

**Outcome**  
**after modern neurosurgical care and formalised rehabilitation following**  
**severe brain injury**

**Ann Sörbo**



UNIVERSITY OF GOTHENBURG

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Institute of Neuroscience and Physiology  
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Outcome after modern neurosurgical care and formalised rehabilitation following severe brain injury

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## **ABSTRACT**

### *Aims:*

The overall aims were to evaluate the results of the treatment concepts for severe brain injury including decompressive craniectomy (DC), early rehabilitation and long-term follow-up, primarily according to the psychosocial consequences of the brain damage and life satisfaction. The first study was a cross-sectional study to assess and compare the consequences for outcome for two groups with severe traumatic brain injury (TBI) or subarachnoid haemorrhage (SAH), one group that received early, long-term formalised rehabilitation and the other that received late or no formalised rehabilitation. The second study was a descriptive, prospective study with follow-up until five years after severe TBI/SAH. The third was a retrospective study of the long-term outcome in patients with malignant middle cerebral artery infarction (MMI) who were treated with DC, while the fourth was a prospective one-year follow-up study of patients with different diagnoses who were treated with DC.

### *Methods:*

The main outcome measures were the structured form for the Swedish Neuro Database, the Glasgow Outcome Scale (GOS), the Extended Glasgow Outcome Scale (GOSE), the Functional Independence Measure (FIM), the Head Injury Evaluation Chart (HIEC), the Community Integration Questionnaire (CIQ), the National Institutes of Health Stroke Scale (NIHSS), the Barthel Index (BI), the short form health survey (SF-36) and the life satisfaction checklist (LiSat-11). Changes over time for the follow-up group and the individuals in the second study, as measured with the GOSE, were analysed using a statistical method that is suitable for small data sets and takes account of the non-metric properties of the data.

### *Results:*

The first study revealed a better outcome for the group that received early formalised specialist rehabilitation and long-term follow-up. No patient remained in a vegetative state in this group as compared with three in the other, 50% were independent as compared with 17% in the other and the frequency of return to work was 55% among the former workers/students as compared to no return to work in the other group.

In the second study, the change over time according to the degree of neurological deficit and day-to-day living abilities (GOSE) was significant at group level until one year after the injury, but important changes were found for some individuals until five years after injury.

In the third retrospective study, the patients who were treated with DC because of MMI remained in an impaired neurological condition. Their life satisfaction was lower as compared with a healthy population, but 83% still rated "life as a whole" as satisfactory.

The fourth study revealed that 20% of the surviving participants had a favourable outcome as measured with the GOSE. Of those who were able to convey their satisfaction with life, 88% reported that life as a whole was satisfactory one year after the injury/onset of disease.

### *Conclusions:*

The studies show that an effective chain of medical and rehabilitation activities can produce a good outcome/living situation and that life can be satisfactory for patients after severe brain injuries in spite of neurological deficits.

*Key words:* outcome, severe brain injury, life satisfaction, early formalised rehabilitation, long-term follow-up, change over time, decompressive craniectomy

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## LIST OF ORIGINAL PAPERS

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This thesis is based on the following four studies, which will be referred to in the text by Roman numerals:

### Paper I

Sörbo A, Rydenhag B, Stibrant Sunnerhagen K, Blomqvist M, Svensson S, Emanuelson I.  
Outcome after severe brain damage, what makes the difference?  
Brain Injury July 2005; 19(7): 493-503.

### Paper II

Sörbo A, Blomqvist M, Emanuelson I, Rydenhag B.  
Psychosocial adjustment and life satisfaction until five years after severe brain damage.  
Int Journal of Rehabilitation Research 2009; 32(2):139-47.

### Paper III

Skoglund T, Eriksson-Ritzén C, Sörbo A, Jensen C, Rydenhag B.  
Health status and life satisfaction after decompressive craniectomy for malignant middle cerebral artery infarction.  
Acta Neurol Scand 2008; 117(5):305-10.

### Paper IV

Sörbo A, Eriksson-Ritzén C, Emanuelson I, Rydenhag B.  
Outcome and life satisfaction one year after decompressive craniectomy.  
Submitted 2010.

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## ABBREVIATIONS

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ADL	Activities of Daily Living
ATLS	Advanced Trauma Life Support Laboratory
BI	Barthel Index
CIQ	Community Integration Questionnaire
CRS	Coma Remission Scale
CRS-R	Coma Recovery Scale - Revised
CT	Computed Tomography
DC	Decompressive Craniectomy
DECIMAL	DEcompressive Craniectomy In MALignant middle cerebral artery infarction
DECRA	DEcompressive CRAniectomy trial
DESTINY	DEcompressive Surgery for the Treatment of malignant INFarction in the middle cerebral artery trial
DI	Diffuse Injury
DOC	Disorders of Consciousness
DSM-IV	Diagnostic and Statistical Manual of mental disorders, fourth edition
FIM	Functional Independence Measure
GCS	Glasgow Coma Scale
GOAT	Galveston Orientation and Amnesia Test
GOS	Glasgow Outcome Scale
GOSE	Glasgow Outcome Scale Extended
HAMLET	The Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial
HIEC	Head Injury Evaluation Chart
HRQL	Health Related Quality of Life
ICD-10	International Classification of Diseases, tenth revision
ICF	International Classification of Functioning
ICH	Intracerebral Haemorrhage
ICIDH	International Classification of Impairments, Disabilities and Handicaps
ICP	Intra Cerebral Pressure
ICU	Intensive Care Unit
LiSat-11	Life Satisfaction Questionnaire (eleven item version)

MCA	Middle Cerebral Artery
MMI	Malignant Media Infarction
MRI	Magnetic Resonance Imaging
mRS	Modified Ranking Scale
NICU	Neuro Intensive Care Unit
NIHSS	National Institutes of Health Stroke Scale
NSE	Neuron Specific Enolase
PTA	Post Traumatic Amnesia
QoL	Quality of Life
RC	Relative Concentration
RCT	Randomised Controlled Trial
RESCUEicp	Randomised Evaluation of Surgery with Craniectomy for Uncontrollable Elevation of intracranial pressure
RLS85	Reaction Level Scale 85
ROC	Relative Operating Characteristic
RP	Relative Proportion
SAH	Subarachnoid Haemorrhage
S-100B	S-100 calcium binding protein B
SF-36	Short-form health survey
SFRM	Svensk Förening för Rehabilitering och Fysikalisk Medicin (Swedish Association for Rehabilitation and Physical Medicine)
s-GFAP	serum Glial Fibrillary Acidic Protein
SU	Sahlgrenska University Hospital
TBI	Traumatic Brain Injury
WFNS	World Federation of Neurological Surgeons scale
WHO	World Health Organisation

## PREFACE

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### **On brain injury, neurosurgery, rehabilitation and gardening**

In my work as a physician in rehabilitation medicine, I meet patients with severe brain injuries in my role as a consultant at the intensive care unit (ICU). I also have the opportunity to follow the struggle of patients and their next of kin during the post-acute phase and, in most cases, during a lengthy rehabilitation phase. In the late 1980s and early 1990s, these patients sometimes had to wait for rehabilitation and were usually followed up for a short period after discharge. I observed that the patients who came to our rehabilitation ward at an early stage appeared to have a better prognosis and a more favourable outcome.

In 1990, I went on a journey, visiting different rehabilitation centres in the USA, which inspired me to start a project together with my team, to organise a structured programme for the early rehabilitation of brain-injured patients in the County of Södra Älvsborg. Two years later, I returned to the USA to visit centres that had specialist programmes for very early rehabilitation. New methods for early rehabilitation were implemented in Borås in 1994-96. Another part of the process of care that had to be further developed and structured was the long-term follow-up. This work was successfully done by my colleagues during the same period.

At a brain injury conference in Denmark in 1996, we met a neurosurgeon from Gothenburg who was interested in evaluating new treatment methods in neurosurgery and was also very interested in what happens to patients after surgery. A very stimulating co-operation was initiated. I was subsequently inspired to start this research and a neurosurgeon thus became my main tutor.

This work has given me the opportunity to evaluate our work at the clinic and to focus on and stress the importance of offering brain-injured victims an effective chain of medical and rehabilitation activities. The subject for this thesis is both neurosurgery and rehabilitation.

*“Brain injury can be a catastrophic event which dramatically changes a person and their family. A host of emotional responses may result. Over time, people often find that they adjust to the changes created by the brain injury. Adjustment doesn't mean that people are happy about changes, rather, it means that they recognize that they cannot be changed, and rather than struggle toward the impossible, begin to set goals and make decisions based on the new self.”*

*Reinforce the behaviors you would like to see increase. Like a garden, “water the behaviors you'd like to grow.”*

*Brain Injury Association of America*

*In conclusion, I would like to point out that I was not able to recover as far as I have without the help of others. BUT, nobody could recover for me! I had to make the effort. “You only get out of a thing, what you put into it.” My parents told me.*

*Craig Brandt, TBI, car accident 1992.*



## INTRODUCTION

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### Definitions

*Measurement* is simply the quantification of an observation against a standard, whereas *assessment* also includes the process of interpreting measurement (Wade 1992). In practice, however, the word “measurement” refers both to the process of discovering the extent of the phenomenon and to the results obtained.

The first thing is to define the purpose of the assessment (discriminative, predictive, or evaluative) and to determine whether the purpose of a study is to evaluate the efficacy or effectiveness of an intervention. The result of a measure can be simply categorisation, or can produce an ordinal, an interval, a ratio scale, quantitative discrete data and quantitative continuous data and this will determine the statistical tests that can be used (Wade 1992; Svensson 2005).

#### *Outcome after brain injury*

Outcome can be defined as “A change to a situation resulting from an action” (WHO 2000). Outcome is a word used for the sequelae, consequences, end point or specific findings that result from the brain injury (Rosenthal 1999).

Outcomes after brain injury are determined by different factors, such as pre-injury personal factors, the extent and nature of the primary brain injury, the subsequently developing manifestations of secondary brain damage, the medical treatment, the rehabilitation interventions and personal and environmental factors.

#### *Rehabilitation*

Nowadays, the word “rehabilitation” is used with many different meanings. It can be derived from *re* and *habilitas* (fitness). Back in 1903, rehabilitation was defined as *giving back to somebody his former rights or position* (Borg et al. 2006) or “reinstatement in dignity” (Bautz-Holter et al. 2007). Olle Höök defined rehabilitation as an umbrella term for the *interventions of medical, psychological, social and vocational character* (Höök 2001).

Rehabilitation is defined by the World Health Organisation (WHO) as follows: *Rehabilitation of people with disabilities is a process aimed at enabling them to reach and maintain their optimal physical, sensory, intellectual, psychological and social functional levels. Rehabilitation provides disabled people with the tools they need to attain independence and self-determination* (WHO 2010).

#### *Rehabilitation medicine*

In Sweden, in 1969, rehabilitation medicine became a speciality called Rehabilitation and Physical Medicine. Since 1992, it has been called Rehabilitation Medicine. It focuses on patients with medical conditions that lead to chronically complex functional disabilities. Different professions work in teams together with the patient to realise defined goals. The goal of rehabilitation is to optimise the conditions for healing the body structures and body function, as well as training the patients to become active members of the community. Rehabilitation medicine may also be defined as the multi- and interdisciplinary management of a person’s functioning and health (Stucki et al. 2002).

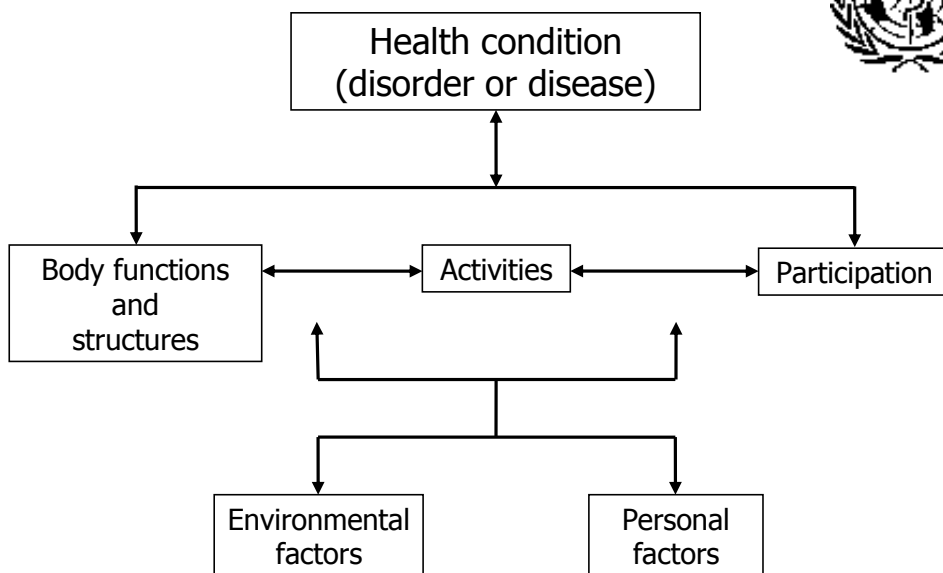
#### *Rehabilitation, ICIDH and ICF*

Back in 1988, Axel and Kerstin Fugl-Meyer presented a paradigm based on a concept of health and the ability to act rather than focusing on disease and disability (Fugl-Meyer and

Fugl-Meyer 1988). They related their paradigm to the WHO's International Classification of Impairment, Disability and Handicap (ICIDH 1980) and suggested that the loss of ability to gratify individual needs designates handicap. Their definition of handicap was therefore not normative (in contrast to the ICDH) but relative, as it was related to the realisable goals of the individual.

The ICIDH labelled limitations at societal level and failed to incorporate environmental and personal factors into the classification. The follow-up, the International Classification of Functioning, Disability and Health, ICF, was published in 2001 (WHO 2001), see Figure 1. Traditional health indicators are based on the mortality rates of populations. The ICF shifts the focus from cause to impact and to "life" and health, i.e. how people live with their health conditions and how they can be improved to achieve a productive, fulfilling life. Instead of terms based on limitations, it denotes ability. Function and disability are viewed as a complex interaction between the health condition of the individual and the contextual factors of the environment, as well as personal factors. The ICF can improve communication between different professions, be used as a "common language" and provide a scientific basis for understanding and studying health and health-related states, outcomes and determinants that are relevant to rehabilitation medicine, see Figure 1.

**Figure 1. Components of the ICF**



#### *Quality of life and life satisfaction*

There are several definitions of quality of life and life satisfaction. Health-related quality of life (HRQL) can be defined as "the value assigned to duration of life as modified by impairments, functional status, perceptions and opportunities influenced by disease, injury, treatment and policy" (Patrick 1993). HRQL encompasses domains related to physical, mental (emotional and cognitive), social and role functioning, as well as an individual's perception of health and well-being. Quality of life (QOL) can be defined as "a personal assessment of the good or satisfactory characteristics of life" (Finch et al. 2002). Dijkers distinguishes between subjective well-being and objective or "outsiders'" assessments of quality of life that utilise externally defined indices of an individual's life situation (Dijkers 2004).

It is beyond the scope of this thesis to further expound on the different definitions of Quality of Life (QoL) and life satisfaction. In this thesis, life satisfaction is defined as the degree to which an individual experiences him/herself as being able to attain his/her goals, a definition found in the work of Fugl-Meyer et al. (Fugl-Meyer and Fugl-Meyer 1988; Fugl-Meyer AR 1992). Based on this consideration, life satisfaction is an indicator of the extent to which individuals have adapted to their new situation in life, as proposed by Roland Melin in his thesis “On life satisfaction and vocational rehabilitation outcome in Sweden” (Melin 2003).

## **Epidemiology**

### *Traumatic brain injury (TBI)*

Head injury is the most common cause of death and severe disability among young people in the United States and Europe (Emanuelson and v Wendt 1997; Andersson et al. 2003). In different studies, the incidence of severe TBI in Sweden varies between 3-12/100,000 per year (Asgeirsson et al. 1994; Kleiven et al. 2003), resulting in between 240 and 960 persons who are affected every year and require extensive resources from the health care system. Males have an overall rate that is around 1.5-2.1 time higher than that of females (Andersson et al. 2003; Kleiven et al. 2003). The external causes are dominated by falls, followed by traffic accidents and persons hit by objects (Andersson et al. 2003). In a study of the annual head injury incidence rate in Sweden from 1987 to 2000, there was a decline in younger ages experiencing a head injury, while the number of head injuries among elderly people increased (Kleiven et al. 2003). Concussion was about three times more frequent than fractures. Haematoma and diffuse or focal contusions had a lower incidence rate than concussion. Concussions and fractures decreased over time. Diffuse or focal injuries showed a steady rate of occurrence over the study interval, while haematoma increased (Kleiven et al. 2003).

