EPIDEMIOLOGICAL ASPECTS OF CONTRALATERAL HIP FRACTURES

Doctoral (Ph.D.) thesis

KRISZTINA JUHÁSZ M.D.

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Prof. József Bódis M.D., Ph.D., D.Sc.

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1. INTRODUCTION

Hip fractures have outstanding significance among osteoporotic fractures because of healthcare, social, and economic burden. There is an increasing tendency with aging society, resulting in an increasing public health problem worldwide.The number of hip fracture was estimated 1.2 million in 1990, with an estimated increase to 8 million by 2050.

There is a changing trend depending on age, gender and geographic region. The lowest incidence was reported in Africa (Nigeria 2/100.000), the highest in Northern European countries (Denmark 574/100.000, Norway 563/100.000, Sweden 539/100.000). Based on literature data the incidence of second hip fracture is between 2 and 20 % among patients suffered from hip fracture. The cumulaive incidence of second or further hip fracture was found 9% in Netherland, 5,08% in Finland, 2,2% among women in Taiwan and 1.8% among men in Taiwan.

Several national studies report on correlation between the incidence of hip fracture and different risk factors. The risk factors of primary hip fracture are the followings: age, female gender, bone density, body mass index, estrogen deficiency, frequent falls, disability, immobilization, low physical activation, low calcium intake, osteomalacia, thyreotoxicosis, smoking, alcoholism, diabetes mellitus. Age, female gender, alcoholism, previous hip fracture, location of hip fracture, functional status, dementia and osteoporosis are reported as the risk factors of second hip fracture, however there is not enough mostly Hungarian data about what are the factors and how they influence the incidence of further or second hip fracture, which can explain the parallel epidemiological investigation of these fracture with primary hip fracture.

The average time until the second hip fracture can change within wide range in the studies published in the topic and using varios methodologies. Detection of the factors influencing the time until second hip fracture can contribute to the identification of patients with high risk.

Among the osteoporotic fractures the health care costs of hip fractures are extremely high. 600.000 new hip fractures occurred in European Union in 2010. The health care costs were estimated 20 billion euro, which represent the 54% of cost associated with osteoporotic fractures. According to some estimates with the increase in the number of hip fracture from 79.000 to 104.000 the health care and social costs will increase from 2 billion pounds to 3 billion pounds.

The complication after the treatment of second hip fracture are wound infection, dislocation, cardiac and pulmonary complication, urinary tract infection, and death. Compared to primary hip fracture the second hip fracture are associated with higher mortality. The one year mortality was detected 15,9% by patients with primary hip fracture, the five year mortality 45,4%, while others found it 24,1% and 66,5% by patients with second hip fractures. A Scottish study reported on 68%

one year survival by patients with primary hip fracture, while the one year survival by patiets with further hip fracture was found 63%.

Considering the occurrence, the incidence of complication, the high mortality, the high health care costs of second hip fracture published in the international literature, and the partial or complete deficiency of Hungarian data of second hip fracture, there is a need of epidemiological analysis based on Hungarian data, to develop efficacious prevention and treatment strategies.

2. AIMS

The dissertation focuses on the incidence of contralateral hip fracture after femoral neck fracture, the trend in incidence of contralateral hip fracture, the risk factors of contralateral hip fracture, the time until the contralateral hip fracture, the mortality of contralateral hip fracture, and its prognostic factors. The aims of the dissertations are the followings:

1. To overview and analyze data associated with incidence, mortality, treatment, complications, costs and rehabilitation of hip fractures based on Hungarian data.
2. To analyze the incidence and distribution of contralateral hip fracture after femoral neck fracture in patients over 60 years.
3. To evaluate the correlation between the incidence and prognostic factors of contralateral hip fractures after femoral neck fracture.
4. To evaluate the prognostic factors influencing the time until the contralateral hip fracture after femoral neck fracture.
5. To analyze the 30 and 365 days mortality after contralateral hip fracture, and the evaluation of 365 days mortality per monthly .
6. To evaluate of the prognostic factors related to the 30 and 365 days mortality after contralateral hip fracture in patients over 60 years.

