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Early Predictors for Long-Term Functional Outcome After Mild Traumatic Brain Injury in Frail Elderly Patients

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Objective: To identify the effect of frailty and early postinjury measures on the long-term outcome after mild traumatic brain injury in elderly patients. **Setting:** Patients admitted to 3 Dutch hospitals designated as level 1 trauma centers. **Participants:** The elderly (≥60 years) with mild traumatic brain injury ($N = 161$). **Design:** A prospective observational cohort study. **Main Measures:** Posttraumatic complaints and the Hospital Anxiety and Depression Scale determined 2 weeks postinjury; the Glasgow Outcome Scale Extended and Groningen frailty indicator determined 1 to 3 years postinjury. **Results:** A total of 102 nonfrail (63%) and 59 frail elderly (37%) patients, mean age of 70.8 (6.3) years were included. Most patients (54%; 72% nonfrail and 24% frail) recovered completely 1 to 3 years postinjury. Two weeks postinjury, 81% had posttraumatic complaints (83% frail and 80% nonfrail elderly), and 30% showed emotional distress (50% frail and 20% nonfrail). Frailty (odds ratio, 2.1; 95% confidence interval, 1.59-2.77) and presence of early complaints (odds ratio, 1.13; 95% confidence interval, 1.01-1.27) (Nagelkerke $R^2 = 46\%$) were found to predict long-term outcome, whereas age was not a significant predictor. **Conclusion:** The frail elderly had worse long-term outcome, and early complaints were found to be a stronger predictor of unfavorable outcome than age. Understanding the implications of frailty on outcome could help clinicians recognize patients at risk of a poor outcome and allocate care more efficiently. **Key words:** *aging*, *brain injuries*, *depression*, *follow-up studies*, *frail elderly*, *outcome assessment (healthcare)*, *prognosis*, *rehabilitation*

THE RISK of sustaining a traumatic brain injury (TBI) increases with age.[1,2] In recent years, the epidemiological pattern of injury has changed, with more injuries occurring among elderly patients (>60 years) caused by low-energy accidents such as falls.[1,3,4] Mild TBI (MTBI) accounts for approximately 80% to 90% of all traumatic brain injuries, and most patients recover within 6 months after MTBI without specific treatment.[2,5] However, a subgroup (20%-25%) experiences persistent posttraumatic complaints, which interfere with resumption of daily activities and work.[6,7]

The number of elderly patients who sustain a TBI is expected to increase due to demographic changes. By 2050, 40% of all trauma patients will comprise adults 65 years or older.[8] The elderly population is generally the biggest consumer of health services and critical care resources. Elderly individuals not only have an increased risk of sustaining a TBI, but advanced age is also a risk factor for higher mortality and morbidity rates after a TBI.[9] It is reported that, on average, 76% of elderly patients who survived a trauma returned home 6 months postinjury.[10,11] Previous studies showed that lower levels of resilience and perceived social support were associated with a reduced quality of life in patients with MTBI.[12] However, specific information is lacking about the long-term outcome and activities of daily living of the subgroup of elderly patients with MTBI.

Corrigan and colleagues[13] stated that, among preinjury characteristics, age accounts for the most variance in outcomes after TBI. Age is associated with

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comorbidities such as hypertension, chronic renal failure, and diabetes, which reflects a higher frailty index and could negatively influence the outcome after MTBI.[4] Frailty is defined by a loss of physiologic reserves and consequent inability to maintain homeostasis to overcome a disease or injury.[10,14–16] This can be caused by a range of factors, which may lead to an adverse health outcome.[16–18] The most common signs of frailty are weight loss, fatigue, weakness, low activity level, and decreased cognitive performance.[14] The prevalence of frailty increases with age and is higher in women.[17,19] In recent years, frailty has emerged as an independent predictor of risk of adverse outcome (such as mortality and disability) in older people. These risks are independent of the associated comorbidities that could be present.[14,20,21] Therefore, it might be beneficial to assess the role of frailty for prognosis after MTBI in elderly patients. In addition, poor recovery after MTBI has been associated with preinjury mental health status and early emotional distress.[22] Since posttraumatic complaints are strongly related to emotional distress, these factors have to be taken into account when evaluating the effect of frailty.

