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Cognitive Impairment and 1-Year Outcome in Elderly Patients with Hip Fracture

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Hip fracture is common in elderly patients. However, few effective studies had linked cognitive impairment to patient clinical outcome.

Material/Methods: A total of 244 elderly hip fracture patients were prospectively followed up for 12 months. At 30 days, 6 months, and 1 year after hip repair surgery, patients and/or primary caregivers were interviewed by phone by trained, blinded interviewers. Functional evaluation, from pre-injury through 1 year after the operation, was assessed using the Barthel Index.

Results: Among 244 patients, 43 were diagnosed as having cognitive impairment (Mini-Mental State Examination score <24). Compared to those without cognitive impairment, the 30-day, 6-month, and 1-year mortalities in the impaired patients were significantly higher than that of the cognitively intact patients. Six months after hip repair surgery, the cognitively intact patients presented significantly higher activities of daily living (ADL) scores than the cognitively impaired patients, and only 38.5% of impaired patients returned to their pre-operation baseline levels afterwards. The ADL scores in the impaired patients were similar to the intact ones at 1 year after the operation.

Conclusions: Although they had a higher risk of mortality in hip fracture, functional gain in the cognitively impaired patients was similar to that in the cognitively intact patients at 1-year follow-up.

MeSH Keywords: **Hip Fractures • Mild Cognitive Impairment • Mortality**

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Background

Fracture of the hip in elderly persons is a significant healthcare concern, with mortality in the first year after hip fracture at about 18–33% [1,2]. The survivors often suffer from impaired quality of life. Moreover, in an aging society, the exponentially increasing incidence of age-related hip fracture results in extra economic burden to the healthcare welfare and social security.

Previous studies have suggested that cognitive impairment, which has been found in 31–88% of elderly patients experiencing hip fracture, was a predictor of poor functional recovery after hip fracture surgery [3,4]. Other studies demonstrate that although cognitively impaired patients may not be able to achieve the same level of functional recovery as their cognitively intact counterparts do, they may, in fact, achieve positive outcomes [5]. Furthermore, investigators specializing in geriatric rehabilitation reported that the cognitively impaired patients could actually achieve functional gain similar to that achieved by the cognitively intact patients [6].

However, most published data were from retrospective studies via queries of databases. The cognitively impaired patients may have had more pre-existing co-morbidities than the cognitively intact patients, which may highly bias the results. We designed a prospective study to identify the prevalence of cognitive impairment in elderly individuals and to determine whether cognitive impairment affects up to 1-year functional gain outcome in elderly patients with new fracture.

Material and Methods

Patients

From August 2007 to August 2009, 343 patients diagnosed with acute hip fracture were admitted to the Department of Orthopedic Surgery at the Beijing Army General Hospital, a trauma and rehabilitation center for elderly patients. Inclusion criteria were: patients aged 61–99, diagnosed with acute hip fracture and who then underwent hip repair surgery; patients must be ambulatory at home before admission; and patients had no end-stage disease or cancer within the past 6 months. Acute hip fractures caused by motor vehicle accident, or infiltrated by tumors, or treated non-surgically were excluded.

Study design

This was a prospective cohort study. Consented and eligible patients were categorized into 2 groups based on cognitive status – with and without cognitive impairment. The study was approved by the Institutional Review Board (IRB) of our hospital.

The hip fracture research team consisted of several surgeons, psychiatrists, and nurse practitioners. Upon patient arrival at the rehab service center, a designated nurse practitioner would be assigned to interview the patient and/or primary caregiver, conduct a physical examination, collect patient data on demographics and co-morbidities, and then identify cognitive status. Eligible patients were classified into 2 groups based on the Mini Mental State Examination (MMSE) score [4]: impaired cognition (score ≤ 23) and intact cognition ($24 < \text{score} \leq 30$). The American Society of Anesthesiologists (ASA) grading system was also used to measure the severity of patient health status at admission. ASA grades were defined as: Grade I: physical fitness, good nutrition, and normal function of various organs; Grade II: mild co-morbidities, functional compensation is sound; Grade III: coexistence of serious illness, limited physical activity, but still able to cope with daily activities; Grade IV: serious co-morbidities, loss of ability to perform activities of daily living, and often facing life-threatening illness. Fracture type was also recorded by an orthopedic surgeon. Patients were discharged if they gained the following functions: transferring to bed and chair independently, eating, bathing, and walking with a walker or able to use a wheelchair. In-patient rehab service was available either on the orthopedic floor or in a nursing home until they met these criteria.