Detailed methodology, results and discussion are given in the next parts based on our previous publications.

3. DETAILED ANALYSIS

3.1. Multidisciplinary approach of hip fractures based on Hungarian data

Hip fractures are described by increased mortality, loss of quality of life, functional decline and burden of diseases. They show a growing number worldwide. The aim of the present study is to summarise the existing data on the incidence, mortality, complications, costs and rehabilitation of hip fractures, which relevance is reported only by few studies. To reduce the mortality and complications of hip fractures the authors emphasize the importance of primary treatment within 12 hours, appropriate selection of surgical methods corresponding to the fracture type after the assessment of femoral head viability, vitamin D supplementation, same conditions for primary treatment during everyday of the week, and an adequate acute treatment and rehabilitation for patient's general health status. In the future integrated processing of multidisciplinary results of hip fractures based on Hungarian data can support the development of efficient treatment and prevention strategies, which can be advantageous for the patient, families, health care system, and the society, too, by the reduction of costly complications of hip fracture healing and mortality.

TIMING OF SURGERY
• **Perform surgery on the day or the day after admission.**
• **Identify and treat correctable comorbidities immediately so that surgery is not delayed by anaemia, anticoagulation, volume depletion, electrolyte imbalance, uncontrolled diabetes, uncontrolled heart failure, correctable cardiac arrhythmia or ischaemia, acute chest infection, exacerbation of chronic chest conditions.**
SURGICAL PROCEDURES
• **Operate on patients with the aim to allow them to fully weight bear (without restriction) in the immediate postoperative period.**
• **Offer replacement arthroplasty (total hip replacement or hemiarthroplasty) to patients with a displaced intracapsular hip fracture.**
• **Offer total hip replacement rather than hemiarthroplasty to patients with a displaced intracapsular hip fracture who were able to walk independently out of doors with no more than the use of a stick and are not cognitively impaired and are medically fit for anaesthesia and the procedure.**
• **Use cemented implants in patients undergoing surgery with arthroplasty.**
• **Consider an anterolateral approach in favour of a posterior approach when inserting a hemiarthroplasty.**
• **Use extramedullary implants such as a sliding hip screw in preference to an intramedullary nail in patients with trochanteric fractures above and including the lesser trochanter (AO classification types A1 and A2).**
• **Use an intramedullary nail to treat patients with a subtrochanteric fracture.**
MOBILISATION STRATEGIES
• **Offer patients a physiotherapy assessment, and mobilisation on the day after surgery, unless medically or surgically contraindicated**.
• **Offer patients mobilisation at least once a day and ensure regular physiotherapy review.**

Table 1
Managament of hip fracture according to NICE (National Institute for Health and Care Excellence) (https://www.nice.org.uk/guidance/cg124)

3.2. Risk factors for contralateral hip fractures following femoral neck fractures in elderly: analysis of the Hungarian nationwide health insurance database

Objectives: To investigate the significance of demographic and clinical factors on incidence of contralateral hip fracture in elderly Hungarian population using the nationwide health insurance database.

Patients and methods: The study included a total of 3783 patients (917 males, 2866 females) treated for primary monotraumatic femoral neck fractures caused by low-energy trauma in the year 2000. Cox regression, Kaplan-Meier survival analyses, and log-rank test were performed to evaluate the following prognostic factors: age, gender, place of living, type of primary fracture and surgical intervention, hospital providing treatment for primary fracture, and comorbidities.

Results: A total of 312 patients (8.2%) suffered second hip fractures. The univariate Cox regression analysis showed a significantly higher risk for second hip fracture in patients having advanced age (p=0.001), female gender (p=0.022), living in capital (p=0.024), and having arthroplasty (p=0.001). Advanced age (p≤0.001) and having arthroplasty (p=0.004) were significant risk factors for contralateral hip fractures according to multivariate analysis (*Table 2*). Log-rank test showed significantly longer survival in females (p<0.001) than in males and in patients with arthroplasty (p=0.013) compared with those having osteosynthesis (*Table 3*).