There is limited information on frailty as possible outcome predictors after MTBI. Therefore, the main purpose of this study was to investigate the effect of frailty (in addition to well-known factors like emotional distress, posttraumatic complaints, and preinjury mental health) on the long-term outcome after MTBI in elderly patients defined as those 60 years or older.

MATERIAL AND METHODS

Participants

This study, conducted between January 2013 and January 2015, was part of a large observational cohort study (UPFRONT study) that included patients with MTBI admitted to 3 Dutch hospitals designated as level 1 trauma centers. MTBI was defined as an injury to the brain with loss of consciousness of 30 minutes or less and/or duration of posttraumatic amnesia of less than 24 hours and a Glasgow Coma Scale score of 13 to 15 at the emergency department.[23] For the current study, only patients 60 years and older were included; the following age groups were created: 60-64, 65-69, 70-74, and more than 74 years. Patients were excluded because of insufficient comprehension of the Dutch language, addiction to alcohol and drugs, or the presence of concomitant dementia or psychiatric diseases. The study was approved by the Medical Ethical Committee of the UMCG, and all patients gave written informed consent.

Collection of data

The following patient and injury characteristics were retrieved: sex, age, medical history, presence of preinjury mental health problems, computed tomography (CT) assessments, mechanism of trauma, and vital parameters on admission. Comorbidities (eg, diabetes and cardiovascular disease) were documented. A CT scan was performed at the emergency department and scored by an experienced radiologist according to the Marshall score (ranging from 1 to 6).[24] Marshall scores were dichotomized into normal CT (score 1) and abnormal CT (scores 2-6). Patients received questionnaires at 2 weeks, 3, 6, and 12 months after injury. For this study, data from the questionnaires assessed at 2 weeks were used and additional information was collected at 1 to 3 years postinjury. This additional information comprised questions regarding satisfaction with life, specific physical impairments, psychosocial well-being (eg, experiencing psychological problem and maintaining social contacts), participation in social life, and mobility. These additional questions assessed at 1 to 3 years postinjury were based on common items measured in other frailty instruments.[25] For the assessment of frailty, we used the Groningen frailty indicator (GFI; described later), which is a valid instrument to measure frailty from a multidimensional perspective.[20,26] The interval between injury and determination of long-term outcome varied between 1 and 3 years, with a mean interval of 30.1 (6.2) months.

Early measures assessed at 2 weeks postinjury

Emotional distress

The Hospital Anxiety and Depression Scale (HADS) contains 14 items, with 7 items measuring depression and 7 items measuring anxiety; scores range from 0 to 21.[27] HADS scores were dichotomized, with a score 8 or more indicating the presence of anxiety and/or depression.

Posttraumatic complaints

The Head Injury Symptom Checklist[7,28] contains 21 common posttraumatic complaints rated on the following scale: 0 = never, 1 = sometimes, and 2 = often. Total scores range from 0 to 42 with correction for preinjury complaints. Presence of posttraumatic complaints was defined as reporting one or more symptoms, and dichotomized into 0 (no complaints) and 1 (complaint).

Long-term measures assessed at 1 to 3 years postinjury

Satisfaction with life

Patients were asked to give their life satisfaction a score between 1 and 10. A score of 1 indicates total dissatisfaction and a score of 10 indicates total satisfaction with their lives.

Postinjury frailty

Frailty was assessed with the GFI.[26] The GFI comprises 15 items and measures functions in 4 domains: physical, cognitive, social, and psychological (see Appendix 1). Scores range from 0 to 15; patients with a sum score of 4 or more were considered frail.[20,26]

Long-term outcome

The Extended Glasgow Outcome Scale (GOSE) was used to assess functional outcomes.[29,30] The GOSE is an 8-point scale, ranging from death (score 1) to complete recovery (score 8). For presentation of data, we combined the following GOSE scores: upper and lower severe disability (GOSE scores 3 and 4) into severe disability and upper and lower moderate disability (GOSE scores 5 and 6) as moderate disability. For regression analysis the GOSE scores were dichotomized into favorable (GOSE 8) and unfavorable outcomes (GOSE 1-7).

