

Updated periodic evaluation of standardized neurointensive care shows that it is possible to maintain a high level of favorable outcome even with increasing mean age

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Abstract

Background Periodic evaluation of neurointensive care (NIC) is important. There is a risk that quality of daily care declines and there may also be unrecognized changes in patient characteristics and management. The aim of this work was to investigate the characteristics and outcome for traumatic brain injury (TBI) patients in the period 2008–2009 in comparison with 1996–1997 and to some extent also with earlier periods. **Methods** TBI patients 16–79 years old admitted from 2008 to 2009 were selected for the study. Glasgow Coma Scale Motor score at admission (GCS M), radiology, surgery, and outcome (Glasgow Outcome Extended Scale) were collected from Uppsala Traumatic Brain Injury Register.

Results The study included 148 patients (mean age, 45 years). Patients >60 years old increased from 16 % 1996–1997 to 30 % 2008–2009 ($p<0.01$). The proportion of GCS M 4–6 were similar, 92 vs. 93 % (NS). In 1996–1997 patients, 73 % had diffuse injury (Marshall classification) compared to 77 % for the 2008–2009 period (NS). More patients underwent surgery during 2008–2009 (43 %) compared to 1996–1997 (32 %, $p<0.05$). Good recovery increased and mortality decreased substantially from 1980–1981 to 1987–1988 and to 1996–1997, but then the results were unchanged in the 2008–2009 period, with 73 % favorable outcome and 11 % mortality. Mortality increased in GCS M 6–4, from 2.8 % in 1996–1997 to 10 % in 2008–2009 ($p<0.05$); most of the patients that died had aggravating factors, e.g., high age, malignancy. **Conclusions** A large-proportion favorable outcome was maintained despite that patients >60 years with poorer prognosis doubled, indicating that the quality of NIC has increased

or at least is unchanged. More surgery may have contributed to maintaining the large proportion of favorable outcome. For future improvements, more knowledge about TBI management in the elderly is required.

Keywords Traumatic brain injury · Standardized neurosurgical intensive care · Periodic evaluation · Outcome · Quality register

Introduction

It has been shown by many that the outcome after traumatic brain injury (TBI) improves with the development of neurointensive care (NIC) [2, 3, 6, 9, 10, 12, 19]. There has not yet been any breakthrough for neuroprotective drugs [11] and high-quality NIC is still crucial for further improvements of treatment results. We have earlier been able to demonstrate successively improved results by comparing the time periods 1980–1981, 1987–1988 [19], and 1996–97 [6]. During the last time period, we had implemented standardized management protocols for the NIC and maximum attention was paid to the importance of avoiding secondary insults through staff lectures and the introduction of new routines where the occurrence of secondary insults should be reported orally at the bedside rounds and recorded in checklists by the responsible nurses [6, 14]. Since the last period, the Uppsala Traumatic Brain Injury Register for quality assurance of NIC has been established [13]. The principles for our NIC have not been changed. There is always a risk that the quality of daily routine care declines and there may also be unrecognized changes in patient characteristics and small shifts in management. Therefore, we found it desirable to evaluate another 2-year period 10 years after the last review and take advantage of the

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information available in The Uppsala TBI register. The specific aim was to investigate the treatment results and characteristics of the patients of 2008–2009 in comparison with the previously most recent reported period of 1996–1997 and to some extent also with earlier periods.

Materials and methods

Referral of patients and the TBI register

The Department of Neurosurgery at the University Hospital in Uppsala, Sweden, provides neurosurgical care for the central part of Sweden with a population of approximately 2 million people. Most patients are initially managed at local hospitals according to ATLS principles and then referred to Uppsala (the most distant local hospital 382 km away) [7]. Since 2008, all patients with TBI admitted to our NIC are included in the Uppsala Traumatic Brain Injury register [13] from which all data can be extracted.

