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ORIGINAL ARTICLE

Higher age is a major driver of in-hospital adverse events independent of comorbid diseases among patients with isolated mild traumatic brain injury

Barbara R. Schmidt[1] · Rudolf M. Moos[2] · Dilek Könü-Leblebicioglu[3] · Heike A. Bischoff-Ferrari[4] · Hans-Peter Simmen[1] · Hans-Christoph Pape[1] · Valentin Neuhaus[1]

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Abstract

Purpose The goal of this study was to investigate if and to what extent age, independent of comorbid diseases, is a risk factor for negative in-hospital outcome with mTBI.

Methods In a retrospective cohort study, we identified 1589 adult patients treated for isolated mTBI in our level-1 trauma center between 2008 and 2015. We used logistic regression analyses to assess the odds of any adverse event by age group (< 65, 65–75, 76–85, and 85+), adjusting for gender and chronic diseases.

Results The prevalence of any adverse event during in-hospital care among mTBI patients was 3.2% overall, 1.8% among those younger than age 65 years, 2.1% among those age 65–75 years, 8% among those age 75–85 years, and 19% among those age 85+ years. The odds of any adverse event were similar in patients aged 65–75 years, but increased among senior patients 4.4-fold for age 75–85 years (OR 4.4, 95%CI 2.0–9.8, $p < 0.001$), and 18-fold for age 85+ years (OR 18.0, 95%CI 8.7–37, $p < 0.001$). Additionally, chronic alcohol abuse (OR 7.0, 95%CI 3.2–15, $p < 0.001$), diseases of the musculoskeletal system (OR 4.3, 95%CI 1.5–13, $p = 0.008$), and diabetes mellitus (OR 2.7, 95%CI 1.2–6.5, $p = 0.023$) increased the odds of any adverse events independent of age and all other covariates.

Conclusions The odds of sustaining an adverse event increased exponentially after age 75 independent of gender and any comorbid diseases. Our data support international efforts to manage senior patients in interdisciplinary geriatric trauma units.

Keywords Adverse events · Minor traumatic brain injury · Risk factors · Senior patients

Introduction

Traumatic brain injury (TBI) represents one of the most common reasons for admissions to emergency departments. People with increased risk of sustaining TBI include children, adolescents and people over 65 years of age [1]. Currently, nearly 20% of the population in industrialized countries are older than 65 years. In view of the postulated demographic changes, the group of patients over 65 years suffering from TBI will increase significantly during the next decades [2–4]. This senior patient group has even a higher risk of sustaining severe TBI with intracranial bleeding due to concomitant comorbidities and polypharmacy with anticoagulants and anti-platelet drugs [5–7].

TBI in general was defined by the WHO as "any injury to the brain resulting from the application of external forces to the skull that can lead to a spectrum of problems including concussion, contusion or diffuse injuries that cause more severe neurological damage"[8]. The severity of TBI can be classified by the Glasgow Coma scale (GCS) into mild (GCS 13–15; mTBI), moderate (GCS 9–12) and severe (GCS 3–8) [9, 10]. This is independent from morphological cranial injuries. Mild traumatic brain-injured patients typically do not

✉ Valentin Neuhaus
valentin.neuhaus@gmx.ch

[1] Division of Trauma Surgery, Department of Surgery, University Hospital Zurich, University of Zurich, Raemistrasse 100, 8091 Zurich, Switzerland

[2] Medical Directorate, University Hospital Zurich, Zurich, Switzerland

[3] Department of Neurosurgery, University Hospital Zurich, University of Zurich, Zurich, Switzerland

[4] Department of Geriatrics, University Hospital Zurich, University of Zurich, Zurich, Switzerland

exhibit severe neurological problems; however, they complain of amnesia, unconsciousness, awareness disturbances, seizures and minor symptoms such as nausea, vertigo and cephalgia. These complaints are commonly treated symptomatically while the patients are hospitalized for more than 24 h [8, 11, 12]. Morphological injuries, such as fractures and intracranial lesions, can cause diverse symptoms (depending on the location), are rather associated with a higher severity, increase the risk of neurosurgical intervention and warrant a close observation.

