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PhD THESIS

**COGNITIVE IMPAIRMENT AND QUALITY OF LIFE
IN ELDERLY PATIENTS WITH HIP FRACTURES**

ABSTRACT

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INTRODUCTION

Over the past decades, the industrialized regions of the world have faced the phenomenon of population ageing. (1) In this context, the cost of the elderly care becomes a challenge for health systems. Both dementia and hip fractures are two conditions specific for the elders, and the optimization of care strategies for such patients becomes very important.

In Romania, the information available on elderly patients with hip fractures is limited, and cognitive assessment in the Orthopaedic departments is not a routine. The only survey carried out for investigating this pathology in the western part of Romania indicates that the incidence rate of hip fracture, per 100,000 inhabitants, increases with age, from 122 in women and 127 in men, for the 65-69 age group, up to 1100 in women and 950 in men, for the ≥ 85 age group. The mortality rate was of 10% one month, 20% four months and between 21 and 30% one year after the traumatic event. (2) The data included in the international medical literature are also scarce. (3,4).

The current study is the first one assessing the cognitive impairment, quality of life and post-fracture functionality of hip fracture patients. Knowing such characteristics of this group of Romanian patients will emphasize aspects that, at the current moment, are not taken into consideration when establishing the care strategies for elderly patients with hip fracture.

GENERAL PART

HIP FRACTURE IN ELDERLY PATIENTS AND ITS RELATIONSHIP WITH COGNITIVE IMPAIRMENT

I. ORTHOPAEDIC THEORETIC CONSIDERATIONS ON PROXIMAL FEMORAL FRACTURES

The fractures of the proximal end of the pelvic limb are classified as: femoral head fractures, femoral neck fractures, and fractures of the trochanteric area, including: fractures of the lesser trochanter, fractures of the greater trochanter and pertrochanteric fractures.

The fractures of the femoral neck can be included in one of the following categories, according to the Garden classification: type I: incomplete, type II: complete non-displaced, type III: complete partially displaced, type IV: complete, completely displaced. Pertrochanteric fractures can be classified as: cervico-trochanteric fractures, simple and complex pertrochanteric fractures, intertrochanteric fractures and subtrochanteric fractures. The femoral neck and pertrochanteric fractures occur mainly in the patients aged over 65, usually as a result of an accidental fall. An adequate surgical or orthopaedic treatment most often results into fracture healing, but, in elderly patients with co-morbidities and mobility impairment, prognosis is not optimistic. (5)

II. ACCIDENTAL FALLS - A PUBLIC HEALTH PROBLEM

Approximately 37.3 million falls severe enough to require medical attention occur each year worldwide. Due to cognitive, sensory and physical impairments associated with ageing, the most frequently affected group of population is represented by the elderly. (6) One of the most important consequences of falls occurring in the elderly is hip fracture. (7) Risk factors for falls can be divided into two categories: intrinsic and extrinsic. Intrinsic factors are related to individual particularities: advanced age, chronic conditions, muscle weakness, impaired mobility and balance, and cognitive dysfunction. Extrinsic factors include: the medication used, environmental elements and activities being carried out. (8) Among the patients suffering from dementia, the reported annual rate of accidental falls is between 47 to 90% (9,10). Recently, the WHO has pointed out the importance of prioritizing scientific research in the field of fall prevention strategies intended for elderly people and of establishing effective risk reduction policies. (11)

III. DEMENTIA AND HIP FRACTURES

There is a two-way relationship between dementia and hip fractures: on the one hand, people suffering from dementia are at high risk of undergoing this type of fracture, and, on the other hand, hip fractures lead to the development and accentuation of cognitive impairment. The high risk of hip fracture faced by a person with dementia is due to the occurrence of three important mechanisms: the existence of risk factors common to both conditions: age, vitamin D deficiency, lifestyle and genotype ApoE4; the occurrence of some factors mediating the risk for an elderly person with dementia to suffer a hip fracture, such as: accidental fall, osteoporosis, and vitamin D deficiency; the adverse effects of psychiatric medication administered to patients with dementia increase the risk of hip fracture. (12)

IV. PATIENTS WITH DEMENTIA IN GENERAL HOSPITALS

About 30-40% of the elderly patients admitted in general hospitals suffer from dementia. (13, 14) The medical staff in general hospitals is still under-skilled in recognizing dementia and its associated symptoms, and when this pathology is not identified, patients' treatment is suboptimal. (14) In order for a hospital to comply with the concept of "dementia-friendly", the following elements are mandatory: the presence of qualified staff and devotion of the necessary time for these patients, involvement of the next of kin and the creation of a partnership with the latter, assessment and early identification of dementia in the hospital, personalized care, and configuration of the environment for the needs of the person with dementia. (15)

