Energy Balance out of Balance after Severe Traumatic Brain Injury

KAROLINA KRAKAU
Dissertation presented at Uppsala University to be publicly examined in Robergsalen, A40, Akademiska sjukhuset, ingång 40, 5 tr., Uppsala, Thursday, March 25, 2010 at 13:00 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

The overall aim of the research presented here was to expand the knowledge on metabolic course and nutritional outcome in patients with severe traumatic brain injury and to analyze the use and accuracy of different methods of assessment.

Study I, a systematic review of 30 articles demonstrated consistent data on increased metabolic rate, of catabolism and of upper gastrointestinal intolerance in the majority of the patients during early post injury period. Data also indicated a tendency of less morbidity and mortality in early fed patients.

Study II, a retrospective survey, based on medical records of 64 patients from three regions in Sweden, showed that the majority of patients regained their independence in eating within six months post injury. However, energy intake was set at a low level and 68 % of the patients developed malnutrition with 10 to 29 % loss of initial body mass during the first and second month post injury.

Study III, a questionnaire based study addressed to 74 care units caring for patients with severe traumatic brain injury showed that resources in terms of qualified staff members were reportedly good, but nutritional guidelines were adopted in less than half of the units, screening for malnutrition at admission was rarely performed and surveillance of energy intake declined when oral intake began. Moreover, assessment of energy requirements relied on calculations and the profession in charge to estimate energy requirement varied depending on nutritional route and unit speciality. At transferral between units nutritional information was lost.

Study IV and V, a prospective descriptive study on metabolic course, energy balance and methods of assessment in six patients showed that patients were in negative energy balance from 3rd week post injury and lost 8-19 % of their initial body weight. Concurrent nutritional problems were difficulties in retaining enteral and/or parenteral nutrition delivery routes until oral feeding was considered satisfactory. The majority of methods for predicting energy expenditure agreed poorly with measured energy expenditure. The Penn-State equation from 1998 was the only valid predictive method during mechanical ventilation.

This thesis concludes that patients with moderate or severe traumatic brain injury exhibit a wide range of increased metabolic rate, catabolism and upper gastrointestinal intolerance during the early post-injury period. Most patients regain independence in eating, but develop malnutrition. Suggested explanations, other than the systemic disturbances early post injury, could be the use of inaccurate predictions of energy expenditure, deficient nutritional routines and difficulties in securing alternative nutritional routes until oral feeding is satisfactory. The impact of timing, content and ways of administration of nutritional support on neurological outcome after a severe traumatic brain injury remains to be demonstrated.

Keywords: Energy expenditure, Traumatic brain injury, Metabolism, Nutrition

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To our patients
LIST OF PUBLICATIONS

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.

I  *Metabolism and nutrition in patients with moderate and severe traumatic brain injury: A systematic review.*
Krakau, K., M. Omne-Ponten, T. Karlsson, and J. Borg,

II  *Nutritional treatment of patients with severe traumatic brain injury during the first six months after injury.*
Krakau, K., A. Hansson, T. Karlsson, C.N. de Boussard,
C. Tengvar, and J. Borg,
Nutrition, 2007. 23(4): p. 308-17 *

III  *Resources and routines for nutritional assessment of patients with severe traumatic brain injury.*
Krakau, K., A. Hansson, A. Ödlund Olin, T. Karlsson,
C.N. de Boussard, and J. Borg,
Scand J Caring Sci. In press *

IV  *Energy balance and metabolism after severe traumatic brain injury; a pilot study using doubly labelled water.*
Krakau, K., L. Ellegård, B.M. Bellander, T. Karlsson,
C.N. de Boussard, M. Karlsson and J. Borg,
Manuscript

V  *Prediction of energy expenditure in patients with severe traumatic brain injury – a validation study by use of continuous indirect calorimetry and doubly labelled water.*
Krakau, K., L. Ellegård, B.M. Bellander, T. Karlsson,
C.N. de Boussard, and J. Borg,
Manuscript

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by
Mattias Krakau
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ABBREVIATIONS

AEE Activity Energy Expenditure
ATP Adenosine Triphosphate
BMI Body Mass Index
BMR Basal Metabolic Rate
BW Body Weight
cal Calorie
CO₂ Carbon dioxide
DLW Doubly Labelled Water
EE Energy Expenditure
ES-PEN European Society of Clinical Nutrition and Metabolism
FIM Functional Independence Measure
GCS Glasgow Coma Scale
GOS Glasgow Outcome Scale
²H Deuterium
IC Indirect Calorimetry
IL Interleukin
IR Interquartile Range
J Joule
kcal Kilocalories
MUST Malnutrition Universal Screening Tool
n Number
N Nitrogen
O₂ Oxygen
¹⁸O Oxygen-18
PEG Percutaneous Endoscopic Gastrostomy
REE Resting Energy Expenditure
RLAS-R Rancho Los Amigos Cognitive Scale Revised
RLS85 Reaction Level Scale 85
SD Standard Deviation
SIRS Systemic Inflammatory Response Syndrome
SWA SenseWear Armband
TEE Total Energy Expenditure
TEF Thermic Effect of Feeding
TNF-α Tumor necrosis factor-alpha
1. INTRODUCTION

Clinical observations

I work as a registered nurse at a rehabilitation unit for patients with severe brain injuries. One of my responsibilities is to see to it that the patients receive adequate nutrition. The term “adequate” includes many different aspects determined by the needs of the patient and hold many challenges. The normal regulation of hunger may no longer function. Even if it does, the patient may not be able to express it. To administer nutrition may also be difficult as some patients are easily stressed by discomfort, e.g. by tubes. When the recovery of the patient advances, care has to be taken due to difficulties in eating – the patient may not be able to chew and swallow correctly or it may be hard to see what’s on the plate or to interpret the situation during a meal. The senses of taste and smell may also be altered.

What started this project was from the observation that patients with severe brain injury very rapidly lost weight. Also, patients were exposed to many different infections and their length of stay at the hospital tended to be fairly long; matters that partly could be explained by consequences of malnutrition. Malnutrition was however very seldom diagnosed in the medical records. Also, estimations of energy requirements seemed unreliable as the body weight of the patient continued to diverge even though nutritional goal was achieved. It was not possible to evaluate if this problem was unique for our department alone. Studies reporting on this subject were mainly from the U.S., but no national data was available. Further, the possible influence of malnutrition on neurological recovery was far from clear. Thus, I wanted to explore this field more closely to see what we should do to reduce the risk of malnutrition and maybe also to improve the recovery of the patients.
1.1 Traumatic brain injury

1.1.1 Incidence
A traumatic brain injury (TBI) occurs when mechanical energy to the head from external physical forces injures the brain. The annual incidence of patients hospitalized for TBI is around 200-300 per 100,000 inhabitants or more [1-6]. In children and elderly, the most common injury mechanism is fall, while in adolescents and adults (15-64 years) vehicle-related events dominate followed by falls with a men-to-women ratio of about 2:1 [6] and often under the influence of alcohol [4, 5]. Incidence peaks occurs at the ages of 16-20 and above 65 years of age [1].

1.1.2 Severity
The severity of TBI is classified as mild, moderate or severe depending on the initial level of consciousness, which is most often scored by use of the Glasgow Coma Scale (GCS) [7]. The total GCS score is determined by the reaction to defined stimuli with regard to eye opening, verbal response and motor response. The proportion of patients within each of these severity categories varies between studies, but the vast majority of patients, 70-90 % are diagnosed with a mild TBI (GCS score 13-15), around 10 % with a moderate TBI (GCS score 9-12) and less than 5 % with a severe TBI (GCS 3-8) [1, 2, 4, 5, 8-10]

1.1.3 Primary and secondary injury
Once the patient is subjected to the primary injury, secondary processes start (e.g. blood flow disturbances, inflammation, production of reactive free radicals and oedema formation [3]). Systemic events, e.g. hypotension, infections and insulin resistance interact and may result in secondary injuries of the brain. Thus, prognosis of TBI is not only dependent on the initial severity based on GCS:score, but also on avoidable factors described in Figure 1. When planning the nutritional treatment of the patient, caution needs to be taken to these factors.
1.1.4 Advancements of outcome

It was already in the late seventies reported that prevention and treatment of secondary events, such as epileptiform seizures, high intracranial pressure and fever, improves clinical outcome [11]. The prehospital and neurosurgical intensive care have achieved major advancements since then. In patients subjected to a moderate or severe TBI, mortality rates have decreased from 40% (pre-neurosurgery period) to 27% (basal neurosurgery period) to 2.8% (secondary insult program) and more patients recover with favourable outcome [12]. The relative risk for morbidity and mortality also seems to be reduced in early fed patients compared to patients given standard nutritional treatment [13, 14]. In addition, early formalized neurorehabilitation improves outcome even further compared to late initiation or unformalized rehabilitation [15-18]. Thus, maximized functional recovery in patients with moderate to severe TBI is favoured by standardized programs designed to prevent specific avoidable events and to include early neurorehabilitation.
"In addition to the demands placed on the brain, the body suffers a systemic metabolic response. Thus, the patient must overcome two insults – those of the brain and the overall systemic response”  Linda Ott and Byron Young [19] pages 223-224.
1.2 Systemic metabolic response

1.2.1 Metabolic response to trauma

The metabolic response to trauma is mediated by different body systems. It includes the nervous system, the endocrine system and the inflammatory response as described in Table 1. These systems interact to increase oxygen and energy supply for vital organs, to mobilize the substrates and mechanisms needed to prevent infection and activate repair processes. The magnitude of the metabolic response is generally proportional to the severity of the trauma, but also to secondary complications (e.g. infections) and treatment interventions (e.g. surgery).