### *Non-traumatic subarachnoid haemorrhage (SAH)*

Subarachnoid haemorrhage has the highest incidence between the ages of 40-60 years. The total incidence of SAH in Sweden, including every degree of severity, is approximately 9-15/100,000 per year for men and 11-21/100,000 for women, with the highest incidence in northern Sweden (Ingall et al. 2000). The WHO MONICA project has shown very large variations in attack rates of SAH across 11 populations in Europe and China. The generally accepted view, that women run a higher risk of SAH than men, did not, however, apply to all the populations in the study. Case fatality rates were consistently higher in Eastern than in Western Europe. Despite improvements in surgical, medical and rehabilitation treatment, the morbidity and the number of people severely disabled because of severe brain injury after SAH have been reported to be high (Lambert et al. 2002).

### *Malignant middle cerebral artery infarction (MMI)*

The incidence of first-ever stroke in Sweden is about 200-300/100,000 per year of whom 20% of the victims are < 65 years old. An investigation in Gothenburg showed that, as different from myocardial infarction, stroke incidence and mortality did not change in 1987-2006 (Harmsen et al. 2009). Stroke is the third most common cause of death among all diseases in Sweden. The incidence of large anterior circulation infarct with both cortical and subcortical involvement in Sweden is around 40/100,000 (Johansson et al. 2000). About 10% of all patients with middle cerebral artery (MCA) infarction suffer from clinical deterioration caused by brain swelling, increased intracranial pressure and brain herniation called malignant media infarction (MMI). This is the most common cause of death during the first week after an ischemic stroke.

### *Intracerebral haematoma (ICH)*

ICH accounts for around 10-15% of all strokes. The incidence of intracerebral haemorrhage without relation to trauma, tumour, aneurysm, malformations or dural fistulae in Sweden is around 13-35/100,000 per year. The main cause is hypertension causing small-vessel cerebral disease. The mortality and morbidity are higher compared with occlusive stroke (Mitchell et al. 2007).

## **Classification of severe brain injury in the very early phase**

The classification of severity and the definition of severe brain injury vary in the literature. Traditionally, a scale for measuring changes in consciousness and function is used.

*The Glasgow Coma Scale (GCS)* (Teasdale and Jennett 1974) is a ranking scale that is often used for rating neurosurgical patients in terms of a ranking order of deficit severity in the acute stage. The GCS is based upon eye-opening, verbal response and motor responses and is well known all over the world. Severe brain injury is defined as GCS 3-8.

*The Reaction Level Scale (RLS85)* (Starmark et al. 1988) has been recommended since 1990 and was mainly used in Sweden at the time of our studies. Today, following the introduction of the Advanced Trauma Life Support Laboratory concept (ATLS concept) (Sims 1979) in Sweden, the GCS is again more frequently used. The RLS85 is a single scale with eight steps (1-8) for assessing overall patient responsiveness. It is based on the same concept as the GCS. In a study, Starmark et al. demonstrated that basically the same information as that found in the separate eye, motor and verbal scales of the GCS can be combined directly into the RLS85 and that it has better interobserver agreement and better coverage than the GCS sum score (Starmark et al. 1988). Severe brain injury can be defined as Reaction Level Scale 4-8.

Patients with intracranial aneurysms can also be classified using the *Hunt and Hess classification* (Hunt and Hess 1968) to estimate the surgical risk according to the meningeal inflammatory reaction, the severity of neurological deficit and the presence or absence of significant associated disease, see Table I.

**Table I. The Hunt & Hess score is based on clinical status (I-V)**

---

I = asymptomatic or minimal headache and slight nuchal rigidity
II = moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy
III = drowsiness, confusion, or mild focal deficit
IV = stupor, moderate-to-severe hemiparesis, possibly early decerebrate rigidity and vegetative disturbances
V = deep coma, decerebrate rigidity and moribund appearance

---

Neuroimaging is a complement to the clinical examination. Computed tomography (CT) is still the most frequently used method for the acute examination. Magnetic Resonance Imaging (MRI) is superior in detecting non-haemorrhagic lesions, such as contusions or shearing lesions, but for practical reasons it is more complicated to use in the very acute stage and is therefore still not used for the primary examination.

*Marshall's classification of diffuse injuries* (Marshall 1991) was constructed for diffuse injuries (DI) after traumatic brain injury. The classification is based on information from the initial CT scan, see Table II. A relationship has been found between the different diagnostic categories and mortality rate.

**Table II. Marshall's classification of diffuse injury (I-IV)**

---

I = DI with no visible intracranial pathology
II = DI with cisterns present and a midline shift of 0-5 mm and/or lesion densities present, no high- or mixed-density lesion > 25 cc
III = DI with compressed or absent cisterns, a midline shift of 0-5 mm, no high- or mixed-density lesion > 25 cc
IV = DI with a midline shift of > 5 mm, no high- or mixed-density lesion > 25 cc
SDH = subdural haematoma, SAH = traumatic subarachnoid haemorrhage

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The *Fisher grading scale* (Fisher et al. 1980) is a scale for classifying the severity of injury for patients with non-traumatic SAH which is constructed on the basis of the amount of subarachnoid blood on the CT scan; 1 = none, 2 = diffuse only, 3 = clot or thick layer, 4 = diffuse or none, with cerebral or ventricular blood.

*Post Traumatic Amnesia (PTA)* reflects the time from injury to the return of memory of ongoing events or the time of a return of the ability to lay down continuous memories. A number of different instruments are available. *The Galveston Orientation and Amnesia Test (GOAT)* (Levin et al. 1979) is commonly used. In a study in which three different methods for measuring PTA were tested, Tate et al. found that significant variability occurred in the number of days it took to emerge from PTA according to the scale used (Tate et al. 2000). Severe injury can be classified as PTA 1-7 days and very severe TBI as PTA > 7 days.

## **Classification of severe injury in the post-acute and long-term perspective**

Severity of injury is also commonly classified according to the *duration of impaired consciousness* or *length of coma*. For this estimation, the scales described above (GCS and RLS) can be used. At the time of our first studies, no more specific scales were available for measuring resolution from coma, which was validated for Swedish conditions. We therefore translated the *Coma Remission Scale (CRS)* (Schönle 1995) into Swedish for the first study. This scale was introduced in Germany by a working group for neurological and neurosurgical rehabilitation to monitor cases of protracted coma remission in early rehabilitation. It has been found to have good psychometric properties and is still recommended in Germany.

Nowadays, the *Coma Recovery Scale Revised (CRS-R)* (Giacino et al. 2004) to assess disorders of consciousness (DOC) is the most widespread and frequently used scale. It is good at detecting the Minimally Conscious State. It has recently been translated into Swedish and the Swedish version is in the process of being authorised by the constructor Josef Giacino.

*The National Institutes of Health Stroke Scale (NIHSS)* (Brott et al. 1989) can be used to classify the severity of a stroke. A score of between 15 and 25 indicates severe impairments and >25 indicates very severe neurological impairments.

*The Glasgow Outcome Scale Extended (GOSE)* (Teasdale et al. 1998) will be further described below. It is an eight-grade ordinal scale that is used to measure outcome after brain injury. When results are dichotomised, unfavourable outcome is GOSE 1-4 and favourable outcome is GOSE 5-8.

## Predictors of outcome after severe brain injury

In the early stages after traumatic brain injury, it appears that measuring *depth of coma* (GCS) (Machamer et al. 2003), *length of coma or DOC* (Katz et al. 2009) and *PTA duration* (Sandhaug et al. 2010) does help in predicting the extent of difficulties or outcome. Nowadays, the coma length and depth are more difficult to measure, as the modern acute medical treatment includes sedation and “waking up” the patients for scoring is debatable.

With the passage of time, however, other factors or components, as described in the ICF above, become more important for outcome, as described by Morton and Wehman (Morton and Wehman 1995).

Jeremitsky et al. presented a study of secondary brain injury factors (Jeremitsky et al. 2003). The records of adult blunt trauma patients were retrospectively reviewed, searching for the following 11 secondary brain injury factors in the first 24 hours post-injury: hypotension, hypoxia, hypercapnia, hypocapnia, hypothermia, hyperthermia, metabolic acidosis, seizures, coagulopathy, hyperglycemia and intracranial hypertension. Hypotension and hypothermia were independently related to mortality. As have been found in previous studies, *hypoxia* and *hypoperfusion* in the acute stage were identified as predictors of a poor outcome (Maas et al. 1997) and should be taken into account when grading the severity of the injury.

Wortzel and co-workers recently presented a study (Wortzel et al. 2009) in which they found that the presence of paratonia and primitive reflexes (“frontal release signs”), such as glabellar, snout, suck, grasp and palmomental responses, after TBI predicted performance on bedside cognitive assessments, level of functional independence and duration of acute inpatient rehabilitation.

There are also some interesting studies of *biochemical markers* of brain tissue damage and correlations with outcome after TBI. De Boussard and co-workers found that abnormal S-100 serum concentrations and symptoms or signs of cognitive impairment were not significantly associated in patients with mild TBI and a GCS score of 14 or 15 (de Boussard et al. 2005). Stålnacke et al. concluded, however, that the association between S-100B and disability supported the notion that the long-term consequences of a mild brain injury may be partly a result of brain tissue injury (Stålnacke et al. 2005). Townend and Ingebrigtsen published a review article in which they concluded that patients with high levels of S-100B (>2.5microg/L) at initial assessment may represent a high-risk group for disability after head trauma (Townend and Ingebrigtsen 2006). Olivecrona et al. found that S-100B and neuron specific enolase (NSE) were significantly higher in subjects with GCS 3 and in those who died (GOS 1) compared with those with GCS 4-8 and GOS 2-5. At follow-up at 3 and 12 months after trauma, there were, however, no differences in prognostic values between the markers and there were no clinically significant values of the markers as predictors of clinical outcome (Olivecrona et al. 2009). Nylén et al. studied serum Glial Fibrillary Acidic Protein (s-GFAP) levels in the acute stage after TBI (Nylén et al. 2006) and SAH (Nylén et al. 2007) and found correlations between serum maximum levels and unfavourable outcome as measured with the GOS and GOSE respectively.

Rivero-Arias et al. found that *CT Fisher grading*, *the World Federation of Neurological Surgeons (WFNS) scale grade*, *aneurysm location* and *time from SAH to intervention* were statistically significant baseline predictors of delayed ischaemic deficit and poorer outcome after SAH (Rivero-Arias et al. 2009). Lindvall et al. concluded that, despite the correlation to outcome, both Hunt and Hess and the Fisher grading scale had a limited predictive value of outcome due to low specificity and/or sensitivity (Lindvall et al. 2009). Güresir et al. found that the *presence of an ICH* is a predictor for unfavourable outcome. To achieve a favourable outcome, ultra-early treatment with haematoma evacuation and aneurysm obliteration appears to be mandatory (Guresir et al. 2008).

In the case of MMI, Oppenheim et al. (Oppenheim et al. 2000) and the DEcompressive Craniectomy In MALignant middle cerebral artery infarction (DECIMAL) study (Vahedi et al. 2007) demonstrated that an *infarct volume of*  $>145\text{cm}^3$  on diffusion MRI was required to develop a malignant infarction. Young *age* and *early surgery* appear to be predictors of a better outcome for patients with MMI undergoing DC (Kakar et al. 2009). Chen et al. found that surgery within 24 hours and an age of  $< 60$  years were prognostic factors associated with a good outcome (Chen et al. 2007). *Early stroke severity* (the day-5 NIHSS scores) and *infarct volume measures* have been found to predict an excellent outcome at 3-months (Johnston et al. 2009).

For ICH, the *state of consciousness at presentation*, *preictal status in relation to ADL and age* appear to be relevant factors in determining the prognosis according to mortality at the 6-month follow-up (Garibi et al. 2002). The *volume of the haematoma*, its deep location, surgical treatment and the preictal status in relation to activities of daily living (ADL) were independent factors for patient outcome measured with the modified Ranking Scale (mRS) (Garibi et al. 2002). Garibi et al. also observed that age, GCS at admission and the volume of the haematoma were the main factors influencing the neurosurgeon's decision regarding surgical treatment.

A study by Alexander et al. of *genetic factors* and TBI revealed that those individuals with the apolipoprotein E 4 allele had a slower recovery rate (Alexander et al. 2007). Olivecrona et al. found that the presence of the apolipoprotein E epsilon4 allele was not associated with long-term clinical outcome (Olivecrona et al. 2009). In the future, genetic studies may have some useful implications, including the identification of genetic markers for the determination of specific molecular profiles in individuals and assessments of phenotype risk as proposed by Dardiotis in a recently published review article (Dardiotis et al. 2010).

As Kakar et al. state, it is important to recognise that poor neurological status alone on presentation does not necessarily equate with irreversible cerebral injury and a poor outcome for an individual (Kakar et al. 2009).

## **Medical treatment at the Neuro Intensive Care Unit (NICU)**

The maintenance of adequate cerebral blood flow is necessary to avoid secondary injuries to the brain. Pathological processes involving the blood-brain barrier, endothelial factors and catecholamines influence the microcirculation. Cerebral oedema and impaired autoregulation can result in the disruption of normal self-stabilising feedback mechanisms for maintaining cellular homeostasis. A vicious circle of raised ICP, reduced cerebral blood flow, ionic dysfunction, impaired substrate delivery, energy failure and progress of the oedema can cause secondary damage to the brain. Accepted treatment procedures include head elevation to around  $30^\circ$ , CSF drainage by venticulostomy, osmotic diuretics and, in severe cases, treatment with barbiturates. Another important part of the treatment is the use of enteral nutrition and the avoidance of overnutrition.

There are standardised protocol-driven therapies, but they vary across different centres.

### *TBI*

The Lund Concept for the treatment of severe brain trauma was introduced at the NICU in Lund in the early 1990s (Asgeirsson et al. 1994) and shortly thereafter in Gothenburg. The Lund therapy considers the consequences of a disrupted blood-brain barrier for the development of brain oedema and the specific consequences of a rigid dura/cranium for general cerebral haemodynamics. It is mainly based on hypotheses originating from basic physiological principles relating to brain volume and cerebral perfusion regulation (Grände et al. 2002). The main goals are a) to reduce or prevent an increase in intracerebral pressure (ICP) and b) to improve perfusion and oxygenation in the pericontusional areas, which is achieved by normal blood oxygenation and by maintaining normovolemia with normal haematocrit and plasma protein concentrations (Grände 2006).

Sedation is included in the protocol. Barbiturates reduce ICP by metabolically induced vasoconstriction and also have a sedative effect. High-dose therapy has side-effects such as electrolyte, renal and cardiovascular complications, pulmonary complications and fever.

P O Grände thus recommends lower doses for a limited period of time (Grände 2006).

The Lund concept can be applied to all patients with severe traumatic brain injuries and should be applied at an early stage to antagonise increases in ICP and secondary injuries. Outcome studies have indicated favourable results (Naredi et al. 1998; Eker et al. 2000; Wahlström et al. 2005).

### *SAH*

Subarachnoid haemorrhage is a serious condition that can be complicated by the pronounced activation of the sympathetic nervous system and systemic reactions such as cardiac arrhythmias, myocardial infarction, pulmonary oedema and cerebral vasospasm. The emergency treatment of SAH focuses on preventing re-bleeding, as well as the treatment of brain swelling, hydrocephalus, vasospasm and stress reactions (Naredi et al. 2000; Stern et al. 2006). Vasospasm and bleeding can cause secondary infarcts with brain oedema. In the period following embolisation or surgery, advanced monitoring techniques such as continuous electroencephalography, brain tissue oxygen monitoring and microdialysis can detect harmful secondary insults (Komotar et al. 2009).

### *MMI*

There have been advances in the early treatment of stroke, with thrombolytic agents and thrombectomy that can limit the ischemic injury (Alberts 2001).

Despite optimal medical therapy, with the administration of mannitol, barbiturates and intensive care with mild hyperventilation, about 10% of all patients with middle cerebral artery infarction still develop life-threatening malignant media infarctions with brain swelling and the risk of transtentorial herniation (Silver et al. 1984; Schwab et al. 1998). For selected patients nowadays, the next step is surgery, treatment with decompressive craniectomy (DC).