V. THE TREATMENT, REHABILITATION AND MORTALITY RATE AFTER HIP FRACTURE

In the orthopaedic department, the treatment of a patient with dementia and hip fracture is difficult, first because these patients tend to develop temporal and spatial disorientation conditions when leaving the normal living environment, which results into psychomotor agitation and hinder the therapeutic approach. There are three major intervention categories efficient in improving the outcome of this patients: multidisciplinary interventions, pharmacological and multifactorial interventions (including, among others, cardiovascular treatment, vision correction, physiotherapy, occupational therapy, medication management, elimination of environmental risk factors at home). (16) In the first 30 days after surgery, elderly patients with hip fractures and comorbid dementia are at high risk for medical and surgical complications. (17) The 30 days and 6 months mortality rate is double in those having dementia. (18) 1 year after the fracture, mortality rate is of one third for those with dementia, and of 18% for the non-affected patients (19).

DELIRIUM ASSOCIATED WITH HIP FRACTURES

According to the American Academy of Orthopaedic Surgeons, 48% of the patients aged over 65, having a hip fracture, suffer from perioperative delirium (before, during or after surgery), and this percentage significantly increases the duration of hospitalization, care costs and risk of institutionalization. (20) The most important risk factors for post-operative delirium in elderly patients undergoing surgery for hip surgery are the pre-existing cognitive impairment, old age and institutionalization. (21) There are clues indicating that these patients present, in the long term, a greater cognitive decline than patients without dementia. (22) Objective assessment tools are currently available, and while preventive and pharmacological treatment methods did not prove to be clearly efficient, two meta-analyses conducted in 2015 support the use of non-pharmacological multi-component interventions to prevent delirium. (24, 25)

THE QUALITY OF LIFE AFTER HIP FRACTURE

In an elderly person's life, a hip fracture marks the beginning of a period of difficulties, such as hospitalization, surgery, pain, the addition of new medicines, immobilisation, followed by movement difficulties, recovery period, dependence on others, and limitation in day-to-day activities. The studies that evaluated the quality of life after hip fracture unanimously indicated a deterioration of the functional capacity and quality of life. (26) Besides the need for pre-morbid care, cognitive impairment also determines a low quality of life at the end of the patient's acute-care period. (27)

In the medium to long term, hip fractures in elderly patients lead to a decrease of the quality of life, by affecting mobility, self-care, day-to-day and social functionality. Only 40 - 60% of the patients manage to reach the previous level of mobility 1 year after the fracture, and only 40-44% of the patients who were previously independent in terms of mobility regain this independence. The hip fracture is followed by a general deterioration process affecting the general health condition and cognitive function, and 10 to 20% of the patients who used to live in their own homes become institutionalized within 6-12 months. (28) One of the most important psychological consequences of the hip fracture occurring by accidental fall is the fear of a new fall. This is an important determinant for a lower quality of life in the elderly due to its negative impact on lifestyle, self-confidence and emotional state. (29)

SPECIAL PART

RESEARCH METHODOLOGY

The main objective of the research was to establish the degree of cognitive impairment in the elderly patients with a hip fracture in the western part of Romania. Our most important **secondary objectives** have been the following: assessing the patients' quality of life and functionality 1 year after the fracture and their relationship with both the previous cognitive status, and premorbid functionality; identifying the prevalence of post-operative delirium; testing the utility of the clock drawing test as a quick and reliable tool for assessing, while in hospital, the patient's cognitive performance and risk of developing post-operative delirium; reporting the survival rate at 3 months and 1 year after hip fracture and identifying the premorbid risk factors.

The study complies with the fundamental **ethical** principles of medical research involving human subjects, included in the Good Clinical Practice (GCP), originating from the Declaration of Helsinki, adopted in 1964 and amended in 2008.

The current project is the result of the collaboration between the Orthopaedic Clinic I and II and the Liaison Department of Psychiatry within "**Pius Brînzeu**" **Clinical Emergency County Hospital in Timisoara**, a hospital unit providing medical services to the population in the western region of Romania.

The studied group included 100 patients who were consecutively admitted in the Orthopaedic Clinic I or in the Orthopaedic Clinic II of "Pius Brînzeu" Clinical Emergency County Hospital in Timisoara between March and October 2016. The subjects included in the study were ≥ 65 years old, and their main diagnosis was fracture of the proximal end of the femur occurring by accidental fall.