**Table 1.** The inflammatory and neuro-endocrine response to trauma

<table>
<thead>
<tr>
<th>Mediators of the metabolic response to trauma</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Postganglionic neurons</td>
<td>↑ Norepinephrine</td>
</tr>
<tr>
<td>Pituary gland</td>
<td>↑ Adrenocorticotropic hormone</td>
</tr>
<tr>
<td></td>
<td>↑ Antidiuretic hormone</td>
</tr>
<tr>
<td></td>
<td>↑ Growth hormone</td>
</tr>
<tr>
<td>Suprarenal gland</td>
<td>↑ Epinephrine</td>
</tr>
<tr>
<td></td>
<td>↑ Cortisol</td>
</tr>
<tr>
<td></td>
<td>↑ Aldosteron</td>
</tr>
<tr>
<td>Macrophages</td>
<td>↑ Cytokines (IL-1, IL-6, TNF-α)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>↑ Glucagon</td>
</tr>
<tr>
<td></td>
<td>↑ Insulin</td>
</tr>
</tbody>
</table>

*Sources: Adapted from various sources [20-22].*
The unmodified response to a major trauma is characterized by two phases; the ebb and flow phase. Ebb phase, or shock phase, comprises the immediate period after injury and is associated with hypovolemia and tissue hypoxia. The following flow phase includes both the acute response when catabolism predominates and the adaptive response when anabolism predominates. During acute phase (Table 2), cardiac output and metabolic rate is increased. To secure the supply of glucose (vital for the brain) and mobilize the substrates needed for defense and repair, metabolism is redirected to accelerate proteolysis, gluconeogenesis and lipolysis. In addition, target cells become insulin resistant and hyperglycemia is observed. Acutely, the shock and acute response serves to protect the individual, but with prolonged and sustained hypermetabolism, the patient can develop Systemic Inflammatory Response Syndrome (SIRS) with risk for multiple organ failure [22].

Table 2. The acute response during flow phase

<table>
<thead>
<tr>
<th>Acute response to trauma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemic effect</td>
</tr>
<tr>
<td>Cardiac output</td>
</tr>
<tr>
<td>H₂O retention</td>
</tr>
<tr>
<td>Metabolic rate</td>
</tr>
<tr>
<td>Muscle catabolism</td>
</tr>
<tr>
<td>Glycogenolysis</td>
</tr>
<tr>
<td>Gluconeogenesis</td>
</tr>
<tr>
<td>Lipolysis</td>
</tr>
<tr>
<td>Acute-phase protein synthesis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>At site of injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood flow</td>
</tr>
<tr>
<td>Inflammation</td>
</tr>
<tr>
<td>Oedema</td>
</tr>
</tbody>
</table>

Sources: Adapted from various sources [20-22].

1.2.2 Nutritional treatment goal during catabolism

The protein breakdown depends not only on the hormonal situation, but also on nutritional intake, *i.e.* catabolism increases if energy intake is less than the energy expended and if protein intake is sparse. The goal of nutritional support is therefore to minimize starvation and catabolism by providing adequate nutrition meeting the protein and energy needs, preventing or correcting fluid imbalance and any specific nutrient or electrolyte deficiency.
1.2.3 Metabolic response to severe TBI

It was in the early 1980:s that attention first was drawn to the concerns of the increased metabolism and catabolism in patients with severe TBI. High metabolic rates of varied degree [23-34] and depletion of protein stores, comparable with those seen in patients with multiple injuries or burns were reported [35]. The impaired immune system identified in patients with severe TBI [36] may well be a consequence of the metabolic strains.

The levels of counterregulatory hormones increased with severity of injury [37-39]. High levels of cytokines [40] were identified and have been confirmed as probable mediators of the metabolic response (Table 1). Different factors were investigated to distinguish which, apart from the brain injury itself, contributed to the increased metabolic rate. There seemed to be no added effect by accompanied non-cranial injuries [41], minor effect by the thermic effect of feeding [42] and significant effect due to sepsis and increased body temperature [43] while metabolic downregulation was observed by sedatives [39, 42, 43]. Thus, many factors interact but their impact on energy expenditure is not possible to foresee on individual basis. Repeated measurements of the metabolic rate are necessary to guide the nutritional treatment. Furthermore, these patients may have problems with gastric emptying and swallowing [44-46]. Without assessment to assure adequate function of the gastrointestinal system, the nutritional route may lead to aspiration and pneumonia.
1.3 Malnutrition

1.3.1 Definition
Malnutrition means faulty nutrition and implies deviations from normal nutrition. There is no universal agreement upon definition, but the following has been suggested.

“Malnutrition is a state of nutrition in which a deficiency or excess (or imbalance) of energy, protein, and other nutrients causes measurable adverse effects on tissue/body form (body shape, size and composition) and function, and clinical outcome.” Marinos Elia 2000, [47], page 3.

Thus, malnutrition arises from a wide range of conditions and its development, characteristics and treatment vary due to its cause (over- or undernutrition, primary or secondary), the type of nutrients involved (macro- or micronutrients, single or multiple nutrients), its severity (subclinical, mild, moderate or severe) and due to the age of the person (adult or child) [47].

1.3.2 Consequences of Protein Energy Malnutrition
Protein Energy Malnutrition, secondary to disease, is the most common form of undernutrition and is a well recognized health problem in European hospitals [48-62]. With its detrimental effects on physiological function and clinical outcome (Figure 2), major efforts in the prevention of malnutrition have been accomplished. Guidelines developed by the European Society of Clinical Nutrition and Metabolism (ESPEN), initiated by the European Council [63-65] form the basis for the Swedish nutritional guidelines [66, 67]. According to these, all patients should be screened for nutritional risk when admitted to hospital. Indicators used are e.g. body mass index (BMI) combined with recent weight loss and information on eating difficulties.

In patients exposed to or in danger of developing malnutrition, the multiple causes should be investigated and followed by a treatment plan where dietary goals and measures taken are defined. Different staff categories should be clearly assigned with respect to nutritional care and information on the nutritional treatment process should proceed to the next caregiver.
Figure 2. Effects on physiological function (middle circle) and clinical outcome (outer circle) from protein energy malnutrition in adults. The illustration is based on the extensive clinical database on prevalence and treatment of disease related malnutrition by Rebecca Stratton, Ceri Green and Marions Elia [68].
1.4 Energy expenditure

1.4.1 Calorimetry
To determine the energy balance over time, energy intake and energy expenditure needs to be measured. Calorimetry is the science of measuring heat from chemical reactions or physical changes and the unit for heat production is joule, but in nutritional literature the calorie concept is more commonly used \( (4.184 \text{ J} = 1 \text{ cal}) \). To measure the generated heat directly from a person, he needs to stay in an isolated chamber or wear a calorimeter suite. Thus, direct calorimetry gives information on the energy expended in an artificial setting and very little information on the true energy expended during normal living conditions. Moreover, it is not possible to apply in a hospital setting when frequent attending of the patient is needed. Instead, some indirect techniques are used.

Energy expenditure is then calculated from the measured oxygen consumption and/or carbon dioxide production. This is possible due to the fact that there is a constant relationship between the amount of oxygen \( (O_2) \) consumed and carbon dioxide \( (CO_2) \) produced in the production of chemical energy \( (\text{adenosine triphosphate (ATP)}) \). By knowing this relationship and the caloric equivalent of our fuels; glucose, lipid and protein, the energy equivalent for \( O_2 \) and \( CO_2 \) is derived. However, the combustion of protein is incomplete; nitrogen is excreted from the body via the urine, skin and stool. Withdrawals are therefore made by the formula used to calculate energy expenditure, the Weir equation \([69]\). Thus, indirect calorimetry is rather a measure of the production of chemical energy, than of the energy expended as heat, but the convention is to describe this quality as the energy expended. Although, both the doubly labelled water technique and measurements of pulmonary gas exchange are indirect methods, it is the latter that is referred to when “indirect calorimetry” is mentioned.

1.4.2 Indirect calorimetry
Assessments of pulmonary gas exchange \( (\text{of } O_2 \text{ and } CO_2) \) are available for continuous measurement at bedside in both mechanically ventilated and spontaneously breathing patients. Expired air is collected in different ways, e.g. directly from the tracheal tube, from a mouth-piece or from a canopy placed
over the head of the patient. The accuracy of indirect calorimetry measurements are dependent on patient, environment and equipment variables, thus careful attention to preparations and technical factors are necessary [70]. With indirect calorimetry, different levels of energy expenditure are measurable; the basal metabolic rate (BMR), resting energy expenditure (REE) and total energy expenditure (TEE). BMR is the amount of energy expended after twelve hours of (overnight) fasting, while at rest and in a neutral temperature environment. It reflects the minimal compound of energy consumed to sustain normal function of vital organs and homeostasis of the body. REE measurements are also done at rest after an overnight fast, but light physical activity is allowed prior to measurements, and REE is hence slightly higher than BMR [70]. If continued for 24 hours, indirect calorimetry can provide a quantification of TEE. Thus, in addition to BMR or REE, TEE includes components for thermic effect of feeding and for the energy expended in physical activity, as delineated in Figure 3.