In our daily practice, we see many patients with an mTBI without morphological injuries on a CT scan. There is scarce data on in-hospital adverse events among these patients and the knowledge about distinct risk factors for an adverse outcome may influence hospital admission policies and management [13–20].

Therefore, the primary goal of this study was to investigate if and to what extent age, independent of any comorbid diseases, is a risk factor for negative in-hospital outcome after sustaining an isolated mTBI without morphological injuries. The second goal was to evaluate other independent predictors for adverse events.

Patients and methods

In a retrospective cohort study, the recorded electronic data of all patients admitted to a level 1 trauma center between October 2008 and December 2015 were analyzed. The local IRB approved the study (KEK-ZH-No: 2011-0382).

The inclusion criteria were adult patients (older than 17 years) with an isolated mTBI and a computer tomography of the head (cCT) at admission. An mTBI was defined as patients with a temporal impairment of awareness following head trauma with signs of amnesia, no new focal neurological deficiency and a GCS at admission of 13–15. Patients with intracranial hemorrhage or skull fractures as well as patients that sustained concomitant injuries were excluded.

The standard procedure for patients with mTBI at this level one trauma center was: every patient with mTBI has a CT scan of the head at admission, followed by a standardized in-hospital neurological observation for 24 h by monitoring GCS, pupillary reflex and motor function and sensibility of the extremities as well as vital parameters in an interval of 30 min for the first 3 h, followed by an hourly monitoring for the next 9 h and every 4 h for the next 12 h. Patients are usually discharged after 24 h with normal observation.

In-hospital data included demographics (age, sex, residence before and after admission, type of insurance), comorbidities, interventions, length of stay and complications. Comorbidities were coded using the International Classification of Diseases, 10th revision (ICD 10) [21], encoded by professional medical coders. The procedures were encoded using the Swiss Operative Classification System (CHOP) [22]. The corresponding ICD codes for urinary tract infection, acute delirium, distinct complications after surgical intervention, respiratory complications, thromboembolism, sepsis, acute anemia, reanimation and acute renal insufficiency were used as marker of adverse events.

More than 20,000 patients were admitted to the trauma center in this time period. Around 8000 patients had a traumatic brain injury and 1589 adult patients with an isolated mTBI and a normal cCT at admission remained for further analysis (Table 1).

Statistical analysis was performed using IBM SPSS Statistics (SPSS, Inc., Chicago, IL, USA). Death and suffering any complications were the outcome parameters. Independent factors were age, sex, as well as chronic comorbidities. Categorical data were reported in absolute numbers (n) and percentages (%), and numerical data as mean, median and standard deviation ($\pm$SD). The Pearson Chi square (χ^2) or Fisher's exact test were used to compare categorical data, while the Mann–Whitney U test was used to compare numerical data. Statistical significance was set at $p < 0.05$ for the analysis. Stepwise backward logistic regression was used to identify the odds of mortality and any adverse event by age group (<65, 65 to 75, 76 to 85, and 85+), plus adjusting for gender and chronic diseases. Chronic diseases were included in the regression analysis if 30 or more patients exhibited that factor and the p value in the bivariate analysis was $p < 0.1$.

Results

Description of the cohort

The mean age of these 1589 patients with an isolated mTBI was 45±21 years. Twenty-two percent of patients were seniors (older than 65 years), 4.9% of patients were older than 85 years. Overall, the majority (63%) of patients were male. However, the rate of female seniors was 54%, with even rising numbers in the older age groups (63% in patients older than 85 years). Most patients sustaining an mTBI (95%) resided at home before admission to the hospital. In the age group of 65–74 years, 98% of the patients were living at home. The percentage of patients with assisted living increased with age, being 21% in patients older than 85 years living in nursing homes or senior residences. However, 85% of seniors of 75–84 years and still 75% of seniors 85 years and older were living at home without professional assistance (Table 1).