### *ICH*

The emergency treatment of ICH focuses on preventing re-bleeding, the treatment of brain swelling and reducing or preventing an increase in intracerebral pressure (ICP) and hydrocephalus via cerebrospinal fluid drainage by the venticulostomy. The medical treatment regimen follows the principles described above. If lowering the blood pressure, the risk of secondary ischemic infarcts due to overly aggressive blood pressure reductions must be taken into account.



## Surgical treatment

For TBI with epidural, subdural or contusion bleeds, the surgical evacuation of the haematomas may be necessary.

For non-traumatic SAH, the primary treatment is either coiling or clipping to prevent re-bleeding and, in some cases, the evacuation of the haematoma. Malformations can be treated with stereotactic radiosurgery or endovascular embolisation, while haemangioblastomas are usually treated by surgical removal. Moreover, haematomas caused by a SAH or an ICH may call for evacuation.

Further steps in the treatment, if the ICP cannot be kept below 20mmHg, are drainage of cerebral fluid from the ventriculostomy and if the ICP levels are still unacceptable, decompressive craniectomy.



### *Decompressive craniectomy*

Decompressive craniectomy (DC) is not a new therapy. It was described by Kocher in 1901 (Kocher 1901) and subsequently by Harvey Cushing who, in 1905, described the method to relieve intracranial pressure (Cushing 1905). Initially, it was used in the management of inoperable brain tumours, but Cushing went further, using it in the treatment of post-traumatic oedema and vascular malformations. For large hemispheric infarction, it was first reported in case reports from 1956 (Scarcella 1956; Gupta et al. 2004).

The treatment is designed to achieve satisfactory cranial volume expansion. There are different techniques, but DC can be defined as the removal of a large area of skull to increase the potential volume of the cranial cavity. There can be a unilateral or bilateral and temporo-parieto occipital, frontal or occipital decompression, with or without dural opening and with or without the evacuation of parts of the damaged brain. Typically, the dura is opened and enlarged by a duraplasty using pericost or a dura substitute. The reduction of ICP after DC was statistically significant in a study by Olivecrona et al. (Olivecrona et al. 2007).

The indications and timing of the surgery are still discussed in the literature and vary across centres in Sweden and throughout the world. Age is one of the factors to take into account, when making the decision to perform a DC. There is some agreement that the prognosis is better at a younger age (Munch et al. 2000; Gupta et al. 2004; Malm et al. 2006; Chen et al. 2007) and that early DC, within 24 hours (Schwab et al. 1998) or within 48 hours after onset (Schirmer et al. 2007; Vahedi et al. 2007), is better than late.

There is still a lack of data from randomised, controlled studies of the benefits of DC for TBI patients. There are currently two ongoing studies of DC and TBI, RESCUEicp (United Kingdom) (Hutchinson et al. 2006) and the Decompressive Craniectomy trial DECRA (Australia). No results are available at this time, see Table III.

Recently, the results of a pooled analysis of three European randomised trials (Vahedi et al. 2007), DECIMAL (Vahedi et al. 2007), DESTINY (Juttler et al. 2007) and HAMLET (Hofmeijer et al. 2009), examining early decompressive large hemicraniectomy in patients with MMI, revealed that surgery was beneficial in all predefined subgroups as measured by the modified Ranking Scale (mRS) at 12 months. Vahedi et al. found that, in patients with MMI, decompressive surgery undertaken within 48 h after stroke onset reduced mortality and increased the number of patients with a favourable functional outcome as measured by the mRS (75% favourable outcomes versus 24% for conservatively treated patients) (Vahedi et al. 2007). The decision to perform decompressive surgery should, however, be made on an individual basis in every patient and should be fully discussed with the relatives, as has also been pointed out by others. Both DECIMAL and DESTINY interrupted the recruitment process because of slow enrolment, the opportunity for pooled analysis and interim analysis at 30 days suggesting that DC reduced mortality (Kakar et al. 2009), see Table III.

From the study of SAH published in 2007 by Schirmer et al., the authors conclude that DC is a useful adjunct modality for the management of refractory intracranial hypertension in patients with high-grade SAH, even in the absence of large intraparenchymal haemorrhages (Schirmer et al. 2007). The long-term outcome was better in patients who underwent early (within 48 hours) intervention. However, in a review article published in 2008, they point out that there are still insufficient data to support the routine use of DC in TBI, stroke or SAH (Schirmer et al. 2008). Decompressive craniectomy can also be the treatment of choice if there are huge secondary ischemic lesions because of vasospasm in non-traumatic SAH patients. The timing of surgery in these cases is not related to the onset of the SAH but to the time of the infarction and oedema.

In a comparison of outcome between different diagnoses which was made by Kim et al., DC with dural expansion was found to be more effective in patients with ICH or TBI than in the MMI group, according to mortality and Glasgow Outcome Scale (GOS) scores (Kim et al. 2009).

Decompressive craniectomy has created ethical dilemmas because of the large number of disabled survivors. Recently, in their review article from April 2009, Kakar et al. summarised the recent evidence base for DC for the most common indications; TBI and MMI (Kakar et al. 2009).

Despite some concerns, class 1 evidence and high-quality, non-randomised evidence suggest improved outcomes in young patients undergoing DC for MMI, including left-hemispheric infarcts.

Class 1 data are awaited for TBI, but it is increasingly clear that DC, combined with modern neurointensive care, offers the potential to save life with acceptable functional outcome (Kakar et al. 2009). As Kakar et al. and others conclude, the decision to perform DC for intractable intracranial hypertension, irrespective of diagnosis, still needs to be individualised.

**Table III. Summary of randomised studies for decompressive craniectomy in traumatic brain injury and malignant infarction of the middle cerebral artery**

<i>Study</i>	<i>Diagnosis</i>	<i>Design/comparison</i>	<i>Age</i>	<i>n</i>	<i>Conclusions</i>
<b>RESQUEicp</b>	TBI	Multicentre Prospective Randomised DC vs barbiturate coma	10-65	est 600	Results are awaited
<b>DECRA</b>	TBI	Multicentre Prospective Randomised DC vs medical treatment	15-60	est 250	Results are awaited
<b>Taylor et al.<sup>x</sup></b>	TBI	Single centre Prospective DC vs medical treatment	Children > 4 years	27 (13 surg +14 contr)	Reduced mortality Moderate improvement in ICP and outcome Not statistically significant
<b>DECIMAL</b>	MMI	Multicentre Randomised, controlled Sequential, single-blind DC vs medical treatment	18-55	38	Recruitment stopped due to slow enrolment and significant difference in mortality rate in favour for surgery
<b>DESTINY</b>	MMI	Multicentre Prospective, sequential Randomised, controlled	18-60	32	Recruitment stopped due to significant benefit of surgery
<b>HAMLET</b>	MMI	Multicentre Prospective Randomised, controlled	18-60	64	Reduced case fatality Reduced poor outcome
<b>Pooled analysis</b>	MMI	Multicentre Randomised, controlled  Pre-planned pooled data from DECIMAL, DESTINY and HAMLET	18-60	93 51 surg+ 42 med	“Good outcome” = mRS≤4 75% in surgical group vs 24% in med (medically treated group) Mortality 22% in surgical group versus 71% in medically treated group

est=estimated <sup>x</sup>(Taylor et al. 2001) surg=surgery contr=controls MMI=malignant media infarction  
TBI=traumatic brain injury

*Complications of DC – “the syndrome of the trephined” or “the sinking flap syndrome”*

Complications that can occur are subdural hygroma formation, osteomyelitis, bone flap resorption and wound infections. “The syndrome of the trephined”, also known as “the sinking flap syndrome”, can be defined as a secondary neurological deterioration in the presence of a sinking skin flap (Schorl 2009). It can produce symptoms such as motor disturbances, headaches, seizures, irritability, cognitive and psychiatric symptoms (Stiver 2009). Cerebral perfusion is reported to be disturbed (Sakamoto et al. 2006; Schorl 2009). The frequency of the sinking flap syndrome after MMI was recently calculated by Sarov et al. as a quarter, including asymptomatic cases (Sarov et al. 2010).

### *Cranioplasty*

The requirement for a cranioplasty needs to be considered at the time of the initial decision to perform DC, as mentioned by Kakar et al. (Kakar et al. 2009). The use of an autologous bone flap is a common method of cranioplasty. The bone flap can be preserved in a deep freezer (around -80°C is recommended) or in the abdomen, thigh or scalp. A review article of 449 cranioplasty procedures reported that bone grafts and polymethylmethacrylate remain the best materials for reconstruction (Moreira-Gonzalez et al. 2003). Little guidance exists on the practical issues of bone flap storage, such as the maximum time and place of storage.

Sakamoto et al. (Sakamoto et al. 2006) reported that CT perfusion imaging suggests improved cerebral perfusion after cranioplasty and Winkler et al. reported that cranioplasty appears to affect postural blood flow regulation, cerebrovascular reserve capacity and cerebral glucose metabolism markedly (Winkler et al. 2000).

The best time for cranioplasty is not well known. Kakar et al. recommend early cranioplasty (weeks rather than months) when ICP control permits but comment that active systemic infection and multiple cranial procedures increase the risk of infection from overly early cranioplasty (Kakar et al. 2009). Sarov et al. suggested that it may be justifiable to replace the bone defect during the first two to three months post stroke (Sarov et al. 2010). Early cranioplasty is preferred to restore cranial integrity and protect from trauma. Several authors have reported neurological improvement after cranioplasty (Dujovny et al. 1997; Dujovny et al. 1999; Gottlob et al. 2002; Liang et al. 2007; Stiver et al. 2008). It may speed up rehabilitation (Kakar et al. 2009) and is important for cosmetic and psychological reasons.

## **Rehabilitation**

### *Rehabilitation after severe brain injury*

The methods for rehabilitating patients with severe brain injuries have primarily been developed during the last 15-20 years in Europe and the USA. In Israel, a “coma centre” was set up back in the 1970s for war victims (Loewenstein 2007). In Denmark, there is a law that guarantees that all persons with severe brain injuries receive rehabilitation in the early phase. In Norway, there is currently an ongoing debate about how to organise the health care system on a national basis for this group. The availability of rehabilitation still differs for patients living in different parts of Sweden.

### *Early rehabilitation after severe TBI*

Early rehabilitation interventions after severe brain injury include assessment and treatment to improve a patient’s level of function and to prevent secondary complications (Mackay et al. 1992; Mazaux and Richer 1998). For the appropriate patients, it should include physical and occupational therapy and speech/language pathology on the intensive care ward. The interventions must be extremely sensitive to the patient’s medical status and needs at the time. Support for the family is part of the programme. The patients are mobilised to sitting and standing positions as soon as possible, even if they still need respiratory assistance. Preventing complications such as infections and contractures is essential. The treatment of spasticity with splints, casting and botulinum toxin may be necessary. Sensory stimulation is part of the programme. When early rehabilitation treatment is initiated, only a few of the patients fulfil the criteria for coma, but they are usually in a vegetative state or minimally conscious state (Giacino 1997; Giacino 2004).

There are still only a few studies of “early rehabilitation” for persons with severe traumatic brain injury that support early intervention. Back in 1982, Cope and Hall suggested that patients who were offered rehabilitation at an early stage (within 35 days post injury) do

better (Cope and Hall 1982). Mackay et al. presented a study in 1992, in which 38 patients with severe head injuries received treatment at the same rehabilitation facility, where the 17 who received acute services with formalised early intervention had shorter durations of coma and rehabilitation stays compared with the patients in the non-formalised programme (Mackay et al. 1992). Mean cognitive levels at discharge were significantly higher for the patients in the formalised programme and they facilitated a significantly higher percentage of discharges to home. In a summary report from 1999, Chesnut et al. concluded that there was not enough scientific evidence for early rehabilitation to issue international guidelines or standards (Chesnut et al. 1999) and more recent studies have not produced the final answer. Eilander and colleagues have evaluated a programme of early intensive rehabilitation for children and young adults in a prolonged unconscious state and almost two-thirds of the patients regained full consciousness (Eilander et al. 2005). Khan et al. presented a retrospective comparison of performance before and after introduction of an integrated TBI programme in a level 1 trauma centre. Length of stay was reduced from 30 days to 12.5 days (Khan et al. 2002). Engberg et al. presented results after centralised subacute rehabilitation versus decentralised rehabilitation. GOS score at discharge was significantly better for the group that had received centralised rehabilitation (Engberg et al. 2006). In a study made by Lynne Turner-Stokes, a synthesis of best evidence compiled from a Cochrane Review of randomized, controlled trials was compared with literature assembled for the UK National Service Framework for long-term neurological conditions, using a new typology based on evaluations of research quality irrespective of study design (Turner-Stokes 2008). The studies included in the Cochrane Review failed to address the impact of early rehabilitation, but the non-trial-based studies provided strong evidence.

#### *Early rehabilitation after stroke*

I have not found any specific studies of early rehabilitation programmes for MMI, severe SAH or ICH, but, for stroke in general, there is some evidence that early rehabilitation is beneficial and there is strong evidence to suggest that treatment at stroke units is superior to treatment at other, non-specialist units (Socialstyrelsen 2009). Stroke units have reduced mortality (case fatality), reduced functional dependence and reduced the risk of dying or living in an institution. Salter et al. conclude that patients admitted to stroke rehabilitation within 30 days experienced greater functional gains and shorter length of stays than those whose admission to rehabilitation was delayed beyond 30 days (Salter et al. 2006). Rehabilitation commencement time and intensity, after adjusting for admission functional status and severity of stroke, remained important predictors of stroke outcomes in a study from Taiwan (Ming-Hsia et al. 2010). Musicco et al. found that patients who initiated the rehabilitative procedures “early” (within 7 days) had better long-term outcomes compared with those who initiated the rehabilitation after more than 1 month (Musicco et al. 2003). Powell et al. highlight the need for structured support and treatment after surgery for SAH to reduce persisting mood disturbance and increase independence and participation (Powell et al. 2002).

#### *Rehabilitation after decompressive craniectomy*

Akins and Guppy point out that the neuro-intensive care team should be prepared to diagnose and treat a spectrum of decompressive craniectomy complications (Akins and Guppy 2008). This is also the case for the rehabilitation team. DC patients can be mobile after a very short time but suffer from motor disturbances, severe cognitive deficits, anosognosia and epileptic seizures. Assuring security and protecting the “unprotected” brain from further injuries is a challenge.

### *Formalised rehabilitation – an effective chain of medical and rehabilitation activities*

Since 1996, a well-integrated process of care for adult patients with severe brain damage has existed in western Sweden. There is close co-operation between the neurosurgical clinic and the rehabilitation clinic. The brain injury team offers early rehabilitation at the local intensive care unit or acute wards. The intervention starts as soon as possible after the intracerebral pressure has stabilised. If the patient cannot be transferred directly from the NICU to the rehabilitation ward, the members of the brain injury team work as consultants at the ICU or on the emergency wards at the local hospital. The programme is influenced by the concept presented by Mackay et al. at the Saint Francis Hospital and Medical Center, Hartford, CT, USA, which includes very early rehabilitation and an interdisciplinary approach to the individual with a brain injury (Mackay et al. 1992). The specific programme protocols that are used have direct intervention guidelines following the format of the Rancho Los Amigos Levels of Cognitive Functioning Scale (Hagen et al. 1972). The programme is also influenced by the rehabilitation programme for very severely brain-injured patients at Therapiezentrum Burgau, Bavaria, Germany (Burgau). The brain-injury rehabilitation team is trained to offer rehabilitation activities every day. The programme is goal oriented and holistic. Short-term goals are formulated and revised every week. A successful therapeutic intervention requires close collaboration between patient, relatives and team. The teams typically include rehabilitation nurses and nurse assistants, physical and occupational therapists, speech-language pathologists, almoners, neuro-psychologists and physicians. Timing for the choice of the different therapies is essential. The goal is that all patients with severe brain injuries living in the County of Southern Älvsborg should receive at least three to four weeks' early assessment and treatment at the specialist unit. In the long term, it requires the patient to participate actively in the process of understanding the complexity of his/her neuropsychological deficits and his/her personal reactions to those deficits. Relatives or significant others are actively involved in the rehabilitation activities. Group treatment is also part of the programme on the rehabilitation ward. After a period of in-patient rehabilitation, the patients are usually transferred to an out-patient day programme. Some patients with severe injuries are also offered follow-up from an Outreach Brain Injury Rehabilitation Programme, including contact approximately once a month for one to four years after discharge. Others have their follow-up from a specialist team that is organised by the Adult Habilitation Services.