![Figure 3. The energy components of total energy expenditure (TEE) in adults. Resting energy expenditure (REE) contributes with the majority of energy expended and varies with age, gender, body mass and body composition while the thermic effect of feeding (TEF) is relatively constant at ~10%. The activity energy expenditure (AEE) is the most dynamic component and range from sedentary living to extreme athletic levels of physical activity [21, 70].](image)

1.4.3 Doubly labelled water

The doubly labelled water technique is the golden standard to measure TEE and gives information on TEE over a period of 2-3 weeks. At onset, the patient receives a defined amount of stable isotopes deuterium (²H) and oxygen-18 (¹⁸O) to drink. The CO₂ production is then estimated from the difference in elimination rate of the two isotopes, analyzed from urine samples. This is possible as ²H is eliminated from the body as water while ¹⁸O is eliminated as both water and carbon dioxide. The difference between the elimination rates of the two isotopes is a measure of CO₂ production. TEE can then be determined from the energy equivalent of CO₂ [71].
1.4.4 SenseWear Armband

A possible approach to approximate TEE is said to be by the use of a portable metabolic monitor, the SenseWear Armband, worn on the upper arm of the patient where it records physiological body signals; skin temperature, near body temperature, rate of dissipated heat, galvanic skin response and physical movement of the patient (2-axis accelerometer). These data and constitutional and behavioural data (age, body height, body weight, sex, handedness and smoking habits) enter an algorithm in the computer software, which calculates physical activity parameters, including the TEE. Different versions of this monitor and of its software have been developed over time. However, the results from studies on the validity of TEE data obtained by such monitoring are not conclusive [72-85] and only a few of these consider the specific impact of various diseases [78, 85].

1.4.5 Predicting energy expenditure

In the absence of technical equipment for assessment of energy expenditure it may be predicted from different formulas. These are manifold, but one of the oldest, the Harris & Benedict equation [86] developed early in the 20th century and based on data from healthy subjects, is still frequently used despite inaccurate predictions both during the early period in critically ill [87] and during the first couple of months after a severe TBI [88]. This calculation includes gender, age, body weight and height of the individual.

1.4.6 Hyper- and hypometabolism

The REE/BMR ratio expresses the metabolic rate and defines the magnitude of hyper- or hypometabolism. In most studies the Harris & Benedict equation is used as the standard for BMR against which REE measurements are compared. For hypermetabolism, different cut-off values are seen in literature, either the 1.1 or the 1.3 quote, i.e. if measured REE is ≥10 % or ≥30 % above the predicted BMR this is defined as hypermetabolism. Hypometabolism is defined as any REE/BMR ratio < 1.0.
2. AIMS OF THE THESIS

The general aim of the work presented in this thesis was to expand the knowledge on metabolic course and nutritional outcome in patients with severe TBI and to analyze the use and accuracy of different methods of assessment; a basis necessary for future intervention studies.

The specific aims of the five studies included were:

I  to examine the evidence on the metabolic state and nutritional support in patients with moderate and severe TBI.

II to describe the current nutritional treatment policies and nutritional outcome in patients with severe TBI up to six months post injury or until the patients were independent in nutritional administration.

III to delineate the resources and routines for nutritional management until six months after severe TBI.

IV to explore the course of energy balance in patients with severe TBI, from time of injury until twelve weeks post injury.

V to evaluate the accuracy of methods to predict energy expenditure in patients with severe TBI.

Each paper presents the questions asked more in detail.
3. METHODS

3.1 Study designs and selection procedures

Study I
To examine the evidence a systematic review of the literature overlooking the period 1993-2003 was carried out (I). Selection procedure of studies followed three steps:

1. From the computerized and manual search (1547 titles/abstracts), studies on nutritional and/or systemic metabolic status of human adults with acquired brain injury were selected (232 studies).
2. These were reviewed in full text with regard to specific inclusion criteria (presented in paper I); 36 studies were selected.
3. The included articles were then assessed for quality according to a standardized protocol assessing scientific merits, clinical relevance, key results and conclusions; 30 articles were accepted.

All studies related to one or more of the study questions. Some data were presented in more than one article. Twenty of the articles concerned the hypermetabolic/catabolic status of patients with TBI [14, 39, 41-44, 89-102], twelve articles concerned the upper gastrointestinal function [14, 44, 93, 98, 103-110] and two reviews [14, 111] and seven trials [93-99, 109, 112] concerned the effect of nutritional treatment.

Study II and III
To delineate nutritional treatment policies, nutritional outcome (II) resources and routines for nutritional management (III) a retrospective descriptive study of medical records combined with questionnaires to the care units involved was conducted.

Selection procedure of patients (II, III):
- All patients with severe TBI, 16 to 64 years old and admitted to Neurosurgical Intensive Care at three regional hospitals (Stockholm, Uppsala and Gothenburg), between 1/7/2003 and 30/6/2004, a total of 111 patients, were considered for the study. When screened for exclusion criteria (presented in paper II) 84 patients remained to be contacted and 64 chose to participate.

For patient characteristics, see Table 3 or Paper II.
Selection procedure of care units (III):
- All care units where the 64 patients had been treated during the first six months post injury or until they were independent in eating (a total of 81 care units in 38 different hospitals) were asked to participate. Seventy-eight units accepted.

From 226 questionnaires directed to three professional categories per unit, distributed between March and July 2005, 161 were returned from 74 units; 61 answered by registered nurses, 52 by nursing assistants, 44 by physicians and 4 unknown. Fifty of the respondents worked at intensive care units, 68 at mixed wards (surgical, orthopaedic, neurological, stroke units and nursing home), 39 at rehabilitation units and 4 were from unknown units. To view the questionnaire, see appendix.

**Study IV and V**
To explore the energy balance during recovery from severe TBI (IV) and to evaluate methods to assess energy expenditure (V), a prospective descriptive study of a small cohort was conducted.

Selection procedure of patients (IV, V):
- All patients, 16 to 64 years old, admitted to the Neurosurgical Intensive Care at Karolinska University Hospital between Sept-2007 and Feb-2009, with an isolated, closed, severe TBI and citizens of Stockholm were eligible. Inclusion also required a computed tomography examination according to trauma protocol, a probable survival and informed consent from closest relative. Twenty three patients met these criteria. Exclusion criteria were prior metabolic disease ($n = 3$) and an expected need for in-hospital care of less than 2-3 months due to fast recovery ($n = 14$). Six patients were left for inclusion. Patient characteristics are demonstrated in Table 3 and in Paper IV and V.

Selection procedure of controls (IV, V):
- One of the measuring techniques required controls. Eligible were contemporary patients with severe brain injury (vascular insults or trauma) with informed consent from closest relative. Three patients were included.
Table 3. Demographic data on the patients included in studies II-V

<table>
<thead>
<tr>
<th></th>
<th>Study II-III</th>
<th>Study IV-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>64</td>
<td>6</td>
</tr>
<tr>
<td>Age (mean±SD)</td>
<td>35±15.7</td>
<td>37±16.7</td>
</tr>
<tr>
<td>Women (n)</td>
<td>11</td>
<td>3</td>
</tr>
<tr>
<td>Men (n)</td>
<td>53</td>
<td>3</td>
</tr>
<tr>
<td>Body weight (mean kg±SD)</td>
<td>75±12.6</td>
<td>74±15.1</td>
</tr>
<tr>
<td>BMI (mean kg/m² ±SD)</td>
<td>24±4.3</td>
<td>24.5±3.7</td>
</tr>
<tr>
<td>GCS 3-5 (n)</td>
<td>29</td>
<td>5</td>
</tr>
<tr>
<td>GCS 6-8 (n)</td>
<td>35</td>
<td>1</td>
</tr>
</tbody>
</table>

3.2 Ethical considerations

Patients, closest relative or authorized representative were informed about the research both in writing and orally. Confidentiality was assured and it was emphasized that withdrawal at any time, or refusal to participate in the studies would have no effect on treatment. Names and telephone numbers on research members were clearly presented. Questionnaires used to members of the staff (III) were anonymous.

The studies (II – V) were approved by the Regional Ethical Review Board of Uppsala University.

Informed consent from unconscious patients (IV, V)

Patients with severe TBI, while unconscious, are dependent on others to make decisions on their behalf. During recovery, altered ability to communicate, interpret or remember may prolong this dependency, thus, close family members and friends are extremely important interpreters of personality and desires of the patient. However, at time of injury, even family members may be incapable to apprehend information. Making decisions on behalf of the patient may also be very burdensome. Thus, prior to contact, the physician in charge determined the appropriateness for contact.

Information directed to the patient was adjusted to their current cognitive level, beginning with a brief presentation repeated at each contact to enable the possibility to deny participation. When patients were ready to comprehend a larger amount of information, this was presented orally and on paper, sometimes using both text and pictures for clarity.

Informed consent after hospital stay (II, III):

As this was a retrospective study, patients had already completed their hospital stay. Prior to contact, information on current need for assistance was obtained. Patients were then contacted either directly with a letter and phone call or indirectly by an authorized representative.
3.3 Measurements and definitions

An overview of the data collection is presented in Table 4. Below follow more detailed information on definitions and measuring methods used.

Table 4. Overview of the data collected to the five studies

<table>
<thead>
<tr>
<th>Study design</th>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
<th>Study V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Systematic literature review</td>
<td>Retrospective descriptive study</td>
<td>Questionnaire-based descriptive study</td>
<td>Prospective descriptive study</td>
<td>Prospective descriptive study</td>
</tr>
<tr>
<td>Data collection: source and context</td>
<td>From 30 articles published between 1993 and 2003.</td>
<td>From patient records of 64 patients from time of injury until the patients became nutritionally independent or, if not, until six months post injury.</td>
<td>From 161 questionnaires addressed to professional staff caring for patients with severe TBI during acute and recovery phase and from medical and nursing records of patients with severe TBI.</td>
<td>From patient records and measurements of 6 patients from time of injury and during recovery.</td>
<td>From patient records and measurements of 6 patients during mechanical ventilation and at 3rd to 5th week post injury.</td>
</tr>
<tr>
<td>Data collection: type of data</td>
<td>Data on hypermetabolism, catabolism and upper gastrointestinal dysfunction and data on effects of different timing, content and way of administration of nutritional treatment.</td>
<td>Data on duration of parenteral, enteral nutrition and assisted feeding, gastrostomy, energy intake, basal metabolic rate, body weight, possible important factors for malnutrition and neurologic recovery.</td>
<td>Data on personnel resources, nutritional guidelines, nutritional screening methods, personnel assignments, energy intake recordings, nutritional information at transferrals between units.</td>
<td>Data on energy expenditure measurements (by indirect calorimetry and doubly labelled water), infections, inflammatory response, nitrogen balance, energy intake, activity level, nutritional problems, general body compositional data and neurologic recovery.</td>
<td>Data on energy expenditure measurements (by indirect calorimetry and doubly labelled water) and predictions (equations and metabolic monitor).</td>
</tr>
</tbody>
</table>

Assisted nutrition (II)

Assisted nutrition was defined as the state when help was required for administering nutrition parenterally, enterally or orally. Any verbal or physical guidance needed for initiation or completion of meals was also considered as assisted feeding. If no rating scale on level of independence in eating had been used and only scarce nutritional notes were found, we used change in
bodyweight as a proxy measure. Thus, patients with considerable weight loss or weight gain were not defined as independent in eating although they might have been allowed to eat unassisted.

