Health related quality of life in Critically ill Patients

A study of health related quality of life in critically ill patients admitted on the Intensive Care

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Gezondheidsgerelateerde kwaliteit van leven bij ernstig zieke patiënten

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Contents

List of abbreviations

HRQOL: Health Related Quality of Life
ICU: Intensive Care Unit
SF-36: Short-Form 36
PF:Physical Functioning
RP:Role limitation due to Physical problems
BP:Bodily Pain
GH:General Health
MH:Mental Health
RE:Role limitation due to Emotional problems
SF: Social Functioning
VT: Vitality
Health transition item: evaluation of current health with one year
PCS: Physical Health Summary Score
MCS: Mental Health Summary Score
EuroQol-5D: EQ-5D
NHP: Nottingham Health Profile
SIP: Sickness Impact Profile
APACHE- and III: Acute Physiology, Age and Chronic Health Evaluation
ROC: Receiver operating characteristics
AUC: Area under the curve
MPII: Mortality Probability Model
SAPS II: Simplified Acute Physiology Score
MANOVA: Multivariate Analysis of Variance
MANCOVA: Multivariate Analysis of Covariance
IQR: Interquartile Range
PPV: Positive predictive value
NPV: Negative predictive value
LR: Likelihood ratio
CI 95%: Confidence interval
MOF/MODS: Multiple organ failure
QALY: Quality-Adjusted Life Year
PTSD: Post traumatic stress disorder
ALI: Acute Lung Injury
ARDS: Acute Respiratory Distress Syndrome
SIRS: Systemic Inflammatory Response Syndrome
LOS: Length of stay

Chapter 1.

Introduction and aim of this thesis

1.1 Introduction and aim of this thesis

Health related quality of life (HRQOL) is a relevant outcome measure for patients admitted to the intensive care unit (ICU). Long term outcome for physical and psychological factors, functional status and social interactions are becoming more and more important both for doctors and nurses as well as for patients and their relatives (1;2). Therefore doctors and nurses want to know what a "reasonable" quality of life means to their patients. The main reason for HRQOL research described in this thesis is the lack of knowledge about the outcome of HRQOL in critically ill patients admitted to an ICU. Especially, the time course of changes in HRQOL following discharge from the ICU and during a general ward stay has not been studied. In HRQOL studies in general as well ass in critically ill patients, there is a lack of a clear framework for defining and describing HRQOL. One of the difficulties in HRQOL research is defining what one means by health related quality of life: there is no universally accepted definition. QOL, health status, functional status, and HRQOL are often used interchangeable in the literature (3). Yet each of these terms may reflect different aspects of an individual's well-being (4). This also may lead to different measurement approaches which may lead to different results. Quality of life is described as a "unique personal perception" (5), influenced by social, psychological, cultural, familial, relational and individual factors. The World Health Organization defines "health" as not only the absence of infirmity and disease but also as a state of physical, mental and social well-being (6). Accordingly, an assessment of health related quality of life should reflect the patients' physiological and psychological status, social functioning and perception of health. The quality of life applied to health, or HRQOL, takes into account not all dimensions of the quality of life, but those that can be changed by the disease or its treatment. Finally, quality of life may be defined as a concept encompassing a broad range of physical and psychological characteristics and limitations that describe an individual's ability to function in their environment and derive satisfaction from so doing. Health related quality of life describes the level of well-being of the individual's life as affected by accident, injury, disease and treatments (7). Recent studies in critically ill patients have measured HRQOL, but an evaluation of conceptual issues is usually missing. **In Chapter 2**. we therefore discussed conceptual issues specifically related to HRQOL measurement in critically ill patients such as: "why measure HRQOL in critically ill patients?"; "how to define and standardize domains of HRQOL?", "what utility measures are used in research pertaining critically ill patients?"; "can proxies provide useful information about HRQOL in critically ill patients?"; "does response shift occur in critically ill patients?" and "do post-traumatic stress disorders occur in critically ill patients?". Evaluating these specific conceptual issues did not yield conclusive results. Some studies reported moderate agreement between patients and their proxies, although lower levels of agreement may be reported for psychosocial or physical functioning. Vigilance for symptoms of post-traumatic stress disorders (PTSD) is needed and early interventions implemented to prevent PTSD. Nursing care while in the ICU and intensive care follow-up may have an important role in recognizing and treatment of psychological problems after hospital discharge. Furthermore, response shift seems an important phenomenon and likely to be present, but is seldom measured when estimating HRQOL in critically ill patients.

To assess the effects of critical illness and intensive care treatment on HRQOL, measurements should be performed on admission to the intensive care. However this is rarely possible as the patient's condition on admission usually limits the filling out of a questionnaire. Nevertheless, assessment of the HRQOL on admission provides valuable information that could support the intensivist in decisions on admission and treatment policies. As most of the patients cannot fill in questionnaires at time of admission proxies must frequently be used.

However, can proxies provide useful information on HRQOL in critically ill patients? The literature concerning agreement between HRQOL assessment by patients and their relatives before ICU admission is not very conclusive. Some studies in critically ill patients reported moderate agreement between individual patients and their proxies, although lower levels of agreement may be reported for psychological or physical functioning (8;9). Other groups have raised concerns of proxy estimations of HRQOL (10). In **Chapter 3,** we studied whether the SF-36 questionnaire can be used to assess the patient's quality of life on admission to the ICU by use of proxies in both scheduled and emergency admissions**.**

Important is the time course of changes in HRQOL of patients following discharge from the ICU, during a general ward stay and after hospital discharge. Studies on the effect of critical illness on HRQOL show contradicting results. While some studies report impaired HRQOL following critical illness (11-13)**,** others show that a slow return to pre-morbid HRQOL occurs (14). Patients take both the burden of treatment as well as the functional outcome into account when deciding whether or not to accept treatment (15). It is therefore important to know the effect of critical illness on HRQOL in order to adequately advise patients and /or relatives. In addition, knowledge of the time frame and the potential of recovery of HRQOL is relevant. Recent studies have shown that poor HRQOL on admission is associated with the development of multiple organ failure during the stay in the intensive care (13) increased hospital mortality (16;17) and worsened HRQOL following discharge (18). Therefore assessment of the quality of life on admission provides valuable information that could support the intensivist in decisions on admission and treatment policies.

In **Chapter 4**. we studied the impact of critical illness and ICU stay on perceived HRQOL during ICU treatment, hospital stay, and after hospital discharge.