Functional outcome assessment

All patients received rehabilitation therapy offered by the Department of Orthopedic Rehabilitation immediately after surgery. Static quadriceps contraction was required on post-operative day 1 and ambulation after 7 days. At 30 days, 6 months, and 1 year after hip repair surgery, the patients and/or primary caregivers were interviewed by telephone by a trained blinded assistant. Functional evaluation, both at before-injury and up to 1 year after the hip repair surgery, was assessed by board-certificated psychiatrists using the Barthel index (original version). The Barthel index, which ranges from 0 (total dependence) to 100 (total independence), is a functional index for the assessment of performance in activities of daily living (ADL) with a certain degree of independence. For patients who died within the follow-up period (up to 1 year), date and cause of death were recorded.

Statistical analysis

All of the statistical analyses were performed using a statistical software package (SPSS for Windows, version 16.0; SPSS; Chicago, IL). Differences in demographics, medical co-morbidities, type of fracture, and length of hospital stay between the 2 groups were compared using the t-test, chi-square test, or Fisher exact test. Kaplan-Meier survival analysis was conducted to compare the overall mortality between patients with and without cognitive impairment. We also used a multivariate

Table 1. Demographic and clinical characteristics of elderly hip fracture patients with or without cognitive impairment.

| Variable | | Cognitively impaired (n=43) | Cognitively intact (n=201) | P |
|-------------------------------|--|--------------------------------|-------------------------------|-------|
| Epidemiologic characteristics | Age (≥75) | 20 (46.5%) | 75 (37.3%) | 0.302 |
| | Sex (male) | 27 (62.8%) | 78 (38.8%) | 0.002 |
| | Femoral neck Fracture | 15 (34.8%) | 97 (48.2%) | 0.110 |
| Medical co-morbidities | Peripheral vascular disease | 21 (48.8%) | 74 (36.8%) | 0.142 |
| | Cardiovascular disease | 20 (46.5%) | 48 (23.8%) | 0.003 |
| | Pulmonary disease | 11 (25.6%) | 80 (39.8%) | 0.246 |
| | Parkinson disease | 6 (13.9%) | 15 (7.5%) | 0.259 |
| | Diabetes | 11 (25.6%) | 35 (17.4%) | 0.214 |
| | Renal disease | 10 (23.2%) | 23 (11.4%) | 0.040 |
| | Number of co-morbidities (two or more) | 13 (30.2%) | 42 (20.1%) | 0.184 |
| | ASA grading (Grade III+IV) | 4 (9.2%) | 7 (3.4%) | 0.095 |
| Length of stay (days) | | 17.13±7.32 | 14.22±5.32 | 0.588 |

ASA – American Society of Anesthesiologists.

analysis proportional hazards regression model adjusted for confounders (e.g., age and gender) to determined hazard ratio (HR) in those patients. ADL scores between hip fracture with or without cognitive impairment were compared using the 2-tailed t-test. P values less than 0.05 were considered significant.

Results

Baseline characteristics of patients

Between August 2007 and August 2009, 343 patients were admitted to the Department of Orthopedic Surgery Beijing Army General Hospital with a diagnosis of hip fracture. Of those patients, 244 met the study inclusion criteria and were enrolled in the study. Ninety-nine were excluded from the study, of which 23 cases did not meet the age criteria, 15 cases were not able to live independently at home, 3 had pathologic fractures, 2 had motor vehicle injuries, and 56 had received non-surgical treatment. Among all eligible patients, 43 were diagnosed as having cognitive impairment prior to the surgery. Table 1 summarizes the baseline demographics, co-morbidities, and ASA grade of patients. Among cognitively impaired patients, there were significantly more males than females ($P < 0.05$). Among the cognitively impaired patients, there were more patients aged 75 or older than among the cognitively intact patients. There were more patients with ASA grade III+IV in the cognitively impaired group than in the cognitively intact group. More cardiovascular disease and renal disease were present

