CLINICAL SCIENCE

IMPACT OF DELIRIUM ON MORTALITY AND COGNITIVE AND FUNCTIONAL PERFORMANCE AMONG ELDERLY PEOPLE WITH FEMORAL FRACTURES

Maria Elizabet Furlaneto, Luíz Eugênio Garcez-Leme

OBJECTIVE: To evaluate the evolution of cognitive and functional performance and mortality among elderly patients who were delirious during hospitalization due to femoral fracture.

STUDY TYPE: Prospective cohort.

LOCATION: Orthopedics and Traumatology Institute of HC-FMUSP; geriatric orthopedic ward.

PATIENTS: 103 patients, aged 60 years or over, who were hospitalized in the geriatric orthopedics ward with femoral fracture in 2001-2002. Thirty of them (29.1%) presented with delirium during their hospital stay and were compared with another 73 (70.9%) who did not present with delirium. There were six deaths, and 97 patients were discharged from the hospital. We obtained information on 85 of these patients four years after discharge; 42 patients were still alive and 43 had died at the time of the evaluation.

METHODS: Data on vital status was obtained for 85 patients. For the 42 survivors, we acquired information on their basic activities of daily living (ADL), instrumental activities of daily living (IADL), and cognitive performance (BDRS) by means of telephone interview with the same caregivers who had provided information at the time of the hospitalization. We compared this data with that obtained during their hospitalizations four years prior. For the 43 patients who died, we obtained information regarding their deaths and used this data in the analysis of mortality.

RESULTS: No relationships were observed between delirium and mortality, delirium and cognitive loss, or delirium and functional loss, after four years from discharge of elderly patients with hip fractures. An initial cognitive deficit was a predictor for mortality (RR = 2.54; p = 0.016), functional loss (OR = 1.80; p = 0.027) and cognitive loss (OR = 1.53; p = 0.024). Cognitive loss was also related to age.

CONCLUSIONS: Delirium had no impact on mortality or functional or cognitive losses in long term evolution (2 years) among elderly patients with femoral fractures. An initial cognitive impairment may identify patients at risk of mortality, functional and cognitive losses over the long term evolution.

KEY-WORDS: Delirium. Elderly. Femoral fracture. Mortality. Cognitive state. Functional state.

INTRODUCTION

Delirium is a neuropsychiatric syndrome caused by a

Department of Orthogeriatrics - Institute of Orthopedics and Traumatology, - Hospital das Clínicas, São Paulo University Medical School-São Paulo/SP, Brazil.
Email: marieli@uol.com.br

transient rupture of cerebral homeostasis subsequent to systemic or central nervous insults (e.g., physical disease, drug intoxication or drug withdrawal). It manifests as attention and awareness deficits, loss of cognitive and perceptive functions, alterations in the sleep-wakefulness cycle, and alterations in psychomotricity. It generally develops acutely, has a fluctuating course over the day, and frequently has a transitory evolution.[1,2] It is the most common complication among hospitalized elderly people, and particularly among

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those who have suffered femoral fracture.[3] Several studies have found associations between the presence of delirium and a poor prognosis for functional recovery, increased mortality, increased length of hospital stay, increased institutionalization following discharge, and increased incidence of dementia.[4-21] In the present study, we re-evaluated patients, assessed during their hospitalization due to femoral fracture, four years after discharge. Groups with and without delirium were compared in terms of mortality and functional and cognitive evolution.

Sample and Methods

Between January 2001 and June 2002, we followed 103 patients, aged 60 years or over, who were hospitalized with femoral fracture. The data from this study have been reported elsewhere[22]. To summarize, we included consecutive patients aged 60 years or older, male and female, who were admitted to the orthogeriatric ward with hip fracture. We excluded patients who didn't have a usual caregiver, and patients with aphasia, deafness, blindness, or inability to speak Portuguese. Patients with cognitive impairment were included.

Baseline physical function and instrumental performance was assessed using Kat's Index (ADL)[23] and Lawton´s Index (IADL)[24], by asking caregivers about the patient's ability to perform physical and instrumental activities before the occurrence of hip fracture. We considered subjects who were independent in all ADL, or needed assistance with only one function, as physically independent. The same criterion was used for instrumental independence using the IADL Index.

We estimated the baseline cognitive function by asking the caregiver to complete the Blessed Dementia Rating Scale (BDRS)[25] considering the 6 months before the admission. We assumed a score of 4 or more indicated dementia. Although we applied the Mini-mental[26] and the Clock Drawing Tests[27] to all patients during their hospitalizations, we didn't consider them to be indicators of dementia or delirium. Because hip fracture is a highly stressful circumstance, any test applied directly to the patient would have questionable reliability, and these tests might not distinguish delirium and dementia.