Can specific diseases, such as sepsis, influence the HRQOL of the patients after ICU treatment, and if yes, how much? Many patients admitted to the ICU have disorders in vital systems caused by sepsis. Severe sepsis is frequently complicated by organ failure that accounts for a persisting high mortality rate (19;20). Patients surviving severe sepsis might have impaired HRQOL like survivors of Acute Respiratory Distress Syndrome (ARDS). It is therefore important to know the effect of critical illness on HRQOL in severe sepsis patients and its recovery over time. It is difficult for doctors to predict whether a critically ill patient will survive ICU treatment. We have seen that HRQOL after ICU discharge is very important for patients and their relatives. In **Chapter 5**. we studied the impact of critical illness and ICU stay of patients with severe sepsis on perceived HRQOL during ICU treatment, hospital stay, and after hospital discharge.

Mortality in patents admitted to the ICU remains high (21). An increasing number of in-hospital patients die in the ICU (22). Can HRQOL before ICU admission be used as a predictor of mortality in patients and what is the value in clinical practice of using the pre-admission HRQOL to provide useful predictive information in order to inform decision making?. The advantages of a validated strategy to identify those patients who will not benefit from ICU treatment are evident. Providing critical care treatment to patients who will ultimately die in the ICU is accompanied by an enormous emotional and physical burden for both patients and their relatives. Furthermore, ICU resources are scarce, and identifying those patients who will not survive ICU treatment allows us to make better use of what resources are available (23). The available tools, including the Acute Physiology Age and Chronic Health Evaluation (APACHE) II score, are based on a combination of pre-morbid factors and acute physiology items recorded during the first 24 hours of admission. The use of these systems in individual patients is limited because they have been validated at the group level. Consequently, ICU doctors must rely upon their clinical experience in their decision making. The predictive value of clinical experience in this regard is also limited (24). The perceived HRQOL pre-admission ICU of patients also reflects components of ‘physiological reserve’ and could possibly, as such, act as a predictor of mortality. We examined HRQOL in critically ill patients before ICU admission and evaluated the predicting ability of survival at six months after ICU discharge in comparison with the APACHE II score in **Chapter 6**.

Every day, in Intensive Care Units, family members ask doctors and nurses questions like: “What will happen to my family member? Will she live? What will his life be like after this illness?” It is a challenge to link ICU care to quality of life experienced by patients and the burden of disease. What can we do to help our patients? To answer these questions we have to know what HRQOL means to patients and what the experiences of patients are pertaining to their stay in the ICU. Experiences of critically ill patients are an important aspect of the quality of the care in the ICU (25-27). The current treatment preference for patients requiring mechanical ventilation is to have patients non-sedated whenever feasible (28). Due to this non-sedation regime and the currently more used daily-wake up call when sedated, memories of patients’ experiences in the ICU are increasing. Patients’ memories of the ventilation period are especially related to the difficulties, in accepting, the inability to speak. Communication between patient and nurse is important and feelings of anger and low mood have been reported, which can lead to reduced rehabilitation (29). Both verbal and non-verbal communication can have a major impact on the patient’s stability and perceived care (26;28;30-32). Memories of hallucinations are a source of discomfort recalled by patients even after discharge. These experiences, also known as delusional memories, can be a sign of the so called ICU syndrome/delirium, which is a predictor of mortality (33). Furthermore the development of post-traumatic stress disorder (PTSD) symptoms may be related to delusional memories (34). Although functional sequelae seem to depend more on co-morbidities and on the critical illness of the patient, neuropsychological sequelae depend not only on the acute critical illness but also on the ability of patients to deal with the memories they retain from that period (34;35). Several studies have sought to identify factors that can function as stressors during an ICU stay, with the aim of preventing of decreasing them (36;37). Granja et al. suggested that neuropsychological consequences of critical illness, in particular the recollection of ICU experiences, may influence subsequent HRQOL (38). Nursing care for patients while in the critical care environment can have a positive effect on psychological well-being. In particular, the way the ICU nurse supports the patient during critical illness and subsequent recovery-periods is seen as an important factor in the patients’ contentment and perceived HRQOL post discharge. It is important to study the experiences of critically ill patients. However, such an understanding of patients experiences would have little value if it did not allow us to provide patients and relatives with follow up care. It is important to help patients in the coping with their experiences, in addition to physical and psychological complaints after ICU ultimately, influencing the perceived HRQOL. A follow up clinic following their discharge from hospital can be improving the speed and the quality of recovery from critical illness. In **Chapter 7.** we assessed patient experiences during ICU stay with specific attention to the perceptions of patients regarding support and nursing care.

If specific populations in the ICU are examined such as cardiac patients, a specific instrument can be used to give information and comparisons. However as ICU patients are a group with different diagnoses, there is a need for generic outcomes that can be used across medical and surgical critically ill patients, as well as condition-specific ones (39). Black et al.

published a literature review over the period from 1970 to August 1998 and concluded that the poor current state of knowledge of appropriate outcome measures for adult critical care survivors means that it is impossible to make clear recommendations as to which particular measures should be used and when and how they should be administered (39). Additionally Black et al. stated that there is an urgent need for rigorous assessment of the measurement properties being used in critical care research (39). In 2002 a consensus conference recommended the Short-form 36 (SF-36) and EuroQol-5D (EQ5-D) as the most appropriate instruments for future research (40). The EQ5-D requires significantly less time to complete compared with the SF-36. We chose the SF-36 because the SF-36 covers much more domains and is more precise compared with the EQ5-D, although imbalances between the different domains in the SF-36 are present. In **Chapter 8**. we performed a review from 1998 to 2007 of measurement properties of instruments that have been used in critically ill patients. The findings of this study and the implications for patient care and further research are discussed in **Chapter 9**.

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Chapter 2.