## **Adaptation after severe brain injury**

### *Adaptation and rehabilitation in the long-term perspective*

One of the main goals of rehabilitation is to support the persons during the adaptation process, which normally takes years. There are several studies of rehabilitation and long-term follow-up and the possibility of improvement during a period of many years for persons with severe brain injuries. In 1999, Willer and co-workers presented a control study of individuals with severe TBI who received residential-based, post-acute rehabilitation. The group who received residential-based, post-acute rehabilitation displayed a statistically significant increase in functional abilities when compared with a group who received support from a traditional (home-based) service group. They showed a significantly greater improvement in motor skills and cognitive abilities (Willer et al. 1999).

Tomberg et al. from Estonia conducted two studies of adaptation, one on SAH (Tomberg et al. 2001) and the second on TBI (Tomberg et al. 2005). One of the aims of the study of SAH was to investigate the psychological coping strategies and their adaptive role for these patients. They found that SAH patients used social/emotional support strategies (getting

sympathy or emotional support from somebody) less than control persons and that they showed a tendency to use acceptance-oriented strategies (accepting the fact that the stressful event has happened and is real) instead. Task-oriented coping styles (planning, active coping, suppression of competing activities, positive re-interpretation and growth and humour) were less frequently used by patients with a severe initial state, who had more marked late disability and dependence in daily living (Tomberg et al. 2001).

In the study of TBI, the participants reported using task-oriented and social/emotional coping strategies less often and avoidance-oriented strategies (behavioural and mental disengagement, denial, restraint coping, avoidance) more often than the control persons. The social support network, satisfaction with it and optimism and life orientation were lower for the TBI group. The authors point to the importance of a social network. To achieve effective rehabilitation and to enhance patients' well-being, it is important to improve the quality of coping and the amount of social support, as well as supporting patients' adequate coping efforts to promote an active lifestyle (Tomberg et al. 2005).

No specific studies of adaptation after malignant media infarction or decompressive craniectomy were found.

## **Outcome**

### *Outcome measurement in rehabilitation medicine*

All outcome measurements selected for research or clinical practice in general should have sound psychometric properties. The important psychometric properties are reliability, validity, sensitivity and responsiveness. The evaluation can be made by the team as a consensus using team measures, or by individual team members, using a profession-specific measure. For measurements of interventions, a measurement should be sensitive to important clinical changes. Clinimetrics (the study of rating scales and indices for the description of clinical phenomena) in rehabilitation medicine has progressed considerably (Dekker et al. 2005). Despite this progress, however, several issues remain. The ICF provides the conceptual basis for measurement and policy formulations for disability and health assessment. While rehabilitation medicine has attained a consensus in its approach to the measurement of activities, i.e. Activities of Daily Living, there has not been a similar development in the methods for measuring participation and environmental factors. Fuhrer states that evaluations of the outcomes of rehabilitation medicine are incomplete if they ignore the subjective well-being of the individual (Fuhrer 1994). He emphasises individually held expectations rather than externally defined criteria.

The time of the assessment is also crucial. In a study of children and adolescents to investigate outcome 10 years after severe or moderate TBI, Horneman and Emanuelson conclude that severity of injury is also an important factor for outcome 10 years after the injury. The study group obtained poorer results in most of the neuropsychological tests compared with healthy controls, even if the severely injured group showed a substantial recovery. Assessments of final outcome for children and adolescents should not be made before the subjects reach adulthood (Horneman and Emanuelson 2009).

### *Outcome in different studies*

A very commonly used measurement in outcome studies is the Glasgow Outcome Scale (GOS), which will be described below. Return to work is another commonly used outcome variable. Table IV gives an overview of some results of psychosocial variables from different TBI and SAH studies over the years. Many outcome studies do not present separate results for moderately and severely brain-injured patients. See Table IV.

**Table IV. Psychosocial outcome from different TBI and SAH studies**

<i>Author (et al.)</i>	<i>Year</i>	<i>Injury severity</i>	<i>Time of assessment</i>	<i>Outcome type</i>	<i>%</i>
Tyerman A <sup>a</sup>	1984	Severe TBI	7 months (2-15)	Depression	60
Naredi S <sup>b</sup>	1998	Severe TBI/SAH	12 months (5-28)	GOS	GR+MD: 71
Annoni JM <sup>c</sup>	1992	Severe TBI	3 years	Work	45
Mackay LE <sup>d</sup>	1992	Severe TBI	At discharge	Discharged home	94
Olver JH <sup>e</sup>	1996	Moderate-severe TBI	2 and 5 years	Work Depression Anxiety	57 and 40 resp 54 and 56 resp 51 and 53 resp
Dombovy M <sup>f</sup>	1998	Severe SAH	28 months (8-65)	Work full time Drive	0 41
Marquardt G <sup>g</sup>	2000	PMSAH	23 months (5-41)	Work	41
Kersel DA <sup>h</sup>	2001	Severe TBI	12 months	Work Depression Leisure activities Divorced	30 49 44 38
Pössl J <sup>i</sup>	2001	Severe TBI	7-8 years	Work at pre-morbid level or reduced	53
Lipper-Grüner M <sup>j</sup>	2002	Severe TBI	1 year	Work	46
Harradine PG <sup>k</sup>	2004	Severe TBI	18 months	Work/study	44
Engberg AW <sup>l</sup>	2004	Moderate+Severe TBI	5,10 and 15 years	Work/study full time or limited	66/51/62 resp
Morris PG <sup>m</sup>	2004	SAH	16 months (14-23)	Depression Anxiety	20 40
Livingston DH <sup>n</sup>	2009	Moderate+Severe TBI	3.3 years	Work	49
Jacobsson LJ <sup>o</sup>	2009	Severe TBI	10 years (6-15)	Work GOS	53 GR+MD: 53
Andelic N <sup>p</sup>	2009	Moderate+Severe TBI	10 years	Work Depression GOSE	58 29 GR+MD: 92

<sup>a</sup>(Tyerman and Humphrey 1984) <sup>b</sup>(Naredi et al. 1998) <sup>c</sup>(Annoni et al. 1992) <sup>d</sup>(Mackay et al. 1992)

<sup>e</sup>(Olver et al. 1996) <sup>f</sup>(Dombovy et al. 1998) <sup>g</sup>(Marquardt et al. 2000) <sup>h</sup>(Kersel et al. 2001)

<sup>i</sup>(Pössl et al. 2001) <sup>j</sup>(Lipper-Grüner et al. 2002) <sup>k</sup>(Harradine et al. 2004) <sup>l</sup>(Engberg and Teasdale 2004)

<sup>m</sup>(Morris et al. 2004) <sup>n</sup>(Livingston et al. 2009) <sup>o</sup>(Jacobsson et al. 2009) <sup>p</sup>(Andelic et al. 2009)

Glasgow Outcome Scale (GOS): MD = moderate disability, GR = good recovery

GOSE= Glasgow Outcome Scale Extended TBI=traumatic brain injury SAH=subarachnoid haemorrhage

PMSAH=perimesencephalic subarachnoid haemorrhage



## Initiation of the studies

For many years (i.e. decades), patients with severe brain damage have been given high priority for rehabilitation at the rehabilitation clinic in Borås. The subjective opinion was that people with severe brain damage can also lead a good life in the long term. In 1996, however, there were just a few studies describing the recovery process and long-term consequences and very few studies of the patient's satisfaction with life after severe TBI and SAH. Recently, a new concept for treating patients with severe brain injuries at the NICU in Gothenburg had been introduced. There was an interest in studying outcome for these patients in the long-term perspective.

In a project designed to establish a well-integrated chain of care for patients with severe brain damage in western Sweden (Sörbo and Rydenhag 2001), and in the early phase of the long-term follow-up, we noted the presence of regional variations in the rehabilitation programmes that were offered to patients with severe TBI and SAH. This initiated Studies I and II.

Remaining questions regarding the use of hemicraniectomy for cerebral hemispheric infarction that involved patient selection, timing of surgery, use for dominant-sided strokes and efficacy at restoring function and quality of life, irrespective of diagnosis, inspired us to start Studies III and IV.

## AIMS

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The overall aim was to evaluate new treatment concepts and describe outcome for patients with severe TBI, SAH, MMI and ICH, with the emphasis on early rehabilitation, decompressive craniectomy and long-term follow-up, mainly according to the psychosocial consequences of the brain damage.

The specific aims were:

- Paper I To assess and compare the consequences for outcome after severe TBI/SAH, mainly according to the components of activity and participation, for two groups, one that received early formalised rehabilitation and long-term follow-up compared with one that received late or no formalised rehabilitation
- Paper II To assess the long-term consequences of severe TBI/SAH up to five years and to determine whether and/or when psychosocial outcome according to activity, participation and life satisfaction is stable over time
- Paper III Retrospectively to investigate the long-term outcome for patients with malignant middle cerebral artery infarction who were treated with decompressive craniectomy
- Paper IV Prospectively to study the long-term outcome after severe brain injury for a single-centre population, with the diagnoses of TBI, SAH, MMI and ICH, that had been treated with decompressive craniectomy

## METHODS

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### Design

- Paper I The first study was a cross-sectional, descriptive study. Early formalised rehabilitation was defined as formalised interventions by a specialised brain-injury rehabilitation team within 50 days after the injury, while the others were late or no rehabilitation. Data were collected from medical records to include the group with late or no rehabilitation. The patients were assessed using standardised outcome measurements at a mean of 26.6 months (SD 4.2, median 25, range 14-41) post TBI/SAH during the period September to October 2000.
- Paper II The second study was a single-centre, descriptive, prospective study. The participants were included consecutively at the NICU and assessed at six months, one, two, three, four and five years after the TBI/SAH. The assessment procedure took place between November 1997 and March 2004 using standardised outcome measurements.
- Paper III The third study was a retrospective study. By using search routines in the computerised system, the patients could be identified. The patients had been treated with DC between 1998 and 2004. The follow-up time was at a mean of 2.9 years (range 1-6) after the insult. The assessments were made between April and June 2005 with commonly used measurements.
- Paper IV The fourth study was a prospective, single-centre study. The participants were included consecutively at the NICU and assessed one year after the injury/insult. The assessment procedure took place between March 2004 and September 2007.

### Outcome measures – instruments in these papers

#### Paper I

*The Functional Independence Measure (FIM)* (Hamilton et al. 1987) was developed by a joint task force of the American Congress of Rehabilitation Medicine to establish a uniform standard for the assessment of functional status during medical rehabilitation at admission and just before discharge, for different diagnoses. It has been used in many countries and has been used for many years in Sweden for comparisons of different rehabilitation centres (Grimby et al. 1996). The FIM is an ordinal scale and assesses self-care, sphincter management, transfer, locomotion, communication, social interaction and cognition in 18 items and is defined as dealing primarily with activity (in the ICF), even if some items also deal with body function.

#### Papers I, II and IV

*The former non-web-based structured form for the Swedish Neuro Database* was used mainly for questions about pre-injury factors, living situation and dependence. The version used in these studies dealt with activity, environmental factors and personal factors according to the ICF.

Papers I, II, III and IV

*The Glasgow Outcome Scale (GOS)* (Jennet 1975) was constructed in the UK in 1975 to present the “degree of neurological deficits and day-to-day living abilities” after severe brain damage. It is an ordinal scale and has been used widely all over the world.

*The Glasgow Outcome Scale Extended (GOSE)* (Teasdale et al. 1998) is a further developed version of the GOS. The extended version was of interest, as the upper three criteria are subdivided with good inter-rater reliability. To my knowledge, there is still no validated Swedish version. For this reason, we used the structured interviews by Wilson et al. (Wilson et al. 1998).

The GOS and the GOSE cover the components of body functions, activity and aspects of participation, as classified by the ICF.

**Table V. Instruments and time of the assessments in Paper II**

Document/ Instrument	Pre- hosp	Acute record B/S/A/SU	NICU SU	ICU Borås	Acute ward B/S/A/SU	Rehab admis- sion	Rehab dis- charge	3 months	6 months	1 year	2,3,4 years	5 years
Acute rec case sheet		x		x	x							
NICU case sheet			x									
Rehab case sheet				x		x	x	x	x	x	x	x
RLS85	x	x	x	x	x	x	x					
GCS	x	x										
FIM						x	x	x	x	x	x	x
HIEC						x		x	x-	x-	x-	x-
GOS									x	x	x	x
GOSE									x	x	x	x
CIQ	x								x	x	x-	x
LiSat-11										x	x	x

B=Borås Hospital  
S=Skene Hospital  
A=Alingsås Hospital  
SU=Sahlgrenska University Hospital

NICU=Neuro Intensive Care Unit  
ICU=Intensive Care Unit

Rec=Record  
x-=Parts of the instrument

For the instruments (abbreviations), see page 6-7 or 26-28

**Paper II**

*The RLS85* was introduced in 1988 in Sweden by Starmark et al. to assess responsiveness in the acute stages and to grade the severity of acute brain disorders (Starmark et al. 1988). The RLS has been recommended in Sweden since 1990 by the Swedish Society for Neurosurgery and Anaesthesiology and Intensive Care for use all over Sweden. It is, however, less frequently used today, as described above. It deals with the component body functions as classified by the ICF.

*The Head Injury Evaluation Chart (HIEC)* (Cudmore and Pentland 1996) was the result of work by the European Brain Injury Society (Brussels, Belgium) to assess early and late outcome after brain injury. The aim was to make one instrument suitable for clinical practice and for scientific research. It was translated into Swedish by Axel Fugl-Meyer and co-workers just before the start of Study II. To my knowledge, it has not been further tested for validity and reliability either in Europe or in Sweden.

It consists of two parts, one for initial information and the second for follow-up, with 175 items covering all the components in the ICF. After one year, we decided to make a selection of items for the rest of the assessments (151/175 items), as using the whole instrument was too time consuming.

*The Community Integration Questionnaire (CIQ)* (Willer et al. 1994) is used to assess home integration, social integration and productive activities for persons with TBI. It was designed by an expert group in 1990 and modified in Detroit, Michigan, USA. It is a 15-item ordinal scale that provides a total score for community integration and subscale scores for home integration, social integration and productive activity. The CIQ has been translated into Swedish by Professor Gunnar Grimby. This instrument was selected as it deals primarily with activities and participation according to the ICF.

#### Papers II, III and IV

*The Life Satisfaction Questionnaire/Checklist (LiSat-9)*, by Fugl-Meyer et al. 1991 Sweden, was designed to measure self-response levels of happiness (Fugl-Meyer 1991). We used the *LiSat-11* checklist (Fugl-Meyer et al. 2002), which is an extension of the LiSat-9. The participants are asked: "How satisfactory are these different aspects of your life. Indicate the number that best suits your situation". It consists of one global item "Satisfaction with life as a whole" and another ten domain-specific items that are scored on a six-grade ordinal scale. Population-based reference values for Sweden are provided (Fugl-Meyer et al. 2002). According to the ICF, a person's subjective opinion of satisfaction with life is in some way included but not clearly classified, as described below in the SF-36.

#### Paper III

*The Barthel Index (BI)* (Mahoney and Barthel 1965) was developed to measure functional independence in personal care and mobility. It has been widely used all over the world to measure Activities of Daily Living (ADL). There are several Swedish translations. It is a 10-item, performance-based instrument, with the items feeding, bathing, grooming, dressing, bowels, bladder, toilet use, transfer, mobility and stairs. Each item is weighted differently and reflects the relative importance of each type of disability in terms of assistance required. It deals primarily with the components of body functions and activity in the ICF.

*The National Institutes of Health Stroke Scale (NIHSS)* (Brott et al. 1989) is a quantitative measure of stroke-related neurological deficits that has been found to have predictive validity for long-term stroke outcome. It includes items about level of consciousness, gaze, visual fields, facial palsy, motor strength, ataxia, sensation, language, dysarthria and extinction/inattention. It deals with the component of body functions according to the ICF.

*The Medical Outcome Study Short-Form Health Survey (SF-36)* (Ware and Sherbourne 1992) addresses social and community life in conjunction with physical function. It was introduced as an indicator of perceived health status and is a generic measure that can be used in general and specific populations. A second version was introduced in 1996. The results can be compared with scores for the general population (Jenkinson et al. 1993; Sullivan 2002). It includes eight multi-item scales measuring physical functioning, role limitations owing to physical health problems, bodily pain, general health perceptions, vitality, social functioning, role limitations owing to emotional problems and mental health. It can be self-administered or administered by trained interviewers either in person or by telephone.

When linking the ICF categories to the items on the SF-36, specific difficulties may be encountered, one of the most important of which may be linking items that ask about a person's health in general. To overcome this difficulty, the code *nd* (not definable) can be chosen (Cieza et al. 2002). Eleven of 51 items were linked *nd* in the paper by Cieza et al.