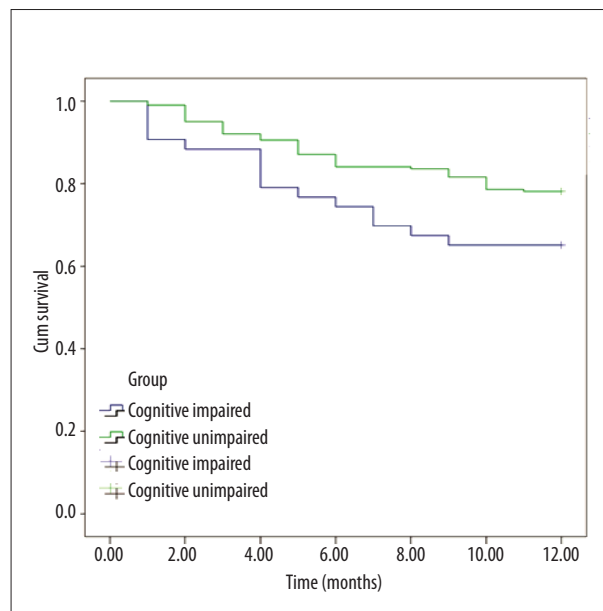


Figure 1. Kaplan-Meier in elderly hip fracture patients with or without cognitive impairment.

in the cognitively impaired group than in the cognitively intact group ($P < 0.05$).

Mortality

The effect of cognitive impairment on survival is shown in Figure 1. In patients with cognitive impairment, the mortality

Table 2. Relative risks of mortality in hip fracture patients with and without cognitive impairment.

| Endpoint | Number of deaths (%) Cognitive impairment | Number of deaths (%) Cognitive Intact | Crude RR | Adjusted RR |
|----------|--|--|------------------|------------------|
| 30-day | 5 (11.2%) | 16 (7.9%) | 1.87 (1.43,2.26) | 1.55 (1.20,1.98) |
| 6-month | 11 (25.6%) | 31 (15.4%) | 1.75 (1.32,1.99) | 1.54 (1.30,1.72) |
| 1-year | 15 (34.9%) | 44 (21.8%) | 1.90 (1.58,2.43) | 1.65 (1.41,1.78) |

Table 3. Cause of death in elderly hip fracture patients with or without cognitive impairment.

| | Hip fracture patients with cognitive impairment, n,% | Hip fracture patients without cognitive impairment, n,% |
|-----------------------------|---|--|
| Chest Infection | 7, 46.6% | 9, 20.5% |
| Cardiovascular disease | 3, 13.0% | 15, 34.1% |
| Cerebrovascular accident | 1, 6.7% | 8, 18.1% |
| Renal failure | 1, 6.7% | 3, 6.8% |
| Urinary infection | 1, 6.7% | 3, 6.8% |
| Pulmonary embolism | 1, 6.7% | 0, 0.0% |
| Gastrointestinal hemorrhage | 1, 6.7% | 0, 0.0% |
| Sepsis | 0, 0.0% | 1, 1.6% |
| Pancreas infection | 0, 0.0% | 3, 6.8% |
| Biliary infection | 0, 0.0% | 2, 4.5% |

Table 4. ADL Scores in hip fracture patients with or without cognitive impairment.

| | Cognitively impaired | Cognitively intact | P value |
|--------------------------|----------------------|--------------------|---------|
| Pre-injury | 70.63±15.97 | 73.62±15.02 | 0.124 |
| 6 months after operation | 53.92±14.43 | 72.19±13.56 | 0.000 |
| 1 year after operation | 669.15±15.97 | 70.45±19.36 | 0.891 |

was 11.2% (5/43) at 30 days, 25.6% (11/43) at 6 months, and 34.9% (15/43) at 1 year. In contrast, the mortality in cognitively intact patients was 7.9% (16/201), 15.4% (31/201) and 21.8% (44/201). Table 2 shows the crude and adjusted hazard ratios (HRs) and their 95% confidential intervals between the 2 groups for 30-day, 6-month, and 1-year following hip fracture between groups. Cognitively impaired patients were approximately 1.5–1.9 times more likely to die within 1 year than the cognitively intact patients. The most common cause of mortality following hip fracture was pulmonary infection in cognitively impaired patients and cardiovascular disease (myocardial infarction) in cognitively intact patients (Table 3).