Delirium was diagnosed by daily evaluation using the Confusion Assessment Method (CAM).[28,29] Thirty patients (29.1%) were identified as being delirious during their hospital stay. The other 73 patients (70.9%) that did not present with delirium were considered to be controls.

During their hospitalization, six deaths occurred: five in the delirium group and one in the control group (p=0,19). Thus, 97 patients (25 cases and 72 controls) were discharged from hospital.

Follow-up evaluation

Patients discharged from the hospital were contacted by telephone 4 years after discharge. We succeeded in contacting 85 patients, 25 cases and 60 controls, who constitute the present sample.

After obtaining authorization, questionnaires on functional evaluation (ADL), instrumental evaluation (IADL), and mental evaluation (BDRS) were applied to the same caregivers who had previously been interviewed at the time of the hospitalization. These questionnaires were applied to the caregivers of patients who were still alive. The person answering for a patient who had died was asked to give the date and cause of death. The contacts were made by telephone, as was the application of the questionnaires, always taking care to interview the same caregiver who had previously been interviewed during the patient's hospitalization.

For the survival analysis, the study considered the 85 patients for whom it was possible to obtain information four years after the initial event. For the functional and cognitive analysis, the sample considered was that of the 42 patients surviving at the time of the present investigation.

The study was approved by the Institutional Ethical Committee.

Data Analysis

We used SPSS 13.0 for Windows (Statistical Package for the Social Sciences) to analyze the data.

The Kaplan-Meier method was used to estimate the survival function. The effects of variables upon mortality were analyzed with Cox proportional hazards models. Variables with p less than or equal to 0.2 were entered into Cox multiple regression to calculate the relative risks.

For functional and cognitive status, we used repeated measures analysis of variance to compare the baseline and follow-up ADL, IADL, and BDRS of individual patients. The analysis of within-individual performance was quite powerful (Wilcoxon, p<0.0001), allowing us to compare the changes in functional and cognitive performances between cases and controls.

The association between baseline and follow-up measures (delirium x non-delirium groups) was made using Fisher and Mann-Whitney tests. The logistic regression analysis included variables that achieved p d" 0.1 in the univariate association with delirium.

Considering continuous scores or nominal data (independent vs. dependent) did not change the results.

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RESULTS

The main characteristics of the study population are presented in Table 1. There were no significant differences between the groups with regard to age, sex, previous diseases, or postoperative intercurrences. Better functional and mental performance was observed in the control group than in the delirium group.

Table 1 - Sample characteristics

Variable	Controls (60)	Delirium (25)
Mean age (standard deviation)	80.02 (8.3)	80.84 (8.1)
Median	79.5	80.0
Sex: female/male (%)	48/12 (80.0%)	23/2 (92.0%)
Previous diseases		
0 (%)	04 (6.7%)	02 (8.0%)
1 (%)	14 (23.3%)	03 (12.0%)
2 (%)	12 (20%)	05 (20.0%)
3 or more (%)	30 (50%)	15 (60.0%)
Initial functional evaluation		
ADL (independent)	42 (70%)	12 (48%)*
Initial instrumental evaluation		
IADL (independent)	19 (32%)	3 (12%)*
Initial mental evaluation		
(no evidence of dementia)	39 (65%)	9 (36%)*

*p<0.05; ADL = activities of daily living; IADL = instrumental activities of daily living

Survival

The mean overall survival was 39.58 months (standard deviation = 2.41; confidence interval = 34.86-44.31). The survival curves for the two groups are presented in Figure 1.

A greater mortality (that was not statistically significant) was observed among patients in the delirium group. It was noted that the differences in mortality between the two groups became more evident beyond the first year af-
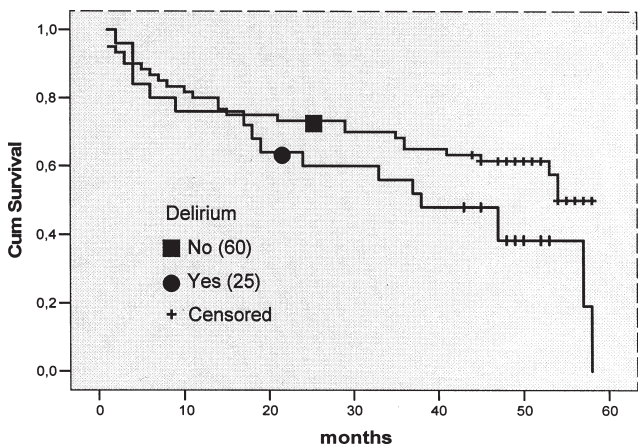

Figure 1 - Kaplan-Meyer survival curves for patients or without delirium. No significant difference occurs between the 2 groups.

ter hospitalization. At 24 months, the mortality estimated for the control group was 26%, versus 36% for the delirium group. At 48 months, the mortality estimated for the control group was 40%, versus 60% for the delirium group.