The instruments in this thesis were selected with the joint aim of dealing with all the dimensions/components of the ICIDH/ICF.

**Table VI. Instruments and the ICF**

<i>Instruments</i>	<i>Body functions</i>	<i>Activity</i>	<i>Participation</i>	<i>Environmental factors</i>	<i>Personal factors</i>
<b>FIM</b>	x	x			
<b>Swedish Neuro Database</b>	x-	x		x	x
<b>GOS/GOSE</b>	x	x	(x)		
<b>HIEC</b>	x	x	x	x	x
<b>CIQ</b>		x	x		
<b>LiSat-11<sup>#</sup></b>					
<b>BI</b>	x	x			
<b>NIHSS</b>	x				
<b>SF-36<sup>##</sup></b>	x	x	x		

x- We did not use the complete form # Not definable ##11 items were linked not definable (*nd*) (Cieza et al. 2002)

(x) Aspects of participation

For the instruments (abbreviations), see page 6-7 or 26-28

## Study groups

The patients had either been admitted directly to the neurosurgical department at Sahlgrenska University Hospital or referred from 13 county or local hospitals. The region of Västra Götaland has around 1.8 million inhabitants.

For Studies I and II, the inclusion criteria were severe TBI or severe non-traumatic SAH at the age of 18-65 years. The included patients had to live in the catchment area of Hospital A or B. Another criterion was the need for intensive care for at least five days. The definition of severe injury was RLS 4 (Reaction Level Scale 85) or worse, corresponding to GCS 8 (Glasgow Coma Scale) or worse at pre-hospital treatment or at the hospital before sedation and intubation. The patients were recruited consecutively at the NICU (Hospital A) and from the patient register at the NICU and/or Department of Rehabilitation (Hospital B). The case records were checked for data about the initiation and amount of rehabilitation.

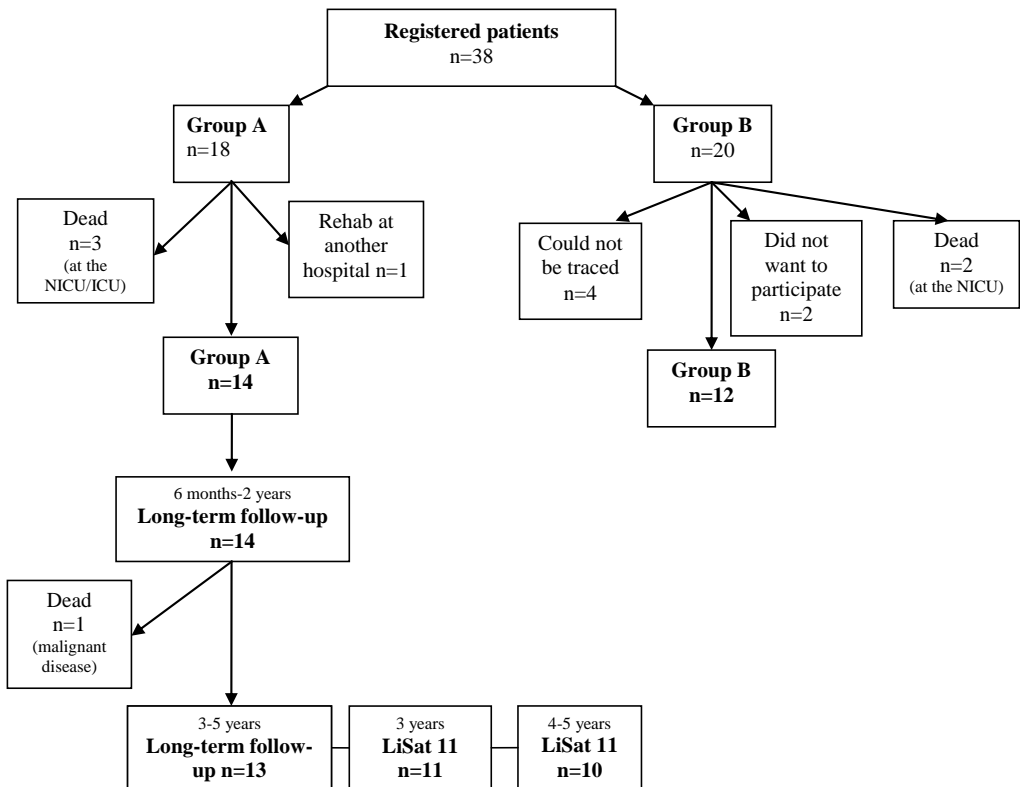
Early rehabilitation was defined as the start of specialised rehabilitation within 50 days.

Two groups were included in Study I. Group A (n=14) were living in the catchment area of Hospital A (270,000 inhabitants) and all these participants received early formalised rehabilitation at Hospital A. Eleven men and three women (mean age 47, range 15-61 years), TBI 7 and SAH 7, were included.

Group B (n=12) consisted of eight men and four women (mean age 44.5, range 21-64 years), TBI 7 and SAH 5, who were living in the catchment area of Hospital B (800,000 inhabitants) and had received late formalised rehabilitation at Hospital B (n=8) or no formalised rehabilitation at small local hospitals (n= 2) or received no rehabilitation at all (n=2), see Figure 2 and Figure 4.

Patients who had received rehabilitation within 50 days after the TBI/SAH at Hospital B were not included in the study. They did not meet the inclusion criteria for either Group B (late rehabilitation) or Group A because they had recovered well during the acute admission and had been selected for early rehabilitation at Hospital B. These patients (n=8) were identified after the study and were therefore not assessed.

**Figure 2. Included patients and drop-outs in Papers I and II.**

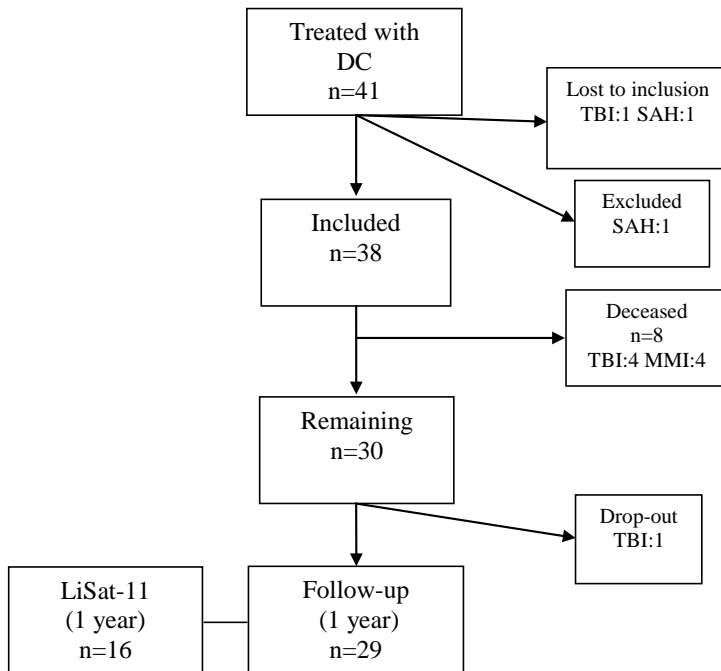


Group A participated in the long-term follow-up study that is presented in Paper II. The follow-up group consisted of 11 men and three women (mean age 47, range 15-61 years), TBI 7 and SAH 7, the same as in Study I. One participant died after two years because of a malignant disease, n=13. The remaining thirteen patients participated in all the assessments throughout the study, see also Figure 2. Two of the 13 were, however, unable to complete the LiSat-11 form. They were unable to communicate due to the severity of their brain injury. Up to three years, eleven participants completed the LiSat-11, but after that one participant deteriorated in terms of performance and was unable to complete it. At years four and five, ten participants completed the LiSat-11.

By using search routines in the computerised system, 18 patients (13 men and five women) who underwent decompressive craniectomy due to a malignant MCA at the neurosurgery unit at Sahlgrenska Hospital, Gothenburg, Sweden, between 1998 and 2004 and met the inclusion criteria could be identified and included in Study III. The medical records of all these selected patients with a mean age of 52 years (range 37-66) were reviewed. Four were deceased and 14 therefore participated in the long-term follow-up. Two of the 14 long-term survivors were unable to complete the LiSat-11 form because of aphasia.

For the fourth study, which is presented in Paper IV, we consecutively included all patients who underwent decompressive craniectomy at Sahlgrenska Hospital between March 2003 and July 2006 because of a traumatic brain injury or a vascular disease. We found that two patients had been lost to inclusion. One patient with SAH was excluded. Thirty-eight patients (25 male and 13 female) with TBI:20, MMI:13, SAH:3, one with sinus thrombosis and one with non-traumatic intracerebral haematoma (ICH) were therefore included. Their mean age was 40.6 years (range 14-63 years). Eight died before the one-year follow-up and one dropped out because of difficulty obtaining reliable data from the nursing home (n=29), see Figure 3. Six patients were unable to fill in the LiSat-11 form because of their severe injury and three did not answer. Four were of a young age and the LiSat-11 form was not distributed to them, as many of the items are not for children or adolescents. Sixteen participants filled in the LiSat-11 form. Seven of the participants with MMI were the same as in Study III.

**Figure 3. Included patients and drop-outs in Paper IV.**



## **Treatment**

All the participants had received acute medical treatment as described above at the NICU at Sahlgrenska University Hospital, Gothenburg, for at least five days.

Group A in Study I received early formalised rehabilitation at Hospital A. At the time of the study, the Department of Rehabilitation at Hospital B offered a rehabilitation programme with early admission primarily for less severely injured patients, which made it possible to identify Group B to make a comparison. The patients included in Study II (the same as in Group A) had all taken part in the formalised rehabilitation programme with early rehabilitation and a long-term follow-up at Hospital A. The programme is further described above.

All patients in Studies III and IV were treated with decompressive craniectomy at Sahlgrenska University Hospital (SU), but one in Study IV was operated on at another university hospital and was referred early to the NICU at SU. A wide hemicraniectomy was performed for all the patients involving the removal of parts of the frontal, temporal and parietal bone. Infarcted brain tissue was not resected. A duraplasty had been performed in all cases except one in Study III and one in Study IV. Specialist rehabilitation had been offered to 27/29 participants in Study IV.

## **Procedure – data collection**

Clinical features were collected from case records for all four studies. Different outcome measures were used during the measurement process, as described below.

The participants in Study I and II were also classified, for severity of injury, by a neurosurgeon using the methods developed by Marshall et al. (Marshall 1991) for TBI, Fisher et al. (Fisher et al. 1980) and Hunt and Hess (Hunt and Hess 1968) for SAH. The assessment of both groups in Paper I was made by the same occupational therapist at the reception at the Departments of Rehabilitation at Hospital A and B or at the patients' homes. For demographic data, basic data and psychosocial outcome, all the patients were interviewed using the former non-web-based but structured form for the Swedish Neuro Database, with two supplementary questions about previous diseases and abuse. Interviews were also conducted with relatives and/or staff providing care when relevant. The data provided by the patients could thus be checked.

In Study II, the assessments were made by the same rehabilitation nurse and the undersigned. Some data in this study were collected by telephone, but most assessments were made at the Department of Rehabilitation or at the patients' homes. All the long-term follow-up data were collected by personal contacts.

In Study III, the cerebral CT scans performed prior to the craniectomy were analysed and classified by an experienced neuroradiologist. All long-term survivors were interviewed and examined by a neurosurgeon (the main author) and a research nurse in their present home. The patients' relatives or caregivers were also interviewed. The follow-up assessments were performed at least one year after the insult.

In Study IV, the patients were assessed one year after the injury/onset of disease, either at the rehabilitation centres by a rehabilitation team member, or via a telephone interview conducted by a research nurse. Interviews were also conducted with relatives when relevant.



## Data analysis and statistics

Scales with ordered categories (ordinal scales), giving only rank orders and not numerical values, were mainly used in the studies. Traditional statistical tests such as the Sign test and McNemar's test for paired proportions do not use the information in the data effectively from a clinical perspective. Numerical data were analysed using Statistica version 6.0.

The Wilcoxon test has been used to compare the degree of injury as measured by the Fisher, Marshall and Hunt & Hess scores in Study I.

We used Svensson's method (Svensson 1998; Svensson and Starmark 2002) for the analyses of the GOSE results in Paper II. This method made it possible separately to measure systematic group changes and individual changes that are not consistent with the pattern of the group changes. The occasion-specific categorical distributions appear as marginal distributions of the contingency table. The group change is shown graphically by plotting the cumulative proportions of the two distributions together with the point (0,0) yielding an ROC (relative operating characteristic) curve (Svensson and Starmark 2002; Svensson 2010). The difference between the probability of the classification being shifted towards higher categories and the probability of the classification being shifted towards lower categories on the second occasion defines a measure called relative proportion (RP). The difference between the probability of the marginal distribution on the second occasion being concentrated relative to the first and vice versa defines the measure of relative concentration (RC). Possible values range from -1 to 1. Values of RP and RC close to zero indicate a negligible change for the group over time. The corresponding ROC curve will be close to the main diagonal. This statistical method is suitable for small data sets (Svensson and Starmark 2002), which are common in rehabilitation research.

In Paper III, the Mann-Whitney U-test was used for the analysis of the SF-36 data and Spearman's rank test was used for testing correlations. For the analysis, we used SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

The results of Paper IV were presented in numerals, mean, median and range. We decided not to do any statistical calculations as the population was a mix of different diagnoses and the sub-groups were small.

## RESULTS

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### Outcome after severe brain damage, what makes the difference?

The main findings in Study I were as follows.

We did not find any explanation for the more favourable outcome for Group A compared with Group B, according to *demographic data, clinical features, time until assessment or time until arrival* at the hospital, as

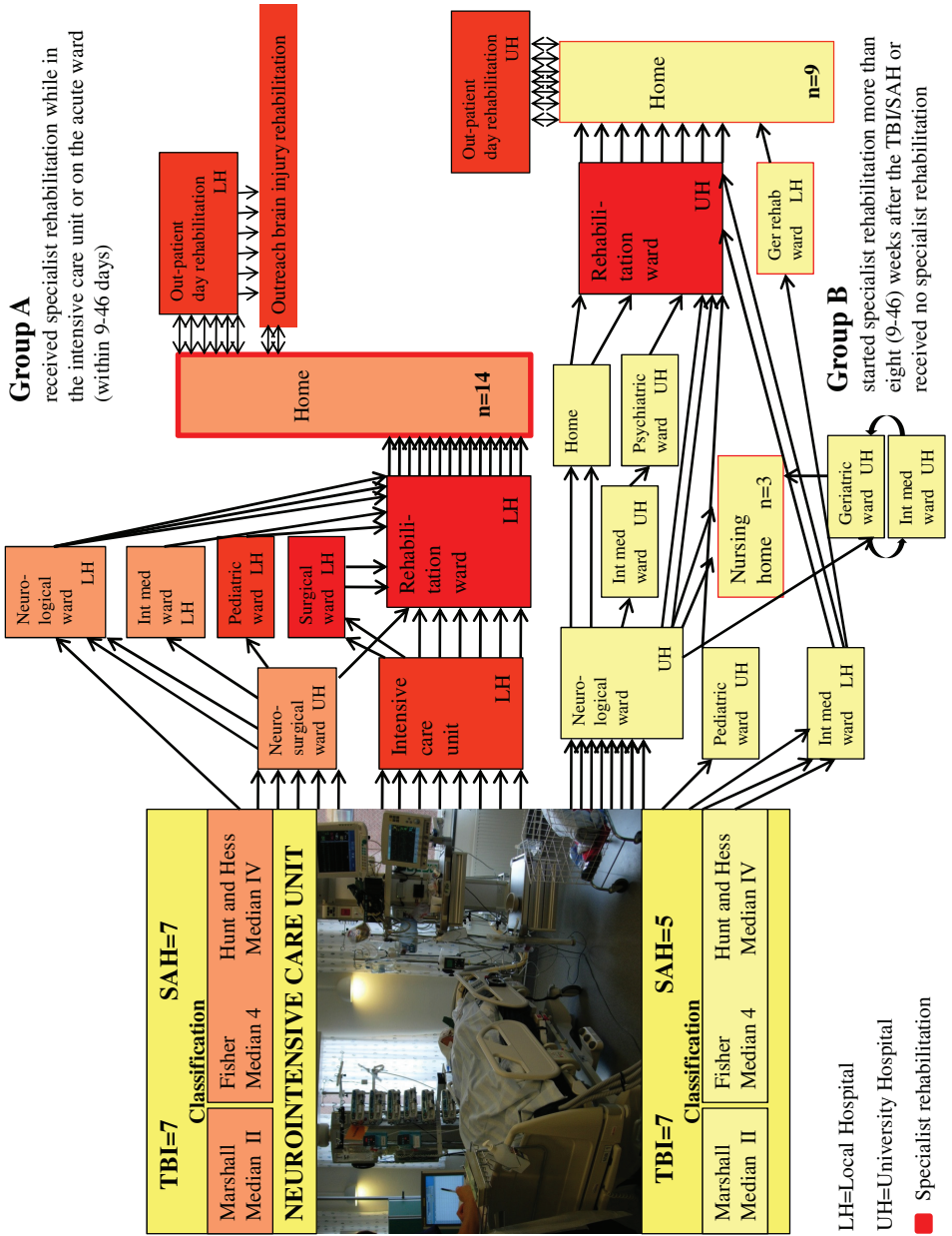
- There were no significant differences in age or gender between the groups.
- There was a lower frequency of unemployment but a higher frequency of disability pension in the group that received early rehabilitation (Group A) as compared with the other that received late or no rehabilitation (Group B).
- The groups did not differ significantly in terms of the degree of injury as measured with the scales of Hunt and Hess, Fisher and Marshall.  
See also Table I (page 497) in Paper I for the clinical characteristics of the patients.
- Seventeen of 26 patients were assessed at two years, at a mean of 26.6 months (SD 4.2, median 25, range 14-41 months), post TBI/SAH. The time of assessment did not differ between the groups.
- Eleven patients in Group A had primarily been referred to one of the emergency departments at the three local hospitals in the catchment area of the Department of Rehabilitation at Hospital A. Two had been directly transported to the NICU and one had primarily been referred to a local hospital close to the NICU.  
In Group B, two patients had been transported to a hospital close to the NICU and two were injured and treated abroad. Eight patients in Group B had been transported directly to the NICU.
- The mean time until arrival at hospital was shorter for Group B (mean 40.5 minutes, SD 36.9, median 25.5, range 18-126), compared with Group A (54.7 minutes, SD 29.8, median 45, range 22-115).

