



The impact of gender differences on mortality in elderly patients after hip fracture

Uticaj polnih razlika na mortalitet starijih bolesnika nakon preloma kuka

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Abstract

Background/Aim. Hip fracture is one of the leading causes of death in elderly population. We evaluated the impact of gender differences on mortality rate in elderly patients with hip fracture. **Methods.** The study included all hospitalized elderly patients (aged over 65 years) with hip fracture during 2013. The patients were classified into four risk groups in accordance with institutional Šišli Etfal risk factor assessment scale ISERFAS to estimate postoperative mortality. Clinical, laboratory and risk score results were gender matched between survived and deceased patients. Hospital mortality was monitored as well as mortality at intervals of three and six months. The prediction effect of gender and overall risk variables on mortality rate were determined by univariate and multivariate logistic regression analyses. **Results.** The complete sample included 434 female and 163 male patients. Average age of men was 77.95 years and 79.18 years for women. Femoral neck fracture was more often seen in women (44.5%), but with no statistically significant difference ($p = 0.57$). Significant difference between

the genders in relation to the risk score values was determined ($p = 0.024$). It was observed that the values of risk score was lower in the female patients and higher in the male patients. Cumulative mortality was 6% during hospital stay, 17.8% after three months and 25% after six months, respectively. In-hospital and six months after the hip fracture, the mortality rates were similar in both genders. The mortality rate was significantly higher in male patients ($p = 0.035$) three months after the hip fracture. The overall risk observed at all mortality intervals was a significant predictor by itself ($p = 0.000$). Independent gender prediction effect disappeared in joint effects of patients' overall risk. **Conclusion.** Gender can be defined as a significant mortality predictor in patients with hip fracture. A risk assessment system to estimate postoperative mortality for hip fractures would be helpful in planning treatment for each patient.

Key words:
hip fractures; aged; risk factors; sex; mortality; comorbidity; serbia.

Apstrakt

Uvod/Cilj. Prelom kuka je jedan od vodećih uzroka smrti u starijoj populaciji. Analiziran je uticaj polnih razlika na stope mortaliteta starijih bolesnika sa prelomom kuka. **Metode.** U studiji su bili uključeni svi hospitalizovani bolesnici stariji od 65 godina sa prelomom kuka tokom 2013. godine. Bolesnici su bili podeljeni u četiri grupe rizika, mali, srednji, visok i veoma visok, u skladu sa institucionalnom Sisli Etfal skalom za procenu faktora rizika postoperativnog mortaliteta (institutional Šišli Etfal risk factor assessment scale – ISERFAS). Klinički, laboratorijski i rizik rezultati upoređeni

su prema polu između preživelih i umrlih bolesnika. Praćen je bolnički, tromesečni i šestomesečni mortalitet bolesnika. Prediktivni uticaj pola i ukupnog rizika na stope mortaliteta testirane su univarijantnom i multivarijantnom regresionom analizom dobijenih rezultata. **Rezultati.** Kompletni uzorak činilo je 434 ženskih i 163 muških bolesnika. Prosečna starost muškaraca je bila 77,95, a žena 79,18 godina. Prelom vrata butne kosti bio je češći kod žena (44,5%), bez statistički značajnosti ($p = 0.57$). Pokazana je značajne razlike u odnosu na muškarce razlika između polova u odnosu na rizik skor ($p = 0,024$). Kod ženskih bolesnika primećen je niži stepen rizika, dok je kod muškaraca

primećen viši. Kumulativni mortalitet bio je 6% tokom hospitalizacije, 17,8% nakon tri, odnosno 25% nakon šest meseci. Stope bolničkog i šestomesečnog mortaliteta bile su slične kada je u pitanju pol, jedino su muškarci značajno češće umirali ($p = 0.035$) tri meseca nakon povrede. Ukupan rizik je na svim posmatranim tačkama mortaliteta ($p = 0.000$) bio značajan prediktor sam po sebi. Samostalni prediktorni uticaj pola se gubio u sadejstvu sa ukupnim rizikom. **Zaključak.** Pol se može definisati kao značajan prediktor

mortaliteta kod bolesnika sa prelomom kuka. Sistem ocenjivanja rizika u proceni postoperativne smrtnosti usled prelom kuka mogao bi biti od pomoći u planiranju tretmana za svakog bolesnika.