The research was conducted in three **phases**. The first phase took place during hospitalization, at the patient's bed, and mainly consisted of assessments of the cognitive function, delirium, functionality and quality of life before fracture. The following two phases were conducted by telephone 3 months and one year after the fracture, and were aimed at assessing the quality of life, functionality and survival rate. The cognitive function was assessed using three standardized **tools**: Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and the Clock Drawing Test in the 4 point version. (30 - 32) Delirium was investigated using the Confusion Assessment Method (CAM), both in its ordinary version and in the version intended for intubated patients. (33,34) The quality of life was assessed using the scale: Quality of Life in Alzheimer's Disease (QOL-AD). (35) The functionality assessment was carried out using: the Barthel Index of Activities of Daily Living. (36)

Statistical analysis of data was performed using the IBM SPSS v.20, SPSS v.17 and R v.3.2.3 statistical packages.

RESULTS

Summary of the main results:

- 92% of the elderly patients hospitalized for hip fractures in the west of the country have a degree of cognitive impairment that may classify them, based on the MMSE score, in the dementia category, and the percentage of those previously diagnosed is of only 14%;
- the delirium associated with hip fracture, occurring before or after surgery, affects 66% of the patients, and post-operative delirium has an incidence of 42%; its main predictors are age and previous cognitive status;
- the most important novelty element of the current research is the fact that it proves the utility of the clock drawing test for predicting postoperative delirium; each additional point obtained by the patient at this test decreased the risk of developing post-operative delirium by 6.54 (1/0.153);
- mortality 3 months and one year after the fracture was of 21, respectively 30%, and the age and functional impairment, before the fracture, were identified as independent predictors of death risk;
- from the functional point of view, the impact of hip fracture in the medium and long term is a major one, and it is not limited to mobility decrease, but it also affects all functionality aspects of everyday life;
- among those who survived 12 months after surgery: 26% became immobilized in bed and only 34% regained the ability to move independently, 25% developed "de novo" sphincter incontinence, and between 12 and 33% of the patients were greatly affected in terms of independence in various aspects of self-care: personal hygiene, toilet use, dressing, bathing, feeding;
- all patients experienced a lower quality of life 12 months after the fracture, which was influenced by: a decreased capacity to carry out household activities, lack of energy, deterioration of self-image, indisposition, degradation of health and loss of ability to carry out recreational activities;
- from a statistical point of view, both functional decline, and the decrease of quality of life, proved to be significantly related to previous cognitive impairment;
- the vast majority of those suffering a hip fracture have fallen before, and the average time span between the first fall and the current one is of 3 years;
- the time and circumstances of the fall vary among the studied subjects, but they are correlated with the degree of cognitive impairment.

DISCUSSIONS

Demographic characteristics of the studied group

According to this study, among the Romanian elderly patients with hip fracture, women predominate, by 76%. The mean age is 83 (78-86), the education level is low, and the number of co-morbidities is high. The similarity noticed between the demographic characteristics of the patients in the current group (mean age, female predominance) and the data reported in medical literature increases the reliability level of the results of this study, especially regarding the statistical risk estimation. (37-39)

Cognitive impairment before the surgery

Although, in addition to proving the objective cognitive impairment, the diagnosis of dementia is also based on cerebral imaging evidence, these results suggest a very high level of dementia among elderly people with a hip fracture in our country. Compared to the 29 - 42% of elderly people with a cognitive impairment among those admitted for hip fractures, according to the international reports, the discrepancy between our results and those presented in the international literature is quite major. (40,41)

Delirium associated with hip fractures

Out of the 100 patients included in the study, 42 developed delirium in the first hours after the fracture, before undergoing surgery. Statistically, pre-operative delirium was significantly related to the degree of cognitive impairment ($p < 0.001$). Out of the 98 patients undergoing surgery, 65 (66%) developed post-operative delirium. After having excluded the patients known to have suffered from dementia before the hip fracture, as well as those with preoperative delirium, the incidence of post-operative delirium was determined as follows: 24/57 (42%), 95% CI (29%, 56%). Statistically, preoperatively measured cognitive impairment was significantly related to the occurrence of post-operative delirium. Thus, in all three scales used for this purpose, MMSE, MoCA and TC-4, the performance of patients who subsequently developed post-operative delirium was significantly lower compared to those without delirium. The average MMSE score was 22 (20-25) in those without delirium, compared to 14 (11-17) in those with delirium ($p < 0.001$). The total MoCA score was 19 (15-21) in the first group, compared to 7 (5-11), in the second group ($p < 0.001$). Except for the subscale used for testing the capacity for abstract thinking and the visual-spatial function, where all the patients in the group performed very poorly, all the other subscales of the MoCA test revealed the poor cognitive status of the patients who developed post-operative delirium. After the statistical adjustment of possible confounding factors (cognitive impairment, patient's sex, pre-operative occurrence, confusional syndrome), age proved to be a significant and independent predictor of post-operative delirium, each additional year increasing the risk of developing delirium by 1.32 times.