There was a difference between the groups according to marital status. More participants were living alone in group B.

There were differences between the groups according to *the process of care*, as shown in Figure 4, including time until onset of rehabilitation and access to formalised specialist rehabilitation, as

- All 14 patients had received early (started within 50 days) formalised rehabilitation during the acute stage at Hospital A. Six patients were referred directly from the local intensive care unit (ICU) to the rehabilitation ward.  
Eight patients in Group B received late (started after 50 days) yet formalised brain injury rehabilitation at Hospital B.
- Two patients in Group B were referred directly to a nursing home and one received rehabilitation at a geriatric ward before referral to a nursing home
- All the patients in Group A went home, whereas three patients in Group B were referred to nursing homes.

*The amount of rehabilitation* was more extensive per patient for those patients receiving rehabilitation in Group B compared with Group A, see Table VII.



**Table VII. Time before onset and amount of specialist rehabilitation (mean)**

<i>Group</i>	<i>A (n=14)</i>	<i>B (n=12)</i>
Time before onset of specialist rehabilitation, days	26.6 (n=14)	107.4 <sup>#</sup> (n=8)
In-patient rehabilitation, length of stay, days	97.3 (n=14)	122.4 <sup>#</sup> (n=8)
Out-patient day rehabilitation, length of stay, days	27.5 <sup>#</sup> (n=6)	64.8 <sup>#</sup> (n=7)
Total length of stay at a rehabilitation ward, days	109.1 (n=14)	133.3 <sup>#</sup> (n=8)
Outreach Brain Injury Rehabilitation, months	18.3 <sup>#</sup> (n=8)	0

<sup>#</sup>For those who received the rehabilitation

#### *Activity and participation*

There were differences between the groups according to dependence. The definition of independence was getting through the day and night without any help from the community or significant others, see also Table VIII.

- According to the definition above, 7/14 patients in Group A were independent compared with 2/12 in Group B.
- The FIM scores showed a difference between the groups, with a better outcome for Group A, as analysed by median scores. We found higher median scores for Group A for the motor items (a total of 13 items) of grooming, bathing, dressing, walking/wheelchair and climbing stairs. According to the cognitive items, we found higher scores for expression, social interaction, problem-solving and memory but not for comprehension. The median total scores for motor/cognitive items were 91/33 for Group A and 85/31 for Group B. The maximum total scores on the FIM were 91/35.

**Table VIII. Dependence, residence, employment and permission to drive before and after the TBI/SAH, %**

<i>Group</i>	<i>A(n=14)</i>		<i>B (n=12)</i>	
	<i>Before</i>	<i>After</i>	<i>Before</i>	<i>After</i>
<b>Independent</b>	100	<b>50</b>	100	<b>17</b>
<b>Living at home</b>	100	<b>93</b>	100	<b>67</b>
<b>Sheltered accommodation</b>	0	<b>7</b>	0	<b>8</b>
<b>Nursing home</b>	0	<b>0</b>	0	<b>25</b>
<b>Work/study, full time</b>	79	<b>21.4</b>	83	<b>0</b>
<b>Work/study, part time</b>	0	<b>21.4</b>	0	<b>0</b>
<b>Unemployed</b>	0	<b>0</b>	17	<b>0</b>
<b>Disability pension or sickness benefit 100%</b>	21	<b>57<sup>#</sup></b>	0	<b>100</b>
<b>Driving</b>	71	<b>43</b>	83	<b>17</b>

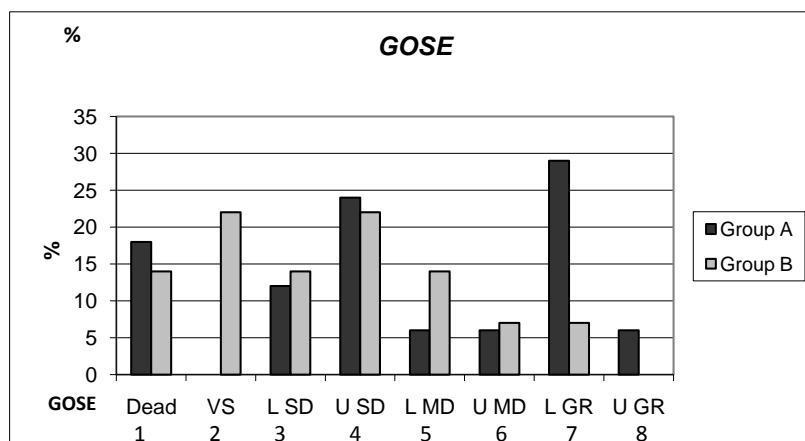
<sup>#</sup>One of the participants returned to work but was on sick leave due to medical problems not related to the TBI at the time of assessment.

- Of the 11 who worked/studied full time before the TBI/SAB in Group A, 55% had returned to work/study full time (n=3) or part time (n=3) at the time of assessment. In Group B, nobody worked or studied.
- Six of 14 patients had received permission to drive in Group A as compared with 2/12 in Group B. All drivers had been assessed by a neuropsychologist and an inspector from the Swedish National Road Administration before regaining permission to drive.

*The neurological deficits – body functions, activity and participation*

- The scores for the *GOS* and the *GOSE* showed a better outcome for Group A, see Figure 5. No patient has remained in a vegetative state in Group A, but, in Group B, three were still in a vegetative state at the time of assessment. The mean for the *GOS* in Group A was moderate disability (4), while it was severe disability (3) for Group B. For the *GOSE*, the mean in Group A was lower moderate disability to upper moderate disability (5.5), while in Group B it was upper severe disability (4.0).

**Figure 5. Glasgow Outcome Scale Extended**



VS = vegetative state, L SD = lower severe disability, U SD = upper severe disability, L MD = lower moderate disability, U MD = upper moderate disability, L GR = lower good recovery, U GR = upper good recovery

VS: Unable to obey even simple commands.

L SD: Needs frequent help or someone to be around at home most of the time.

U SD: Should be able to look after him/herself for up to 8 hours during the day but is unable to shop without assistance and/or is unable to travel without assistance.

L MD: Only able to work in a sheltered workshop or non-competitive job or currently unable to work. Unable to participate. Rarely, if ever, takes part in social and leisure activities. Disruption and strain, typical post-traumatic personality changes are observed daily and are intolerable.

U MD: Reduced work capacity. Participates much less, less than half as often as before the injury in social and leisure activities. Disruption and strain: typical post-traumatic personality changes are observed once a week or more but are tolerable.

L GR: Able to work. Participates a little less, at least half as often in social and leisure activities. Disruption and strain: typical post-traumatic personality changes are observed occasionally, less than weekly.

U GR: There are no current problems relating to the injury which affect daily life.

## **Psychosocial adjustment and life satisfaction until five years after severe brain damage**

The main findings in Study II were as follows.

### *Mortality*

- One participant (1/14, 7%) died between the two- and three-year follow-ups. The cause of death was cancer.

### *Psychosocial adjustment – demographic data – personal factors and environmental factors*

- At the five-year follow-up, 12/13 (93%) of the surviving participants were living at home.
- Marital status was stable over time and there were no differences between participants living alone and cohabiting/married participants according to satisfaction with life as a whole.
- Three participants had a history of overuse of alcohol. Two had an abuse, as defined in DSM-IV, before the TBI and one was a “high consumer” (drinking beer and/or drinks every day) but functioned well socially. Two relapsed, but there were no signs or reports of abuse or overuse among the other 12.

### *Psychological reactions –body functions*

- Anxiety (3/14) was not as commonly reported as depression (10/14) among the participants during the follow-up period.

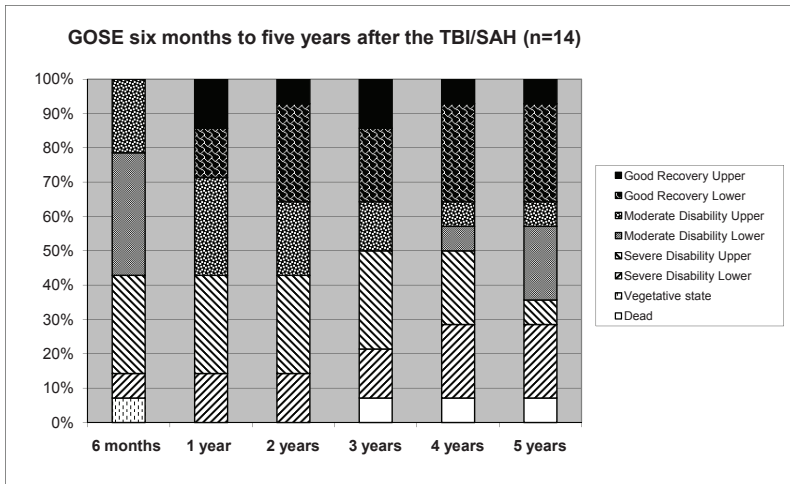
### *Activity and participation*

- In all, 7/14 (50%) went back to work. Of the surviving participants who worked before the TBI/SAH, 6/10 (60%) had gone back to work at the five-year follow-up. They were working at a level of 50% (n=4) and at a level of 100% (n=2). The maximum level was achieved within one to two years after the TBI/SAH for four of the participants and within three years and five years respectively for the other two.
- Fifty per cent of the former drivers regained permission to drive within two years. One had to wait for permission until two years after a seizure because of post-traumatic epilepsy. One lost it after the two-year follow-up because of visual impairment and one who did not drive before obtained a licence three years after the injury. At the end of the study, 70% of the former drivers were therefore driving again.
- The frequency of leaving home increased over time for 10 of the 13 participants, as measured by one item in the community integration questionnaire (CIQ). For one, it was stable, making visits to friends or relatives > 5 times a month, and for two participants it deteriorated between one and five years.

### *Neurological deficits – body functions, activity and participation*

- The SAH patients improved more than the TBI patients and the TBI patients changed for the worse to a greater extent during the study compared with the SAH patients.
- Changes according to the GOSE were seen from six months to five years, as shown in Figure 6. The change was significant (analysed with Svensson’s method) at group level between six months and one year but not for the other assessments.

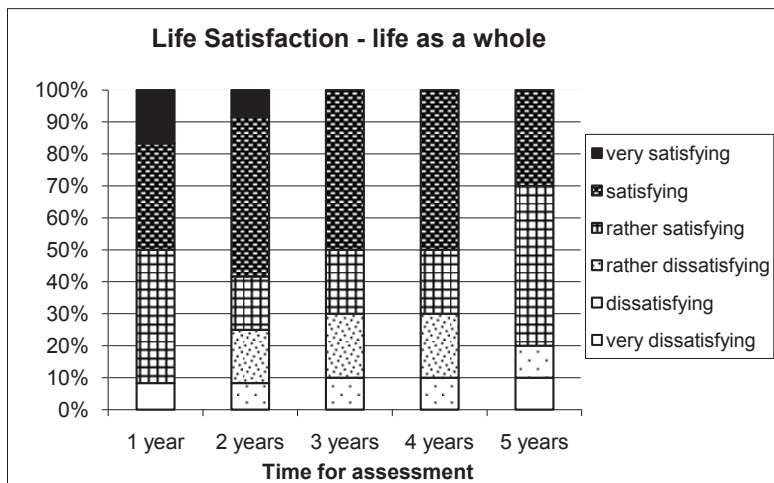
**Figure 6. GOSE over time**



*Life satisfaction*

- Satisfaction with life as a whole was not stable over time for the individuals. The participants were most satisfied at the one-year assessment.
- Eighty per cent rated their life as satisfactory and 20% as unsatisfactory to some degree at the five-year follow-up, as seen in Figure 7.

**Figure 7. Life as a whole (LiSat-11) over time**



- Generally, the figures are lower and satisfaction with sexual life was especially low, as compared with the population-based reference values. Satisfaction with physical health displayed the smallest differences, see also Table 4 in Paper II (page 145).

## **Health status and life satisfaction after decompressive craniectomy for malignant middle cerebral artery infarction**

The main findings in Study III were as follows.

### *Status before surgery*

- Thirteen men and five women at the age of  $52.0 \pm 8.9$  (range 37-66) years were included. Sixteen patients scored 6-8 on the GCS, while two scored 9-12. Anisocoria (sign of a third nerve palsy caused by uncal herniation) had been found in 12/18 (67%) of the patients. The mean time from onset of symptoms to DC was  $54.5 \pm 28.7$  hours (range 19-120).

### *The analysis of the CT scans*

- The majority of the 18 patients had had the infarction in the right hemisphere (15/18, 83%). Eleven of 18 (61%) had their infarction only in the MCA territory and 6/18 (33%) had an additional infarction in the anterior cerebral artery territory. Only one (1/18, 6%) had an additional infarction in the posterior cerebral artery territory. The mean midline shift was  $12.6 \pm 4.0$  mm (n=16).

### *Mortality*

- The acute mortality defined as mortality until discharge from acute care was 17% (3/18) and long-term mortality (until the follow-up examination) was 22% (4/18).

### *Body functions*

- Most patients were severely affected by their stroke. The mean NIHSS score at the long-term follow-up was 13.8 (range 6-20). No patient was left in a vegetative state.

### *Body functions and activity*

- All participants required assistance for ADL. The mean BI was 63.9 (range 5-100), but for seven patients the BI exceeded a score of 60, which can be used as a cut-off level for being independent.

### *Body functions and activity (participation)*

- All patients were classified as GOS 3, which means that they were “able to follow commands but unable to live independently”.

### *Life satisfaction*

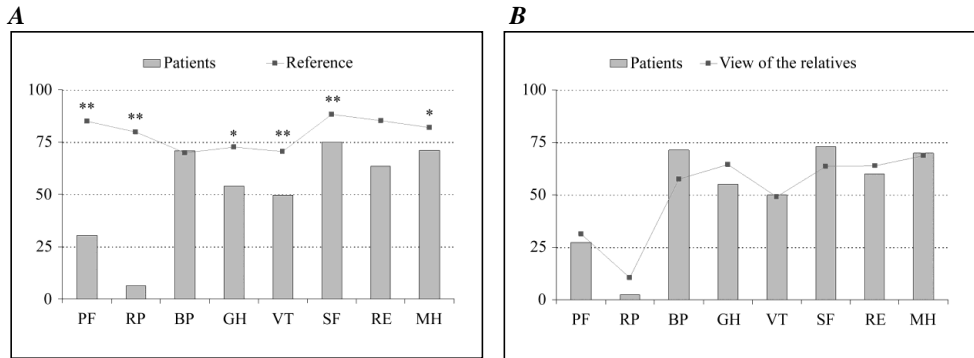
- Five of 12 patients (42%) found life as a whole “satisfying” or “very satisfying” and another five patients (42%) found it “rather satisfying”. Two of 12 (17%) found life as a whole “rather dissatisfying” or “dissatisfying”. Two patients could not fill in the form because of aphasia.
- There was no correlation between age, time from onset of symptoms to surgery versus NIHSS scores, BI scores or GOS scores.