Ključne reči:

kuk, prelomi; stare osobe; faktori rizika; pol; mortalitet; komorbiditet; srbija.

Introduction

Hip fracture is one of the leading causes of death in elderly population. Mortality rates have not changed in the last four decades and ranges from 2% to 8% during hospitalization, 8%–10.5% within thirty days after the fracture, about 17% after three months, 11%–28% after six months and 22%–36% after a year^{1–3}.

As for gender structure of the world's population, female population dominates over male population in all elderly groups^{4,5}. Almost all the publications confirmed the hip fractures were more common in women than in men in relation between 1.7:1⁶ and even 4.5:1⁷. Predominance of hip fractures in the female population is a universal phenomenon. In China (Shenyang province) and in Turkey, where men work hard physical labor, the female / male ratio of hip fracture is reversed^{8,9}.

Chronic, multi-systemic and more or less controlled diseases are characteristic for a person with the hip fracture (on average, 3.7 comorbidities). Such person can have cognitive impairment in high percentage and is given multiple medications¹⁰.

A lot of variables affecting the treatment outcomes in the patients with fracture were described and include: age, gender¹¹, interval between admission and the surgery, the level of surgery risk, functional and mental status before the fracture^{12,13}, cognitive impairment¹⁴, presence of multiple diseases before the fracture, American Society of Anesthesiologists (ASA) score¹⁵, hemodynamic disorders¹⁶, type of treatment (surgical or non-surgical) and type of surgical technique¹⁷.

Many studies have indicated gender as an important factor that affects mortality after the hip fracture. This gender conversion is interesting and can be seen in higher incidence rates in women and in higher mortality rates in men^{18,19}.

Statistically significant difference in mortality rate in men in comparison to women is even 2.38 times higher²⁰. Generally, mortality rate is higher in men and is in the range between 32% and 62% annually, and in women it ranges between 17% and 29%^{21,22}.

Methods

The study enrolled all the patients with the proximal femoral fracture over the age of 65 years, hospitalized at the Orthopaedic and Traumatology Clinic of the Clinical Center Niš and Kragujevac, Serbia. All the data, including anam-

nesitic (gender, age), clinical (type of fracture, type of treatment, type of surgery treatment and implant type), laboratory and radiography data were collected using hospital discharge database for the patients hospitalized in both clinical centers.

In accordance with the institutional Šišli Etfal risk factor assessment scale²³ (Table 1), comprising the data on patients' age, daily activities, osteoporosis, dementia, cardiac diseases, etc., the patients were classified into low, moderate, high and very high risk groups.

Individual data were also obtained from the Institute of Statistics Death Registry – Republic of Serbia, six month after the injury, to assess survival rate, obtain the diagnosis by identifying the immediate cause of death and determine factors responsible for mortality in patients with the hip fracture. Mortality rate in elderly patients can be monitored at different intervals. Generally speaking, there are two main periods: in-hospital mortality occurring during the hospital stay and post-discharge mortality occurring after the discharge from hospital. These data are important for survival rate analysis after the fracture (three, six and twelve months). In our study, in-hospital mortality as well as three-month and six-month mortalities were evaluated.

Clinical findings (general health status evaluation, the presence of associated diseases, quantity and type of medication, mobility assessment, type of fracture and injury location), laboratory findings and risk score were gender compared between survived and dead patients.

Complete statistical analysis of the data was done with the statistical software package, SPSS Statistics 17 (Chicago, IL, USA). Most of the variables were presented as the frequency of certain categories, while statistical significance of differences was tested with the χ^2 test.

In case of continuous data, the variables were presented as the mean value \pm standard deviation (SD) and the statistical significance of differences was tested by *t*-test.