Conclusion: Our study demonstrates that the risk of suffering from contralateral hip fractures is higher in females, elderly population, those living in the capital, and patients having undergone arthroplasty. Identification of high-risk groups for contralateral hip fractures is needed to establish.

PROGNOSTIC FACTORS	Univariate analysis			Multivariate analysis		
	HR	(95% CI)	P value	HR	(95% CI)	P value
AGE						
years	1.59	(1.20 - 2.10)	0.001	1.03	(1.02 – 1.05)	**0.000**
GENDER						
female/<u>male</u>	1.43	(1.05 - 1.94)	0.022	1.27	(0.93 – 1.73)	0.14
PLACE OF LIVING						
capital / <u>village</u>	1.43	(1.05 – 1.95)	0.024	1.34	(0.89 – 2.01)	0.165
town / <u>village</u>	1.32	(0.94 – 1.85)	0.116	1.24	(0.88 – 1.76)	0.227
city / <u>village</u>	1.05	(0.77 - 1.44)	0.749	1.00	(0.86 – 1.92)	0.983
no data / <u>village</u>	1.08	(0.63 – 1.86)	0.771	1.06	(0.59 – 1.92)	0.851
TYPE OF HOSPITAL PROVIDING CARE FOR THE PRIMARY FRACTURE						
capital / <u>county</u>	0.99	(0.75 - 1.32)	0.951	1.09	(0.81 – 1.46)	0.587
town / <u>county</u>	1.14	(0.85 - 1.55)	0.380	0.99	(0.67 – 1.48)	0.972
national inst.,university clinics/<u>county</u>	1.22	(0.87 - 1.71)	0.258	1.00	(0.69 – 1.46)	0.992
TYPE OF PRIMARY FRACTURE						
extracapsular/ <u>intracapsular displaced</u>	0.86	(0.65 - 1.13)	0.275	0.97	(0.73 – 1.28)	0.818
intracaps. undisplaced/<u>intracaps. displ.</u>	0.78	(0.52 - 1.17)	0.230	0.84	(0.56 – 1.27)	0.416
ICD GROUPS OF ACCOMPANYING DISEASES						
1/<u>0</u>	0.96	(0.67 - 1.37)	0.810	0.86	(0.60 – 1.24)	0.423
2/<u>0</u>	1.18	(0.81 - 1.72)	0.400	1.04	(0.71 – 1.53)	0.845
≥3/<u>0</u>	1.00	(0.62 - 1.60)	0.999	0.83	(0.51 – 1.34)	0.448
TYPE OF SURGICAL INTERVENTION FOR PRIMARY FRACTURE						
arthroplasty / <u>osteosynthesis</u>	1.60	(1.20 - 2.10)	0.001	1.56	(1.56 – 2.09)	**0.004**

The reference values are underlined, HR: Hazard Ratio, CI: Confidence Interval, ICD: International Statistical Classification of Diseases and Related Health Problems

Table 2 *Cox regression analysis of prognostic factors for contralateral hip fracture*

PROGNOSTIC FACTORS	Average survival time (days) **(95% CI)**	Median survival time (days) **(95% CI)**	p-value
GENDER			
female	1567.89 (1519.94 - 1615.83)	1310.00 (1205.42 - 1414.58)	**0.000**
male	1240.64 (1160.41 - 1320.86)	795.00 (672.24 - 917.76)	
TYPE OF PRIMARY FRACTURE			
arthroplasty	1659.75 (1542.65 - 1776.86)	1528.00 (1239.18 - 1816.82)	**0.013**
osteosynthesis	1463.46 (1419.24 - 1507.68)	1115.00 (1027.11 - 1202.89)	
PLACE OF LIVING			
capital	1519.73 (1431.27 - 1608.19)	1307.00 (1106.30 - 1507.69)	0.732
town	1473.25 (1395.45 - 1551.04)	1118.00 (963.47 - 1272.52)	
city	1481.80 (1379.24 - 1584.37)	1113.00 (920.87 - 1305.12)	
village	1456.86 (1379.84 - 1533.88)	1110.00 (975.65 - 1244.34)	
no data	1599.45 (1410.47 - 1788.42)	1387.00 (948.46 - 1825.53)	

CI: Confidence Interval

Table 3
Kaplan-Meier survival and log-rank analysis of contralateral hip fractures according to prognostic factors.