**Energy intake (II, IV)**

Data on the daily intake of energy was collected from nutritional protocols in both studies. In study IV energy intake was specially monitored when patients started eating orally. They received food on which weight, volume, energy and nutrient content of each component of the meal were specified and also, the tray, served to the patient, was photographed before and after each meal. All nutritional protocols were then checked on consistency to delivery notes of the specially ordered food and to photographs and recalculated before analysis.

**Energy expenditure (IV, V)**

To measure the energy expenditure, different techniques were used at different intervals:

- a side stream metabolic cart, the Datex-Ohmeda M-COVX module was used for continuous indirect calorimetry measurements during mechanical ventilation (IV, V)
- the Deltatrac™ II metabolic monitor was used for intermittent indirect calorimetry under basal conditions twice a week from when patients could breathe satisfactory on normal air (IV).
- a doubly labelled water period starting at two weeks post injury (IV, V) and, if possible, repeated at two months (IV).

Prior to analysis, raw data on energy expenditure were filtered to eliminate technical flaws (the Datex-Ohmeda M-COVX ) and non-steady state data (the Deltatrac™ II). Doubly labelled water data was rectified to control for shifts of isotope levels caused by enteral and parenteral nutrition.

To predict the energy expenditure, 14 equations (see Table 2 in paper V) and the SenseWear Armband were used (V).

**Energy balance (II, IV)**

In study II, data on the total energy expenditure according to indirect calorimetry was too sporadic to allow any evaluation of the energy balance. Instead the energy intake of the patients, was related to the BMR by use of the Harris & Benedict equation [86].

In study IV, energy balance was calculated from the daily energy intake and TEE measured with continuous indirect calorimetry during mechanical ventilation and to doubly labelled water from two weeks post injury.
Malnutrition (II, III)
Two definitions of malnutrition were used; one in order to guide respondents of the questionnaire in defining patients at risk for malnutrition (III) and one to determine high risk limits of weight loss and BMI (II). The first one used in the questionnaires reads:

Patients with eating difficulties and/or with involuntary weight loss (>5 % in one month or >10 % in 3-6 months) and/or patients with low BMI (<20).

The anthropometrical data available in study II to evaluate malnutrition were body mass index (BMI) and weight change over time. We used the high risk criteria of the Malnutrition Universal Screening Tool (MUST) [64] to set the limits of weight loss and BMI in the patients studied. According to MUST a patient at high risk for malnutrition is:

1. A patient with BMI less than 18.5 kg/m².
2. A patient with involuntary weight loss exceeding 10 %.
3. A patient with both BMI 18.5 - 20 kg/m² and an involuntary weight loss of 5 to 10 %.

Factors with a possible impact on malnutrition (II)
The data abstracted from medical records and analyzed on relation to malnutrition were; age, gender, GCS score, accompanied fractures, days on sedation, days of fever or of hypothermia, physical anxiety, upper gastrointestinal intolerance, length of stay and length in intensive care unit.

Nitrogen balance (IV)
The nitrogen balance was derived by balancing nitrogen intake and excretion to reflect the anabolic or catabolic situation (negative nitrogen balance=catabolism). Nitrogen losses were calculated from urinary urea analysis and predicted also from losses via skin and stools at 5, 20, 40 and 80 days post injury. Nitrogen intake on these days was collected from the nutritional protocols.

Body weight (II, IV)
In study II, body weight was measured according to the standards of the care units involved.
In study V, body weight was measured daily during early post injury period and once to twice a week during rehabilitation. Measurements were performed in the morning with weight of clothes and sheets withdrawn.
Glasgow Coma Scale (GCS) (II, IV, V) and Reaction Level Scale 85 RLS85 (II)

The level of consciousness was rated by GCS [7] or RLS85 [113] scores during the early post injury period according to standard procedure, *i.e.* by the nurses and physicians at the ward, several times a day, unless contradiicted by high intracranial pressure.

Rancho Los Amigos Cognitive Scale Revised (RLAS-R) (IV)

From two weeks post injury and each fortnight from then on, cognitive level was rated by one of the authors (KK) using RLAS-R [114], a 10-level rating scale of cognitive function which reflects different stages of the awakening from a severe brain injury. The first part includes the period when patient is in need of total assistance, from being non-responsive to being able to localize stimuli (level 1-3). Next period holds the cognitive functioning levels of a stressed, confused and disoriented patient; from an non-purposeful agitated state with maximal assistance (level 4) to an automatic and appropriate behaviour with minimal assistance (level 7). Final level (level 10) is characterized by purposeful and appropriate behavior with modified independence.

Functional Independence Measure (FIM) (II, IV)

In study II, FIM [115] was rated according to standard procedure and in study IV ratings began at two weeks post injury and each fortnight from then on. With FIM, 18 separate functions are rated; self care (to eating, grooming, bathing, dressing and toileting), sphincter control (bladder and bowel), transfers (to/from bed, chair, wheelchair, tub/shower), locomotion (walking/wheelchair, stairs), communication (auditory/visual comprehension and expression), social cognition (social interaction, memory, problem solving). Based on observations on what the patient actually performed, each function was scored from 1 (total dependency) to 7 (totally independent). Nursing assistants in charge of the daily care of the patient were consulted by one of the authors (KK) at each rating.

Glasgow Outcome Scale (GOS) (IV)

Outcome of patients in study V was rated with GOS [116] by the clinical follow-up coordinator at the Neurosurgery Department, at six months and one year post injury. With this scale, outcome is scored into five categories; death, persistent vegetative state (patient exhibits no obvious cortical function), severe disability, (conscious but disabled - patient depends upon others for daily support due to mental or physical disability or both), moderate disability (independence in activities of daily living but disabled of varying degrees, including *e.g.* dysphasia, hemiparesis, ataxia, memory deficits or personality changes) and good recovery (resumption of normal activities even though there may be minor neurological or psychological deficits).
3.4 Statistical analysis (II-V)

Descriptive statistics and tests were performed by use of the software package SPSS (version 13.0 and 16.0). Frequencies and quote data was presented as mean values and standard deviations (SD) or, when non-normal distributions, as median values and interquartile range (IR). Statistical tests used in study II and V are summarized in Table 5. Variables of possible influence on malnutrition (II) and energy expenditure (V) were tested for independent association by use of multiple regression analysis with backwards elimination, but as methodological weaknesses were identified, these findings were not included in the papers.

**Table 5. Statistical tests used in study II and V**

<table>
<thead>
<tr>
<th>Evaluation</th>
<th>Study II</th>
<th>Study V</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinical factors of influence on body mass; Malnourished patients versus non-malnourished</td>
<td>Agreement between measured and predicted energy expenditure</td>
</tr>
<tr>
<td>Tests for measures of difference</td>
<td>Person Chi-square test</td>
<td>Wilcoxon two-sample test</td>
</tr>
<tr>
<td>Tests for measures of correlation and agreement</td>
<td>Spearman’s correlation test</td>
<td>Intraclass correlation</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Modified Bland-Altman test</td>
</tr>
</tbody>
</table>
4. RESULTS

**Table 6. Overview of the results of the studies**

<table>
<thead>
<tr>
<th>Study I</th>
<th>Study II</th>
<th>Study III</th>
<th>Study IV</th>
<th>Study V</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aims</strong></td>
<td>To examine the evidence on the metabolic state and nutritional support</td>
<td>To describe the current nutritional treatment policies and nutritional outcome</td>
<td>To delineate the resources and routines for nutritional management</td>
<td>To explore the energy balance</td>
</tr>
<tr>
<td><strong>Main results</strong></td>
<td>-Variations in measurement methods between studies.</td>
<td>-At six months post injury, most patients had regained their independence in eating.</td>
<td>-Resources in terms of qualified staff members were reportedly good.</td>
<td>-Patients were in negative energy balance from 3rd week post injury.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Energy intake was low.</td>
<td>-Nutritional guidelines were adopted in less than half of the units.</td>
<td>-Concurrent nutritional problems were difficulties in retaining enteral and/or parenteral nutrition delivery routes until oral feeding was satisfactory.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Two thirds of the patients developed malnutrition during the first two months post injury.</td>
<td>-Screening for malnutrition at admission was rarely performed.</td>
<td>-Surveillance of energy intake declined when oral intake began.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-Sparse data beyond the first month.</td>
<td>-Assessment of energy requirements relied on calculations.</td>
<td>-The profession in charge to estimate energy requirement varied depending on nutritional route and unit speciality.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>-A tendency towards less morbidity and mortality in early fed patients.</td>
<td>-Nutritional information was lost at transfers.</td>
<td></td>
</tr>
</tbody>
</table>
4.1 Metabolism and nutritional treatment (I)

**Hypermetabolism**
From the 30 studies included in this systematic review, a total of 316 patients with moderate and severe TBI had been examined with indirect calorimetry. Mean REE/BMR ratios in non-sedated patients varied between 1.05 and 1.6 and in the sedated between 0.96 and 1.32 [41-44, 89, 93, 95, 102]. However, the procedure for measuring REE differed between the studies and the metabolic measurements were mainly carried out during the early post injury period. Thus, comparisons of REE/BMR quote were slightly hampered and information on duration or frequency of hypermetabolism could not be derived.