Conceptual issues specifically related to HRQOL in critically ill patients

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In part submitted

2.1 Abstract

Introduction *In the last years there is more attention for the quality of survival in critical care. Health related quality of life (HRQOL) is an important issue for both patients and family. Furthermore admission to intensive care (ICU) can have psychological effects in critically ill patients. Recent studies in critically ill patients have measured HRQOL, but an evaluation of conceptual issues is usually missing. We therefore discussed several conceptual issues specifically related to HRQOL measurement in critically ill patients.*

Measurements *Several conceptual issues were discussed such as: “why measure HRQOL in critically ill patients?”; “how to define and standardize domains of HRQOL?”; “what utility measures are used in research pertaining critically ill patients?”; “can proxies provide useful information about HRQOL in critically ill patients?”; “does response shift occur in critically ill patients?”; and “do post-traumatic stress disorders occur in critically ill patients?”.*

Results and conclusions *Evaluating these specifically conceptual issues did not yield conclusive results. Some studies reported moderate agreement between patients and their proxies, although lower levels of agreement may be reported for psychosocial or physical functioning. Vigilance for symptoms of PTSD is needed and early interventions to prevent PTSD implemented. Nursing care while in the ICU and intensive care follow-up may have an important role in recognizing and treatment of psychological problems after hospital discharge. Furthermore, response shift seems an important phenomenon and likely to be present, but is seldom measured when estimating HRQOL in critically ill patients.*

2.2 Introduction

Traditionally the assessment of critical care has focused largely on survival. Indeed, mortality in ICU patients remains high (1). However, there is more attention for the quality of that survival in the last years, which is an important issue for the patients and their family (2;3). Patients recovering from critical illness may show impaired functional status with an associated reduced HRQOL. In addition, the focus of doctors and nurses about people’s feelings in relation to prolonging patient lives is rising. The ideal outcome for the patient is to return to their preexisting functional and psychological status or a status acceptable for the patient (4), whereas the ideal outcome for society is the efficiency of care (5). Nevertheless, the long term impact for the patient and his family of ICU admission is increasingly recognized (6). Recent studies in critically ill patients have measured HRQOL, but an evaluation of conceptual issues is usually missing (7). Several questions could be asked such as: “why measure HRQOL in critically ill patients?”; “how to define and standardize domains of HRQOL?”; “what utility measures are used in research pertaining critically ill patients?”; “can proxies provide useful information about HRQOL in critically ill patients?”; “does response shift occur in critically ill patients?”; and “do post traumatic stress disorders occur in critically ill patients?”. We have chosen to discuss these conceptual issues specifically related to HRQOL measurement in critically ill patients because in HRQOL critical care literature these issues are usually missing however considered important.

2.3 Results

We discussed conceptual issues specifically related to HRQOL measurement in critically ill patients pertaining:

1. Why measure HRQOL in critically ill patients?
2. Definition and domains of HRQOL
3. HRQOL and utility measures in critically ill patients
4. Can proxies provide useful information on HRQOL in critically ill patients?
5. Response shift in critically ill patients
6. Post-traumatic stress disorders in critically ill patients

2.3.1. *Why measure HRQOL in critically ill patients?*

Development of ICU technology has seen a rapid growth in the last few years. This enables ICU staff to sustain and restore life of critically ill patients who would have otherwise died. In the past, survival alone was enough to justify all interventions, but the high costs makes ICU staff more and more aware about the importance of measuring the quality of life (8). The costs of ICU treatment are high and frequently a significant fraction of these costs are spent on patients with a poor prognosis and a large chance to die. It seems necessary to look at cost effectiveness and cost utility for developing guidelines in using ICU resources (9;10). However, how do ICU patients feel and function? This information seems essential for making decisions at the bedside, but is also important in the evaluation of the efficacy and efficiency of ICU interventions (11). HRQOL investigation in critically ill patients can make a contribution to answering these questions of long term prognosis (11).

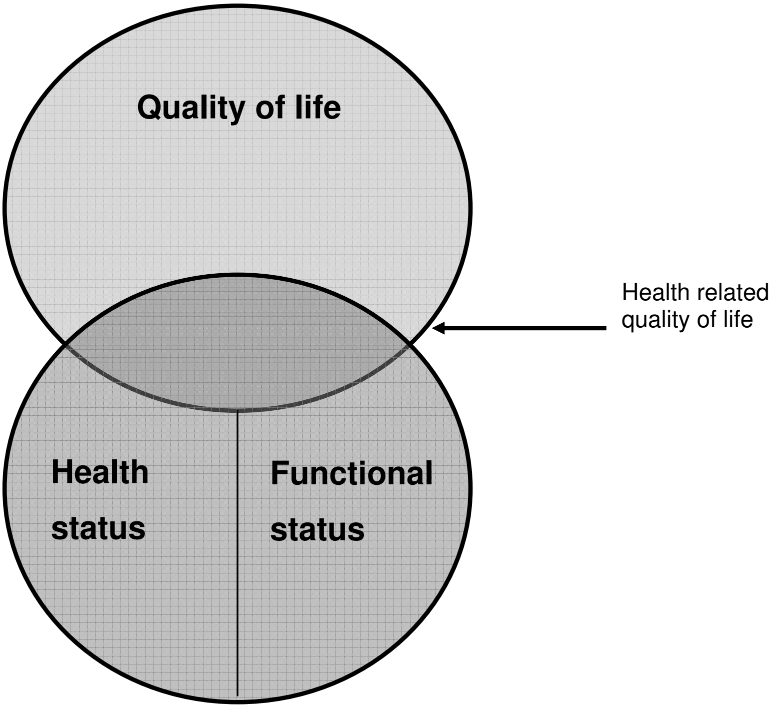
2.3.2 *Definition and domains of HRQOL in critically ill patients*

In HRQOL studies in general as well as in critically ill patients, there is a lack of a clear framework for defining and describing HRQOL. One of the difficulties in HRQOL research is defining what is meant by health related quality of life: there is no universally accepted definition. QOL, health status, functional status, and HRQOL are often used interchangeably in the literature (12). Yet, each of these terms may reflect different aspects of an individual's well-being (Fig.1) (11). This may lead to different measurement approaches, and thus different results. Measuring HRQOL is in essence evaluating the health status of individuals, both mental and physical, together with their own sense of well being (13). The World Health Organization defines health as not only the absence of infirmity and disease but also as a state of physical, mental and social well-being (14). By using this definition we can define HRQOL, which can be divided into several dimensions, including physical, psychological and social functioning. The physical domain contains items describing physical capacities of a patient and the physical complaints he or she has doing this activities, like bathing or dressing, walking, climbing stairs, pushing a vacuum cleaner, biking, carrying groceries or having pain. The psychological domain contains items describing psychological complaints, like feeling depressed or anxious, or positive feelings like satisfaction, feeling full of energy and happiness. The social domain contains items describing to what extent illness interfered with usual social activities with family, friends, neighbors or groups. Besides that, patients can also give their overall opinion of the three domains. This overall opinion shows what the influence is of illness and the associated treatment on the current health of the patient (14).