Patients

To be able to compare the results with the previous period [6, 19], we used the same inclusion and exclusion criteria. All TBI patients between the age of 16 and 79 years admitted to the NIC unit at the Uppsala University Hospital between 2008 and 2009 were eligible for the study. In total, 168 patients were identified, and after exclusion of 20 patients, 148 patients remained in the study. The patients were excluded for the following reasons: (1) the patients were admitted to the NIC unit ≥ 5 days after the trauma ($n=4$), or were treated successfully at the NIC unit within 24 h ($n=6$); (2) patients had both pupils wide and non-reacting on arrival at the NIC unit ($n=3$) (i.e., patients with an obvious predestined fatal clinical course [1, 4] in whom it could not be assessed retrospectively if active treatment had been initiated); (3) patients had gunshot injuries ($n=1$) and patients lost to follow-up ($n=6$).

Neurointensive care

All patients were treated according to the same standardized management protocols as in the previously evaluated time period of 1996–1997 [6]. The standardized management protocols are summarized below.

Basal treatment

Head elevation was 30° to facilitate venous outflow and prohibit ventilator-associated pneumonia. Unconscious patients (Glasgow Coma Motor Score (GCS M) 1–5) were intubated and received propofol infusion (Propofol-LipuroB, Braun Medical AB, Danderyd, Sweden) as sedation and morphine

injections or infusions as analgetics. The sedation was interrupted repeatedly and neurological wake-up tests were performed [16]. The patients were initially moderately hyperventilated (PaCO₂ 4.0–4.5 kPa) but gradually normoventilated as early as possible when the intracranial pressure (ICP) allowed. Extracerebral hematomas and contusions causing significant mass effect were surgically evacuated except in cases where coagulopathy was resistant to therapy. ICP was monitored in all patients with GCS M 1–5 using an intraventricular drainage catheter if possible or intracerebral probes if the ventricles were compressed.

Treatment goals were as follows: ICP ≤ 20 mmHg, cerebral perfusion pressure (CPP) ≥ 60 mmHg, systolic blood pressure >100 mmHg, CVP 0–5 mmHg, pO₂ >12 kPa, blood glucose 5–10 mmol/l, electrolytes within normal range, normovolemia and body temperature $<38^\circ\text{C}$. Prophylactic anticonvulsants were not given.

If no mass effect existed, intermittent drainage of small volumes (approximately 1–2 ml) of cerebrospinal fluid (CSF) was applied. The reason for not using a continuously open drainage system early was to maintain control over the intracranial dynamics and to avoid the development of slit ventricles and inaccurate ICP readings during the period when the risk of expanding mass lesions was highest. If the ICP was controlled by intermittent drainage for a reasonable period of time (around 1–3 days) without signs of progressive impairment or inadequate ICP registration due to compressed ventricles, the ventricular drainage was kept open and CSF was drained against a pressure level of 15–20 mmHg. This was always preceded by a CT-scan to exclude expanding mass lesions and slit ventricles. If the ICP was increased despite basal treatment, the following steps were followed:

Step 1a - Continuous sedation and stress reduction

Re-evaluation with the purpose of identifying significant mass lesions requiring surgery, existing avoidable factors, or inadequate sedation level. No wake-up tests until stabilization of ICP. Infusion of 0.2–0.3 mg/kg/24 h $\beta 1$ -antagonist Metoprolol (Seloken, AstraZeneca AB, Södertälje, Sweden) and injections of $\alpha 2$ -agonist Clonidin (Catapresan, BoehringerIngelheim AB, Stockholm, Sweden) (0.5–1.0 $\mu\text{g}/\text{kg} \times 8$ or the same dose as an infusion) were given to reduce the physiological stress response and thereby avoid ICP spikes and aggravation of cerebral edema [5].

Step 1b - Barbiturate coma treatment

If previous treatments are insufficient to reduce the increased ICP, thiopental infusion was used (Pentocur, Abcur AB, Helsingborg, Sweden). The infusion was started with a bolus dose of 4–8 mg/kg given as repeated 50 mg doses until ICP < 20 mmHg or blood pressure became unstable. After this, a continuous infusion of 5–10 mg/kg/24 h was given for around

6 h and thereafter 2–5 mg/kg/24 h. The lowest possible dose to keep ICP < 20 mmHg was used and burst-suppression on electroencephalogram was not a goal. During this treatment, a CPP of 50 mmHg was allowed. Thiopental concentrations > 380 $\mu\text{mol/l}$ were avoided.