3.3. The analysis of prognostic factors influencing the time until contralateral hip fracture in Hungarian aging population

Introduction: The aim of the study is to evaluate the incidence of contralateral hip fracture after femoral neck fracture, and the effect of prognostic factors on time until contralteral hip fracture.

Patients and methods: In the analysis patients older than 60 years, were operated in year 2000 with femoral neck fracture were investigated, who suffered from contralateral hip fracture until 2008. December 31. Age, gender, comorbidity, type of surgical intervention for primary fraction, place of living and type of hospital providing care for primary fracture were evaluated by one way ANOVA considering the time until contralateral hip fracture.

Results: 312 patients met the criteria. The annual incidence of contralateral hip fracture after femoral neck fracture changed between 1.5 and 2.1%, and the cumulative incidence was 8.24%. The average time until contralateral hip fracture was 1159.8 days. There was no significant alteration between the annual incidence of contralateral hip fracture (*Table 4*). Significantly shorter time was detected in patients with higher age (p=0.010) (*Table 4*).

Conclusions: There was no significant difference between the annual incidence of contralateral hip fracture in patients over 60 years with femoral neck fracture. The shorter time until the contralateral hip fracture by the older age groups highlights the need of elaboration of prevention strategies.

PROGNOSTIC FACTORS	I. Contralateral hip fracture		II. Time until contralateral hip fracture (day)	III. p value
	cases	(distribution %)	average (day)	
GENDER				
female	263	84,3	1141,82	0,414
male	49	15,7	1256,06	
AGE GROUPS				
60-69 year	53	18	1416,62	0,010
70-79 year	148	47	1207,43	
80-89 year	97	31	1015,62	
90 year	14	4	682,14	
COMORBIDITY				
presence	274	87,8	1128,98	0,104
absence	38	12,2	1381,71	
TYPE OF FEMORAL VACK FRACTURE				
intracapsular undisplaced	67	21,5	1166,19	0,627
intacapsular displaced	219	70,2	1177,08	
extracapsular	26	8,3	997,27	
TYPE OF SURGICAL INTERVENTION FOR PRIMARY FRACTURE				
osteosynthesis	251	80,4	1205,17	0,070
arthroplasty	61	19,6	972,90	
PLACE OF LIVING				
village	76	24,4	1241,22	0,566
town	78	25	1132	
city	58	18,6	1179,47	
capital	84	26,9	1054,02	
no data	16	5,1	1391,81	
TYPE OF HOSPITAL PROVIDING CARE FOR THR PRIMARY FRACTURE				
town	104	33,3	1256,34	0,398
county	88	28,2	1184,15	
capital	72	23,1	1031,78	
national institutes and university clinics	48	15,4	1097,77	

Table 4.
Number and distribution of contralateral hip fracture (1. column), time until contralateral hip fracture (2. column), and the value of ANOVA analysis (III. column) according to the prognostic factors

3.4. Analysis of mortality and its predictors in patients with contralateral hip fracture after femoral neck fracture

Introduction: There is a high mortality with not well understood risk factors after the second hip fracture.

Aim: Analysis of the 30 and 365 day mortality and its risk factors in patients with contralateral hip fracture.

Method: Patients with contralateral hip fracture between 01 Jan 2000 and 31 Dec 2008 were identified among those who suffered their primary hip fracture in Hungary in 2000. Risk factors as age, sex, concomitant and chronic diseases, type of fracture and surgery, surgical complications, day of admission were analyzed by logistic and Cox regression as well as Kaplan-Meier analysis.