Calculations of odds ratios (OD) and their 95% confidence intervals (CI) were done to determine the association between risk factors and outcomes (survival). For that purpose, the most promising independent variables as a single risk factor were incorporated into binary logistic regression analyses. All the analyses were estimated at $p < 0.05$ level of statistical significance.

The prediction effect of gender and overall risk variables on mortality rate were determined by logistic regression analysis; univariate analysis was performed as the first and then multivariate analysis as the second one.

Table 1

Šišli Etfal Research and Training Hospital Risk Scoring System before hip fracture surgery²³

Patient's characteristics	Score		
Age (years)			
< 70	0	Diabetes Mellitus	1
70–79	1	Vascular occlusion	1
80–89	2	Gastrointestinal disease	1
> 90	3		
Daily activity degree before fracture		Lung pathologies	
free	0	asthma	1
one crutch	1	infection	1
walker	2	Chronic obstructive lung disease	
bedridden	3	tumor	1
		tuberculosis	1
Osteoporosis (Singh)		Electrocardiogram	
0–3	0	normal	0
4–5	1	aritmia	1
6	2	infarction sign	2
Dementia (Hagerawa criteria's)		ST-T changes, AV block	3
normal	0	Blood tests	
borderline	1	Hb (g/dL) 11<	1
predementia	2	Hb (g/dL) 11>	0
dementia	3	Total protein (< 6 g)	1
Heart Pathologies		Total protein (> 6 g)	0
myocardial infarction	1	Neurological disease	
angina pectoris	1	hemiplegia	1
right heart failure	1	parkinson	1
ventricular extrasistol	1	Genitourinary disease	1
cardiac aritmia	1	Obesity	1
hypertension	1	Cancer	1

Total risk score: 0–5 – Low risk; 6–10 – Moderate; 11–15 – High; > 15 – Very high.

Results

The complete sample consisted of 597 patients, 434 (72.7%) female and 163 (27.3%) male patients. Average age of women was 79.18 years (age ranges from 65 to 101 years) and 77.95 years for men (age ranges from 65 to 92 years). Intertrochanteric fractures were present in 241 (55.5%) female patients and in 95 (58.3%) male patients. Fractures of the femoral neck were present in 193 (44.5%) females and 68 (41.7%) males. The difference was not statistically significant ($p = 0.57$). As for the injury location, there was a statistically significant difference between male and female patients, namely, 380 (87.6%) women got fractures indoors in comparison to 41 (25.2%) men who got injured outdoors ($p = 0.000$).

Before the hip fracture, 234 (53.9%) women were able to walk independently, 199 (45.9%) required some kind of assisting device and one (0.2%) patient walked with the help of another person before the fracture. On the other hand, 112 (68.7%) males walked independently, 50 (30.7%) required some kind of assisting aid and one (0.6%) male patient walked with the help of another person. The χ^2 test showed significant difference between the genders and mobility before the fracture ($p = 0.003$).

The level of creatinine ($p = 0.001$) was significantly more increased in 61 (37.4%) males in comparison to 100 (23%) females. The level of hemoglobin was lower in 207 f (47.7%) emales in comparison to 64 (39.3%) males.

Of 23 most frequently occurring morbidities among the elderly with hip fracture who were followed in our study, there were only 7 morbidities with a significant difference between men and women (Table 2). Out of 21 groups of medications, the gender difference in medication consumption was registered only in 4.

The χ^2 test also showed significant difference between the genders in the risk score values ($p = 0.024$). In the female patients, the values of low risk score (13.8%) and moderate risk score (46.1%) were observed while in the male patients the risk score was high (49.1%) and very high (1.8%), (Tables 3). Tables 4, 5 and 6 show distribution values of in-hospital, three-month and six-month mortality according to the gender and risk score.

Table 7 shows in-hospital, three-month and six-month mortality rates. In-hospital and six-month mortality rates were similar in both genders. Only three-month mortality rate after the hip fracture was significantly higher in male patients ($p = 0.035$).