Thirty-seven percent of the patients had at least one comorbid disease. The rate of comorbidities was highest (72%) in patients 75–84 years. Arterial hypertension in 46%, atrial fibrillation in 21%, cancer in 18% and dementia in 17%

Table 1 Demographic overview

Parameter	Total, $n=1589$		Under 65 years, $n=1245$ (78%)		65–74 years, $n=141$ (8.9%)		75–84 years, $n=125$ (7.9%)		85 years or older, $n=78$ (4.9%)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex										
F	580	37	394	32	60	43	77	62	49	63
M	1009	63	851	68	81	57	48	38	29	37
Residence before admission										
At home	1323	95	1055	96	121	98	93	85	54	75
At home with outpatient care	5	0.4	1	0.1	0		2	1.8	2	2.8
Nursing home	21	1.5	4	0.4	0		7	6.4	10	14
Senior residence	10	0.7	1	0.1	1	0.8	3	2.8	5	6.9
Psychiatric hospital	8	0.6	7	0.6	0		1	0.9	0	
Other hospital	24	1.7	21	1.9	1	0.8	2	1.8	0	
Penal institution	4	0.3	4	0.4	0		0		0	
Other	5	0.4	3	0.3	0		1	0.9	1	1.4
Type of insurance										
General	756	83	611	87	68	79	48	69	29	62
Private	150	17	92	13	18	21	22	31	18	38
Comorbidity present	699	44	462	37	92	65	90	72	55	71
Any complications during hospitalization	57	3.6	24	1.9	5	3.5	11	8.8	17	22
Death	3	0.2	0		1	0.7	1	0.8	1	1.3
Type of discharge										
Regular	1425	91	1148	93	127	91	98	82	52	70

Table 1 (continued)

Parameter	Total, $n=1589$		Under 65 years, $n=1245$ (78%)		65–74 years, $n=141$ (8.9%)		75–84 years, $n=125$ (7.9%)		85 years or older, $n=78$ (4.9%)	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Against medical advice	32	2.0	29	1.4	2.4	2	1	0.8	0	
Transfer	36	2.3	18	1.5	3	2.2	10	8.3	5	6.8
Death	3	0.2	0		1	0.7	1	0.8	1	1.3
Discharge rehabilitation center	9	0.6	4	0.3	1	0.7	2	1.7	2	2.7
Discharge care facility	25	1.6	5	0.4	1	0.7	6	5.0	13	18
Discharge psychiatry	35	2.2	28	2.3	4	2.9	2	1.7	1	1.4

	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD
Age in years	45	42	21	36	34	14	69	68	3	80	80	3	88	88	3
Length of stay in days	2	1	1	1	1	1	2	1	2	2	1	2	2	2	2
Hours of intensive care (since 2012)	1	0	6	1	0	4	3	0	18	0	0	3	0	0	0
Hours of mechanical ventilation (since 2009)	0	0	4	0	0	5	1	0	5	0	0	4	0	0	1