The analysis of the individual variables is shown in Table 2. Sex, age, type of underlying diseases (e.g., cardiovascular diseases, chronic obstructive pulmonary disease, cancer, previous femoral fracture, and chronic renal failure), and number and types of postoperative intercurrences (e.g., pneumonia and cardiovascular events, urinary tract infections) were found not to have had any significant influence on mortality. Although acute renal failure had a high correlation with mortality, it must be weighed that there were only three cases of this complication. The functional indicators (ADL and IADL) and the cognition indicator (BDRS) were strong predictors of mortality when analyzed in a univariate manner. The presence of three or more underlying diseases also showed a positive correlation. Delirium did not have any significant effect on mortality (RR = 1.83; p = 0.05).

The significant variables were tested in a Cox multiple regression model (Tables 3, 3A). Cognitive state was shown to be a predictor for mortality.

Table 2 - Univariate analysis for mortality.

Variable	RR	p value
Delirium (+)	1.829	0.055
Sex (female/male)	0.709	0.382
Age (80 years or over)	1.473	0.215
Three or more underlying diseases	1.458	**0.017***
Postoperative intercurrences _ ARF	11.223	**<0.001***
Functional evaluation (Independent/Dependent)	3.185	**<0.001***
Instrumental evaluation (Independent/Dependent)	2.495	**0.038***
Mental state (Blessed >= 4)	3.575	**<0.001***

ARF= acute renal failure; RR = relative risk

Table 3 - Cox regression model 1 for mortality

Model 1	Adjusted RR	p value	95% confidence interval
Cognitive deficit	**2.40**	**0.027**	**1.10 - 5.21**
Functional deficit	1.05	0.184	0.98 - 1.13
Delirium	1.28	0.466	0.66 - 2.47
ARF	5.96	0.009	1.55 - 22.97

ARF= acute renal failure; RR = relative risk

Table 3A - Cox regression model 2, excluding ARF

Model 2	Adjusted RR	p value	95% confidence interval
Cognitive deficit	**2.54**	**0.016**	**1.19 – 5.44**
Functional deficit	1.05	0.181	0.98 – 1.12
Delirium	1.42	0.278	0.75 – 2.69

ARF= acute renal failure; RR = relative risk

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Analysis of mortality in the sub-sample without dementia also showed no relationship with delirium.

Functional state

Among the 42 survivors 82% of the controls and 75% of the cases either had been totally independent or presented dependence in only one basic daily activity at the time of their hospitalization. Four years later, 55.9% of the controls and 37.5% of the cases continued to be independent. Functional loss presented a significant univariate association with the number of underlying diseases, as well as with the initial functional and cognitive states measured during hospital stay. There was no correlation between current functional status and age, sex, or delirium (Table 4). Analyzing variables in a multivariate fashion with logistic regression, only initial cognitive impairment could be considered an independent predictor of functional loss (Table 5).

Table 4 - Univariate analysis of present functional evaluation

Variable	OR	95% CI	p
Delirium	2.11	0.43 – 10.28	0.36
Age	1.06	0.97 – 1.16	0.20
No. of diseases	2.56	1.40 – 4.66	0.002
Initial functional evaluation	5.03	1.52 – 16.67	0.008
Initial cognitive evaluation	1.96	1.19 – 3.24	0.008
Sex	2.00	0.32 – 12.33	0.46

Table 5 - Functional loss – logistic regression

Variable	OR	P	95% CI
Diseases	1.67	0.147	0.84 – 3.33
Cognitive evaluation	1.80	0.027	1.07 – 3.00
Constant	0.115	0.11	

Cognitive state

Patients with a score of less than four on the BDRS scale were considered to have no important cognitive deficits. Among survivors (42), 62.5% of the cases and 79.4% of the controls had no important cognitive loss during their hospital stay. Four years later, there were no significant cognitive alterations in 25% of the cases and 52.9% of the controls.