From three studies evaluating a total of 57 patients [39, 42, 43], consistent data showed that sedation reduced the metabolic rates. The impact of other factors, *i.e.* body temperature, thermogenic effect of nutrition, sepsis and associated injuries, were mainly reported on from small clinical descriptive studies and thus only suggestive.

**Catabolism**
There were consistent data in three randomized controlled trials [94, 96, 98], one cohort [39] and three clinical descriptive studies [44, 101, 102] that the majority of the patients exhibits catabolism during the first two weeks after the injury with a negative nitrogen balance of -3 to –16 g N/day. Two case series reported on late status; at day 30-75 post-injury [90-92], the catabolism had stabilized and was almost back to normal, but all patients were by then malnourished with a weight loss of 16 % (n11) and 12.6 % (n10) since injury.

**Upper gastrointestinal dysfunction**
Five studies, including one randomized controlled trail [103], one cohort study [104] and three clinical descriptive studies [44, 105, 110], reported on upper gastrointestinal function in a total of 104 patient. Although, different techniques were used to define gastric function, there were consistent data showing that upper gastrointestinal dysfunction is common after severe TBI. The frequency, as reported in three of the studies, varied from 44 % [110], 80 % [104] to 100 % [105]. All measurements were done during the early post injury period. No data on the persistence of the impairment could be received.
Effects of nutritional treatment
Two systematic reviews [14, 111] and seven randomized controlled trials, described in nine articles [93-99, 109, 112], evaluated various effects of nutritional treatment. Study settings, interventions, outcome measures and randomisation procedure in the trials differed. Thus, the data of these studies cannot be directly combined, which limits evidence-based conclusions and recommendations. However, one systematic review based on eleven RCTs, concluded that early feeding may be associated with a trend towards better outcomes in terms of survival and disability [111].

4.2 Nutritional treatment and nutritional outcome (II)

Care settings during hospital stay and assistance at discharge
The hospital stay for the patients of this study (n=64) varied vastly, from 9 to 356 days, median 77 (IR 95) and included three to eight different care units per patient. For the majority (73 %), the time in hospital included three periods; an intensive care period (median 17 days, IR 14) followed by a period in different ward settings (median 17 days, IR 15) and finally in a specialized rehabilitation setting (median 55 days, IR 68). At discharge from hospital care, 64 % of the patients (n=41) were able to go home without any assistance, while 22 % (n=14) needed further assistance at home. Eight patients (12.5 %) were discharged to nursing homes and one patient died during hospital stay one month post injury due to a major stroke.

Nutritional route
All patients received parenteral nutrition for 2 to 64 days (mean 19 ±12.2). The majority of the patients (86 %) also received enteral nutrition, started on day 4 ±2.9 post injury for 1 to 178 days (median 14, IR 33). 14 patients had a gastrostomy inserted approximately one month post injury (31 ±8.6 days). At six months post injury, 4 were still in use. First swallowing test was done within one month post injury in most patients, median 16 days (IR 22). Time with need for assisted feeding varied a lot, from 9 to 180 days, median 37.5 (IR 61). At six months post injury 54 patients (84 %) had gained total nutritional independence. This group of patients started to receive all their food orally after 4 to 119 days post injury, median 21 (IR 18). Five (8 %) of the remaining still dependent patients, received all their food orally but needed assistance, two (3 %) were fed with a combination of oral and enteral nutrition and two could not swallow any food orally and were given all food enterally. The patient, who died one month post injury, had received parenteral and enteral nutrition throughout this time period.
Energy intake in relation to basal metabolic rate

Energy intake recordings were done in all patients but two at an average of 31 days ±38 (range 1 to 176 days). Daily protocols of energy intake were mainly registered while the patients were on parenteral nutrition and/or enteral nutrition, but when they started to eat, the recordings declined. From the onset of oral feeding the daily total energy intake was registered in only 25 % of the orally fed patients for 8 days ±8. The EI throughout the first month was just below the calculated BMR, and stayed at 21 % above BMR during the second month.

Change of body weight

Weight development was evaluated in 56 patients, but the frequency of measurements varied between individuals as well as between care units, which hampered our evaluation. Compared to the first recorded measurement after 3 ±2.9 days, all patients but four had an initial weight loss. In eight patients (14 %), this was less than 5 %, in another eight it was 5-10 % and in 37 (66 %) more than 10 %. The weight reduction lasted 1-2 months post injury in most patients and was followed by a slow return towards the initial weight.

Malnutrition

Malnutrition was defined according to the high-risk criteria of MUST. In total, the number of malnourished patients according to the criteria was 38 (68 % of the 56 patients evaluated). The majority of patients had their lowest body weight recordings during the second month post injury.

Malnourished patients compared with non-malnourished

The malnourished patients and the non-malnourished patients were compared regarding factors that might have an impact. There was no difference in age, gender, severity, in days of hypothermia, fever or in days of physical anxiety between malnourished and non-malnourished patients. However, associated fractures, days on sedation, upper gastrointestinal intolerance, length of stay and length of stay in intensive care unit differed between the groups. Further analysis by regression analysis (presented here, but not in the paper) showed an independent effect of days on sedation and length of stay. The risk for malnutrition was 6.7 times higher in patients sedated for more than twelve days when compared to those with shorter sedation period and 4.1 times higher in patients with a length of stay exceeding 77 days when compared to those who were discharged earlier. The retrospective design of this study limited the interpretation on these findings, thus, we chose not to report on it in the paper. For an evaluation of reasons for malnutrition, a detailed prospective study on a larger study sample is required. However, this analysis guided us on which patients to include in study IV and V, i.e. patients with an expected hospital stay of 2-3 months.
4.3 Resources and routines for nutritional management (III)

Questionnaires to staff (n161) and the medical records of patients with severe TBI (n64) were compared with regard to nutritional routines and resources.

**Personnel responsible for nutritional policies**

Available personnel with nutrition as a special assignment were represented by a; Dietician according to 83 % of the respondents, Nutrition nurse in 80%, Nutrition nursing assistant in 63 %, Speech- and language pathologist in 73 %, Nutritional support team according to 40 % of the respondents. Ninety percent reported combinations of two or more of these professional competencies and in 27 % all five were available.

**Nutritional guidelines**

More than one third of the respondents, 40 % reported an absence of nutritional guidelines, but 11 % were in the process of developing them. Thus, in 51 % of the units no nutritional guidelines were present.

**Nutritional screening methods**

Guidelines on nutritional screening were only rarely followed according to the questionnaires and BMI was said to be the least used screening tool. When the medical and nursing records of the patients were examined, 45 % of the patients had their body height documented at some time during their total care period. However, transferring body height data between units or remeasuring it at the next caregiver, was seldom performed.

**Access of body weight equipment**

Most common were sitting scales reported by 70 %, hoist scales by 42 %, standing scales by 42 % and bed scales by 23 %. Some had combinations, but in every fifth unit measurements were possible only if patients were able to sit in an upright position or stand up.

**Measurement of body weight; routines**

According to questionnaires, weight control of all patients within the first week from admission was reported as a routine by 37 %. Daily to weekly control intervals in all patients was reported to be the present routine for 62% of the respondents.

When the medical and nursing records of the patients were analyzed, they revealed no data indicating any regular body weight measurements and in 37% of the care unit episodes weight measurements were absent.
Assessment of energy requirement
The use of indirect calorimetry was uncommon; 12 % of the respondents considered indirect calorimetry to be the method of choice to estimate energy requirement of the patients, 14 % reported access to the equipment and only 8 % confirmed they used it. Instead, the majority, 73 % reported use of different calculations to estimate energy requirement.

Definition of energy balance
Almost two thirds reported that no definition of energy balance was used at all in clinical practice. 27 % defined energy balance as the relationship between energy intake and calculated energy requirements. Only one of the respondents referred to the relationship between energy intake and the measured energy expenditure.

Who is responsible for energy assessment?
When patients received parenteral nutrition, the physician was described as being in charge of estimations and prescriptions of energy requirements by the majority of the units, but at the intensive care unit, the physician was distinctly in charge of this task, independently of nutritional route. At the mixed wards and the rehabilitation units it was mainly the task of the registered nurse when patients received enteral or oral feeding. The dietician was not involved in estimating the energy requirements at the intensive care units, but at the mixed wards and the rehabilitation units, especially during enteral nutrition.

The rare and delayed consultation of dieticians in assessing energy requirements was confirmed when examining how this had been carried out in the study patients. According to medical and nursing records, dieticians had been consulted for energy assessment in 22 % of the patients at approximately one month post injury.

Surveillance of energy intake
Half of the respondents clearly reported that the energy intake always was documented in patients needing more than one nutritional route at the same time. This did not correspond to data on how energy intake had been registered. Energy intake was mainly registered while patients were on parenteral and enteral nutrition, but the recording of energy intake decreased to one quarter when patients started to eat. However, fluid intake recordings continued in the majority of the orally fed patients, 92 %.
Who is responsible for documenting nutritional status?
The registered nurse was reported to be responsible for documenting nutritional status and also for reporting it to the next care giver - in 83 % and in 92 % of the questionnaires respectively.

Nutritional data reported between caregivers
Nutritional information passed on mainly concerned ways of administering nutrition and eating difficulties. Information on prescribed energy level, weight development and BMI were less reported on.