F female, *M* male, *n* numbers, *SD* standard deviation

Table 2 Comorbidities

	Total		Under 65 years		65–74 years		75–84 years		85 years or older	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Mental and behavioral disorders	358	23	280	22	39	28	23	18	16	21
Intoxication with psychotropic substances	173	11	148	12	20	14	5	4.0	0	
Nicotine abuse	8	0.5	6	0.5	1	0.7	1	0.8	0	
Chronic alcohol abuse[a]	98	6.2	78	6.3	15	11	5	4.0	0	
Depressive disorder	45	2.8	38	3.1	4	2.8	1	0.8	2	2.6
Dementia[a]	30	1.9	2	0.2	3	2.1	12	9.6	13	17
Neoplasms	217	14	161	13	22	16	22	18	12	15
Arterial hypertension[a]	184	12	55	4.4	37	26	57	46	35	45
Heart diseases										
Coronary artery disease	23	1.4	5	0.4	3	2.1	11	8.8	4	5.1
Cardiac dysrhythmia	50	3.1	8	0.6	9	6.4	17	14	16	21
Atrial fibrillation/flutter	46	2.9	6	0.5	7	5.0	17	14	16	21
Heart failure	4	0.3	0		0		2	1.6	2	2.6
Left heart failure										
NYHA 2	1	0.1	0		0		0		1	1.3
NYHA 4	1	0.1	0		0		1	0.8	0	
Right heart failure	3	0.2	0		0		2	1.6	1	1.3
Diabetes mellitus[a]	64	4.0	32	2.6	12	8.5	13	10	7	9.0
Diseases of the musculoskeletal system and connective tissue[a]	36	2.3	18	1.4	5	3.5	11	8.8	2	2.6
Vascular diseases										
Cerebrovascular disease	23	1.4	12	1.0	4	2.8	4	3.2	3	3.8
Peripheral vascular disease	9	0.6	2	0.2	2	1.4	4	3.2	1	1.3
Disorders of thyroid gland	20	1.3	10	0.8	2	1.4	3	2.4	5	6.4
Paresis/plegia	19	1.2	11	0.9	4	2.8	2	1.6	2	2.6
Hemiplegia	15	0.9	10	0.8	2	1.4	1	0.8	2	2.6
Lipometabolic disorders	18	1.1	5	0.4	3	2.1	7	5.6	3	3.8
Esophagitis, GERD, gastrointestinal ulcera, gastritis, duodenitis	16	1.0	9	0.7	4	2.8	2	1.6	1	1.3
Chronic pulmonary disease	13	0.8	5	0.4	3	2.1	4	3.2	1	1.3
Diseases of the liver										
Chronic hepatitis C	12	0.8	11	0.9	0		0		1	1.3
Alcoholic liver disease	11	0.7	9	0.7	1	0.7	1	0.8	0	
Other diseases of the liver	8	0.5	8	0.6	0		0		0	
Fibrosis or cirrhosis of liver	1	0.1	1	0.1	0		0		0	
Chronic hepatitis B	1	0.1	1	0.1	0		0		0	
HIV	7	0.4	7	0.6	0		0		0	
Obesity	6	0.4	5	0.4	1	0.7	0		0	
Renal insufficiency ≥ Stadium III										
With moderate restriction	4	0.3	0		3	2.1	1	0.8	0	
With severe restriction	2	0.1	0		0		0		2	2.6
Chronic renal failure—renal dialysis	2	0.1	0		1	0.7	1	0.8	0	

ERD gastroesophageal reflux disease, *HIV* human immunodeficiency virus, *n* numbers, *NYHA* New York Heart Association functional classification

[a]Entered into multivariate analysis

were most commonly encountered. Overall, 4% of patients sustaining an mTBI suffered from diabetes mellitus, and in the senior patients older than 65 years 9.3% had diabetes. In the age group > 85 years, 44.9% had diabetes mellitus. Compared to diabetes, psychiatric diseases were similarly distributed between all age groups (22.5% in patients < 65