Univariate analysis indicated that individual gender prediction effect was defined as a significant mortality predictor only three months after the fracture ($p = 0.032$) while its significance was not registered for in-hospital and six-month mortality rate. Overall risk for patients (ISERFAS) at all mortality intervals is by itself a significant predictor ($p = 0.000$) (Table 8).

Table 2

Groups of morbidities and medications with significantly evident gender differences

Morbidity	Women, n (%)	Men, n (%)	<i>p</i>
Anemia	211 (48.6)	65 (39.9)	0.056
Epilepsy	4 (0.9)	7 (4.3)	0.006
Kidney disease (chronic renal insufficiency, nephropathy, azotemia, etc.)	98 (22.6)	55 (33.7)	0.005
Diseases of the genitourinary tract	4 (0.9)	6 (3.7)	0.019
Hearing problems	6 (1.4)	8 (4.9)	0.011
Thyroid disease	14 (3.2)	0 (0.0)	0.020
Gastritis, ulcer of the stomach /duodenum	14 (3.2)	15 (9.2)	0.002
Medications			
antiepileptics	4 (0.9)	6 (3.7)	0.019
bronchodilators	42 (9.7)	26 (16.0)	0.032
thyroid hormones	10 (2.3)	0 (0.0)	0.051
stomach protector	125 (28.8)	64 (39.3)	0.014

Table 3

Difference between the gender according to the risk score values

Gender	Risk score, n (%)				Total
	low	moderate	high	very high	
Women	60 (13.8)	200 (46.1)	168 (38.7)	6 (1.4)	434 (100.0)
Men*	10 (6.1)	70 (42.9)	80 (49.1)	3 (1.8)	163 (100.0)
Total	70 (11.7)	270 (45.2)	248 (41.5)	9 (1.5)	597 (100.0)

* *p* = 0.024 vs. women.

Table 4

Distribution values of in-hospital mortality according to the gender and risk score

Gender	Risk score, n (%)				Total
	low	moderate	high	very high	
Survivors					
women	60 (14.7)	198 (48.5)	148 (36.3)	2 (.5)	408 (100.0)
men	10 (6.5)	70 (45.8)	71 (46.4)	2 (1.3)	153 (100.0)
total	70 (12.5)	268 (47.8)	219 (39.0)	4 (0.7)	561 (100.0)
Non-survivors					
women		2 (7.7)	20 (76.9)	4 (15.4)	26 (100.0)
men		0 (.0)	9 (90.0)	1 (10.0)	10 (100.0)
total		2 (5.6)	29 (80.6)	5 (13.9)	36 (100.0)

Table 5

Distribution values of three-month mortality according to the gender and risk score

Gender	Risk score, n (%)				Total
	low	moderate	high	very high	
Survivors					
women	58 (16.9)	178 (51.7)	106 (30.8)	2 (.6)	344 (100.0)
men	10 (8.5)	62 (53.0)	45 (38.5)	0 (.0)	117 (100.0)
total	68 (14.8)	240 (52.1)	151 (32.8)	2 (.4)	461 (100.0)
Non-survivors					
women	2 (3.1)	20 (31.3)	42 (65.6)	0 (.0)	64 (100.0)
men	0 (.0)	8 (22.2)	26 (72.2)	2 (5.6)	36 (100.0)
total	2 (2.0)	28 (28.0)	68 (68.0)	2 (2.0)	100 (100.0)

Table 6

Distribution values of six-month mortality according to the gender and risk score

Gender	Risk score, n (%)				Total
	low	moderate	high	very high	
Survivors					
women	58 (18.3)	166 (52.4)	92 (29.0)	1 (.3)	317 (100.0)
men	10 (9.0)	60 (54.1)	41 (36.9)	0 (0)	111 (100.0)
total	68 (15.9)	226 (52.8)	133 (31.1)	1 (.2)	428 (100.0)
Non-survivors					
women		12 (44.4)	14 (51.9)	1 (3.7)	27 (100.0)
men		2 (33.3)	4 (66.7)	0 (0)	6 (100.0)
total		14 (42.4)	18 (54.5)	1 (3.0)	33 (100.0)