4.4 Total energy expenditure and energy balance (IV)
In the six patients included in this study, the injury pattern and secondary events varied, thus so did recovery rate and final outcome. The intended study period was from day of injury until two and a half months post injury. Two patients proceeded accordingly, while for patients participating during a shorter time period, participation to measurements varied.

Energy balance
Indirect calorimetry (IC) measurements continued for 5 to 21 days while patients were on mechanical ventilation. Measurements with doubly labelled water (DLW) began on day 14-18 in five patients and covered a period of approximately three weeks. Energy intake and TEE were approximately balanced during IC period while negative during DLW period. When calculated on a 70 kg individual, energy balance/day of the patients ranged from -168 to 231 kcal/day during IC period and from -7 to -378 kcal during DLW period.

Occurrences of possible influencing factors
The metabolic strains from secondary events were numerous. Several surgery interventions were necessary, infections, especially pneumonia, were common and the inflammatory period in patients was persistent. During recovery, a hyperactive period, of varying degree and length, occurred in all patients; either by periods of high muscle tension and pronounced sweating, persistent movements and fidgeting or characterized by anxious and frequent attempts to leave. At end of the study period, all patients but one were able to walk.
Two patients had persistent problems of slow gastric emptying. Nasogastric tubes and intravenous catheters were frequently removed by the patients and when oral feeding began two patients needed modified consistency on food and fluids at the beginning and one patient with severe dysphagia had a percutan encoscopic gastrostomy (PEG) placed one month post injury.
Two patients with difficulties in initiating activities needed guidance to start each meal. Other factors identified that may have influenced on total energy intake/day were periods of oral mucositis, diarrhoea, occasional fasting preparations before surgery, nausea and repulsion for hospital food.

**Energy balance in relation to body weight and nitrogen balance**

Patients lost 8-19% of their initial body weight and the period of negative energy balance corresponded well to time of weight loss. Moreover, the decrease in energy intake and body weight continued in two patients even after the 5th week. All but one patient were catabolic at first and second measurement, while approximately in balance after 1.5 and 2.5 months post injury. Nitrogen intake related to body mass ranged from 0.07-0.28 g N per kilo body weight and day (equivalent to 0.44-1.75 g protein/kg/day).

### 4.5 Methods to assess energy expenditure (V)

**Accuracy of the SenseWear Armband and equations**

The estimated energy expenditure (EE) according to different equations for prediction of EE and a non-invasive monitor, the SenseWear Armband, were compared with EE in the patients, measured by IC and DLW. During IC period, the majority of methods for predicting EE (n=9/13) differed significantly from the measured EE and underestimated the EE (p≤0.05) and two equations overestimated it (p≤0.05). On group level, the Ireton-Jones equation from 1997 and the Penn-State equation from 1998 correctly estimated the EE. However, the Ireton-Jones equation from 1997 showed poor agreement (intra class correlation <0.4) and did not detect the accurate level of day-to-day, intra-individual variations of EE. Only the three Penn-State equations showed a good or excellent agreement (intraclass correlation ≥0.6) with indirect calorimetry.

Modified Bland Altman plots of the three Penn-State equations demonstrated that the Penn-State 1998 was the most accurate with a mean difference close to zero (+22.3 kcal), with 91% of the plots within limits of clinical acceptance, *i.e.* ±15% of the measured EE (±314 kcal). The Penn-State 1998 also agreed excellently (intraclass correlation ≥0.75), had the highest amount of accurately assessed days and was the only predictive method where EE predictions in all patients were within clinically acceptable level, *i.e.* within ±15% of the measured EE [87].

During DLW measurements, at 3rd to 5th week post injury, two equations and the metabolic monitor were evaluated, but observations were too few for any conclusive statement.
Factors influencing energy expenditure
Clinical and laboratory variables with possible influence on EE were analyzed. However, the findings were not reported on in the papers as the available data was too few to allow any conclusions, but are briefly summarized here for information. In the regression analysis, male gender and increased heart rate ($\geq 77.4$ beats/min) were independently associated with high EE ($\geq 27$ kcal/kg body weight). When the influence of medications was analyzed, Midazolam was independently related to a low EE, while for Clonidine and Morphine, a positive b-coefficient was found. Clonidine was the only agent where dosage had an effect on EE ($p \leq 0.003$). Thus, both the use per se and the dose of Clonidine were related to a high EE.
5. DISCUSSION

Clinical outcome after TBI has improved by early detection and treatment of avoidable factors during early intensive care [12]. Less is known about the possible importance of systemic metabolic disturbances and nutrition with regard to the long-term outcome in patients with TBI. The overall aim of this thesis was to expand the knowledge on the metabolic course and nutritional outcome in patients with severe TBI and to analyze the use and accuracy of different methods for assessment. The following section will commence with a discussion of some of the findings and then of methodological aspects.

5.1 Main findings and comments

Metabolic rate
According to the systematic review (study I) the metabolism in non-sedated patients, varied between 105 % and 160 % and in the sedated between 96 % and 132 % of the predicted metabolic rate.
The fairly large variation of the degree of hypermetabolism; a variability of 11 % in TBI population compared to 3-6 % in normal population [88] probably reflects both patient selection and measurement procedures. The diversity in metabolic rate also raises the question of adequacy of and the precision in estimations of the energy expenditure, as the consequences of under- as well as overfeeding are undesirable. When different methods to estimate energy expenditure were evaluated (study V), only one, the Penn-State equation from 1998 was found accurate. However, its use is restricted to the time in ventilator as it requires data on expired minute volume. So far, indirect calorimetry is the method of choice to measure the individual metabolic rate of the patient. Applying an average need for the whole group of non-sedated TBI patients of 40 % above the predicted basal levels, as recommended in previous guidelines [14], may be practical, but the variation demonstrated in the studies of our review does not support this recommendation. The effort should rather be to install regular indirect calorimetry measurements into clinical practice for these patients [117].
While on mechanical ventilation indirect calorimetry is very easily performed. When patients are breathing spontaneously again, the steady state required for measurements may be difficult to capture in restless patients (study IV), but with an abbreviated measurement protocol, measurements may be facilitated without endangering their accuracy [118]. However, the implementation of this routine, i.e. measuring the energy expenditure instead of predicting it, has been unsuccessful (study III). Indirect calorimetry was seldom used by the care units caring for patients with severe TBI. In addition, the unawareness, found amongst personnel, of the true definition of energy balance (only one out of 74 respondents answered correctly and two thirds reported that no definition was used in clinical practice), reflecting that an essential component of nutritional assessment in clinical practice is neglected. In fact, surveillance of the homeostasis of the patient does not seem to include the evaluation of energy balance.

**Catabolism and change of body weight**

The systematic review (study I) provided consistent data showing that the majority of patients with moderate and severe TBI are hypercatabolic in the early post-injury period. On group level, the daily nitrogen balance ranged from minus 3 to minus 16 g N (study I). In the individuals measured by us (study IV) it was in correspondence; -3.1 to -9.2 g N at 5 days post injury in 5/6 patients and -1.9 to -17.8 in 3/3 patients at 20 days post injury.

The majority of the patients developed malnutrition (study II). The weight development of the patients (study II and IV), showed that body mass continued to decrease for weeks. Assumingly, the duration of hypermetabolism and catabolism was not restricted to the early post injury period, but were extended over a longer time period, or other factors mattered.

**Energy intake**

The quality of nutritional care after a severe TBI is challenged in many ways. During the first and second month post injury, the nutritional route changed frequently and nutrition was not easily administered in the distressed patients. Moreover, the energy intake during the first month in the patients of study II covered merely the BMR and thus, obviously not the energy need of the patients. During the second month energy intake was increased by only 21 %. In study IV, energy intake decreased when patients started eating, indicating that alternative nutritional routes are necessary to maintain until satisfactory oral intake is reached.

Suggestive approaches to optimize delivery include early detection of patients at risk for delayed oral intake by use of GCS and RLAS score [119, 120] and early gastrostomy for those at risk [106, 107, 121-124]. According to ESPEN guidelines (European Society for Clinical Nutrition and Metabolism), PEG should be considered if it is expected that the nutritional intake of the patient is likely to be qualitatively or quantitatively inadequate for 2-3
weeks [125]. As it takes time to await a satisfactory oral intake after a severe TBI and as the reduced energy intake prolongs catabolism, it is our recommendation to follow guidelines and consider early PEG in patients with low GCS or RLAS scores, i.e. GCS score 3-9 or RLAS level 1-2 after time of sedation [119, 120].

**Nutritional routines**

Concurrent with the rapid clinical changes within each patient, we found that patients with severe TBI are subjected to frequent transfers between care units; 3-8 care units/patient (study II). For many reasons, this is not optimal.

Patients with severe TBI require highly specialized care to prevent specific avoidable events and to enable early neurorehabilitation. A basic concept to promote the cognitive recovery of the patient is to encourage the exposure to situations, people and environment that the patient is familiar with and avoid those that are stressful. A frequent change of environment is highly stressful and the late initiation of rehabilitation may prolong recovery or even have an unfavorable effect on outcome [15-18].

Further, from a nutritional perspective, it is a demanding task to maintain optimal nutritional care under such circumstances and to secure adequate information when handing over the patients. If routines for nutritional assessment are missing or inadequate, this most probably endangers the nutritional status of the patients. The results from study III, the one examining nutritional routines and recourses at 74 units from 38 different hospitals in Sweden, were quite discouraging. The lack of routines indicated that in a majority of patients malnutrition was never recognized as a health problem.