Table 3 Complications

	Total		Under 65 years		65–74 years		75–84 years		85 years or older	
	n	%	*n*	%	*n*	%	*n*	%	*n*	%
Urinary tract infection	18	1.1	2	0.2	2	1.4	6	4.8	8	10
Acute delirium	12	0.8	7	0.6	2	1.4	1	0.8	2	2.6
Complications of surgical intervention	9	0.6	6	0.5	1	0.7	1	0.8	1	1.3
Complications during intervention	3	0.2	1	0.1	1	0.7	0		1	1.3
Wound dehiscence	1	0.1	0		0		0		1	1.3
Respiratory complications										
Intubation	7	0.4	6	0.5	0		1	0.8	0	
Pneumonia	6	0.4	0		0		4	3.2	2	2.6
Aspiration pneumonia incl. Mendelson's syndrome	5	0.3	5	0.4	0		0		0	
Respiratory insufficiency	2	0.1	2	0.2	0		0		0	
Early complications in trauma	4	0.3	2	0.2	0		0		2	2.6
Cerebral infarction (thrombosis or embolism)	2	0.1	0		0		0		2	2.6
Acute myocardial infarction	1	0.1	1	0.1	0		0		0	
SIRS	3	0.2	2	0.2	0		0		1	1.3
Sepsis	2	0.1	0		0		0		2	2.6
Acute anemia	2	0.1	1	0.1	0		1	0.8	0	
Traumatic muscular ischemia	2	0.1	1	0.1	0		0		1	1.3
Complications following infusion, transfusion or injections	2	0.1	2	0.2	0		0		0	
Reanimation	1	0.1	0		1	0.7	0		0	
Acute renal insufficiency	1	0.1	0		0		0		1	1.3

n numbers, *SIRS* systemic inflammatory response syndrome

Table 4 Predictors for adverse events

	Sig.	OR	95%CI	
			Lower	Upper
Age > 85 y vs. <65 y	< 0.001	18	8.7	37
Chronic alcohol abuse	< 0.001	7.0	3.2	15
Age 75–84 y vs. <65 y	< 0.001	4.4	2.0	9.8
Diseases of the musculoskeletal system and connective tissue	0.008	4.3	1.5	13
Diabetes mellitus	0.023	2.7	1.2	6.5
Age 65–74 y vs. <65 y	0.510	1.4	0.5	3.9

Dependent variable: any adverse event. Covariates: age group (<65 y, 65–74 y, 75–84 y, and > 85 y), gender, chronic diseases (arterial hypertension, chronic alcohol abuse, dementia, diabetes mellitus, diseases of the muskuloskeletal system and connective tissue). 1589 included cases in analysis, R^2 0.194

CI confidence interval, *OR* odds ratio, *y* years

years and 22.7% in patients > 65 years). Thirty-six patients (2.3%) had diseases of the musculoskeletal system and the connective tissue with half of these patients being younger than 65 years (Table 2).

Outcomes

The mean length of stay was 2 ± 1 days with a range of 1–20 days. Length of stay steadily increased with age ($p < 0.001$). Patients with comorbidities stayed slightly (+ 0.52 day), but significantly ($p < 0.001$), longer. One, or two or more adverse events increased the length of stay significantly (+ 2.2 days and + 3.0 days, respectively; $p < 0.001$).

Three patients (0.2%) with an end-stage disease died during the hospitalization. All of them were older than 65 years.

One hundred and seventy-three patients (11%) had a second CT of the brain during the hospitalization due to a temporarily lowered GCS or severe headache. No neurosurgical procedures had to be done during the hospitalization.

An adverse event was encountered in 3.2% ($n = 51$); however, the rate was highest (19%, $n = 15$) in patients older than 85 years. Urinary tract infection and pneumonia were the most common adverse events ($n = 18$, 1.1% respectively $n = 6$, 0.4%). Only 0.8% of the patients suffered from acute delirium. However, acute delirium was diagnosed most frequently in the age group of 65–74 years (1.4%) (Table 3).

Independent risk factors for adverse events were age older than 85 years (OR 18.0, 95%CI 8.7–37, $p < 0.001$; vs. patients younger than 65 years), age between 75 and 85 years

(OR 4.4, 95%CI 2.0–9.8, $p<0.001$), chronic alcohol abuse (OR 7.0, 95%CI 3.2–15, $p<0.001$), diseases of the musculoskeletal system (OR 4.3, 95%CI 1.5–13, $p=0.008$) and diabetes mellitus (OR 2.7, 95%CI 1.2–6.5, $p=0.023$) (Table 4).