Step 2 - Decompressive craniectomy

Decompressive craniectomy was advised under the following conditions: (1) Step 1b was unsuccessful in reducing ICP < 20 mmHg; (2) Step 1b caused severe adverse effects; (3) If too high doses/concentrations of thiopental were needed with risk of complications.

A hemicraniectomy was done if there was a shift of the mid-line but no significant mass lesions to remove. Bilateral frontotemporal craniectomies with sparing of a bone ridge at the mid-line were done if no shift was present. The ambition should always be to remove as large bone flaps as possible and a duraplasty should be performed to ensure adequate decompression.

Evaluation of outcome

The clinical outcome was assessed after around 6 months by a selected number of persons using structured telephone interviews for the extended Glasgow Outcome Scale (EGOS) [17, 18].

Statistical methods

To compare the groups, Pearson's Chi-square analyses were used. When comparing differences in gender and outcome, Yates' Chi-square was used when expected numbers were less

than 5. A p value < 0.05 was considered as a statistically significant difference.

Results

Patient characteristics on admission

The age distribution had changed from 1996–1997, showing a decreasing number of patients with increasing age, to 2008–2009, which showed a bimodal distribution with the highest number of patients in the age groups 16–29 years and 60–79 years (Fig. 1). The proportion of patients > 60 years had increased from 16 to 30 % between those time periods ($p < 0.01$, Table 1). The distribution in different admission GCS M grades was similar in the two time periods with the majority of patients in GCS M 4–5 grade (Fig. 2, Table 1).

In the 1996–1997 period, 73 % (112/154) patients were classified as diffuse injury I–IV according to the Marshall classification [6, 8] compared to 77 % (114/148) in the 2008–2009 period (NS) (Table 2). Extra-cranial injuries were present in 36 % of the patients in the 1996–1997 period and in 39 % of the patients in the 2008–2009 period (NS) (Table 1). The most predominating causes of trauma were motor vehicle accidents in both periods (29.2 % for 1996–1997 and 29.7 % for 2008–2009) (Table 3).

Surgery

A larger proportion of the patients underwent surgery in the 2008–2009 period compared to the 1996–1996 period (43 % (64/148) vs. 32 % (49/154), $p < 0.05$) (Table 2). Among patients classified as evacuated mass lesions and non-evacuated mass lesions (i.e., all focal mass lesions), 94 % (32/34) of the