Tremendous work has been done at Swedish hospitals to detect patients at risk for malnutrition. Nutritional screening (BMI, loss of body weight and eating difficulties) of all patients at admittance is an obligated routine today. Patients with severe TBI automatically qualify to the high risk group as weight loss is to be expected and as they are dependent on some one else to interpret their nutritional needs. Therefore, measures need to start immediately, before weight loss is a fact. The nutritional goal is to achieve and maintain energy balance from time of injury, until the weight development of the patient has stabilized. To maintain energy balance may sound obvious and easy, but according to our findings, we conclude that it is not.
5.2 Methodological aspects

Study I
The systematic review identified only 30 studies with evidence related to the study questions. The systematic procedure with a thorough literature search, controlled selection process and standardized quality assessment is believed to have diminished bias to a minimum. The search was restricted to studies published during the recent past ten years, as advancements of medical and nursing care during the last decades may have improved the metabolic and nutritional care of these patients. These studies, although few, allowed some important conclusions related to the study questions, but did not allow a meta-analysis.

Study II
The retrospective design enabled the investigation of nutritional treatment without interfering with the treatment process. However, the weaknesses that accompany retrospective studies of medical and nursing records must be considered, e.g. facts may have been missed if left out in the records – only what was recorded could be evaluated and the equipment and procedures for measurements and assessments were not controlled for.

Study III
In this questionnaire based study the response rate was high, representing the majority of care units, which enabled comparison with how the patients had been treated. However, answers may reflect only how the experienced personnel act and not the proceedings of the novice, as the selection procedure of respondents made by the head nurse was performed to find respondents with confident knowledge of the local nutritional resources and routines. This may have given an over-positive picture and may be one explanation to the discrepancies between what was said to be done and what was actually accomplished. The data collected did not admit any evaluation of how the nutritional routines of the units and the development of malnutrition in the patients were connected. However, this does not contradict that failing nutritional routines may increase the risk for malnutrition.

Study IV
This prospective descriptive study was the first study to report on the total energy expenditure by the use of DLW. Apart from valuable information on total energy need, it was allowed us to explore the applicability of this technique on patients recovering from a severe TBI. However, due to limited resources the intended number of patients aimed for was around ten but only six patients were included, thus findings cannot be
generalized. Moreover, the study protocol was meant to cover 80 days post injury, but not all patients fulfilled study protocol.

One further consideration is that standard nutritional treatment may not have been achieved, as the staff in charge of nutritional treatment was not blinded to which patients on the ward that were included in the study. Standard procedure at the neurosurgery intensive care unit is to measure the energy expenditure for 4-6 hours at a time and not all patients are measured. As all our patients had continuous measurements, this most probably resulted in a more precise assessment of energy requirement.

Moreover, when patients began to eat and the plate needed to be photographed before and after each meal, this may have encouraged both the helper (in assisting the patient) and the patient (to actually finish the portion served). Thus, the patients of this study are believed to have received a more accurate nutritional treatment than standard routines would have provided.

**Study V**

In this validation study we desired to evaluate the accuracy of predicting EE, not only between individuals, but also within the individual during indirect calorimetry measurements, why the cases included in the analysis were all observations, *i.e.* each patient contributed with all his/her observations. This increased the degrees of freedom of a small study sample, but also inflated them and increased the risk for false positive results (Type 1 error). Therefore, even though the observations clearly demonstrate weaknesses of the EE assessment methods at study, further prospective studies of larger number of patients with severe TBI are necessary to confirm these results.

An additional limitation relates to the post traumatic fluid retention of the patients. As we used present body weight in the equations and in the metabolic monitor, SWA, this may have lead to inaccurately high EE predictions for this period. However, this did not seem to be the problem as EE was most often underestimated.
6. GENERAL CONCLUSIONS

I Patients with moderate and severe TBI exhibit a wide range of increased metabolic rate, catabolism and upper gastrointestinal intolerance during the early post-injury course, while data concerning the later post-injury period are lacking.

I Available data from previous studies do not allow any recommendation on how metabolic abnormalities should guide the nutritional treatment. The impact of timing, content and ways of administration of nutritional support on neurological outcome after TBI remains to be demonstrated.

II Independence in eating is regained in most patients with severe TBI within the first six months post injury, but in the majority malnutrition is developed.

III Despite good resources of qualified staff, the nutritional routines to assess patients with severe TBI are deficient, resulting in incomplete nutritional data and lost nutritional information.

IV Data suggests that negative energy balance after a severe TBI could not only be explained by the elevated metabolic rate and catabolism induced by the trauma, but also by difficulties in securing alternative nutritional routes in the distressed patient.

V The findings suggest that the Penn-State equation from 1998 is sensitive to changes in energy expenditure both within and between individuals. Thus, data support the use of it to estimate energy expenditure in patients with severe TBI while on mechanical ventilation.
7. FUTURE STUDIES

There are several areas related to the metabolic and nutritional needs of patients with severe TBI that need to be further highlighted.

Available data suggest that nutritional support aiming at meeting the metabolic demands is beneficial. This encourages randomized controlled trials of large study samples. These studies should define the level of energy- and protein intake in relation to energy expenditure during a relevant time period that has the best effect on outcome.

The duration and consequences of upper gastrointestinal intolerance in patients receiving enteral nutrition, the impact of different positioning of the tube and of the administration rate also needs further elucidation.

As failing nutritional routines may increase the risk for malnutrition, evaluation of implemented nutritional routines, such as the following, would be of interest.

- Early assessment of patients with increased risk for prolonged time to achieve total oral feeding, by use of GCS and RLAS, to enable prediction of clinical course and an accurate choice of nutritional route.
- Admission screening on nutritional risk after each transferral.
- Clear assignment on obligations concerning nutrition to all professional staff involved.
- Energy requirement assessed by indirect calorimetry
- Energy goal set and evaluated weekly by measurements of body weight and daily recordings of energy intake until weight development is stabilized.
- Nutritional information at transferrals between units that includes information on; nutritional route, eating difficulties, assessed energy requirement, weight development and BMI.
A fundamental component to enable adequate nutritional treatment is the use of reliable methods to determine the energy expenditure of the patient. As long as measurements with indirect calorimetry are not set into routine, this continues to be a topical area for research:

- Confirmatory studies of the accuracy of the Penn-State equation from 1998 while patients are in ventilator (it requires data on expired minute volume) and of a recently presented equation [126] applicable after the mechanical ventilation period, are warranted.
Efter en svår traumatisk hjärnskada är den metabola påfrestningen stor och den initialt medvetslöse patienten är under en längre tid beroende av andra för att få i sig näring. Då den akuta fasen avslutats och rehabilitering inletts har patienten ofta blivit undernärd. Eftersom undernäring har en negativ effekt på flertalet funktioner i kroppen är strävan med nutritionsbehandlingen att tillgodose energi- och proteinbehovet för att på så sätt minimera nedbrytningen av kroppsvävnad.

Syftet med denna avhandling var att studera metabolismen och nutritionsbehandlingen hos patienter med svår traumatisk hjärnskada, nutritionsrutinerna hos vårdavdelningarna och utvärdera olika bedömningsmetoder.

Studieupplägget innebar därmed: (1) en systematisk litteraturstudie för att ta fram tillgänglig evidens inom fältet, (2) en kartläggning över nutritionsbehandlingen hos patienter som skadats under åren 2003-2004, (3) en enkätsstudie över hur nutritionsrutinerna såg ut hos vårdgivarna till dessa patienter och slutligen (4) en beskrivande studie av den totala energiförbrukningen och energibalansen efter en svår traumatisk hjärnskada med (5) utvärdering av energiberäkningsmetoder.


Kartläggningen över hur nutritionsbehandlingen ser ut under det första halvåret efter skadan eller fram tills dess att patienterna inte behövde hjälp med näringsstillförseln visade att 84 % av de 64 patienterna som ingick blev självsäglande i sitt ätande, men att 68 % hade blivit undernärda under de första två månaderna med viktförluster på 10-29 % av sin initialvikt.
Energimängden som patienterna fått i sig under den första månaden var i nivå med det som de beräknades förbruka i vila och steg marginellt under den andra månaden efter skadan. Vid granskning av nutritionsrutinerna hos de vårdavdelningar där patienterna vårdats framgick det att rutinerna var bristfälliga trots relativt god tillgång på nutritionsansvarig personal. Energiförbrukningen mättes sällan och man förlitade sig på energiberäkningsmetoder. Beräkningar av energiintag avslutas då patienterna övergick från intravenös näringstillförsel och/eller sondmat till att äta. Viktkontroller var oregelbundet utförda och vid en tredjedel av vårdtillfällena saknades de helt. BMI var sällan uträknat och information gällande patientens nutrition förlorades då patienterna bytte vårdavdelning.

Patienterna befinner sig sannolikt i en negativ energibalans under en förhållandevis lång period efter skadan. Möjligheten att uppnå energibalans, d.v.s. då energiintaget motsvarar energiförbrukningen, är, förutom patientens mottaglighet för näringstillförsel, beroende av hur bra beräkningar man kan göra.

9. ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to all those who have helped me in many different ways. In particular I wish to thank:

The patients who participated in the studies, your friends and families. You may not have benefited from this research yourselves, but due to your participation, important aspects on how to optimize nutritional treatment could be identified. This unselfish act in the middle of a chaotic life event is highly honourable and I am deeply obliged to you.

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My dearly beloved family and beautiful friends. Thank you for your incredible patience, your warm support and for distracting me with the pleasures and realities of life. Thanks to you, life has not escaped me.

…Mattias, my love and husband, thank you for always being there and also for your nice drawing on the cover.

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10. REFERENCES


99. Taylor, S.J., S.B. Fettes, C. Jewkes, and R.J. Nelson, Prospective, randomized, controlled trial to determine the effect of early enhanced enteral nutrition on clinical outcome in mechanically venti-


126. McEvoy, C.T., G.W. Cran, S.R. Cooke, and I.S. Young, Resting energy expenditure in non-ventilated, non-sedated patients recover-
Nutritional treatment questionnaire

1. Is there access to any of these professional categories at your department?  
*Please put a cross against either yes or no on each alternative.*

- Nutritional support team\(^1\) \quad Yes \quad No
- Dietician \quad Yes \quad No
- Speach- and language pathologist \quad Yes \quad No
- Nutrition nurse \quad Yes \quad No
- Nutrition nursing assistant \quad Yes \quad No

The responsibility for nutritional treatment policies is organized differently, *i.e.*

Comments………………………………………………………………
…………………………………………………………………………

\(^1\) Meaning a group consisting of at least one physician, one dietician and one registered nurse, with orders to develop nutritional routines. The group is either locally situated at your department or there is an established connection to your department.