Cognitive loss was correlated with the following: three or more comorbidities, an age of 80 years or more, and the initial cognitive evaluation. There was no significant association with delirium (p=0.16), sex, or initial functional evaluation. When analyzed using logistic regression, prior cognitive deficit and age remained significantly correlated with the cognitive evaluation four years later (Tables 6 and 7).

Table 6 - Univariate analysis of present cognitive evaluation

Variable	OR	95% CI	p
Sex	2.80	0.45 – 17. 32	0.27
Age	8.23	1.87 – 36.83	0.05
No. of diseases	1.71	1.06 – 2.74	0.03
Initial functional evaluation	2.14	0.97 – 4.70	0.06
Initial cognitive evaluation	2.03	1.12 – 3.67	0.02

Table 7 - Cognitive loss – logistic regression

Variable	OR	95% CI	p
Age	1.12	1.02 – 1.37	0.024
Cognitive deficit	1.53	1.06 – 2.20	0.024
Constant	0.00		0.019

DISCUSSION

Mortality

In this study, no relationship was observed between mortality and delirium, although the degree of significance (p=0.055) suggests that a relationship might be found in studies with larger numbers of patients. The functional and cognitive states did have strong associations with mortality. Nevertheless, Cox regression showed only the cognitive deficit to be a predictor of mortality.

The medical literature reports non-homogeneous results when correlating delirium and mortality. Several studies have shown that delirium is not correlated with late mortality[7,12,14,15]. Other authors[11,16,20] have positively correlated delirium and mortality, but they have made no adjustment for other variables involved. According to still other studies, although delirium is associated with long-term mortality, it fails to have a predictive, independent effect on mortality. In these studies, mortality is better correlated with comorbidities and functional and cognitive impairment (at baseline) than with delirium[6,8,9,10]. McCusker et al.[19] and Rockwood et al.[13] have reported delirium as a predictor of mortality, but medical conditions and age were co-predictors. A Brazilian study conducted with patients who underwent coronary artery bypass graft surgery has found a mortality rate of 10.8% for those with delirium compared to 2.05% for non-delirium patients, but these rates refer to mortality during the hospital stay for a different sample of elderly patients[30].

Functional and cognitive losses

In the present study, the initial cognitive deficit was a predictor of greater functional and cognitive losses. No association was observed between delirium and functional and cognitive deterioration.

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Regarding functional loss, the international studies have also shown heterogeneous results. Some studies have reported significant functional loss in the early evolution after delirium, but failed to demonstrate a significant association between delirium and functional performance six months after its occurrence.[5,9,10,12,15] One study observed persistent functional loss at 2, 6, and 12 months after delirium, but found dementia to be a better predictor for functional loss than delirium.[18] Francis & Kapoor[6] reported delirium, cancer, age, and marital status as predictors of loss of ability for independent community living in the long term evolution (4 years) of medical inpatients. It is necessary to note that only three of the cited studies have been conducted with patients presenting femoral fractures,[14,15,20] and their results are not homogeneous. Thus, in regards to mortality and functional loss, our data did not contradict those of the current medical literature.

On the other hand, when we consider cognitive loss, our data disagrees with that of previous studies. Delirium has been demonstrated to be a predictor of cognitive decline by several authors.[6,14,17,18] Others have demonstrated that the occurrence of delirium may increase the incidence of dementia, even in patients without evidence of previous cognitive impairment.[4,13,16] A recent review of literature, including nine studies selected by means of methodological criteria, associated delirium with either a greater cognitive decline or higher incidence of dementia.[31]

We believe that the difference observed in the present study results simply from the differences between the samples studied. As well as being of limited size, our sample presented a mean age close to 80 years, thus characterizing it as a cohort of "very old individuals." This consequently presented a larger number of patients with prior cognitive deficiencies and severe clinical conditions.

It also needs to be considered that we were dealing with patients who, as well as being of advanced age, presented with femoral fractures. Hip fractures are often an epiphenomenon related to patients' underlying diseases and frailty, with a particularly high mortality resulting from their organic limitations. Under these conditions, delirium, although still having importance, may lose something of its reliability as an indicator of poor prognosis.

There are several distinct known pathophysiological processes leading to delirium, and there may be a common final pathway. These mechanisms, the relationships among them, and the clinical manifestations of delirium have yet to be clarified. The present study has pointed towards the appropriateness of studying clinically homogenous groups instead of large heterogeneous groups of patients. Homogeneous groups better establish the correlations between clinical conditions and the specific neuropathological processes that lead to damage of the attentional system that precipitates delirium. We believe that the definition of such relationships will probably lead to better strategies for preventing and treating this syndrome, assuring better prognoses for patients who have experienced delirium at one time or another.