Statistical analysis

For the statistical analysis, this study used the Statistical Package for the Social Sciences (SPSS) version 22.0. Nonparametric tests (χ^2, Mann-Whitney *U*) were used with nonnormally distributed data to determine group differences. Correlations between variables were determined by either Pearson or Spearman correlation coefficients. Regression analysis was done with dichotomized GOSE score as the dependent variable. Variables significant in the univariate logistic regression were further analyzed in a multivariate binary logistic regression analysis. A *P* value below .05 was considered significant. In case of multiple comparisons, Bonferroni-Holm corrections were applied.

RESULTS

In total, 188 patients were judged eligible to participate in this study. However, 7 refused to participate, 19 could not be contacted, and 1 patient died. Thus, a total of 161 patients were included in the analysis, 59 (37%) frail and 102 (63%) nonfrail elderly patients.

Patient characteristics

Patient characteristics are displayed in Table 1. The male-to-female ratio was 1:1.2, with a mean age of 70.8 (6.3) years. Falls were the most common mechanism of injury, and 73% of patients were admitted to the hospital ward; almost all patients were discharged to their homes. Patient characteristics for frail and nonfrail patients are presented in Table 2. Injury caused by collision was twice as high in frail patients (31% frail and 17% nonfrail, $P = .12$). Prior to injury, 37% of patients experienced physical impairments (51% of frail, 29% of nonfrail,

TABLE 1 *Patient characteristics*[a]

Patient characteristics	Total N = 162	60-64 N = 27	65-69 N = 54	70-74 N = 38	>74 N = 43	P value
GCS of 15 on admission, %	72	70	65	76	79	.73
ISS, mean (SD)	8.2 (5.9)	10.5 (8.1)	7.0 (3.6)	9.9 (7.5)	7.1 (4.5)	.11
Sex, %						.73
Male	55	52	59	58	49	
Female	45	48	41	42	51	
Hospital admission, %	73	74	74	79	65	.55
Comorbidities, %	65	59	57	74	74	.17
Premental health, %	6	0	6	5	9	.21
CT abnormalities, %	23	33	15	32	19	.20
Mechanism of injury, %						.02
Fall	75	82	70	68	84	
Collision	22	19	20	32	16	
Other cause	3	0	9	0	0	
Discharge destination, %						.07
Home	96	85	100	96	98	
Other hospital	2	11	0	2	0	
Rehabilitation facility	1	4	0	2	0	
Nursing home	1	0	0	0	2	
Long-term favorable outcome, %	54	59	54	55	52	.89

Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale; ISS, injury severity score; SD, standard deviation.
[a] *P* values indicate differences between age groups. Post hoc analysis showed no significant differences (at $P < .008$ level) between separate age groups.

TABLE 2 *Patient characteristics of frail and nonfrail patients*

Patient characteristics	Total $N = 161$[a]	Frail $N = 59$	Nonfrail $N = 102$	*P* value
GCS of 15 on admission, %	72	69	73	.75
Sex, %				.46
Male	55	51	57	
Female	45	49	43	
Mean age (SD)	70.8 (6.3)	71.7 (6.6)	70.1 (5.7)	.02
ISS, mean (SD)	8.2 (5.9)	8.7 (6.2)	7.9 (5.7)	.08
Hospital admission, %	72	76	70	.44
Premental health, %	6	11	3	.06
Mechanism of injury, %				.12
Fall	75	66	80	
Collision	22	31	17	
Other cause	3	3	3	
Comorbidities, %	65	78	57	.05
CT abnormalities, %	23	19	26	.42
Discharge destination, %				.49
Home	96	95	96	
Other hospital	2	1	3	
Rehabilitation facility	1	2	1	
Nursing home	1	2	0	

Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale; ISS, injury severity score; SD, standard deviation.
[a] $N = 161$ due to death of 1 patient.