Table 7

In-hospital, three-month and six-month mortality rates for men and women

Mortality rate	Total		Women		Men	
	n	%	n	%	n	%
In-hospital	36	6	26	6	10	6.1
three-month	100	17.8	64	15.7	36	23.5*
three- to six-month	33	7.2	27	7.8	6	5.1
six-month	133	25	91	23.5	42	28.6

¹ six-month mortality rate is sum of the mortality rates obtained after three and between three to six months after the injury.

p = 0.035 vs. women

Table 8

Univariate analysis of the gender and overall risk as predictors of mortality including patients with hip fractures

Mortality rate	Wald	Sig.	Odds ratio (OR)	95% CI for OR	
				lower	upper
Hospital					
gender	0.004	0.947	0.975	0.459	2.069
risk	32.203	0.000	13.293	5.439	32.487
Three-month					
gender	4.614	0.032	0.605	0.382	0.957
risk	41.362	0.000	3.754	2.508	5.618
Six-month					
gender	0.958	0.328	1.576	0.634	3.917
risk	12.621	0.000	3.029	1.643	5.581

CI – confidence interval; * *p* = 0.000

Multivariate regression analysis that the total joint effect of gender [OR (95% CI) 1.279] and risk score (ISAR-FAS) in in-hospital mortality defined the multiple risk levels as significant predictors (*p* < 0.001). A three-month mortality rate risk score also proved to be a significant predictor and in the low risk patients as well (*p* = 0.006). A six-month mortality rate showed that joint effects of gender and risk score were disappeared, so neither gender, nor the lowest risk score in the patients were no longer predictors, but something else was.

The independent gender prediction effect disappeared in joint effects with a total risk score in the patients and gender was not a responsible mortality predictor according to multivariate regression model.

Discussion

A typical image of a person with proximal femoral fracture can be compared to an old lady in the eight decade of li-

fe living alone, with decreased motility and problems in daily activities and health problems typical of her age. The image accounts for the male patients as well, but the number of male population of the same age is lower in comparison to females⁴.

Autier et al.²⁴ estimated that by 2031 there would be about 600,000 hip fractures in women and about 150,000 in men, unless effective prevention measures in the European Union (EU) were applied. It was estimated that one in three women and one in nine men over the age of 80 years would experience osteoporotic hip fracture.

Hip fracture incidence doubles for each decade of life after the age of 50, so 93% of women who live up to 80 years of age have at least one fracture, accounting for 33% of hip fracture²⁵.

One of the leading etiological factors is osteoporosis that is most common in women since the menopause induces hormonal deficit that causes osteoporosis. Besides, incidence rates of hip fractures are caused by multiple falls in women due to less muscle mass⁶. An important factor is also the longer life expectancy for women in comparison to men^{4,6}.

However, it is well known that the countries promoting prevention mostly in female population (bisphosphonates, calcium and vitamin D) faced less dramatic incidence of hip fractures in women and the fracture rate was steady in men, as reported for Scandinavian countries²⁶. In another study (USA)²⁷, the efficacy of prevention measures were also pointed out as well as higher incidence of fractures in Caucasian female immigrants not involved in prevention strategies.

Identification of patients at a risk and determination of treatment options can be facilitated by understanding predictors of mortality²⁸.

In their study, Hu et al.²⁸ identified 12 preoperative predictors for post-operative mortality in patients with hip

fracture. They included advanced age, male gender, nursing home or facility residence, poor preoperative walking capacity, poor activities of daily living, higher ASA grading, poor mental state, multiple comorbidities, dementia or cognitive impairment, diabetes, cancer and cardiac disease.

During the performance of our study we observed that gender variable had prognostic value on incidence and mortality rates, but in different ways. This gender conversion showed higher incidence rates in women and higher mortality rates in men. It is clear that female gender is considered a risk factor for hip fracture. So, the risk of hip fracture in women aged 50 years was estimated to be 14%, while in men the risk was only 3%²⁹.

This gender difference cannot be clearly explained. One explanation can be that higher morbidity rate of 32% is registered in males one year after the hip fracture unlike the female population with morbidity rate of 18%²¹.