Fig. 1 Age distribution by period

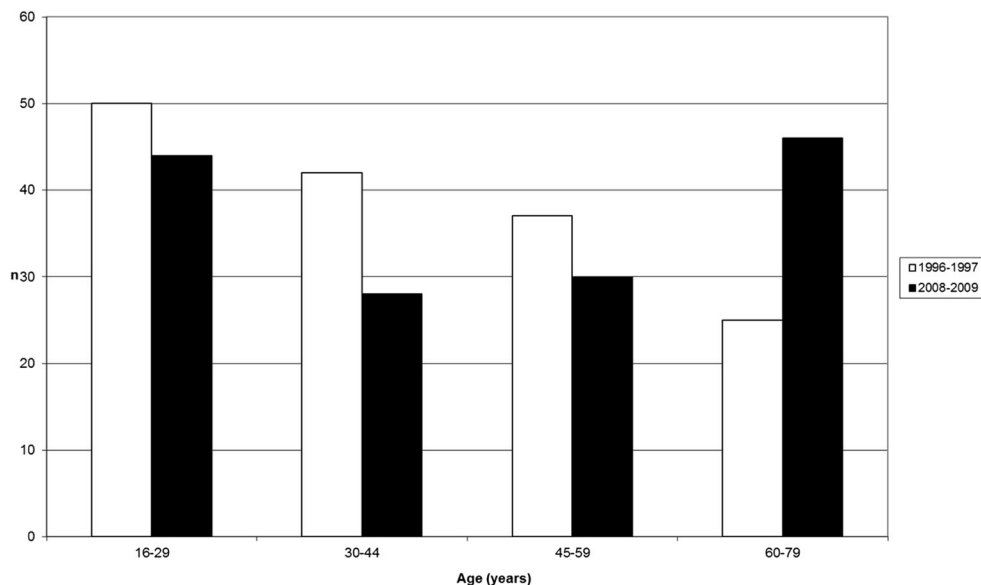


Table 1 Comparative summary of periods

	1980–1981 ^a	1987–1988 ^a	1996–1997 ^b	2008–2009	Chi-square test (1996–1997 vs. 2008–2009)
Numbers	49	72	154	148	
Referrals (%)	75	65	80	82	NS
Mean age, years	37	36	41	45	
>60 years (%)	16	18	16	30	<i>p</i> <0.01
GCS M \geq 4 (%)	40	42	92	93	NS
Epidural hematoma (%)	16	8	9	9	NS
Multiple injuries ^c (%)	18	18	36	39	NS
Outcome GCS M 1–6 (%)					
Mortality	41	31	6	11	NS
Favorable outcome	34	48	78	74	NS
Outcome GCS M \geq 4 (%)					
Mortality	40	27	2.8	10	<i>p</i> <0.05
Favorable outcome	40	69	84	80	NS

^a [19]^b [6]^c Associated chest injury, abdominal injury (requiring surgery), or major fracture (one or more extremity or spinal fracture)

patients were operated on before discharge in 2008–2009 compared to 62 % (26/42) in 1996–1997 (*p*<0.05) (Table 2).

Clinical outcome

Follow-up of the patients treated in 2008–2009 after 10 months in mean (median, 9, range, 1–28) showed that 45 % had good recovery (GR) (33.8 % higher GR and 10.7 % lower GR), 28 % moderate disability (MD) (16.2 % higher MD and 11.5 % lower MD), and 16 % severe disability (SD) (6.8 % higher SD and 9.5 % lower SD). No patient was

in a vegetative state (VS). At the time of follow-up, 17 of the patients (11.5 %) had died. Seven patients had died at the NIC unit and ten patients had died after discharge from the NIC. Figure 3 shows the clinical outcome according to GOS in four time periods. The proportion of patients in GR increased and the proportion of diseased patients decreased substantially from 1980 to 1981, 1987 to 1988, and 1996 to 1997, but then the results did not change significantly to from 2008 to 2009 (Table 1). The patients who died in 1996–1997 had an average age of 48 years, while the patients who died in 2008–2009 had an average age of 61 years (Table 5). The proportions of

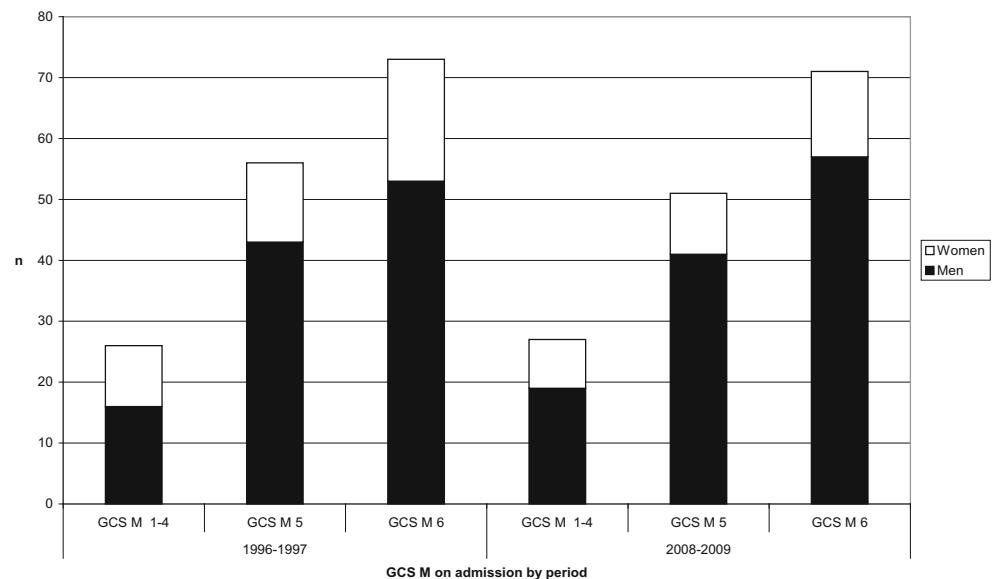
Fig. 2 Glasgow Coma Scale Motor score (GCS M) by period