2.3.3 *HRQOL and utility measures in critically ill patients*

Treatment of patients in the ICU is expensive, and the justification for ICU treatment has been questioned on clinical, ethical and economic grounds (9;15). HRQOL measuring instruments (generic quality of life questionnaires) provide descriptive information about individuals and are used when researchers want to gain understanding about the impact of illness and treatments on patients, but also in changes to patient's health status over time. To incorporate differences in both quality and duration of survival, a unitary measure of outcome, the "Quality-Adjusted Life Year" (QALY), has been introduced (16). For example, a patient who gains ten years of life, with a quality of life of 60 % of normal, has gained six QALYs. Thus, a disease causing only morbidity can be compared with diseases causing mortality. These utility measures, such as the EQ-5D (17), Health Utilities Index (18) and SF-6D (19) assign a single value from 0, representing death or worst health imaginable, to 1, representing optimal health. Combining the utility value with survival data allows an estimate of quality-adjusted life-years (QALY's). Knowledge of outcome in terms of QALYs may potentially be used to assess the efficacy of the treatment in the ICU (16). Quality adjusted survival integrates two of the most basic and important patient-valued and society-valued objectives: to prolong life and to preserve or enhance quality of life. Viewed from this perspective, therapies that selectively improve the quality of life of survivors could be as valuable as therapies that decrease mortality (20).

Figure 1. What is quality of life?



2.3.4 Can proxies provide useful information on HRQOL in critically ill patients?

In critically ill patients it is rarely possible to assess the effects of critical illness or intensive care treatment because the patients condition on admission limits the filling out of a questionnaire. Often a close relative is also asked to function as a decision maker and to represent the patient for different therapeutic options (21). Completing a HRQOL measure on behalf of someone else requires proxies to put themselves in another person's shoes, to imagine what it feels like to be them, and to speculate about the impact of their health care on their experience of life. The literature concerning agreement between patients and their relatives assessment of HRQOL before ICU admission is not very conclusive. We and others have validated the use of proxies and found good agreement between proxy and patient (22). The use of proxies seems sensible, since critical illness itself could have influenced the recollection of the patient's pre-admission health status. However, concerns have been raised about proxy estimations of HRQOL in populations with greater disease severity (21). Scales et al. suggested that predictions of poor ICU outcome may be exaggerated if proxies underestimate HRQOL (21). However, in contrast to the afore mentioned studies, these investigators interviewed patients 3 months after ICU discharge and their proxies at study entry. This makes it entirely possible that survivors of critical illness may overestimate pre-admission HRQOL. Nevertheless, while relatives may not be fully able to express the patients' own perception of well being, their estimation of functional ability may sometimes be the only way to determine baseline HRQOL.

2.3.5 *Response shift in critically ill patients*

Patients accommodate to their illness. An important mechanism in this adaptation process is called 'response shift' which involves internal standards, values and the conceptualization of HRQOL. Response shift is the change in internal standards of values and of conceptualization and consequently in the perception of HRQOL (23). This could be either because patients become accustomed to their illness or chronic disease or because their expectations about their HRQOL have changed. Cohen (1982) stated that coping was a crucial factor for quality of life (24) also patients' coping ability was found significantly positively correlated with quality of life (25). Recent research documents the presence and importance of response shifts in both treatment outcome research and longitudinal observations of HRQOL. Several studies suggest that patients make significant response shifts during treatments, i.e. in patients with cancer (26;27), multiple sclerosis (28), or pancreas-kidney transplants (29). To our knowledge no studies are performed to investigate response shift in critically ill patients.

The question is whether we can measure response shift in critically ill patients. Response shift is not only important in longitudinal observations of HRQOL but also in medical decision making. Lenert et al. used preference-assessment methods common in cost-effectiveness analysis to investigate interactions between preferences and health status. They found that patients in poor health status valued intermediate health status almost as much as near-normal states. Conversely, patients in good health valued intermediate states nearly as little as poor health states. Patients in poor physical and mental health tended to recalibrate their standards for comparing health states in a manner that downplayed current personal problems, and small gains were more valuable to disabled than to healthy persons (30). To measure response shift some investigators used the then-test. The then-test is a method that aims to measure change in reference values by the comparison of a retrospective baseline measurement with a conventional baseline measurement (27). In the then-test, which is conducted at follow-up, patients are asked to provide a renewed judgment about their HRQOL at the time of the conventional baseline measurement. If the then-test is completed with a concurrent follow-up measurement, it is assumed that the same reference value is used for both assessments. Comparing the then-test with a follow up measurement has been proposed as a method to assess change in HRQOL over time, which is not confounded by change in reference values (27).

In conclusion, response shift is a phenomenon which is important and likely to be present but has rarely been investigated in critically ill patients.

2.3.6 Post- traumatic stress disorders in critically ill patients

Memory of traumatic experiences may lead to the development of psychological problems, such as post-traumatic stress disorders (PTSD). Critical illness can be a traumatic event. Emotional distress, anger, sense of loss, depression and anxiety are common problems experienced by people with critical illness (31). PTSD can be triggered by traumatic events and may last for years after the event. Characteristics symptoms include: re-experiencing the events through nightmares or flashbacks, avoidance of the stimuli associated with the event and hyper-arousal symptoms (32;33). The experience of critical care may precipitate symptoms of PTSD after discharge (34). Cuthbertson et al. found not only a high incidence of symptoms of PTSD in general critical care patients 3 months after discharge, but also that it was associated with younger patients and those who had been ventilated for longer, although not necessarily with overall length of stay. Cuthbertson et al. highlight how to identify patients with symptoms of PTSD and raise the possibility of scoring patients at risk before discharge home, assessing their recovery environment and ensuring patients are assessed at the critical care follow up clinic (34). Nursing care for patients while in the intensive care can have a positive effect on psychological well-being (32). Schelling et al.(35) tested the hypothesis that survivors of ALI had an increased rate of symptoms of post-traumatic stress and found that more Acute Lung Injury (ALI) survivors had evidence of post traumatic stress than did hospital control individuals and United Nations soldiers. Post traumatic stress was associated with impaired health-related quality of life and was highly correlated with the patients recollections of traumatic events from the intensive care unit. However a study conducted by Jones et al. (36) found that, although delusional memories of intensive care were associated with symptoms of PTSD, factual memories appeared to be protective. This study suggests that factual memories may allow ICU survivors to reject delusional memories and thereby decrease to reject the symptoms of post-traumatic stress.