Functional outcome

Twenty-six patients with cognitive impairment survived up to 1 year after operation. Table 4 showed the ADL scores for all patients throughout the study period. No significant differences in functional outcomes were identified between the 2 groups before fracture. However, at 6-month follow up, the cognitively intact patients presented significantly higher ($P=0.000$) ADL scores than the cognitively impaired patients did. ADL scores in 38.5% (10/26) of the cognitively impaired patients returned to the pre-injury status, and among cognitively impaired patients, 47.1% (98/208) of cognitively intact patients returned to their previous ADL status. In all survivors, the ADL

scores became similar between the 2 groups at 1-year follow-up (69.15 ± 15.97 vs. 70.45 ± 19.36 , $P=0.89$).

Discussion

Many studies have investigated the effect of the history of cognitive impairment on hip fracture prognosis in elderly patients [5,7–9]. Most results were from retrospective clinical studies, so the prevalence of mortality varied due to selection and information biases.

The data from our prospective study showed a high prevalence of mortality in cognitively impaired patients: 11.2%, at 30-day, 25.6% at 6-month, and 34.9% at 1-year follow-up, compared to 7.9% at 30-day, 15.4% at 6-month, and 21.8% at 1-year follow-up in cognitively intact patients. By using the COX Cox proportional hazard model, cognitively impaired patients had a 50–60% higher risk of death than cognitively intact patients (adjusted HR 1.54–1.65). The underlying mechanism of the close association between cognitive impairment and 1-year mortality was unknown. One of the interpretations is that patients with cognitive impairment may have more clinical multiple comorbidities than those without [10]. Another possible interpretation is that hip fracture, as like other major trauma, triggers an unbalanced local and systemic inflammatory response to trauma, featuring especially the elevation of a group of pro-inflammatory cytokines [11]. The hypothesis of proinflammatory response cascade was supported by our previous human study [11] and animal studies [12] in which anti-inflammatory cytokine antibodies reverse the development of organ dysfunction and decreases mortality. As Because the lungs are the first and primary target organ infiltrated by pro-inflammatory cytokines in the post-injury period, cytokines infiltration in cognitively impaired patients may lead to clinical pulmonary dysfunction and then initiate a multiple organ failures. Chronic trauma would also worsen the systemic inflammatory response and raises increases mortality by amplification of cytokine production [13]. Additionally, cognitively impaired patients usually had long been bedridden and thus more likely to develop pulmonary complications (e.g., infection). In fact, our data showed

that the most common cause of death in the cognitively impaired patients was pulmonary infection compared to that of cognitively intact patients (46.6% vs. 20.5% $P<0.05$). Interesting, ischemic cardiovascular disease was the most common cause of death in cognitively intact patients in our study, which was consistent with the finding by Monvcada et al. [7].

Hip fracture is associated with much lower rates of functional recovery in the elderly population. Even Although surgical repair may increase the possibility of independent living, to live independently, physicians and caretakers often defer the surgery in the cognitively impaired patients because they were concerned that those patients will not benefit from postoperative functional recovery; therefore,. So surgery in cognitively impaired patients may be deferred secondary to concerns that the patient will not receive functional benefit. It was shown in our data that the cognitively impaired patients did h months after surgical repair, but they re-gained daily living function at 1 year post-surgery. Although they might require longer rehabilitation, they seemed to benefit from hip fracture surgery as much as the cognitive intact patients did. Moreover, our results are supported by Goldstein et al. [14] who reported no difference of functional gain in self-care, sphincter control, and locomotion (with the exception of mobility and transfers) between the cognitively impaired and intact patients. Heruti et al. [15] and Rolland et al. [16] also demonstrated that the cognitive status was not associated with the absolute motor function gain. Thus, although this study is limited by the small sample size, these results suggest that some cognitively impaired patients may have functional recovery similar to that of patients without cognitive impairment.

Conclusions

The results of this study suggest that cognitive impairment status should not be used to determine whether the cognitively impaired patients would benefit from hip repair surgery. Therefore, we conclude that although cognitively impaired patients had a higher risk of mortality, functional gain was similar to that in cognitively impaired patients at 1-year follow-up.

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