Table 2 Initial CT Marshall category and surgery

CT-category ^a	Definition	1996-1997 ^b (n / surgery)	2008-2009 (n / surgery)
DI I	No visible intracranial injury on CT scan	0 / 0	1 / 0
DI II	Cisterns present, midline shift 0-5 mm and/or lesion densities present (< 25 cm ³)	70 / 10	85 / 18
DI III	Cisterns compressed or absent, midline shift 0-5 mm. Lesion densities < 25 cm ³	36 / 10	18 / 8
DI IV	Midline shift > 5 m, lesion densities < 25 cm ³	6 / 3	10 / 6
DI I-IV		112 / 23	114 / 32
		N.S.	
EML	Any lesion surgically evacuated	1 / 1	23 / 23
NEML	High- or mixed-density lesion > 25 cm ³ , not surgically evacuated	41 / 25	11 / 9
EML + NEML		42 / 26	34 / 32
		p < 0.05	
Total		154 / 49	148 / 64
		p < 0.05	

^a *DI I* diffuse injury I, *DI II* diffuse injury II, *DI III* diffuse injury III, *DI IV* diffuse injury IV, *EML* evacuated mass lesion, *NEML* nonevacuated mass lesion [8]

^b [6]

patients with SD and patients in VS were virtually unchanged over time (Fig. 3). Patients in higher GCS M on admission had better outcomes in both periods (Fig. 4, Table 4).

Subgroup analysis showed that mortality had increased in patients with GCS M 4–6, from 2.8 % in 1996–1997 to 10 % in 2008–2009 ($p < 0.05$), while the proportion of patients with a favorable outcome (GR+MD) was not significantly changed (Table 1). When mortality in the 2008–2009 period was analyzed

in detail, older patients (60–79 years) had higher mortality ($p < 0.001$) and lower favorable outcome ($p < 0.01$) (Fig. 5). Favorable outcome (GR+MD) was seen in 75 % (88/117) of the men and in 61 % (19/31) of the women (NS). Unfavorable (SD+VS) 13 % (15/117) of the men and in 29 % (9/31) of the women (NS). Of the men, 12 % died (14/117) and 10 % (3/31) of the women (NS). The 17 patients treated in 2008–2009 who were dead at the time of follow-up were judged to have died as a direct or indirect consequence of the trauma (Table 5). Aggravating factors were present in the large majority of the cases, which also applies to 1996–1997 (Table 5).

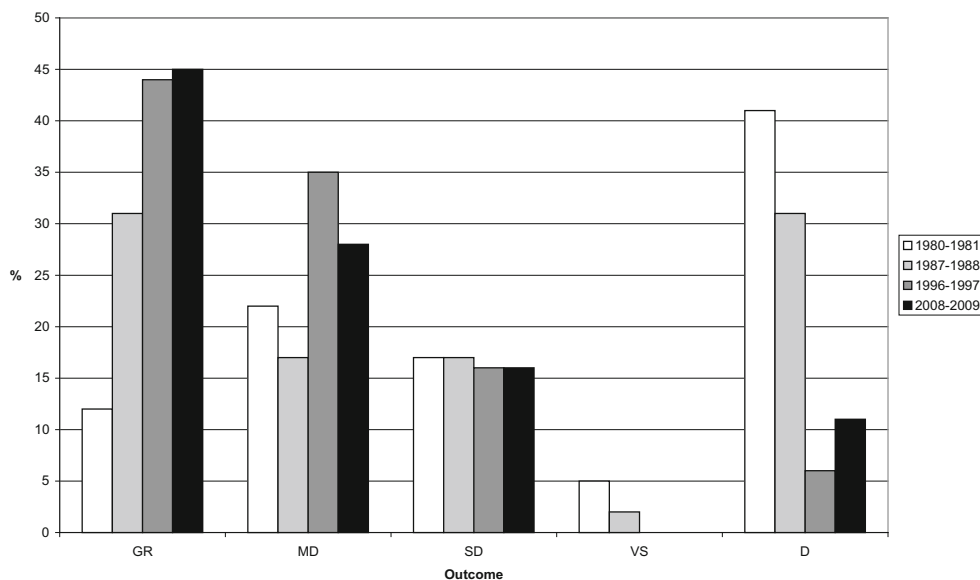
For the 2008–2009 period, 12 of the patients who died were 60 years or older. The youngest patient (patient 1) had a traumatic vertebralbasilar dissection, which led to severe cerebral ischemia. Patient 2 was involved in an explosion accident and arrived to the NIC unit in GCS M grade 2. Patients 3, 4, and 5 all had cancer diagnoses. Patients 6, 7, and 8 all had severe alcohol abuse. Patient 9 had an acute subdural hematoma diagnosed 2 days after the trauma and he was admitted in GCS M 3. Patients 10, 11, and 12 had large acute subdural hematomas, which were evacuated in their local hospitals on vital indication. Two of these patients were admitted in GCS M grade 2–3 and the third was 79 years old. Patients 13 and 14 were found in GCS M 1 at the scene of the accident when the emergency team arrived and patient 13 was also cyanotic. Patient 15 was 78 years