TABLE 3 *Residual impairments and activities of daily living 1 to 3 years after injury*

Residual impairments	Total $N = 161$[a]	Frail $N = 59$	Nonfrail $N = 102$	*P* value
Early impairments[b]				
Posttraumatic complaints, %	81	83	80	.68
Emotional distress, %				
HADS-anxiety	16	24	13	.06
HADS–depression	14	26	7	<.01
Late impairments[b]				
Physical, %				<.01
Sickness	38	59	26	
Reduced strength in hands	23	59	37	
Dropping things out of hand	23	42	12	
Mobility, %				<.01
Inability to drive a car	24	42	14	
Changed to preinjury situation	36	63	21	
Psychosocial, %				<.01
Enjoyment of activities	13	27	5	
Change in social relations	16	25	10	
Satisfaction with life, mean (SD)	7.4 (1.2)	6.7 (1.4)	7.9 (0.8)	<.01
Living situation, %				<.01
Living with partner	76	61	84	
Living alone	20	31	15	
Living with partner + children	3	5	1	
Living with children	1	3	0	

Abbreviations: HADS, Hospital Anxiety and Depression Scale; SD, standard deviation.
[a] $N = 161$ due to death of 1 patient.
[b] Early residual impairments were assessed at 2 weeks postinjury; late residual impairments were assessed at 1 to 3 years.

$P < .01$) and 6% of patients had preinjury mental illness (11% of frail and 3% of nonfrail patients).

Early posttraumatic complaints and emotional distress

Concerning early posttraumatic complaints (assessed at 2 weeks postinjury), 81% of the patients reported more than 1 complaint (mean = 4.8, standard deviation = 3.9). The most frequent prevailing posttraumatic complaints for both groups were dizziness (55%), fatigue (50%), and headache (44%). Only presence of forgetfulness was significantly different between the groups (31% frail and 19% nonfrail, $P = .004$). Regarding emotional distress 2 weeks postinjury, 14% of patients experienced depression (26% frail and 7% nonfrail, $P = .001$) and 16% experienced anxiety (24% frail and 13% nonfrail, $P = .06$).

Long-term outcome and complaints

Overall, 54% of patients completely recovered, 14% had mild disability, 22% had moderate disability, and 11% had severe disability. The majority (72%) of the nonfrail elderly patients completely recovered compared with 24% of the frail elderly ($P < .01$). The frail patients were primarily moderately disabled (41%). The nonfrail elderly had a higher mean GOSE score compared with the frail elderly ($P < .01$). Outcome was not significantly different between males and females.

At 1 to 3 years postinjury, frail elderly patients reported a lower mean score for satisfaction with life (6.7 vs 7.9 for nonfrail, $P < .01$), and more often reported being unhappy with their lives (20% of frail vs 0% of nonfrail, $P < .01$) (Table 3). Since only one patient died 1 to 3 years after injury, no further analyses were conducted on long-term mortality.

Predictive factors for long-term outcome

The univariate logistic regression for the total group, with GOSE as the dependent variable, showed that the presence of complaints (odds ratio [OR], 1.16; 95% confidence interval [CI], 1.06-1.27; $P < .001$), the GFI (OR, 1.87; 95% CI, 1.51-2.31; $P < .001$), anxiety (OR, 1.17; 95% CI, 1.05-1.29; $P = .003$), and depression (OR, 1.2; 95% CI, 1.08-1.34; $P = .001$) were significant predictors of an unfavorable outcome. Other variables (sex, premental health, destination at discharge, living situation, comorbidities, Glasgow Coma Scale, presence of CT abnormalities, and mechanism of injury) were not significant predictors of outcome. In a multivariate logistic regression analysis of the entire group, with GOSE as the dependent variable, only the GFI (OR, 2.1; 95% CI, 1.59-2.77; $P < .001$) and presence of complaints (OR, 1.13; 95% CI, 1.01-1.27; $P = .04$) emerged as significant predictors of outcome, with an estimated explained variance of 46% (Nagelkerke R^2). With increasing GFI scores, patients were twice as likely to have an unfavorable outcome (GOSE scores <8). Age, early anxiety, and depression were not significant predictors of the long-term outcome within this cohort.

DISCUSSION

This is one of the first studies to evaluate the effect of frailty and age on the long-term outcome after MTBI in an elderly population. One main finding was that more than half of the elderly patients showed complete recovery after injury. Approximately one-third of the patients were considered frail, and a favorable long-term outcome was observed in only 24% of these patients. Frail elderly patients more often showed early emotional distress. Furthermore, frailty was found to be decisive for the long-term outcome in the multivariate analysis, whereas age was not.