2. Are there guidelines\(^2\) for nutritional treatment at your department?  
*Please put a cross against all the accurate alternatives that are present at your department regardless the use of them.*

- Yes, we have locally constructed guidelines designed for our patients’ specific needs \square
- Yes, we have guidelines constructed by and our Hospital \square
Yes, we have the National Guidelines (SWESPEN) ☐
No, we have no nutritional guidelines ☐
No, but nutritional guidelines are under construction ☐
Comments........................................................................................................

2 Guidelines that briefly describe the nutritional process, *i.e.* nutritional assessment, diagnose, aim, treatment and follow-up

*If the answer is no on question no 2, please proceed to question no 5.*

3. How accurate are the following statements?
*Please put a cross against either yes or no on each alternative.*

Our guidelines are determined by the management and well established in the personnel.
Yes ☐ No ☐

Our guidelines are determined by the management, but not established in the personnel.
Yes ☐ No ☐

Our guidelines are well established in the personnel, but not by the management.
Yes ☐ No ☐

Our guidelines are less than five years old.
Yes ☐ No ☐

Comments
.....................................................................................................................
4. How well are your guidelines obeyed? Please approximate how much guidelines are obeyed and put a cross.

0% [ ] 20% [ ] 40% [ ] 60% [ ] 80% [ ] 100% [ ]

Comments

5. What nutritional screening is commenced when patients are admitted at your department?

Please put a cross against the most accurate alternative on each statement.

a) Information on any eating difficulties is obtained in

All patients [ ] A few patients [ ] No patients [ ]

b) Information on weight development is obtained in

All patients [ ] A few patients [ ] No patients [ ]

c) Body Mass Index is estimated in

All patients [ ] A few patients [ ] No patients [ ]

Comments

6. Which group of patients is the energy need estimated on?

Please put a cross against the most accurate alternative. Only one of the following statements is eligible.

We calculate the energy need

On all patients [ ] On all patients at risk\(^3\) [ ] Very occasionally [ ]

On no patients [ ]

Comments

\(^3\) Patients at risk, meaning at risk for undernutrition according to the following criteria.

- Patient with eating difficulties.
- Patient with involuntary weight loss (>5 % in one month or >10 % in 3-6 months).
- Patient with low BMI (<20)
If energy need is never estimated, please proceed to question number 12.

7. How is the energy need estimated?
Please answer each statement and put a cross for either yes or no.

a) By predicting energy need with an equation formula  Yes ☐ No ☐

b) By measuring the energy expenditure with indirect calorimetry technique4 Yes ☐ No ☐

Comments

4 Device measuring the amount of oxygen consumed and carbon dioxide produced and though that, indirectly measuring the energy expenditure.

If you answered “No” on question number 7a, please proceed to number 9.

8. Which equation is the most frequently used to calculate the energy need of your adult patients (kcal/day)?
Please put a cross against the most accurate alternative. Only one of the following 7 statements is eligible.

☐ 15-20 kcal/kg bodyweight

☐ 20-25 kcal/kg bodyweight

☐ 25-30 kcal/kg bodyweight

☐ Harris & Benedict’s equation

Harris & Benedict
Men: 66.5 + 13.7W + 5.0H - 6.8A
Women: 655.1 + 9.6W + 1.8H - 4.7A
W = Weight in kg
H = Height in cm
A = Age in years

☐ Harris & Benedict’s formula with corrections according to Long
### Long’s corrections for activity

<table>
<thead>
<tr>
<th>Activity</th>
<th>Correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bedridden</td>
<td>+12%</td>
</tr>
<tr>
<td>Walking</td>
<td>+13%</td>
</tr>
</tbody>
</table>

### Long’s corrections for trauma

<table>
<thead>
<tr>
<th>Trauma Type</th>
<th>Correction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe burns</td>
<td>+21%</td>
</tr>
<tr>
<td>Skeleton trauma</td>
<td>+13.5%</td>
</tr>
<tr>
<td>Severe sepsis</td>
<td>+16%</td>
</tr>
<tr>
<td>Minor operation</td>
<td>+12%</td>
</tr>
</tbody>
</table>

### Energy need with corrections according to The National Food Agency (old version)

<table>
<thead>
<tr>
<th>Predicted energy need/kg body weight</th>
<th>Correction of predicted energy need</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal metabolic rate</td>
<td>If the patient is thin +10%</td>
</tr>
<tr>
<td>Bedridden</td>
<td>If the patient is overweight -10%</td>
</tr>
<tr>
<td>Walking</td>
<td>If the patient is 18-30 years old +10%</td>
</tr>
<tr>
<td>At recovery</td>
<td>If the patient is &gt;70 years old -10%</td>
</tr>
<tr>
<td></td>
<td>For each degree &gt;37º C +10%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Predicted energy need/kg body weight</th>
<th>Basal metabolic rate</th>
<th>22 kcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted energy need/kg body weight</td>
<td>Bedridden</td>
<td>29 kcal</td>
</tr>
<tr>
<td>Predicted energy need/kg body weight</td>
<td>Walking</td>
<td>33 kcal</td>
</tr>
<tr>
<td>Predicted energy need/kg body weight</td>
<td>At recovery</td>
<td>40 kcal</td>
</tr>
</tbody>
</table>

Another equation is most commonly used by us and that is (write the formula)………………………………………………

Comments

………………………………………………………………………

### 9. What are your possibilities for using indirect calorimetry at your department?

Please put a cross against the most accurate alternative on each statement.

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>We have indirect calorimetry device(^4) at our department</td>
<td>☐</td>
</tr>
<tr>
<td>We have a routine for this</td>
<td>☐</td>
</tr>
<tr>
<td>We have staff members skilful in the measuring technique</td>
<td>☐</td>
</tr>
<tr>
<td>We call in a consultant for this measurement</td>
<td>☐</td>
</tr>
</tbody>
</table>

Comments

………………………………………………………………………
10. Who estimates the energy need most frequently at your department?
*Please put a number in each square for each administration route.*
0 = this administration route is not used at our department
1 = estimation of energy need is not used for this administration route
2 = the physician
3 = the dietician
4 = the registered nurse
5 = the nursing assistant

a) When nutrition is administered parenterally

b) When nutrition is administered enterally

Comments

11. Who prescribes the energy need most frequently at your department?
*Please put a number in each square for each administration route.*
0 = this administration route is not used at our department
1 = prescription of energy need is not used for this administration route
2 = the physician
3 = the dietician
4 = the registered nurse
5 = the nursing assistant

a) When nutrition is administered parenterally

b) When nutrition is administered enterally

c) When nutrition is administered orally

Comments
12. How is energy intake registered? What statement is most accurate?
Please put a cross against the most accurate alternative on each statement.

a) Calorie intake registration is recorded
   On all patients ☐   On all patients at risk ☐   Very occasionally ☐   On no patients ☒

b) Calorie intake registration is always recorded when different ways of administering nutrition are used simultaneously.
   Yes ☒   No ☐

c) Calorie intake registration is used to correct the daily energy balance.5
   Yes ☐   No ☒

Comments
……………………………………………………………………………………………………
……………………………………………………………………………………………………
5 Energy expenditure – Energy intake = Energy balance

13. How does your department define energy balance?
Please put a cross against the most accurate alternative. Only one of the following statements is eligible

☐ Calculated energy need minus energy intake
☐ Energy expenditure measured with indirect calorimetry4 minus energy intake
☐ Energy balance is not defined

Comments
……………………………………………………………………………………………………
14. When is body weight and body height measured in the patients?
*Please put a cross against the most accurate alternative on each statement.*

a) Both weight and height is measured within one week after admission
- On all patients [ ]
- On all patients at risk [ ]
- Very occasionally [ ]
- On no patients [ ]

b) Only weight is measured within one week after admission, not height
- On all patients [ ]
- On all patients at risk [ ]
- Very occasionally [ ]
- On no patients [ ]

c) How often is body weight measured
- Daily [ ]
- Every second day [ ]
- Once a week [ ]
- Every fortnight [ ]
- Once a month [ ]
- Weight is not measured [ ]

d) Height is measured
- On all patients [ ]
- On all patients at risk [ ]
- Very occasionally [ ]
- On no patients [ ]

Comments

…………………………………………………………………………

15. What different kinds of weighing equipment are accessible at your department?
*Please put a cross against all accurate alternatives.*

- Bed scales [ ]
- Hoist scales [ ]
- Shower scales [ ]
- Sitting scales [ ]
- Standing scales [ ]

Comments

……………………………………………………………………………………
16. Who, most frequently, documents the nutritional status of the patient?

*Please put a cross against the most accurate alternative. Only one of the following examples is eligible.*

- The physician
- The registered nurse
- The nursing assistant

Comments

17. Who, most frequently, reports the nutritional status of the patient to the next caregiver?

*Please put a cross against the most accurate alternative. Only one of the following examples is eligible.*

- The physician
- The registered nurse
- The nursing assistant

Comments

18. Are there any separate nutritional guidelines for patients with traumatic brain injury at your department?

- Yes
- No

Comments

Please control our answers and contact us if you have any questions.

**Thank you for participating!**

Yours Sincerely
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Acta Universitatis Upsaliensis

Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 523

Editor: The Dean of the Faculty of Medicine

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