Table 3 Causes of accidents

Cause of accident	1996–1997 ^a (n/%)	2008–2009 (n/%)
Motor vehicle occupant	45/29.2	44/29.7
Pedestrian	18/11.7	11/7.4
Cyclist	3/1.9	5/3.3
Work	15/9.7	8/5.4
Domestic	7/4.5	19/12.8
Sport	16/10.4	5/3.4
Assault	6/3.9	10/6.8
Fall under the influence of alcohol	35/22.7	27/18.2
Other	7/4.5	18/12.2
Unknown	2/1.3	1/0.7

^a [6]

Fig. 3 Clinical outcome according to Glasgow Outcome Scale (GOS) by period



old and was on Warfarin medication. Patient 16 had chronic kidney disease and Alzheimer’s disease. Patient 17 was a 72-year-old patient who underwent multiple operations because of expansive hygromas and who had coagulase-negative staphylococcus (CoNS) meningitis. One of the patients who died during the NIC could be classified as “Talk and die”. This patient was 78 years old and on Warfarin treatment (patient 15).

Discussion

A substantial successive improvement of outcome after TBI, have been shown during the development of NIC,

when the periods 1980–1981, 1987–1988 and 1996–1997 have been compared [19, 6] (Fig. 3). The updated evaluation of the standardized NIC in Uppsala for the time period 2008–2009 did not show any significant changes in clinical outcome overall when the results were compared with the 1996–1997 period (Fig. 3). The neurological grade on admission according to the GCS M score was also virtually the same for the two periods (Fig. 2). The major observation was that the proportion of patients >60 years was doubled, which apparently did not influence the overall clinical outcome substantially despite that the proportion of favorable outcome was lower and the mortality higher in this

Fig. 4 Clinical outcome according to Glasgow Outcome Scale (GOS) by admission Glasgow Coma Scale Motor score (GCS M)

