diseases and provide an accurate and predictive measurement (14). In spite of the fact that CPS has been revealed a predictable measurement on mortality, no study has evaluated the independent prediction of CPS on mortality in osteoporotic hip fractures.

The objective of the present study was to assess whether polypharmacy or Comorbidity-Polyphrmacy score could predict the mortality risk in the patients had an osteoporotic hip fracture over age 65.

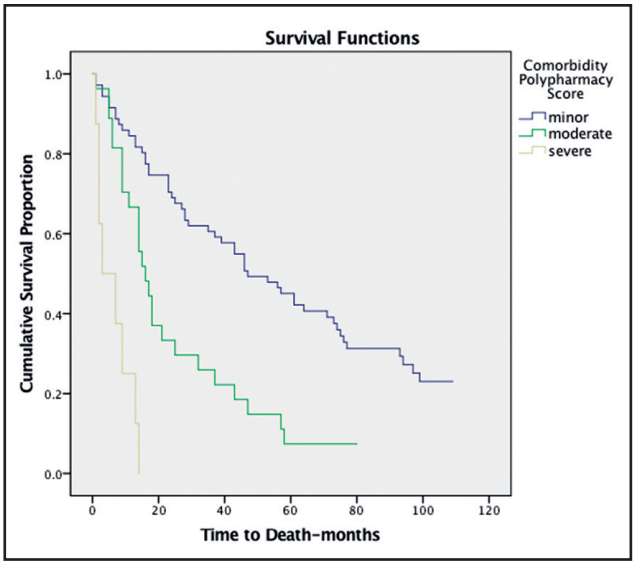

Fig. Kaplan-Meier survival testing among different CPS groups.

MATERIAL AND METHODS

Following Institutional Review Board approval, 133 consecutive patients who were admitted with a preliminary diagnosis of hip fracture and underwent surgery between 2009 and 2013 were enrolled in the present study using the database of Sisli Etfal Training and Research Hospital. Hip fractures occurred following a simple trauma involved in the study. Medical charts and pharmacy records were obtained during admission and following variables were recorded: the etiology of the fracture, additional fractures, comorbid conditions such as diabetes mellitus, epilepsy or etc., medications except for eye drops, intranasal infusers, and topical medications. Eight patients under age 65, six fractures following high energy traumas such as traffic accidents or fall from height, six had T-scores less than -2.5 on the hip or vertebral bone mineral density and four patients had additional long bone fractures required surgery excluded from the study. The remaining 109 patients were included in the study.

The CPS is defined as the sum of the number of medications and all known comorbid conditions as the previous studies (9, 10, 14). For instance, a patient used one medication for (1 point) hypertension (1 point) indicated as 2 points. A patient used two medication(2 points) for a seizure (1 point) and one medication (1 point) for diabetes mellitus (1 point) indicated as 5 points. Patients divided into four groups according to CPS: 0–7 (minor), 8–14 (moderate), 15–21 (severe), or ≥22 (morbid). Polypharmacy status was defined in case of using 5 or more medications based on a previous study (6). Data on deaths were collected via National Death Statement Data. The patients still live were reached via telephone and checked again.

Statistical analysis

Statistical analysis was performed using SPSS version 12 (SPSS Inc, Chicago, IL). Means, frequencies and standard deviations were calculated to summarize the study data. An independent t-test was used to compare the variables between gender and a ^{2} test was used to compare the differences among categorical variables. The survival time was counted in months from the surgery to the day of the death. Survival analysis was performed using Kaplan-Meier/Log-Rank testing. Data were compared for 1-year, 2-year and 5-year mortality using a multivariate logistic regression model. The CPS categories were combined into two groups as minor (0–7 points) and moderate-severe (8–21 points) categories to simplify the analysis. Results of multivariate analyses were reported as adjusted odds ratios (AORs) with 95% confidence intervals (CI) with a threshold significance at $p < 0.05$.

RESULTS

A total of 109 patients with a mean age 80 ± 8.06 were included in the study. The patients were followed to 5 years if they were still alive. Most of the patients were women (n = 71,65%) The mean time to death from the surgery was 42.06 ± 34.9 months. Detailed descriptive information has been presented in Table 1.

No significant difference was found in terms of age, type of fracture, type of surgical procedure and time to death in gender.

The Kaplan-Meier survival curves showed a significant difference in mortality among the CPS groups. (Log-Rank test < 0.001) Overall mortality was as following: 1-year mortality = 27.4%, 2-year mortality = 49.1%, 5-year mortality = 80.2%.

Table 1. Patient characteristics (n = 109)

	Men (n = 71)	Women (n = 38)	P
Age, years (SD)	81.20 (6.5)	79.85 (8.7)	0.41*
Type of the fracture			
collum femoris	22	46	0.84**
pertrochanteric	13	25	
Surgical procedure			
hemiarthroplasty	26	49	0.64**
osteosynthesis	9	22	
Time to death	38.5 (34.6)	43.8 (35.2)	0.47*
CPS			
minor	28	43	
moderate	4	23	
severe	3	5	
Polypharmacy			
(–)	31	50	
(+)	4	21	