The significance of these data lies in the fact that although men are relatively young when sustain a hip fracture, they obviously have poorer general health than women which affects the final outcome of hip fracture³⁰. In a study made by Carpintero et al.³¹, it was found that increased mortality rate in men was due to poor nutritional status, multiple comorbidities, habitual cigarette smoking and excessive use of alcohol. However, Allegri-Lopez et al.³² reported that besides decreased functional activities prior the fracture, female gender was proved to be a predictor of increased mortality.

Mobility degree before the injury was significant in patients with hip fracture in our study as well, since its consequences affect general health status in these patients. Women were less motile in comparison to men, which implies that an indoor or outdoor fracture shows patients' physical and mental status prior to injury. About a half of hip fractures in female population was caused by experiencing a loss of confidence in walking, so they restricted their daily activities and became unable, or, unwilling to leave their homes which was increasing the risk of further fractures³³. Moreover, in a very old woman and men, the risk of hip fracture was equal^{34,35}, suggesting that women and men susceptibility to the occurrence of hip fractures was increasing with age.

The health status before the fracture is the best predictor of recovery after fractures. Up to three quarters of patients had the following diseases on admission (hypertension: 20%–40%; ischemic heart disease: 8%–40%; anemia: 25%–35%; dementia: 10%–35%; chronic obstructive pulmonary disease (COPD): 10%–35%; fibrillation: 9%–20%; diabetes mellitus: 7%–20%³⁶). Comorbidities proved to be significant prognostic factors in our study as well as in some others. Analyzing association between preoperative comorbidity and the risk of postoperative complications and mortality, it was found that in the elderly with hip fracture, the presence of three or more preoperative comorbidities represented the strongest risk factors while respiratory infections and heart failure were the most common post-operative complications and proven lead to increased mortality³⁷.

An association between preoperative abnormal values of creatinine and postoperative mortality was established in a study with smaller number of patients³⁸. Increased values of creatinine in male gender were also found in our study. De-

compensated chronic renal dysfunction in elderly patients, resulting from intraoperative or postoperative complications, oliguria and hyperkalemia additionally worsen kidney function. However, preoperative and postoperative preventive measures for reducing renal function may be effective in reducing mortality rate. Chronic renal dysfunction in elderly patients is decompensated due to intraoperative or postoperative complications, the function of the kidneys is additionally worsen by oliguria and hyperkalemia. However, preoperative and postoperative prevention measures against reducing renal function may be effective in mortality decrease.

The studies on mortality rate after discharge from hospital (most commonly monitored three, six and twelve months)³⁹ showed that the advances in surgery and anesthesiology did not significantly reduce mortality rate²². According to literature data, mortality was mostly registered three to six months following the fracture^{19, 40, 41}. Mortality rate declined after that, although never decreased to the level of mortality rate in general population²². The dominance of male gender as a mortality predictor was also registered in our study.

So, the elderly men, who suffer from more chronic diseases (heart failure, COPD hypertension, diabetes), those who live in nursing homes and those with a higher degree of dependence in daily activities are at the greatest risk of dying during the first year after hip fracture¹³.

Conclusion

The most common result of all the studies is that preoperative health status is the most efficient criterion for postoperative mortality prediction. Short-term mortality is explained by a combination of comorbidity and acute effects of trauma or a combination thereof. However there is an increase in the rate of early mortality even in patients with hip fracture without evident comorbidities, suggesting that at least a certain percentage of mortality was caused by immediate consequences of fractures or surgical intervention. We used the risk assessment scale in our study because its broad content facilitates overall assessment. Mortality rates and scored results were statistically significant and correlated with each other.

This study showed evident gender differences: female gender as a risk factor for hip fracture and male gender as a risk factor for lethal outcome. In-hospital and six-month mortality rates were similar regarding the gender, but three-month mortality, after sustaining the injury, showed that men had higher mortality rate. Thus, gender can be defined as a significant mortality predictor in patients with hip fracture.

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