Study limitations

We re-evaluated 42 surviving patients. This sample is quite small considering that we analyzed and weighted several variables (sex, age, comorbidities, functional and cognitive scales).

Another limitation to be pointed out is the heterogeneity of the sample. If many pathophysiological mechanisms may lead to delirium, it is desirable, although methodologically difficult, to categorize patients for inclusion, mainly regarding baseline and follow-up cognitive evaluations.

While other studies[6] have also used telephone interviews; this is still a serious limitation in clinical investigations. Although we interviewed by phone the same caregivers that we had interviewed during hospitalization of the patients, this limitation remains.

We used the Blessed Dementia Rating Scale to discriminate patients into dementia and non-dementia groups because, in our initial study,[22] because we did not want to exclude delirious patients at admission In that circumstance, the cognitive scales directly applied to patients would not to be reliable. Almost all existing studies used IQCODE,[32,3,18] BDRS[6], mini-mental,[6,13,14,16,18] chart review, and unspecified interviews[4,14,16] to measure cognitive performance. As we know, these methods may not discriminate between grades of cognitive impairment. Some authors have used neuropsychological test batteries in the follow-up cognitive evaluations, but they have not applied the same tests in the initial evaluation for the inclusion of the patients.[4,13,17] We propose that, in future studies, both pre- and post-delirium cognitive evaluations should be be the same.

CONCLUSIONS

The present study did not show any long-term effect of delirium on mortality, or functional and cognitive performance of elderly patients with hip fracture. The baseline cognitive impairment was identified as an independent predictor of mortality, and functional and cognitive deteriorations among those patients four years after the occurrence of delirium.

The frailty and heterogeneity of our sample may have attenuated the effect of delirium as a predictor of poor prognosis.

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Future studies, with more homogeneous samples, are necessary to clarify the roles of delirium in mortality, and functional and cognitive losses, as well as the incidence of dementia after its occurrence.

RESUMO

Furlaneto ME, Garcez-Leme LE. Impacto do delirium sobre mortalidade e desempenhos cognitivo e funcional em idosos com fratura de fêmur. Evolução tardia. Clinics. 2007. 62(5):545-52.

OBJETIVO: Avaliar efeito do delirium na mortalidade e na evolução dos desempenhos cognitivo e funcional em idosos com fratura de fêmur, 4 anos após a alta hospitalar.

ESTUDO: coorte, prospectivo.

LOCAL: Instituto de Ortopedia e Traumatologia do HC-FMUSP; Enfermaria de Ortopedia Geriátrica.

PACIENTES: 103 pacientes com 65 anos ou mais, consecutivos, internados em 2001-2002, na enfermaria de ortopedia geriátrica, por fratura de fêmur. 30 idosos (29,1%) apresentaram delirium durante a internação e foram comparados com os 73 que evoluíram sem delirium (30 casos x 73 controles). Houve 6 óbitos, 97 receberam alta hospitalar. O estudo atual mostra reavaliação de 85 desses pacientes.

MÉTODOS: Dentre os 85 pacientes, temos 43 óbitos e 42 sobreviventes. Foram obtidos dados de atividades básicas de vida diária (ADL), atividades instrumentais de vida diária (IADL), desempenho cognitivo (Blessed), referentes aos sobreviventes, através de entrevista telefônica com os mesmos cuidadores que forneceram as informações durante a internação . Comparamos esses dados com aqueles de 4 anos atrás (42 pacientes). Dos pacientes que foram a óbito, obtivemos data e causa de óbito. Dados referentes aos 85 pacientes entraram na análise de mortalidade.

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RESULTADOS: Não foram observadas relações entre delirium e mortalidade, delirium e perda cognitiva, delirium e perda funcional. Déficit cognitivo inicial foi preditor de mortalidade (RR= 2,54 ; p=0,016), perda funcional (OR=1,80; p=0,027) e perda cognitiva(OR=1,53; p=0,024).

CONCLUSÕES: Delirium não teve impacto sobre mortalidade e perdas funcional e cognitiva na evolução tardia de idosos com fratura de fêmur. O déficit cognitivo inicial pode identificar pacientes em risco para mortalidade, perda funcional e perda cognitiva futuras em idosos com fratura de fêmur. A fragilidade e heterogeneidade da nossa amostra pode ter atenuado o poder preditor de mau prognóstico do delirium.

UNITERMOS: Delirium. Idoso. Fratura de fêmur. Mortalidade. Estado cognitivo. Estado funcional.

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