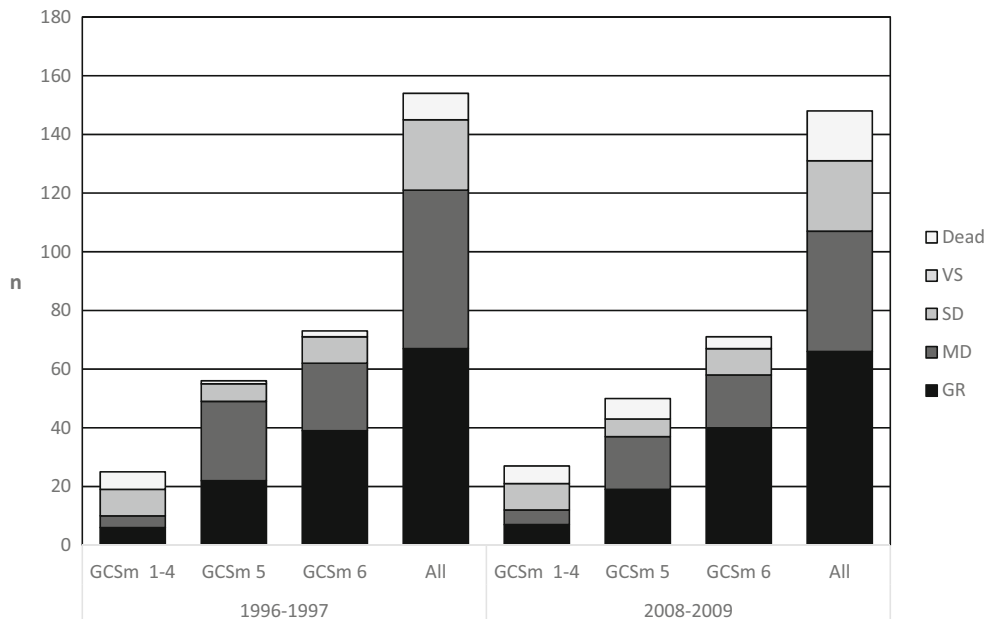


Table 4 Clinical outcome by admission GCS M grade

GOS	GCS M n (%) 1996–1997/n (%) 2008–2009		1–4	All
	6	5		
GR	39 (53)/40 (56)	22 (39)/19 (38)	6 (24)/7 (26)	67 (44)/66 (45)
MD	23 (32)/18 (25)	27 (48)/18 (36)	4 (16)/5 (19)	54 (35)/41 (28)
SD	9 (12)/9 (13)	6 (11)/6 (12)	9 (36)/9 (33)	24 (16)/24 (16)
VS	0 (0)/0 (0)	0 (0)/0 (0)	0 (0)/0 (0)	0 (0)/0 (0)
Dead	2 (3)/4 (6)	1 (2)/7 (14)	6 (24)/6 (22)	9 (6)/17 (11)
Total	73 (100)/71 (100)	56 (100)/50 (100)	25 (100)/27 (100)	154 (100)/148 (100)

age group (Fig. 5). When the mortality for the two time periods was compared for patients in GCS M 4–6, the mortality was significantly higher during the last period. An analysis of mortality by year showed that the increased mortality mainly was ascribed to 2009, 14 % (9/61) compared to 9.2 % (8/87) 2008 and preliminary analysis of 2010 showed 5.0 % mortality (data not presented). Therefore, the observed increased mortality for patients in GCS M 4–6 is probably not an indication that the quality of NIC has decreased in general but more probable a temporary increase in mortality 2009, which appears to be explained by aggravating factors in the large majority of patients with fatal outcomes (Table 5). On the contrary, maintaining the large proportion of favorable outcomes despite that the proportion of patients >60 years with poorer prognosis had increased may indicate that the quality of NIC rather has increased or at least is unchanged. The observation that a larger proportion of patients underwent surgery

(Table 2) may indicate that more active surgery may have contributed to that the large proportion of favorable outcome was maintained.

The larger proportion of elderly in the latest evaluated period was expected. It is well known that the proportion of elderly in the population is increasing. In Sweden, the proportion of people ≥ 65 years old has increased from 13.9 % in 1971 to 17.4 % in 2011 and is predicted to be 22.8 % in the year 2051 [15]. Furthermore, there is also an increase in the general health and activity of living among the elderly. Therefore, health-care faces a tremendous challenge to be able to offer elderly people adequate treatments in the future. We need a better mechanism for selection of elderly patients possible to treat and also to improve our understanding of age-specific pathophysiological mechanisms to be able to give the optimal care.

The finding that the results appeared to be virtually unchanged since the last updated period of 1996–1997 may indicate that the quality of NIC has culminated or is close to culminating. Therefore, in addition to optimizing the care of