We can conclude that vigilance for symptoms of PTSD is needed and early interventions to prevent PTSD implemented. Nursing care while in the ICU and intensive care follow-up may have an important role in recognizing and treatment of psychological problems after hospital discharge.

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Chapter 3.

Quality of life on admission to the Intensive Care: can we query the relatives?

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3.1 Abstract

Objective *To study whether the Short Form-36 questionnaire can be used to assess the patient's quality of life on admission to the ICU by use of proxies in both scheduled and emergency admissions.*

Design and setting *Prospective study involving direct interviews of patients and relatives before or during ICU stay in a 10- bed mixed intensive care unit in a 654- bed university affiliated hospital.*

Patients and participants *Patients before major elective surgery (n=55) or following emergency admissions (n=57).*

Measurements and results *Patients and proxies completed a health questionnaire in the first 72 h following emergency admission or the day before a scheduled admission to the ICU. Internal consistency was evaluated by measurement of Cronbach's α. All dimensions of the SF-36 had adequate internal consistency. On all eight dimensions a significant correlation was found between the patient and their proxy. In general, proxies underestimated the patient's quality of life although differences were small (less than 5%). On most items a good to very good agreement was found (α > 0.6). Quality of life assessment was not affected by the admission status of the patient (acute or elective admission and surgical or medical diagnosis).*

Conclusions *The SF-36 questionnaire completed by a proxy can reliable assesses the quality of life of the critically ill patient on admission to the ICU. Proxies underestimated the patient's quality of life, although the differences were small.*

3.2 Introduction

Surviving critical illness is the most important objective of admission to the intensive care unit (1;2). Subsequently scoring systems to predict changes in survival have been developed and probability of survival has been incorporated in many admission and discharge protocols (1;3). In addition, mortality data are used as a marker of quality of care for within unit and between unit comparisons. Finally, efficacy of new treatment schedules in intensive care is judged on their effect on mortality. However, once survival has been achieved, quality of life is a very important issue for the patient and his/her relatives. Quality of life has therefore been recognized as an important aspect of outcome in intensive care (3). To assess the effects of critical illness and intensive care treatment on quality of life measurements should be taken on admission to the intensive care. However, this is rarely possible as the patient's condition on admission usually limits the filling out of a questionnaire. Therefore all studies have used a retrospective assessments of quality of life on admission at the time when the patient was discharged from the intensive care (4). Relatives in close contact with the patient (proxies) have been found to adequately reflect the patient's quality of life at time of discharge from the intensive care by use of the Short-Form 36 (SF-36) questionnaire (4). Measuring quality of life at time of discharge from the intensive care reveals valuable information only in patients who have survived critical illness. In addition, recent studies have shown that poor quality of life on admission is associated with the development of multiple organ failure during the stay in the intensive care (5), increased hospital mortality (6;7) and worsened quality of life following discharge (8).Therefore assessment of the quality of life on admission provides valuable information that could support the intensivist in decisions on admission and treatment policies.

As most of the patients cannot fill in questionnaires at time of admission proxies must frequently be used. However, the use of proxies at time of admission has not been validated and could be limited by the acute and possibly life threatening condition of their relative.

We therefore studied whether the SF-36 questionnaire could be used to assess the patient's quality of life on admission to the ICU by use of proxies in both scheduled and emergency admissions.

3.3 Materials and methods

Patients and proxies

Patients eligible for the study were those admitted to the intensive care of the Gelre Lukas hospital, a 654-bed university affiliated hospital with a 10 -bed mixed intensive care unit. Between June 1999 and January 2000 we screened 318 admissions, 206 of which were excluded (sedation or an inadequate level of consciousness *n*=105, weekend-admission *n*=50, patients without an appropriate proxy *n*=34, readmission to the ICU *n*=10, other *n*=7). The study thus included 112 patients (mean age 66±13 years), most of whom had cardiovascular, respiratory, or gastrointestinal problems. Two groups were differentiated, those admitted following major elective surgery (*n*=55) and those with emergency admissions (*n*=57). These patients and their proxies completed the SF-36 questionnaire. Socio- demographic data and clinical characteristics of the patients and their proxies included in the study and of patients excluded are presented in Table 1.
The study was approved by the local ethics committee

Table 1 Sociodemographic and health status characteristics of ICU patients and proxies and the patients excluded from the study.

	All patients (*n*=112)	Proxies (*n*=112**)**	Elective admissions (*n*=55)	Emergency admissions (*n*=57**)**	Patients excluded (*n*=206)
Age (years)	66±13	-	63±12	68±13 *	69±11
Sex: M/F (%)	55/45	-	68/32	42/58	53/47
APACHE II	13±7	-	9±4	17±7 *	14±8
ICU Length of stay	2.8±5.2	-	1.7±3.3	3.8±6.4 *	3.0± 6.0
Hospital Length of stay	21.4±22.9	-	19.2±24.3	23.7±21.4 *	23.7 ± 21.4
*Diagnostic groups (%**)***		-	-	-	-
Cardiovascular	43	-	52	33	40
Respiratory	16	-	21	11	18
Gastrointestinal	23	-	18	29	17
Neurological	3	-	-	6	9
Trauma	2	-		4	5
Others	13	-	9	17	11
Type of proxy (%)	-	-	-	-	-
Spouse	-	43	58	23	-
Child	-	46	31	65	-
Brother/sister	-	9	9	12	-
Parent	-	2	2	-	-

* p<0.01 elective vs. emergency admissions

Proxies had to be in close contact with the patient on a regular basis. Patients and proxies were asked to complete the SF-36 within 72 h following emergency admission or the day before a scheduled admission to the ICU. When necessary, instructions and an explanation of the questionnaire were given. When the patient was unable to write, the patient was asked to point out the selected answers. Proxies were asked to answer the questions on behalf of the patient and mark the statement that best described the patient's state of health in the last 4 weeks prior to the admission. Proxies completed the questionnaire in a separate room, when possible at the same time as the patients. All interviews were taken by the same investigator (JH). Data collected on relatives included gender, degree of relationship and whether living with the patient. Demographic data and severity of illness (Acute Physiology and Chronic Health Evaluation II, APACHE II) of the patients were also collected. Proxies were predominantly spouses (43%) or sons/daughters (46%). Two patients (emergency admissions) died during ICU admission, while two emergency admissions subsequently died on the general ward. None of the elective surgery admissions died.