The prevalence rate of frailty, as reported in the landmark study of Rockwood et al,[19] ranged from 70 to 366 per 1000 patients in those 65 years and older. In this study, 36% of all patients and 42% of those older than 74 years were considered frail, figures comparable to those in other studies.[30,31] A higher prevalence of frailty in women has been reported, but that was not present within our cohort.[19,31] Earlier studies have stated that frailty can lead to the adverse outcome.[32] However, in this cohort elderly patients tended to recover after sustaining an MTBI, with 54% of patients recovering completely and 14% experiencing mild disability. Severe disability was observed only in 1 in 10 patients. Moreover, recovery rates did not differ significantly across age groups. This relatively good functional outcome is in accordance with the findings of others who have reported that the majority of elderly patients with MTBI (63%) had a good recovery and were able to live independently.[33] We found that frail elderly patients were 3 times more likely to experience an unfavorable outcome (76%) compared with the nonfrail elderly (28%). This unfavorable outcome for the frail elderly was more pronounced with increasing age.

Previous studies have found that complaints and preinjury characteristics are relevant predictors of outcome after an MTBI. Within the present cohort, the majority (81%) of patients reported at least 1 posttraumatic complaint 2 weeks postinjury.[34,35] The most frequent posttraumatic complaints were dizziness, fatigue, and headache in accordance with previous studies.[7,28] When comparing frail with nonfrail patients, no significant differences were found in the presence of early complaints. However, this study identified the presence of early posttraumatic complaints as a significant predictor of unfavorable long-term outcome for all patients after

MTBI. A previous study, conducted by Cassidy et al,[22] found that the presence of early emotional distress and poor premorbid physical health status were associated with a poor recovery after MTBI. In this study, approximately 1 in 3 patients experienced early emotional distress, and frail elderly patients were nearly 3 times more often considered anxious and depressed in comparison with nonfrail elderly patients. This finding is line with previous findings that, once frailty develops, the likelihood of clinically significant depression and anxiety increases.[36] Frail patients also had a reduced mobility 1 to 3 years after injury, and 29% of the frail patients were activities of daily living dependent; this is higher than what has previously been reported.[37] Only 2 patients (3.5%) were also dependent prior to the accident; the dependency rate increased approximately 8-fold postinjury, in accordance with other studies.[38,39] Moreover, it was noted that frail patients were more likely to be living alone 1 to 3 years after injury in comparison with nonfrail elderly patients (31% vs 15%). Regarding the level of satisfaction with life, frail elderly patients reported a significantly lower score compared with nonfrail elderly patients. We postulate that the presence of psychosocial impairments and the living situation might have negatively influenced satisfaction with life in the frail elderly.

Higher mortality rates and worse functional outcomes are present in elderly patients with TBI, although TBI and concomitant injuries are often less severe compared with younger patients.[3] Furthermore, frailty was previously found to be a predictive factor for the mortality rate.[14] Since only 1 patient in our cohort died, it was not possible to determine the impact of frailty on mortality in this sample.

Studies reporting solely on the outcome of elderly patients after MTBI are scarce, since such studies often included all age categories.[3,33,40,41] Although a number of studies have indicated that increasing age is associated with higher mortality rates and worse outcomes after TBI, the majority of these studies concern individuals with severe TBI.[41–45] Others have explained the association between higher age and a worse outcome by stating that it may be difficult for the elderly to psychologically adjust to the traumatic event, which was not only limited to MTBI.[1,40] In particular, resilience is one factor assumed to contribute to the adverse outcome following MTBI.[12] Conversely, Mosenthal and colleagues[33] found that older patients with MTBI continue to improve after discharge and postulated that age might possibly be a more important predictor of the unfavorable outcome in patients with more severe TBI. The present study identifies frailty and the presence of early posttraumatic complaints as significant predictors of the unfavorable long-term outcome after MTBI, whereas age is not. A possible explanation for this finding could be that the effect of age on outcome diminishes with increasing age.