Results: There were 312 eligible patients identified with 8.3 % mortality rate at 30 and with 38,4% at 365 days respectively *(Figure 1)*. Significant risk factors for the 30 day mortality were intertrochanteric type of fracture (OR: 4.722; HR: 4.129) and non operative management (OR: 7.357; HR: 6.317) while for the 365 day mortality those were older age (OR:1.070; HR:1.050) and type of surgery (OR:0.450). (*Table 5, 6*) *(Figure 2)*

*Conclusion:*Age, type of fracture and type of surgery provide to be risk factors. There is a need to identify further risk factors in order to develope an efficacious prevention strategy for the reduction of the mortality after the second hip fractures.

PROGNOSTIC FACTORS	30 days mortality			365 days mortality		
	OR	95% CI	p value	OR	95% CI	p-value
AGE						
years	1.041	0.980-1.106	0.196	1.070	1.033-1.109	0.000
GENDER						
female/<u>male</u>	0.397	0.148-1.067	0.067	0.577	0.301-1.105	0.097
COMORBIDITY						
presence/<u>absence</u>	n.i.			n.i.		
LOCATION OF HIP FRACTURE						
pertrochanteric/ <u>femoral neck</u>	4.722	1.750-12.742	0.002	1.053	0.609-1.821	0.852
others/ <u>femoral neck</u>	2.428	0.433-13.620	0.313	0.484	0.154-1.520	0.214
TYPE OF INTERVENTION						
arthroplasty/ <u>osteosynthesis</u>	1.116	0.215-5.799	0.896	0.450	0.208-0.975	0.043
none/ <u>osteosynthesis</u>	7.357	1.197-45.229	0.031	3.683	0.748-18.14	0.109
LOCAL COMPLICATION						
presence/<u>absence</u>	1.387	0.045-3.322	0.386	1.496	0.633-3.532	0.359
DAY OF ADMISSION						
weekday/<u>weekend</u>	1.105	0.423-2.888	0.839	1.194	0.685-2.081	0.531

The reference values are underlined. n.i.: not interpretable. OR: Odds Ratio, CI: Confidence Interval.

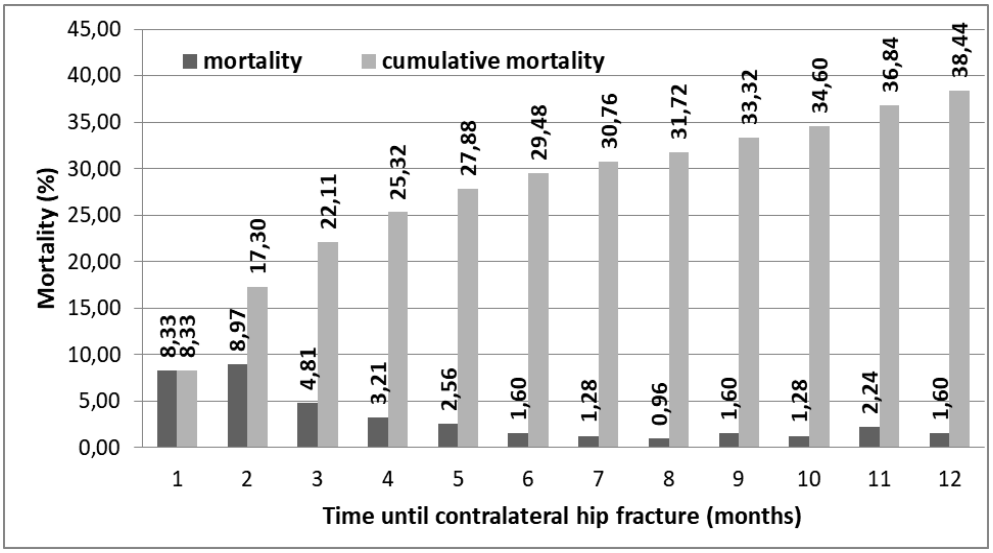
Table 5.