3.3.1 SF-36 questionnaire

The SF-36 is a widely used, standardized generic instrument. The SF-36 contains eight multi-item dimensions (total of 35 items): (a) limitations in physical activity related to health problems (ten items), (b) limitations in role activities because of physical problems (four items), (c) limitations in usual role activities because of emotional problems (three items), (d) vitality (four items), (e) general mental health (five items), (f) limitations in social activities because of physical or emotional problems (two items), (g) bodily pain (two items), and (h) general health perceptions (five items). In addition the SF-36 contains one health transition item (not contained in a dimension): change in health status during the past year is also assessed. Answers to the 36 items were transformed and weighted according to earlier recommendations and subsequent scoring was performed according to predefined guidelines (9). The SF-36 has been validated in primary care, for members of the general population (10;11) and for assessing quality of life following critical illness (12). Translation, validation and norming of the Dutch language version of the SF-36 health questionnaire have been evaluated in 1998 in community and chronic disease populations (13). The time required to complete the questionnaire was 15-20 min.

3.3.2 Statistical analysis

Spearman's correlation coefficient was used to calculate the correlation for the various dimensions of the SF-36 between patients and proxies. As we did not know the expected differences in scoring on the SF-36 questionnaire we included more than 100 patients/proxies with equal number of patients/proxies in the elective and emergency admission groups. In a paired *t*-test this number of patients/proxies can detect a difference of at least 10% (that we thought to be clinically relevant) in the mean SF-36 scores in all dimensions with a power of 0.90 and α of 0.05. Predefined subgroup analysis consisted of schedules vs. emergency admissions. A one-sample *t*-test was used to assess demographic differences between scheduled and emergency admissions. Cronbach's α coefficient was calculated to evaluate the internal reliability of the items of each dimension both for patients and proxies. Dimension reliability was defined as an $\alpha \geq 0.70$ (14). All data are expressed as mean ± SD were appropriate unless otherwise indicated. The level of agreement between patients and their proxies both in emergency and scheduled admission was further analysed using the Bland- Altman method (15) and the Kappa statistics for items of the SF-36. A weighted κ was used for data when the data collected allowed more than two ordered categories, otherwise an unweigthed κ was calculated. A κ value greater than 0.80 was regarded as indicating excellent agreement and one lower than 0.2 as indicating poor agreement between patient and proxy.

A p-value less than 0.05 was considered statistically significant. Data were analyzed using the Statistical Package for the Social Sciences.

3.4 Results

3.4.1 All patients

Cronbach's α varied between 0.76 and 0.93 and was best for physical functioning both for patients and proxies. A significant correlation was found for all eight dimensions between patients and their proxy. Correlation coefficients varied between 0.96 (physical functioning) and 0.76 (role limitation due to emotional problems). Although statistically significant, a low correlation coefficient was found for the general health perception item from the SF-36 (evaluation of current health compared to one year ago, r=0.48, p= ≤ 0.01;(Table 2). The mean weighted score for patients and proxies among SF-36 dimensions are summarized in Table 3. The highest difference was found on physical functioning (1.39±1.7, p< 0.01) and the lowest on role-emotional: (0.004±0.81; NS). On most items good to excellent agreement was found (κ> 0.6). Only two items scored moderate agreement (κ between 0.41-0.6).

Table 2. Summary of Spearman's correlation coefficient between SF-36 dimensions between patients and their proxies for all patients (*n*=112) and for elective (*n*=55) or emergency admissions (*n*=57) separately; all correlations were statistical significant (p<0.01)

	Items	All patients (*n*=112)	Elective *Admissions* (*n*=55)	Emergency Admissions (*n*=57)
Physical functioning	10	0.96	0.96	0.97
Role-physical	4	0.78	0.70	0.84 *
Bodily pain	2	0.86	0.87	0.87
General health	5	0.88	0.89	0.89
Vitality	4	0.86	0.80	0.92 *
Social functioning	2	0.83	0.84	0.81
Role- emotional	3	0.76	0.68	0.72
Mental health	5	0.80	0.78	0.83
Health transition item:				
Evaluation of current health with 1 year ago	1	0.48	0.38	0.59 *

* p<0.01 for the difference between elective or emergency admissions

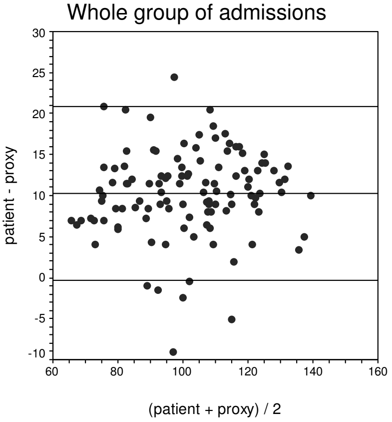
3.4.2 Scheduled versus Emergency admissions

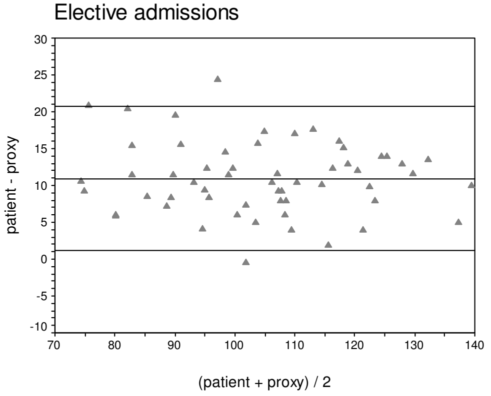
Scheduled admissions were significantly younger and had a significantly lower APACHE II score. Both length of intensive care and hospital stay was significantly longer in emergency admissions (Table 1). Cronbach's α was greater than 0.7 for patients and proxies in all dimensions. Also no significant differences in the Cronbach's α were found. In both scheduled and emergency admissions a significant correlation between patient and proxy was found for all items (Table 2). Both for the dimension role-physical functioning and the vitality dimension the correlation coefficient was significantly different between scheduled and emergency admissions (Table 2). When comparing surgical (*n*=23) and non-surgical patients (*n*=34) in the acutely admitted patients, no significant differences were found in any dimension. Both for elective and emergency admission the proxy underestimated the quality of life of the patient although the differences were small (Table 3). Bland-Altman analyses showed acceptable limits of agreement of the weighted score between patients and proxies for all dimensions (Table 4, Figures). No significant relationship was found between the differences in the weighted score and the mean of this score either in emergency or scheduled admissions. The κ scores for both scheduled and emergency admissions were good to excellent on all items in the physical functioning dimension. In the other dimensions moderate to excellent agreement was found.