CPS – Comorbidty-Polypharmacy Score
* independent t-test, ** χ^2 test

Table 2. Multivariate analyses of variables in mortality

Characteristics	1-year mortality		2-year mortality		5-year mortality	
	AOR (95% CI)	*P*	AOR (95% CI)	*P*	AOR (95% CI)	*P*
Gender						
women	1.00		1.00		1.00	
men	0.2 (0.07–0.7)	0.09	0.7 (0.2–2.05)	0.55	1.46 (0.3–6.4)	0.61
Age (years)	1.1 (1.0–1.2)		1.25 (1.1–1.3)		1.3 (1.2–1.5)	
Surgical procedure						
osteosynthesis	1.00		1.00		1.00	
hemiarthroplasty	2.1 (0.9–6.7)	0.04	1.2 (1.1–1.3)	0.2	0.42 (0.09–1.8)	0.3
CPS						
minor	1.00		1.00		1.00	
moderate-severe	4.2 (1.3–13.9)	0.02	2.9 (1.0–8.5)	0.04	2.1(0.28–15.6)	0.46
Polypharmacy						
(-)	1.00		1.00		1.00	
(+)	2.2 (0.4–10.9)	0.3	1.4 (0.9–8.5)	0.51	0.64 (0.05–7.03)	0.71

AOR – Adjusted Odds Ratio
CPS – Comorbidty-Polypharmacy Score

CPS presented a significant prediction in 1-year (AOR: 4.2, $p < 0.05$) and 2-year mortality (AOR: 2.9, $p < 0.05$) after adjustment for several covariates (including age, gender, surgical procedure) whereas 5-year mortality did not reveal a significance. ($p = 0.46$) Type of surgical procedure revealed a significant prediction only at 1-year mortality (AOR: 2.1, $p < 0.05$) (Table 2).

Polypharmacy did not show significant prediction on mortality in both Kaplan-Meier test (Log-Rank test $p = 0.21$) and multivariate analyses ($p > 0.05$, Table 2).

DISCUSSION

The current study was the first study sought the prediction of the CPS on mortality in the patients underwent surgery for an osteoporotic hip fracture. The most important finding of the study was the overall mortality rate correlated with increased CPS in our cohort. Moreover, the patients with moderate and severe CPS had a 4.2 times more mortality risk in 1 year and 2.9 times more in 2 years while no significant prediction was found in 5-year follow-up. Polypharmacy status which is indicated in patients used more than five drugs was not found as a significant predictor for mortality.

Previous studies mostly evaluated the impact of polypharmacy on mortality in the elderly. Even though some studies determined a significant prediction on mortality associated with excessive polypharmacy, some studies did not find any relation between the use of multiple drugs and mortality (4, 5, 11). Polypharmacy and its effect on mortality still have a controversy. Gnjidic et al. (6) determined that the use of five or more medications increased the rate of the mortality in the older population. In similar Leelakanok et al. (12) reported an association between polypharmacy and death. In a recent study, number of the drugs were not found a predictable for 6-month mortality in the patients had a hip fracture (8). In similar Wimmer et al. reported that polypharmacy was not associated with mortality in 3-year follow-up (18).

The main bias of the aforementioned studies not to distinguish the patients into groups considering the type of fracture or trauma. Previous studies revealed that the CPS has been determined an easy-to-use prognostic tool for the trauma patients (2). Mubang et al. stated that the CPS is an independent predictor for the trauma patients older than 45 years (14). In that study type of the fracture and type of trauma were not considered. Our study assessed the patients in specific groups considering the hip fractures and the patients aged more than 65 years. Hip fractures in our study were osteoporotic fractures and a simple fall was the main reason for the entire cohort. We think that the patients had hip fractures mostly associated with pre-existing conditions and should be assessed seperately than the other fractures occured due to a complex trauma. The patients underwent a hip fracture surgery have already been reported with a high rate of mortality in early term follow-up (at 6 months or 1 year) independently of any covariates (7, 16). Panula et al. found the risk of the mortality in hip fracture patients three times higher than the general population (15). In a similar study, pre-existing conditions were reported the main reason for the mortality in 6 months (7). Our findings also supported the previous studies and revealed that the compexity of the drugs have more impact than the number of drugs. The complexity of the regimen was determined an independent risk factor for poor outcomes and multiple medication use is only one component of complexity (18).

Several reasons may be specified why CPS is a better predictor than polypharmacy following a hip fracture surgery. Even though the drugs may be harmful or

number of comorbid medical conditions may associate with mortality, the number of drugs indicate the severity of the associated medical condition. For instance, using three drugs link to a severe diabetes mellitus whereas using one drug indicates a mild diabetes mellitus. The association between CPS and mortality found in the present study indicates a required intervention to ensure optimal medication in osteoporotic hip fractures. During the admission, comorbidities should be evaluated with a multidiciplinary approach and the possible unnecesary pharmaceuticals should be discontinued.

The present study had also some limitations. First, our study used a retrospective study design, not a randomized study. Second, we did not seek the change in medications during the follow-up. Third, the type of drugs and comorbid diseases were not assessed on its own merits. Finally, our analyses might not have revealed the best cut-off value for the number of the medications to be able to indicate as polypharmacy.

However, evaluating a specified group, only the osteoporotic hip fracture following a simple fall, was the main strength of the study.

CONCLUSIONS

Both comorbidities and the number of the drugs were used have an impact on the mortality in the patients underwent surgery for an osteoporotic hip fracture. CPS is a better predictor than polypharmacy in the first two years follow-up.

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