Multivariate logistic regression analysis of 30 and 365 days mortality after contralateral hip fracture

PROGNOSTIC FACTORS	30 days mortality			365 days mortality		
	HR	95% CI	p value	HR	95% CI	p value
AGE						
years	1.035	0.980-1.093	0.213	1.050	1.024-1.077	0.000
GENDER						
female/ male	0.443	0.181-1.081	0.074	0.639	0.405-1.006	0.053
COMORBIDITY						
presence/ absence	n.i.			n.i.		
LOCATION OF HIP FRACTURE						
pertrochanteric/ femoral neck	4.129	1.637-10.412	0.003	1.176	0.787-1.757	0.429
others/ femoral neck	2.089	0.415-10.507	0.372	0.692	0.276-1.734	0.432
TYPE OF INTERVENTION						
arthroplasty/osteosynthesis	1.046	0.212-5.153	0.956	0.552	0.289-1.054	0.072
none/ osteosynthesis	6.317	1.256-31.769	0.025	2.084	0.837-5.188	1.115
LOCAL COMPLICATION						
presence/ absence	0.392	0.051-3.038	0.37	1.255	0.688-2.290	0.459
DAY OF ADMISSION						
weekday/ weekend	1.128	0.464-2.746	0.790	1.119	0.738-1.696	0.598

The reference values were underlined, n.i.: not interpretable. HR: Hazard Ratio, CI: Confidence Interval.

Table 6.
Multivariate COX regression analysis of 30 and 365 days mortality after contralateral hip fracture