To our knowledge there are no other studies of the influence of frailty on outcome after MTBI in elderly patients. Therefore, this study is the first to report on this issue. As the overall population ages, it will become mandatory to improve the care for elderly patients with MTBI. Frailty is not only a risk factor for sustaining a TBI in general, but it could also complicate treatment for this elderly group. It might seem difficult to disentangle the effects of frailty from those of comorbidities and disability, although the difference lies within the definition.[16,46] Comorbidities refer to the coexistence of clinically manifest diseases diagnosed by clinicians. Conversely, frailty is a multifactorial concept, is rarely limited to a single organ system, and refers to an increased vulnerability to physical and psychological stressors.[16,32] Previous research underlined that frailty can exist without the presence of comorbidity and disability, suggesting that frailty can result from aging-related physiologic changes that are not disease or disability based.[47]

The findings of this study support the hypothesis that frailty is an independent factor that can increase vulnerability to the unfavorable outcome after MTBI. Understanding the implications of frailty on outcome is important to recognizing elderly patients who are at risk of the adverse outcome and in need of early treatment after sustaining MTBI.

Study limitations

We recognize that this study has some limitations. First, this study lacked a comparison group (one that consists of the frail elderly who did not sustain an MTBI) to investigate the effect of frailty alone. However, the sample size of this study is large compared with other studies. Moreover, the differences regarding the long-term outcome between the frail and nonfrail are clearly significant, indicating a substantial effect of frailty upon functional outcomes in patients with MTBI. Although preinjury frailty status was not measured, the findings suggest that measuring frailty postinjury has a significant effect on the long-term outcome. Furthermore, it could be argued that the GOSE is not an applicable instrument to measure outcome in these elderly patients. Moreover, there is partial redundancy between the GOSE and the frailty measure. Nevertheless, the GOSE is a valid scale that is employed worldwide to monitor functional recovery, even several years after injury in all age categories, and earlier studies have reported the clinical relevance and validity of this outcome instrument.[20,30]

Although outcome can be reliably determined by phone, this could result in an overestimation of good outcome, and the effect of frailty could even be greater than measured within the present cohort.[29] This study did not measure cognitive impairments, which made

it difficult to determine whether patients were suffering from age-associated mild cognitive impairment, although none of the patients in this study were clinically diagnosed with dementia.

CONCLUSION

This study shows that the elderly overall tend to recover well after sustaining MTBI. Frail elderly patients showed the less favorable long-term outcome compared with nonfrail patients, exhibiting more residual physical and psychological impairments. These results may have a number of implications for clinicians. For instance, frail elderly patients could benefit from a more extensive follow-up period although they "only" sustained a mild brain injury. Furthermore, this study emphasizes the importance of fall prevention in the elderly; clinicians should focus more on prevention measures in this elderly population.

As frailty is a multidimensional index, future research should investigate which aspects of frailty are the best predictors of the long-term outcome after MTBI. This information could help clinicians improve current rehabilitation programs. Future research should also include all categories of TBI to investigate the effect of preinjury frailty and age in addition to other factors (eg, resilience and coping) on recovery after TBI. This could help allocate care more efficiently and possibly to reduce the associated medical costs.

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APPENDIX 1: Groningen Frailty Indicator

Physical domain

Are you able to carry out these tasks single handedly and without any help? (The use of help resources, such as a walking stick, walking frame, or wheelchair, is considered to be independent.)

1. Shopping
2. Walking around outside (around the house or to the neighbors)
3. Dressing and undressing
4. Going to the toilet
5. What mark do you give yourself for physical fitness? (scale 0 to 10)
6. Do you experience problems in daily life because of poor vision?
7. Do you experience problems in daily life because of being hard of hearing?
8. Have you lost a lot of weight in the last 6 months? (3 kg in 1 month or 6 kg in 2 months)
9. Do you take 4 or more different types of medicine?

Cognitive domain

10. Do you have any complaints about your memory?

Social domain

11. Do you have ever experienced an emptiness around you?
12. Do you long for other people (to socialize with)?
13. Do you feel abandoned?

Psychological domain

14. In the past 4 weeks, did you feel downhearted or sad?
15. In the past 4 weeks, did you feel anxious or nervous?

Scoring:

Questions 1-4: → Yes = 0; no = 1
Question 5: → 0-6 = 1; 7-10 = 0
Questions 6-9: → No = 0; yes = 1
Question 10: → No = 0; sometimes = 0; yes = 1
Questions 11-15: → Yes = 1; sometimes = 1; no = 0