Table 3 Mean SF-36 dimensions scores for patients and proxies for all patients (*n*=112) and for elective (*n*=55) or emergency (*n*=57) separately

	Max. score	All patients(*n*=112)		Elective (*n*=55)		Emergency (*n*=57)	
		Patient	Proxy	Patient	Proxy	Patient	Proxy
Physical functioning	30	22.1±5.8	20.7±5.8 *	23.2±5.3	21.7±5.5 **	20.9± 6.3	19.6±6.0 **
Role- physical	8	6.3±1.7	6.0±1.6	6.1±1.4	5.9±1.6	6.5± 1.7	6.2±1.6
Bodily pain	12	9.4 ±2.7	8.9±2.9 *	9.5±2.4	8.8±2.8 **	9.3± 3.0	8.9±3.0
General health	25	16.1±4.6	14,1±4.7 *	17.0±4.2	14.6±4.4 **	15.2± 4.8	13.5±5.0 **
Vitality	24	15.2±3.7	14.6±3.8 *	16.1±3.4	15.4±3.8	14.3± 3.7	13.7±3.7
Social functioning	10	7.3±1.9	6.8±1.9 *	7.5±1.7	7.0±1.8 **	7.1± 2.2	6.6±2.0
Role- emotional	6	4.7±1.3	4.6±1.2	4.3±1.2	4.3±1.3	5.0± 1.2	5.0±1.1
Mental health	30	21.6±3.8	21.0±3.9 *	22.1±3.4	21.4±3.8	21.2± 4.2	20.6±4.0
Health transition item	5	3.6±0.8	3.7±0.7	3.7±0.8	3.8±0.7	3.5±0.8	4.0±0.8

* p≤ 0.01 for all patients and proxies
** p≤ 0.01 between patients and proxies admitted electively and as emergency





Figures
Bland-Altman analysis of the total weighted scores of patients and proxies, in all patients and in emergency and elective admissions

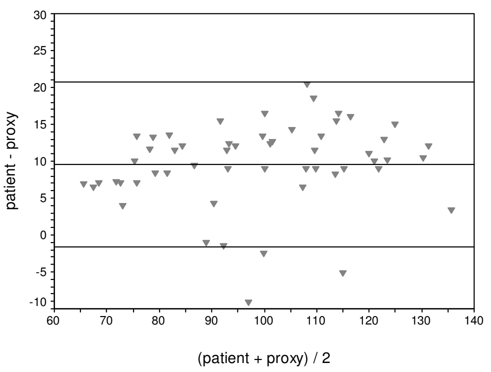


Table 4 Bland- Altman analysis of SF-36 dimensions for all patients and proxies (*n*=112) and for elective (*n*=55) or emergency (*n*=57) separately

	All patients (*n*=112)	Elective admissions (*n*=55)	Emergency admissions (*n*=57)
Bland-Altman analysis			
Mean Difference	102 ± 18	104 ± 16	99 ± 16
Limits of agreement	0 to 21	1 to 21	-2 to 21

3.5 Discussion

This study shows that relatives in close contact with the patient can adequately reflect the patient’s quality of life on admission to the intensive care by use of the SF-36 questionnaire. In general, proxies tended to underestimate the patients quality of life although the differences were small. The proxy best reflected the patient’s functional quality of life. Although we speculated that acute illness and emergency admission to the intensive care could bias the proxies we found no differences in the adequacy of the proxies to assess the patient’s quality of life between elective (all surgical patients) and emergency admissions.

Although survival is the most important objective of admission to the intensive care, quality of life following discharge is an important issue for patients, relatives and the physicians and nurses involved in the patient's treatment. Several factors underscore the assessment of the patient's quality of life. First, intensive care patients with a low quality of life on admission have higher hospital mortality and a worsened quality of life following hospital discharge (6-8). Wehler et al. (5), using the SF-36 questionnaire, found, in still preliminary data, that patients developing multiple organ failure (MOF) had lower physical health scores on admission than non-MOF patients. At follow up MOF patients had lower scores in most areas of physical health than non-MOF patients, whereas domains of mental health did not differ between the two groups. These data underscore the importance of physical health, as assessed by quality of life instruments, in surviving critical illness. Therefore the benefit of intensive care admission in patients with limited quality of life could be limited. Second, knowledge of the quality of life to be expected at discharge can be important for relatives, physicians, and nurses to value the appropriateness of additional interventions and/or further treatment. Third, to study the impact of critical illness and treatment schedules on quality of life adequate assessment on admission should be carried out. Finally, in addition to mortality, quality of life should be part of the evaluation of new therapeutic interventions in intensive care. On admission to intensive care the emergency procedures and abnormal levels of consciousness could limit the assessment of quality of life by the patient. In the current study many patients were not eligible due to sedation or inadequate level of consciousness. In addition, 33% of the patients included required help to adequately fill out the required questionnaire. Therefore the use of proxies to assess the patient's quality of life is often necessary.