1. Figure
Mortality after contralateral hip fracture per months (%) and cumulative mortality (%)

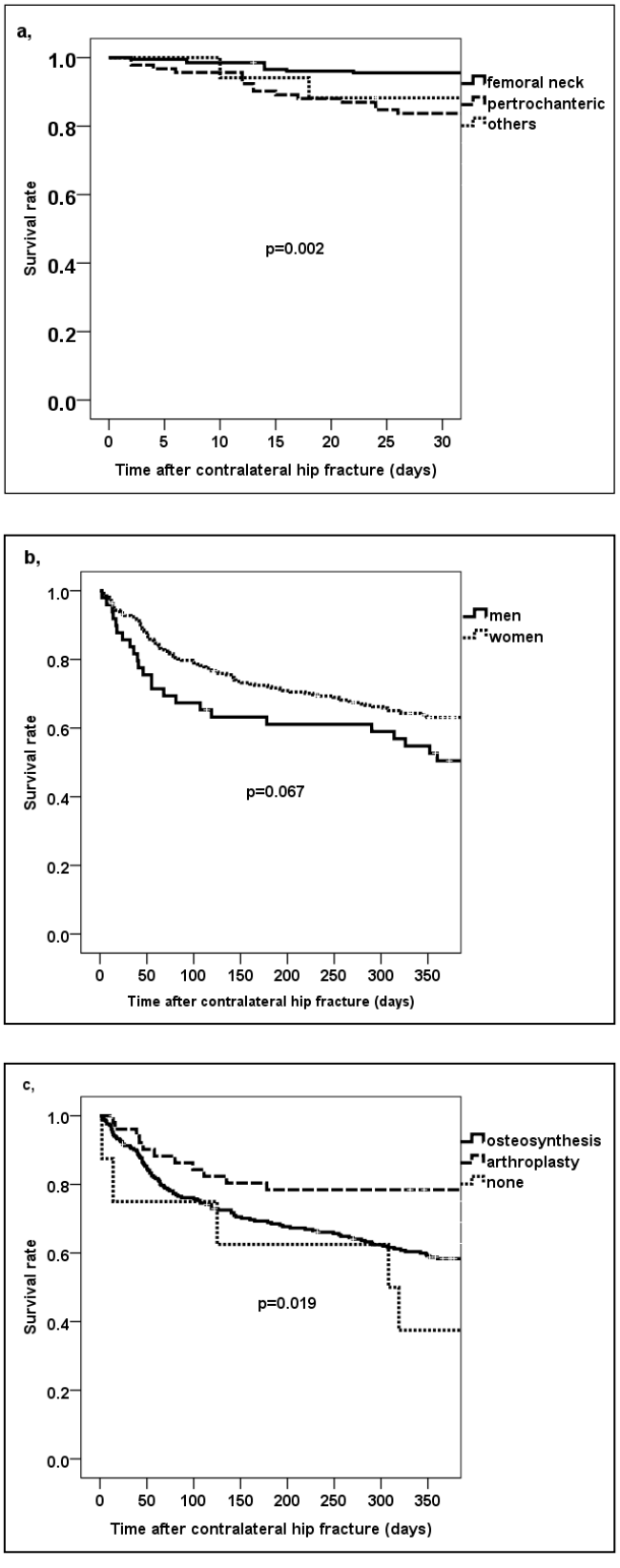


Figure 2.
Kaplan-Meier survival curve 30 and 365 days after contralateral hip fracture according to location of hip fracture (a.), gender (b.), and type of intervention (c.)

4. NOVEL FINDINGS AND PRACTICAL APPLICATION

4.1. Novel findings

1. Evaluation of annual distribution, trend, annual incidence, and comparison, as well as cumulative incidence of contralateral hip fracture after femoral neck fracture.

2. Evaluation of risk factors of contralateral hip fracture after femoral neck fracture by Cox regression analysis with the demonstration of correlation between the female gender, higher age, arthroplastical surgical intervention and living in capital.

3. Evaluation of prognostic factors of time until contralateral hip fracure after femoral neck fracture by analysis of variance with the demonstration of correlation between higher age and shorter time until the contralateral hip fracture.

4. Determination of 30 and 365 day mortality after contralateral hip fracture after femoral neck fracture and the demonstration of 365 days mortality per monthly.

5. Evaluation of prognostic factors of 30 and 365 days mortality of contralateral hip fracture by logistic and Cox regression analysis with the demonstration of correlation between higher mortality and pertrochanteric fracture type, absence of surgery, higher age and osteosynthesis.

6. Shorter 30 days survival was revealed by Kaplan-Meier analysis and log-rank test by patients with pertrochanteric fracture type, and shorter 365 days survival by patients with osteosynthesis and absence of surgery.

4.2. Practical application

Patients with previous hip fracture have higher risk for further hip fracture. There is a need for the analysis of the effect of prognostic factors, which can influence the risk for second or further hip fractures. The results of the dissertation will provide effective basis for professional and health-related political decisions that are aimed to elaboration of integrative prevention strategy in the future. Until then there is a need for enforce the preventive approach in order to optimalisation of health gain exploitable at different levels of healthcare system.

1. We recommend the elaboration of hip fracture management guidelines considering the rehabilitation starting in early postoperative period.

2. We recommend the elaboration of effective and uniform prevention strategy of hip fractures- in particular the identification of risk groups and the beginning of antiosteoporotic therapy- in order to prevent primary and further fractures, to reduce of complication and mortality, and to improve general health status.

3. Until the elaboration of uniform prevention strategy we recommend the integrated cooperation of outpatient care (traumatology)- primary care (general practice) – nursing (institutional and home care, family) – and rehabilitation care axis in order to the prevention.

4. We recommend the use of separate codes of further hip fractures on the same or contralateral side -during the anamnesis and assessment of fracture- as responsibility of health service provider.

5. Similarly to the NICE guideline we recommend the multidisciplinary management of patients with hip fracture, as part of it a multidisciplinary rehabilitation and orthogeriatric multidisciplinary control based on an orotgeriatric assesment are done with the cooperation of specialists of prevention, mental health and bone health and the primary care, outpatient care and social services.

ACKNOWLEDGEMENTS

I express my thanks to:

Andor Sebestyén president (University of Pécs, Clinical Centre, Pécs) for the tutor guidance provided during my doctoral work, and inspiring support.

Imre Boncz professor (University of Pécs, Faculty of Health Sciences) for all the help and advices provided during my doctoral work.

József Bódis professor (University of Pécs, Faculty of Helath Sciences), leader of the Doctoral School, for facilitating my research and studies in the doctoral program.

Horváthné Kivés Zsuzsanna, for her recommendations to my doctoral work.

The collegues of National Health Insurance Fund for all the help and support during my researh.

Last, but not least I am grateful to my family for their support and understanding.