*The patients' view of their health status*

- The patients' view, as measured with the SF-36, was significantly lower compared with an age-matched reference group in all items except bodily pain and emotional role, see Figure 8a.
- No significant differences were found when comparing the patients' own view of their health with their relatives' view, see Figure 8b.

**Figure 8. Results from the short-form health survey (SF-36)**



PF = physical functioning    GH = generally health    RE = role emotionally  
 RP = role physical        VT = vitality                    MH = mental health  
 BP = bodily pain            SF = social functioning

\* $P < 0.05$ ; \*\* $P < 0.01$

A: Results for the patients compared with age-matched reference material.  
 B: Results from the patients compared with scores based on their relatives' views (n=12).

**Outcome and life satisfaction one year after decompressive craniectomy**

The main findings in Study IV were as follows.

*Mortality*

- The mortality rate for the whole group at the centre at one year was 19.5% (8/41).
- The long-term mortality for the included TBI patients was 20%, for MMI 28.6% and for SAH and for OD 0% each.

*Rehabilitation*

- Twenty-seven of thirty of the surviving participants (90%) received rehabilitation at the specialist rehabilitation centres in the region within the first year.
- For those who received specialist rehabilitation, it started a mean of 52.1 days (median 39, range 8-193 days) after the injury/onset of disease.
- The mean stay at the rehabilitation centres for the whole group was 16.1 weeks (median 15.5, range 2-45).

- We saw a trend towards that those with MMI on the non-dominant side had longer rehabilitation stays with a mean of 19.8 weeks (median 24, range 8-32 weeks) as compared with those with MMI on the dominant side and a mean of 13.8 weeks (median 15.5, range 7-19 weeks), see also Table 1 in Paper IV (page 5).

#### *Cranioplasty*

- Twenty-nine of the 30 patients underwent cranioplasty before the follow-up after a mean of 5.5 months (median 5.7, range 0-10).

#### *Late complications, infections*

- Infections in the bone flap occurred in seven patients (24%).
- The mean preservation interval for the whole group was 5.4 months (median 5, range 1-10 months) and the mean was the same for those with uninfected flaps and those with infected flaps.

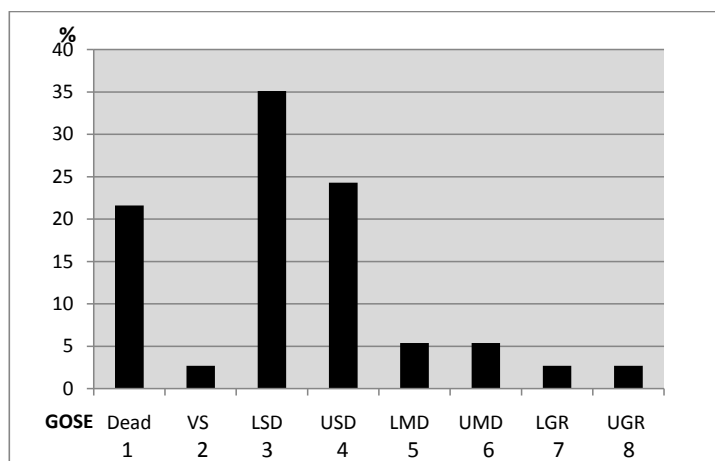
#### *Dependence – activity, participation and environmental factors*

- At the long-term follow-up, 25/29 (86.2%) lived at home, one (3.4%) lived in sheltered accommodation but with no assistance during the night, while another 3 (10.3%) lived in institutions (nursing homes).
- Five (17%) were independent (all with TBI), eight (27%) were unable to get through the day without assistance from a partner or parents and 13 (44%) received assistance from the community or had personal assistants. Those three (10%) who were living in nursing homes were totally dependent.

#### *Body functions, activity and participation*

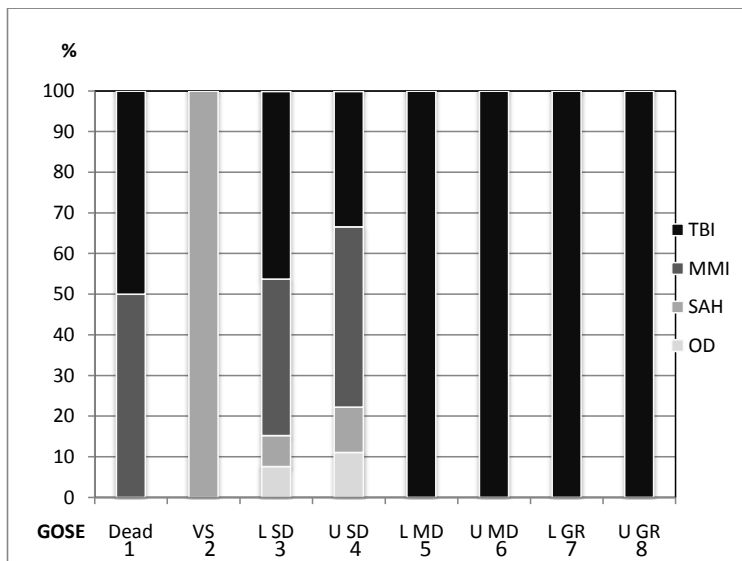
- Six participants (6/29, 20%), all with TBI, had a favourable outcome when dichotomised into unfavourable outcome (GOSE 2-4) and favourable outcome (GOSE 5-8).

**Figure 9. The distribution in the different GOSE categories (n=37)**



VS = vegetative state, L SD = lower severe disability, U SD = upper severe disability,  
 L MD = lower moderate disability, U MD = upper moderate disability,  
 L GR = lower good recovery, U GR = upper good recovery

**Figure 10. The distribution of the different diagnoses (GOSE)**



VS = vegetative state, L SD = lower severe disability, U SD = upper severe disability,  
 L MD = lower moderate disability, U MD = upper moderate disability,  
 L GR = lower good recovery, U GR = upper good recovery

*Life satisfaction*

- Six patients (21%) were unable to fill in the form because of their severe injury and three (10%) did not answer. Four (14%) were of a young age and the LiSat-11 form was not distributed to them, as many of the items are not for children or adolescents. Sixteen participants, 16/29 (55%), filled in the LiSat-11 form.
- Fourteen of 16 patients (88%) rated their life as satisfactory (“satisfying” or “rather satisfying”) and two (12%) as unsatisfactory (“rather dissatisfying”). No patient rated their life as “dissatisfying” or “very dissatisfying”.
- The two who rated their life as “rather dissatisfying” both had a GOSE 4.
- The median score for “life as a whole” was 5 (satisfying) (range 4-6), for the TBI patients, and 4 (“rather satisfying”), (range 3-6), for the MMI patients. For the SAH patient and the other diagnoses, see Table 4 in Paper IV (page 10).
- For all those who were rated as GOSE 3 (all diagnoses), the median score for life as a whole was 4.5 (“rather satisfying/satisfying”), (range 4-6).

## DISCUSSION

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When we designed the first study, we had ethical problems to deal with. There were no randomised, controlled studies of the impact of early and formalised rehabilitation and we therefore conducted a study of this kind. However, as our subjective experience was that patients recovered more rapidly and with fewer complications when rehabilitation was initiated as quickly as possible, it was not possible to randomise to no or late rehabilitation. We thought it was impossible to get patients or relatives to agree to this. An opportunity to conduct a cross-sectional study was, however, presented, due to the different traditions at the two hospitals in the same region at that time.

The literature about early rehabilitation compared with late rehabilitation after severe brain injury is sparse. Turner-Stokes et al. concluded in their Cochrane Review (Turner-Stokes et al. 2005) entitled “Multi-disciplinary rehabilitation for acquired brain injury in adults of working age” that, for moderate to severe injury, there is “strong evidence” of benefit from formalised intervention. In her review article from 2008, Lynne Turner-Stokes highlighted the importance of looking beyond the somewhat restrictive set of trial-based evidence (Turner-Stokes 2008). She found in her study that the trial-based studies provided “strong evidence” that more intensive programmes are associated with more rapid functional gains and “moderate evidence” that continued outpatient therapy can help to sustain gains made in early post-acute rehabilitation. However, the trial-based studies failed to address the impact of early or late rehabilitation, the effect of specialist programmes (e.g. vocational or neuro-behavioural rehabilitation), or cost effectiveness. In contrast, the “non-trial-based” studies provided strong evidence in all these areas, as well as evidence of the cost benefits of rehabilitation.

When we designed the second study, we wanted to obtain as much data as possible about the recovery phase. At that time, it was already evident from the work of Fordyce et al. (Fordyce et al. 1983) and George Prigatano (Prigatano 1989) that neuropsychological deficits or physical impairments such as pareses (e. g. body functions) were not as important for outcome or for the distress of the patients or their families as psychosocial changes. This was also subsequently described by Hop et al. (Hop et al. 1998) and Rosenthal et al. (Rosenthal 1999). We decided not to use neuropsychological tests to evaluate outcome but instead used instruments that focused more heavily on participation and satisfaction, which are often the main goals of rehabilitation.

To measure participation, we selected the CIQ. It had recently been translated into Swedish and asked the important questions. It has, however, been criticised for its shortcomings and not sufficiently good psychometric properties (Minnes et al. 2003; Kuipers et al. 2004). Adding up the scores from the different subscales is not acceptable from a statistical point of view (Svensson 1998). We therefore decided to use only selected questions (4/15 items) from the CIQ in our one- to four-year assessments but to use the whole instrument for the others.

There has been some criticism in the literature about only using return to work as a measure of outcome (Elsass and Kinsella 1987). Return to work is, however, central to social integration for most brain-injured patients and is thus, in my opinion, a relevant outcome measurement.

Small sizes in study groups are common problems in rehabilitation research. In Study I, it took us more than two years to include the number of 14 patients at Hospital B who also participated in Study II. A subsequent control revealed, however, that the groups at Hospital A and B were representative of the catchment areas. We excluded one participant, because of rehabilitation at another hospital, but we did not lose anybody during the follow-up except for

the persons who died. In Study III, all the surviving patients, who were identified by the computerised system, agreed to participate. In Study IV, which was a single-centre study, we lost two to inclusion, one was excluded and one more was lost to the long-term follow-up. The drop-out rate was 4/41 (9.7%) or 4/29 (14%) of the surviving patients. Corrigan et al. found that longitudinal studies of persons with TBI regularly report that one third to half the participants are lost to follow-up (Corrigan et al. 2003). Of the surviving participants, 16/29 filled in the LiSat-11 questionnaire. It should, however, be remembered that 19/29 were expected to participate as six had language disorders and/or very severe injuries and four were too young. The frequency of participation in the investigation group (16/19) can thus be calculated at 84%. It is probable that small studies with few drop-outs produce less bias than huge studies with a very high and perhaps undetected selective loss to follow-up. Investigating the view of life from different aspects for the patients with more severe neurological deficits is difficult but important. To our knowledge, there were no instruments at the time of the study to measure life satisfaction for those with language disorders or very severe injuries. It would have been interesting to use qualitative methods to collect data about life satisfaction for the participants in Studies II, III and IV who were unable to communicate enough to fill in the LiSat-11 questionnaire.

In Study III, we used the commonly used Barthel Index (BI) to rate dependence and found that 50% of the participants reached a BI of > 60, which is often considered to be the cut-off level for independence. Nobody was, however, independent. In a review article (Balu 2009), the cut-off level is discussed and he describes the lack of uniformity of cut-off points in different studies, as well as the inherent ceiling effects of BI, which became apparent in our study. In Study I, we also noted that the FIM had important ceiling effects, although the study comprised patients with severe injuries.

One shortcoming in Studies I, II and IV is the mix of different diagnoses. Although the mechanism of injury for TBI, SAH, MMI and ICH differs, there is, to my knowledge, a similar pattern of recovery to some extent, as well as a similarity in the pattern of the remaining sequelae after severe injuries. This has been described in the case of TBI and SAH by Hellowell et al. (Hellowell and Pentland 2001). All the diagnoses cause both focal and diffuse brain injuries because of the oedema and elevated ICP and the secondary injury cannot be completely prevented.

In our experience, early rehabilitation prevents complications such as infections, contractures, pressure sores, urinary complications and the development of insufficient movement patterns. Depressions can be diagnosed and treated pharmacologically without delay and psycho-stimulating medication can be tried. Rehabilitative interventions, both physiotherapeutic and pharmacotherapeutic (Nudo 2003) and task-specific training (Hubbard et al. 2009), may have benefit via the modulation of neuroplastic mechanisms and thus have an impact on outcome. Being referred to a nursing home without formalised rehabilitation in the early stage (three patients in Group B) could be expected to have a negative impact on the outcome, with a higher risk of patients remaining in a vegetative state. Early rehabilitation also gives the patient and relatives an early insight and goal-oriented strategies to cope with the difficulties. It is well known in rehabilitation that it is easier to educate the family and to create good patterns in the early phase but more difficult to change ingrained patterns. Early rehabilitation could therefore be an important factor and could explain the differences between the groups in terms of dependence, as seen in Table VIII.

In a case report from Australia (Honeybul 2009), the author highlights the need to view patients that are treated with craniectomy as a particularly high risk and recommends that institutions review or establish a specific policy regarding their management.

Many of these patients require surveillance during the night and day and the rehabilitation plans and rehabilitation activities have to be modified. To my knowledge, there are no international or Swedish guidelines about how to protect the unprotected craniectomy site after decompressive craniectomy for the patients that are waiting for cranioplasty. A policy for this would be a great help for the rehabilitation professionals.

A period waiting for cranioplasty can result in substantial costs for the rehabilitation clinic, be dangerous and stressful for the patient, rehabilitation staff and relatives and slow down rehabilitation. The patients have problems setting goals and struggle to reach them until cranioplasty is performed. As one of my patients said, "There is no point struggling now. Who knows if I shall be alive after the operation, my rehabilitation will start after the cranioplasty". There is still a need to shorten the waiting time as this will speed up rehabilitation and shorten rehabilitation in-patient stays, minimise the suffering of the patients and increase accessibility for others who need rehabilitation.

There are different methods, in the acute phase, for classifying and predicting the severity of injury with the aim of making a prognosis for the future. The most common measures are, however, not as reliable as they were before the modern neurointensive care treatment methods were introduced. Some patients are intubated and sedated at RLS 3, when consciousness displays a downward trend. The lowest score for GCS/RLS could therefore not be estimated for the patients in Studies I and II. Reliable information about the length of PTA was not found in the case sheets of most patients (either group) in Study I. Many patients were treated, even during the early recovery phase, with drugs that have an impact on cognitive functions; they include clonidine and sedatives. We used the GOAT to estimate PTA for some of the participants in Study II. The time taken to emerge from PTA is, however, dictated by the method that is used, as described by Tate et al. (Tate et al. 2000; Tate et al. 2006). For these reasons, the use of PTA nowadays for grading injury severity is debatable. We did not use length of PTA for classification in Study I and did not analyse the data for the prediction of outcome in Study II. Predicting outcome after brain damage is a challenge for the specialists in neurosurgery, neurology and rehabilitation medicine. Corrigan et al. found that important aspects of outcome could not be predicted on the basis of premorbid characteristics, injury severity and initial functional abilities (Corrigan et al. 1998). Factors that should be taken into account, when trying to make a prognosis for the possibility of good recovery in the very early phase, are information about whether the patients have had episodes of anoxia or hypoperfusion. In Studies I and II, when looking at the emergency data for the participants with the worst outcome, we found that, with the exception of one individual in each group, they had had episodes of anoxia or hypoperfusion.

The results and differences in outcome between the two groups in Study I are evident. The most important question to ask is whether the two groups differ in some important respects, other than the rehabilitation treatment. We found that injury degree, as measured by the initial RLS85/GCS scores, Hunt & Hess score, Marshall's classification, Fisher grading scale or frequency of anoxia or hypoperfusion, is not able to explain the difference. It was not possible to find reliable PTA data for either group and PTA was therefore not used to classify the degree of injury and inclusion.