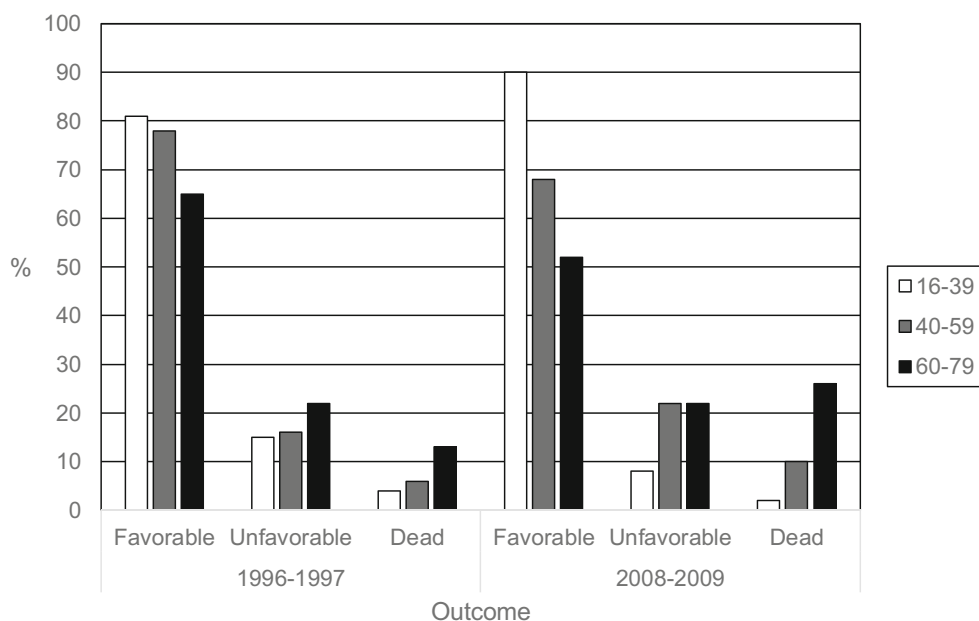
Fig. 5 Clinical outcome according to Glasgow Outcome Scale (GOS) by age

Table 5 Characteristics of patients who died

Patient no.	GCS M admission	GCS M discharge	Age	Aggravating factors
2008–2009				
1	5	4	19	Vertebrobasilar dissection
2	2	D ^c	43	Explosion accident
3	6	6	55	Small cell lung cancer
4	5	6	64	Operated for colon cancer 5 days prior to trauma. Suspected cerebral metastasis
5	5	4	68	Non-small cell lung cancer, severe heart disease
6	6	6	45	Severe alcohol abuse
7	6	6	60	Alcohol abuse, liver cirrhosis
8	2	D	64	Severe alcohol abuse
9	3	3	62	Large acute subdural hematoma diagnosed 2 days after trauma
10	2	D	64	Acute subdural hematoma evacuated at local hospital before transfer to Uppsala
11	3	D	73	Warfarin, acute subdural hematoma evacuated at local hospital before being transferred to Uppsala
12	5	D	79	Acute subdural hematoma evacuated at local hospital before transfer to Uppsala
13	4	4	75	GCS M 1 and cyanotic when EMT ^a arrived
14	5	6	52	GCS M 1, non-reacting pupils, and systolic BP 90 when EMT ^a arrived
15	6	D	78	Warfarin
16	5	D	79	Chronic kidney disease, diabetes mellitus 2, Alzheimer's dementia, and recent myocardial infarct
17	5	6	72	CoNS ^b meningitis, multiple intracranial surgeries
			(Mean 61)	
1996–1997 ^d				
1	6	D	79	Renal carcinoma, chronic myelogenous leukemia, coagulopathy
2	6	4	57	Myeloma, coagulopathy
3	3	6	60	Mastocytosis, coagulopathy
4	3	4	47	Pneumonia 6 weeks after TBI
5	4	D	22	Septic shock
6	3	D	22	Penetrating heart injury
7	3	D	25	Trunk, spine, and extremity injuries
8	3	D	51	
9	3	D	71	
			(Mean 48)	

^a EMT emergency medical technician

^b CoNS coagulase-negative staphylococci

^c D died before discharge

^d [6]

elderly TBI patients, new approaches need to be developed and effective neuroprotective drugs need to be introduced in order to improve the results further.

Conclusions

A large proportion of favorable outcomes (78 %) was maintained despite that the proportion of patients >60 years old with poorer prognosis was doubled (16 to 30 %), which may

indicate that the quality of NIC rather has increased or at least is unchanged. More active surgery may have contributed to that the large proportion of favorable outcomes was maintained. For further improvements of the results in the future, more knowledge about the optimal TBI management for the elderly is required, as well as an introduction of new approaches and effective neuroprotective drugs.

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Compliance with ethical standards

Conflict of interest None.

Research involving human participants The study was approved by the local ethical review board.

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