Patients after an adverse event were significantly more often transferred to another facility (18% vs. 1.7%) or discharged to a rehabilitation center (1.9% vs. 0.5%) or care facility (5.6% vs. 1.5%) ($p<0.001$).

Discussion

Mild traumatic brain injury is often diagnosed in emergency departments, more frequently in senior patients [13, 23]. In our Level I trauma center, mTBI is the most frequent diagnosis in seniors. These patients are commonly multimorbid and on multiple chronic medications and therefore difficult to manage [24–28]. Morbidity of mTBI can be high; however in-hospital data is, to the best of our knowledge, scarce. This study revealed that the in-hospital outcome of patients with an isolated mTBI and a normal cCT at admission was usually uneventful. Nonetheless, patients older than 75 years and patients with diabetes or chronic alcohol abuse were at risk for adverse events and may need special monitoring, whereas young patients without other independent risk factors might not necessarily need neurological monitoring or hospitalization.

One strength of this study was the strict treatment algorithm practiced in our level I trauma center. However, there were several limitations. First, it was a retrospective evaluation of in-hospital patients only with the possibility of reporting aberrancy and coding errors and no long-term outcome. Second, there are low-threshold criteria and limitations to perform a cCT scan in the algorithm practiced in our level one trauma center, so the incidence of mTBI might be overrepresented as well as the number of patients admitted with isolated mTBI. Third, only patients with isolated mTBI were included. On the one hand that reduced the sample size significantly, but on the other hand we could study the effect of mTBI on in-hospital adverse events conclusively. Fourth, the small numbers of adverse events limited multivariate analysis. Last, the severity or prevalence of different diseases (dementia in seniors underreported or unrecognized) and complications (acute delirium might have been underdiagnosed) may not have been appropriately reflected and information on established medication with anticoagulants or anti-platelet drugs had not distinctly been recorded.

The mortality rate in our cohort was 0.2% and all of our three patients that had deceased during hospitalization suffered from end-stage diseases. The end-stage diseases were also the reasons for the fall causing an mTBI. The small number of patients did not allow effective biostatistical analysis. Our mortality rate was similar to the 0.45% in-hospital all-cause death rate reported by Pentland et al. in 2005 [29]. Mortality rate is low in patients with an isolated mTBI and a normal CT of the head at admission.

In our study group, the overall prevalence of complications, mainly urinary tract infection and pneumonia, was 3.2%. Our morbidity rate was similar to the 3.7% rate of adverse events published by Brennan et al. 1991 of the Harvard Medical Practice Study [30]. Nevertheless, we detected an exponential increase in the complication rate in patients older than 74 years. This can be explained by frailty and the associated sarcopenia in higher age with a deficiency of mobility, physical activity, incontinence and immune deficiency. Therefore, we think that hospitalization of patients that have sustained mTBI can be recommended for these distinct patients that are at risk of sustaining adverse events.

In comparison to infectious adverse events, the percentage of acute delirium recorded in our study cohort is underreported. Some doctors seem to accept confusion or mutism as part of traumatic brain injury or demented patients. Inouye et al. stated that as much as 50% of elderly people in hospital suffer from delirium causing costs of US$164 billion per year in the USA [31]. Over the past few years, scoring systems have been implemented into the clinical routine to identify acute delirium and patients at risk. Still, the recognition and appropriate treatment of delirium require further training and algorithms.

In summary, this study showed a very low mortality and a low morbidity of isolated mTBI with a normal CT head. However, there are patients at risk for adverse events. We identified four groups of patients at risk: senior patients ≥ 75 years, patients with chronic alcohol abuse, patients with connective tissue diseases and patients with diabetes mellitus. We think that hospitalization of these patients at risk is advisable. Furthermore, senior patients are ideally treated in specialized orthogeriatric centers that conform to the demands of this specific patient group coming to pharmacy and pharmacokinetics, physiotherapy and fall prevention and nutrition.

Compliance with ethical standards

Conflict of interest There are no conflicts of interest with this topic.

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