The Clock Drawing Test used as an assessment tool of post-operative delirium risk in elderly patients with accidental hip fracture

The logistic regression model used for assessing the possible predictors of post-operative delirium has proved that TC-4 is a strong independent predictor of the risk of post-operative delirium, and each additional point obtained by the patient decreases the risk of developing this pathology by 6.54% (1/0.153).

Quality of life after hip fracture

The average score of the QOL-AD scale, used for measuring the quality of life in this study, has decreased during the 12 months of monitoring by 8 points, on average, which indicates a clear decrease in the patients' quality of life. Statistically, both the variation of the total average score, as well as the initial scores and the 12-month scores were significantly associated with the degree of cognitive impairment before the fracture. In other words, the higher the degree of dementia, the lower the quality of life before and 12 months after the fracture. Similarly, the more advanced the dementia, the lower the quality of life became compared to the initial moment. The following areas assessed in the study proved to have the most significant contribution to the decrease in the quality of life: a decreased capacity to carry out household activities, lack of energy, deterioration of self-image, indisposition, degradation of health and loss of ability to carry out recreational activities.

The current research confirms what the other specialized studies reported unanimously: hip fractures result into a lower quality of life regardless of their type and of the patient's geographic area of origin (Alexiou, 2018). Cognitive impairment present before the fracture is also identified as a risk factor for this decrease (Buecking). To the best of our knowledge, the current study is the first one to describe the QOL-AD profile of patients with hip fractures, with the specific areas affecting the quality of life.

Limitations of the study

The most important limitation of the study is that the diagnosis of dementia was attributed only based on the MMSE score. No cerebral imaging assessments could be performed so as to allow us to comply with the official diagnosis criteria for dementia. Another inevitable limitation is that the assessment of cognitive performance was carried out in the conditions of physical and emotional stress caused by the hip fracture. In the absence of a control group, we cannot appreciate to what extent the impairment of functionality and quality of life can be attributed to the hip fracture, and how much of this deterioration is a result of the aging process.

CONCLUSIONS

In the context of the global population aging phenomenon, hip fractures tend to become a challenge for health care systems, given the direct and indirect costs of care, but also their effects on the patients' quality of life, in the medium and long term. The current study provides, for the first time in Romania, data related to the cognitive deficit, and impairment of functionality and quality of life in the case of elderly population suffering a hip fracture.

Compared to the data reported in the medical literature, the results suggest that the level of cognitive impairment of Romanian elderly patients with a hip fracture is higher, they develop delirium more frequently during hospitalization, and their functionality and quality of life are much more affected one year after surgery. Mortality 3 months and one year after the fracture is also higher. This could be explained by the poor health condition of the Romanian elderly people, the reduced access to health services and the priority level given by the local medical system to the pathology of cognitive impairment.

The most important element of originality, i.e. the fact that we have proved the utility of the clock drawing test in predicting the risk of post-operative delirium, can significantly improve a currently deficient area, namely, the cognitive assessment of the hospitalized elderly patients. A subsequent study on a larger group of elderly patients at risk for post-operative delirium, coming from other surgical specialties, could consolidate these initial results.

The results obtained may find applicability both in the orthopaedic medical practice, as well as in psychiatry and primary care. They can serve as a theoretical basis for the development and implementation of educational programs intended for the medical staff working in the orthopaedic department in order to raise awareness about this pathology with a deteriorating effect on the elderly patients with hip fractures. Improving the skills of the orthopaedic medical staff for identifying the patients at risk for delirium and functional impairment could help prioritize the preventive and treatment measures. For psychiatry and primary care physicians who care for patients suffering from dementia, knowing the high risk of these patients for falls and hip fractures could have huge implications for the prevention process. Also, knowing that patients with dementia are more prone to fail in the post-operative recovery process can help rethink and adapt the rehabilitation programs to their needs. The information on the place, time, and circumstances in which the fracture occurred may be a good start for setting up a counselling program for the patients and their next of kin, aimed at preventing hip fractures.

The data on the medium and long-term functionality and quality of life as of the occurrence of the hip fracture can also be useful in the field of social work. The high level of functional impairment from after the fracture, as well as the deterioration of the quality of life, lead to the identification of a population with real needs for social care. Marking out the areas with the greatest functional deficits can also help guide the intervention programs.