The groups differed in some respects according to pre-injury variables, as can be seen in Table II in Paper I (page 498). Marital status, with a higher frequency of people living alone

in Group B, could have had a negative impact on the frequency of patients returning to their homes, as has also been reported in a study by Tooth et al. (Tooth et al. 2001). Another difference is that Group A came mainly from rural areas, while Group B came from an urban population. It is possible that the social networks, especially employers, are more tolerant and “care-giving” in rural areas, which might have had a positive impact on the psychosocial outcome in Group A. Harradine et al., however, reported a poorer outcome after TBI in rural residents as compared to urban ones (Harradine et al. 2004).

The patients in the group that received late rehabilitation at the hospital had longer mean rehabilitation stays in hospital than the patients in the early group, indicating that “the late patients received more days of rehabilitation at the hospital but with poorer results”. This is in accordance with the findings of Cope et al. and Mackay et al. (Cope and Hall 1982; Mackay et al. 1992)

In 1998, Corrigan presented a study referred to above which was cross-sectional and included every degree of severity of brain injury after TBI. He concluded that outcomes over the first five years after discharge were dynamic, with most change taking the form of improvement, at least after the first two years. In a study presented in 2001 with the aim of investigating correlates of life satisfaction after TBI, Corrigan et al. found that life satisfaction was relatively stable between years. Change that did occur was associated with marital status and depressed mood two years after injury (Corrigan et al. 2001). These results are not in agreement with our findings in Study II, as the participants were discharged to their homes and stayed there and marital status was very stable. This might be a result of the rehabilitation programme that involves the next of kin in the rehabilitation work and supports them to take their loved ones home for the weekends at an early stage. The families could be supported by the outreach brain injury rehabilitation team for many years, if needed. This support and the kind of population (rural, with a tradition of “taking care”) might explain this. There may still, however, be a change in marital status in the future, as described by Harradine et al. (Harradine et al. 2004).

Little guidance exists on the practical issues of bone flap storage, such as the maximum time, temperature and best place for storage. In Study IV, we found a high frequency of infections following cranioplasty (24%), for which we have no explanation. It is possible that the artificial material used for duraplasty could increase the infection rate and also that the delay until cranioplasty could increase the risk of infection. These questions require systematic studies.

We found that most participants, 27/30 (90%), in Study IV had received rehabilitation, which was not the case in Study I. Early rehabilitation was, however, still not offered at a uniform level in the different parts of the Västra Götaland Region. This can be adjusted by an appropriate number of in-patient rehabilitation hospital beds in relation to the number of inhabitants in the catchment area, but also, in my experience, by changing the routines for early assessments and priorities. To assure very early rehabilitation, the brain injury rehabilitation teams can work as consultants on the acute wards. The in-patients’ stays can be shortened if the patients with severe injuries, who are discharged at an early stage to their homes, receive follow-up by specialist home-rehabilitation teams who can also work as consultants in community settings.

At the five-year follow-up, 6/13 participants in Study II reported making visits to friends or relatives > 5 times a month and 5/13 reported visits 1-4 times a month. For those 11/13, there was no decline over the years. Moreover, in the case of the two most severely injured participants, the frequency of leisure activities increased, as one moved to a nursing home and the other received personal assistance.

Thomsen reported that 68% in her sample experienced a reduction in social contact, with two-thirds of her group having no contact with people outside the immediate family and reporting loneliness 10-15 years after the injury (Thomsen 1984) and Olver et al. reported that more than half of their sample had lost friends and had become more socially isolated since the accident (Olver et al. 1996). Elsass and Kinsella noted that the patients themselves were not distressed by a decrease in social contact (Elsass and Kinsella 1987). We suggest that a focus on social re-integration during rehabilitation could change this unfavourable trend.

Seventy per cent of the former drivers in Study II regained permission to drive. One had very severe memory deficits and severe executive problems on the neuropsychological tests but very good results on the assessments by the inspector and was therefore allowed to drive. This shows the importance of offering adequate assessments even to people with severe deficits, as permission to drive a car is crucial for "identity" and gives the experience of independence and thereby satisfaction.

Barbara Wilson suggested that those patients who had returned to work had to use more strategies for memory compensation than those who had not returned to work (Wilson 1992). The Outreach Brain Injury Rehabilitation Programme, including structured work with coping strategies (spread over a long period), and the higher demands of daily living for Group A might thus explain the improved psychosocial outcome. This part of the programme probably influences the score for dependence and the frequency of return to work more than the early intervention. The result for this group, with 43% of all the participants (55% of the former workers) working, some individuals improving and no decline in employment status until five years, is as good as or better than those in other studies, see Table IV. It has been difficult to find studies to compare with, as most studies also include patients with moderate TBI/SAB.

We suggest that the intensive teaching of compensatory strategies and the long-term support from the outreach brain injury rehabilitation team for the participants and their employers, together with co-operation with the local social insurance office, have had a positive impact on vocational outcome in the long-term follow-up.

The frequency of relapse into, or development of, alcohol abuse during the long-term follow-up was lower than expected. Perhaps the fact that one of the former abusers had a severe condition and was totally dependent on others and the fact that this was a population with good social support protected people from relapse. The prolonged support of the outreach rehabilitation team might also have protected the participants from falling into abuse.

Anxiety was not as commonly reported or observed as depression in Study II. Olver et al. reported anxiety and depression in around 50% of their sample (Olver et al. 1996). Tyerman and Humphrey noted that "whilst accurate self-appraisal of the severely head injured will be limited by cognitive impairment (especially lack of insight), it is the subjective impairment which represents distressing reality for these patients and dictates their psychological adjustment" (Tyerman and Humphrey 1984). We suspect that this low frequency of anxiety has nothing to do with our programme but is mainly a matter of definition and/or that frontal lesions may have protected the patients from anxiety, in spite of signs and symptoms of depression.



In a study by Pierce and Hanks (Pierce and Hanks 2006) to determine which components of the ICF are most predictive of global life satisfaction after TBI, restriction of participation in life activities was found to have the greatest impact. Larsson Lund et al. found that perceived participation and problems with participation are determinants of life satisfaction in people with spinal cord injury (Lund et al. 2007).

It is generally assumed that improved function in activities creates better subjective well-being. It is noteworthy that Johnston et al. found a lack of association between frequency of activities and subjective appraisals (Johnston et al. 2005), which means that a higher frequency of activities does not necessarily make patients happier. Correlations between activity-specific satisfaction and general life satisfaction were generally weak and non-significant in their study (Johnston et al. 2009). Dissatisfaction with an activity correlated strongly with a desire to change the activity, but general life satisfaction did not correlate with a desire to change activities. These relationships cannot be assumed and should be assessed on more of an individual level. Gurin et al. stated that a person has to fulfil the demands internalised roles impose upon him or her to become satisfied (Gurin 1960) and Mailhan et al. found that satisfaction with life is not linearly related to disability after severe TBI (Mailhan et al. 2005). We found the same tendency in Study IV. This might explain why the participant who obtained very high scores on the GOSE in Study II was less satisfied at five years, as compared with those with lower scores.

Another finding in Study II was that the participant with the most severe behavioural problems was the one that was most satisfied with contact with friends, partnership, family life and leisure situation. This is in agreement with other studies. Elsass and Kinsella found that the patients themselves were not distressed by a decrease in social contact (Elsass and Kinsella 1987) and Kersel et al. found no obvious relationship between the prevalence of a behavioural problem and the degree of distress associated with it (Kersel et al. 2001).

Satisfaction with the different life domains changed over time, as well as satisfaction with life as a whole. A negative trend can be related to a growing awareness of the consequences of the brain injury for the future (Prigatano 2005) and the lapse between demands and function. Rehabilitation does not necessarily make people happy, although the intention is to guide the patients to set realistic goals. Other life events naturally also have an impact on satisfaction with life as a whole. It was not at all surprising to find that satisfaction with life as a whole and for most other items in Studies II and III was lower compared with a normal Swedish population. It was, however, surprising and pleasing to find that around 80% of those who were able to convey their opinion rated life as a whole as satisfactory in Studies II, III and IV.

As important changes, for better and for worse, took place for individuals, even if they were not statistically significant at group level, a longer period of follow-up than the commonly presented “one-year studies” for patients with severe injuries is warranted.

## CONCLUSIONS

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The availability of rehabilitation for patients with severe brain injuries differs in different parts of the Västra Götaland Region.

Early rehabilitation and a continuum of care results in shorter hospital stays in overall terms after traumatic brain injury and subarachnoid haemorrhage. The outcome was better for those who received early formalised rehabilitation and a follow-up as compared with late or no rehabilitation.

In a five-year follow-up study, the change at group level was significant, as measured with the GOSE, until one year after the injury, but important changes were found for the individuals until five years. The participants were most satisfied with “life as a whole” at the one-year assessment.

A group of patients who were treated with decompressive craniectomy after malignant media infarction remained in an impaired neurological condition but had a fairly good insight into their limitations.

An effective chain of medical and rehabilitation activities can produce acceptable outcome after severe brain injury, as life as a whole can be satisfactory for the majority of patients in spite of neurological deficits and dependence on others. Their life satisfaction scores (for those who were able to fill in the LiSat-11 form) were, however, lower compared with those of a set of reference material.

## CLINICAL IMPLICATIONS AND FURTHER STUDIES

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Although most patients have a favourable outcome, the numbers of persons who survive after severe brain damage with persisting neurological, emotional and intellectual deficits after brain injury is huge. The demand for professional rehabilitation has increased.

Some of the advances in rehabilitation include the task-specific training of cognitive deficits, virtual reality training, computer-aided cognitive remediation and body weight-supported treadmill training for motor deficits. It is also important to find good methods to study when and which of the more traditional interventions are most effective, in order to distribute the resources to as many individuals as possible. There is promising evidence of improved outcome and functional benefits with early induction into a transdisciplinary or interdisciplinary brain injury rehabilitation programme. Still little is known about how to optimise recovery by stimulating the modulation of the brain via neuroplastic mechanisms. We need more knowledge about the way in which persons with severe brain injuries adapt to their new life and benefit from the most effective early and late rehabilitation programmes not only according to the specific training methods. However, TBI research is fraught with difficulties because of an intrinsically heterogeneous population due to age, injury severity and type, functional outcome measures and small samples. Randomised, controlled studies do not always answer the questions and are sometimes impossible to conduct because of ethical dilemmas. More controlled studies are thus needed.

We need to focus more on the components of activity, participation and environmental factors in combination with the patient's subjective opinion and wishes. More studies of home rehabilitation from these aspects are needed.

Decompressive craniectomy is a life-saving treatment, but the "syndrome of the trephined", the long-term outcome and adaptation process are still not very well described. Quality of life is multidimensional. Conclusions from outcome data, relating solely to body functions, activity or participation, have limitations. We are waiting for the results of the ongoing RCT studies of TBI and it is necessary to take account of the patients' own opinion of living with severe neurological deficits. Assessing the most severely injured victims about their opinion is not possible using the instruments available at the moment. It is to be hoped that studies with a qualitative design and/or studies with functional MRI will give us more information.

The assessment of residual brain function in the vegetative state is extremely difficult and depends frequently on interpretations of observed behaviors. As the studies in this thesis show, there is a low incidence of patients who remain in a vegetative state. Nevertheless, there is work to be done to standardise and develop guidelines for the assessment procedures and treatment.

I hope that, in the future, these struggling patients will receive not only the initial neurosurgical treatment and intensive medical care but also sufficient rehabilitation, regardless of where they live.

## SWEDISH SUMMARY

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Att drabbas av en svår hjärnskada får konsekvenser för resten av livet. En svår hjärnskada påverkar hälsan såsom kroppens funktioner, aktivitetsförmågan och förmågan att vara delaktig i olika sammanhang. Andra faktorer av betydelse för hur hälsotillståndet blir efter en skada är personliga faktorer, hur man fungerar och vad man har för egenskaper innan skadan samt omgivningsfaktorer såsom t ex familjesituation och den fysiska miljön. Även om återhämtningen kan vara god även efter en svår hjärnskada blir livet sällan sig helt likt. Omhändertagandet vid det akuta insjuknandet/skadan, den akuta medicinska behandlingen, rehabiliteringen och stöd från sjukvården upp till flera år efter skadan spelar roll för återhämtningen. Det medicinska omhändertagandet i akutskeendet har förbättrats så att flera överlever svåra skador utan mycket svåra resttillstånd. Rehabilitering spelar en viktig roll för att minska konsekvenserna av sjukdom eller skada och påbörjas allt tidigare i förloppet. Det tar olika lång tid för olika individer att anpassa sig, lära sig leva under de nya förutsättningarna. Detta påverkar individens livskvalitet och livstillfredsställelse. Att ha ett omfattande resttillstånd efter en skada behöver inte betyda att livstillfredsställelsen blir dålig. För att bedöma olika tillstånd före och efter en skada, följa återhämtningen och utvärdera olika behandlingsmetoder har standardiserade utvärderingsinstrument konstruerats.

Syftet med denna avhandling var att undersöka resultat och mäta återhämtning efter svår hjärnskada då behandlingsmetoder införts under de senaste två decennierna såsom tidig rehabilitering och dekompressiv kraniektomi. Med dekompressiv kraniektomi menas att en del av skallbenet opereras bort för att ge mer plats för hjärnan som svullnat efter skadan. Operationen görs när svullnaden blir så kraftig att den är livshotande. Skallbenet eller en protes läggs tillbaka i ett senare skede när svullnaden försvunnit. I första hand har den psykosociala återhämtningen och patienternas livskvalitet och livstillfredsställelse undersökts i delstudierna. Ytterligare ett syfte var att undersöka tillgången till kvalificerad specialistrehabilitering i Västra Götalandsregionen för de som drabbats av en svår hjärnskada.

Förutom att genomgångar av sjukhusjournalerna gjordes, användes ett antal olika standardiserade mätinstrument/formulär i de olika delstudierna.

En jämförelse gjordes mellan en grupp patienter med svår traumatisk hjärnskada eller subaracknoidalblödning (blödning under den hårda hjärnhinnan) som fått tidig specialistrehabilitering (påbörjad inom 50 dygn) samt långsiktig uppföljning, och en grupp patienter som fått sen eller ingen specialistrehabilitering alls.

Den grupp som fått tidig rehabilitering följdes också upp regelbundet upp till 5 år efter skadan.

För att ta reda på hur det gått för patienter som behandlats med kraniektomi pga svår stroke, malign mediainfarkt (stopp i ett av hjärnans större blodkärl) gjordes hembesök till en grupp patienter när minst ett år förflutit efter skadan (varierande mellan 1-6 år). Patienterna undersöktes och de närstående, eller i vissa fall personliga assistenter, fick fylla i diverse formulär.

Ett år efter skadan skickades formulär angående återhämtning och livstillfredsställelse ut till patienter som behandlats med dekompressiv kraniektomi pga olika skador/sjukdomar under perioden under mars 2003 till juli 2006 på Sahlgrenska Universitetssjukhuset. Vi undersökte också hur många som fått specialistrehabilitering.

Gruppen som fått tidig specialistrehabilitering och långsiktig uppföljning återhämtade sig bättre än den som fått sen rehabilitering. Färre patienter hade ett mycket svårt restillstånd i den gruppen, fler var oberoende (kunde klara sig helt själva) och fler arbetade jämfört med de som fått sen eller ingen rehabilitering alls.

Långtidsuppföljningen visade att återhämtningen på gruppnivå var störst och statistiskt signifikant under första året efter skadan men att betydelsefulla förändringar kunde ske för individerna under hela 5-årsuppföljningen. Livet i allmänhet skattades ”tillfredsställande” i ngn grad (”ganska – mycket tillfredsställande”) av 80% av de individer som kunde svara på frågor eller själva fylla i formuläret om livstillfredsställelse.

Uppföljningen av patienter med malign mediainfarkt som behandlats med kraniektomi visade att de drabbade hade lägre hälsorelaterad livskvalitet än normalbefolkningen. Det var ingen signifikant skillnad mellan hur de närstående skattade den skadades hälsorelaterade livskvalitet och vad patienterna själva angav. Trots att de levde med omfattande neurologiska skador så skattade 83% livet i allmänhet som tillfredsställande.

Ettårsuppföljningen av de som behandlats med dekompressiv kraniektomi visade att de flesta (90%) hade fått specialistrehabilitering. Tjugo procent hade återhämtat sig mycket väl. Av de som kunde skatta sin livstillfredsställelse angav 88% att livet i allmänhet var tillfredsställande.

Tillgången till specialistrehabilitering efter svår hjärnskada varierar i olika delar av Västra Götalandsregionen. En effektiv vårdprocess med modern medicinsk behandling, tidig rehabilitering och långsiktig uppföljning resulterar i bättre återhämtning och livet kan upplevas tillfredsställande även efter en svår hjärnskada med omfattande restillstånd.

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