A questionnaire used to assess quality of life should meet several conditions. First, the questionnaire used should have relevance to the patient's condition and should be validated in the societal context of the patient. The SF-36 questionnaire has been validated in patients with chronic obstructive pulmonary disease and those with stroke (16;17). In addition, as many different diagnostic groups are present in the ICU, the questionnaire should be robust and not disease specific. The SF-36 is a general instrument covering areas of quality of life without reference to a specific diagnosis (4). Also, the questionnaire should be relatively easy to fill out and should not take to much time. Although some have valued the SF-36 to be a too long and boring questionnaire (18) in our study the average time needed is 15 min. All patients showed much interest in the questions despite their sometimes difficult situation, and none of the eligible patients or proxies refused consent. Finally, when proxies are used to assess the patient’s quality of life, a significant and clinically relevant correlation is found between the patient's quality of life and the assessment made by the proxy. We found the proxies to adequately reflect the patients’ quality of life on admission to the intensive care when the SF-36 questionnaire was used. Others have reported similar results. Rogers et al. (4) and Crispin et al. (12) showed that the use of proxies and the SF-36 reliably assessed the patient’s quality of life at time of discharge from the ICU. Also in specific subgroups, proxies using the SF-36 have been found to adequately reflect the patient’s quality of life (19). However in specific dimensions, especially in the area of mental well- being (role limitation due to emotional problems) agreement between patients and proxy is moderate. Others have reported similar results (4;18;20-22). Relatives are more appropriate in their assessment of the physical characteristics than of psychological characteristics of the intensive care patient. We and others found that the physical health dimension was reflected best by the proxies (4). We speculated that acute illness could influence the perception and valuation of quality of life both by the patient and proxy. In the current study we therefore included both emergency and scheduled admissions to the intensive care. We found no differences in the agreement between patients and proxies in either elective or emergency patients. In both elective and emergency patients the differences in the mean weighted scores were small. Also, no differences were found in the agreement between patient and proxy in surgical and medical acutely ill patients. Recently Crispen et al. (12) reported similar results. However, in this study the patients were questioned at time of discharge from the ICU when the acute illness had already resolved. In addition questioning quality of life at discharge excludes the patients who die in the ICU, and therefore valuable information of the impact of poor quality of life on admission on survival is lost. Many of the seriously injured patients and critically ill patients had to be excluded from our study, as these patients were not able to fill out questionnaires. The current study is therefore limited, as the results from our emergency patients cannot be readily generalised to all emergency admissions. However, as we have found no significant differences in length of stay and APACHE II scores between the excluded and included patients we believe that in our patient population the results can be generalized to the more severely ill patients as well.

Interestingly, in all dimensions the quality of life assessment by the proxy was always lower than the patient although the differences were small. From our data we were unable to explore the reason for these differences. This underestimation was not related to the admission status as in both emergency and elective patients small but significant differences in the mean scores were found.

In conclusion, the SF-36 questionnaire completed by a proxy can reliably assess the quality of life of the critically ill patients on admission to the ICU. Proxies underestimated the patient’s quality of life, although the differences were small. Given the impact of baseline quality of life on morbidity and mortality of critical illness, assessment and subsequent valuation of quality of life on admission should be part of admission guidelines.

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Chapter 4.

The Impact of Critical illness on Perceived Health- Related Quality of Life During ICU treatment, Hospital stay, and After Hospital Discharge; A long- term Follow-up study

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4.1 Abstract

Introduction *The time course of changes in health- related quality of life (HRQOL) following discharge from the ICU and during a general ward stay has not been studied. We therefore studied the immediate impact of critical illness on HRQOL and its recovery over time.*

Methods *In a prospective study, all patients admitted to the ICU for >48 h who ultimately survived to follow up at 6 months were included. The Medical Outcomes study 36-item short form was used to measure HRQOL before ICU admission, at discharge from the ICU and hospital, and at 3 and 6 months following discharge from the ICU and hospital. An age-matched healthy Dutch population was used as a reference.*

Results *Of the 451 included patients, 252 could be evaluated at 6 months (40 were lost to follow up, and 159 died). Pre- ICU admission HRQOL in survivors was significantly worse compared to the healthy population. Patients who died between ICU admission and long term follow up had significantly worse HRQOL in all dimensions already at ICU admission when compared to the long term survivors. HRQOL decreased in all dimensions (p<0.001) during ICU stay followed by a rapid improvement during hospital stay, gradually improving to near pre-ICU admisison HRQOL at 6 months following ICU discharge. Physical functioning (PF), general health (GH), and social functioning (SF) remained significantly lower than pre-ICU admission values. Compared to the healthy Dutch population, ICU survivors had significantly lower HRQOL 6 months following discharge (except for the bodily pain score).*

Conclusions *A sharp multidimensional decline in HRQOL occurs during ICU admission where recovery already starts following discharge to the general ward. Recovery is incomplete for physical functioning, general health and social functioning when compared to baseline values and the healthy population.*

4.2 Introduction

Health-related quality of life (HRQOL) has been recognized as a relevant outcome measure for patients requiring ICU care (1). Predicting long-term outcome using physical and psychological factors, functional status, and social interactions is becoming more important both for doctors and nurses as well as for patients and their relatives (2;3). Various instruments have been described, but there is no uniform test for HRQOL in general, and not for ICU patients in particular. However, in a consensus conference, the Medical Outcomes Study 36-item short form (SF-36) and EuroQol-5D were recommended as the most appropriate instrument in this setting (4). The EuroQol-5D is a generic instrument that includes five dimensions and the EuroQol-5D visual analog scale. The SF-36 contains eight multiitem dimensions and is currently one of the most widely used generic questionnaires used in critical care medicine (5). However, only 2% of outcome studies in the ICU have used these outcome measures (6). Studies on the effects of critical illness on HRQOL have shown contradicting results. Where some studies (7-9) have reported impaired HRQOL following critical illness, others (9;10) have shown that a slow return to premorbid HRQOL occurs. In addition, the magnitude of recovery may differ among the different domains (11). Patients take both the burden of treatment as well as the functional outcome into account when deciding wether or not to accept treatment (12). It is therefore important to know the effect of critical illness on HRQOL in order to adequately advise patients and/or relatives. Second, knowledge of the time frame and the potential of recovery of HRQOL is relevant. The effect of critical illness on HRQOL is, however, difficult to assess as the condition of critically ill patients usually limits the adequate evaluation of their situation (13). We therefore validated the use of proxies to measure the patients'

HRQOL in the period before admission to the ICU (14), allowing us to study the changes in HRQOL during ICU and hospital stay. To our knowledge, no such data are available in the literature. The purpose of this study was to assess the immediate impact of critical illness and ICU stay on HRQOL and to follow the recovery of HRQOL immediately following discharge from the ICU up to 6 months.

4.3 Materials and Methods

All patients admitted for > 48 h to a 10-bed closed-format mixed surgical-medical ICU of a 654 -bed university affiliated hospital in the Netherlands were eligible for the study. Between September 2000 and April 2004, all 2127 patients admitted to the ICU were screened for study participation (Fig 1). In patients readmitted to the ICU (*n*=36), data on HRQOL at discharge from the final ICU admission were included in the study. All patients surviving the 6-months follow-up period were included in the study (*ie*, long-term survivors). Nonsurvivors were defined as all patients who died between ICU admission and the 6 months follow-up. The study was approved by the local ethics committee, and informed consent was obtained at entry into the study from the partner or legal representative of the patient. As soon as possible, informed consent was also obtained from the patient.

4.3.1 *HRQOL Measurement*

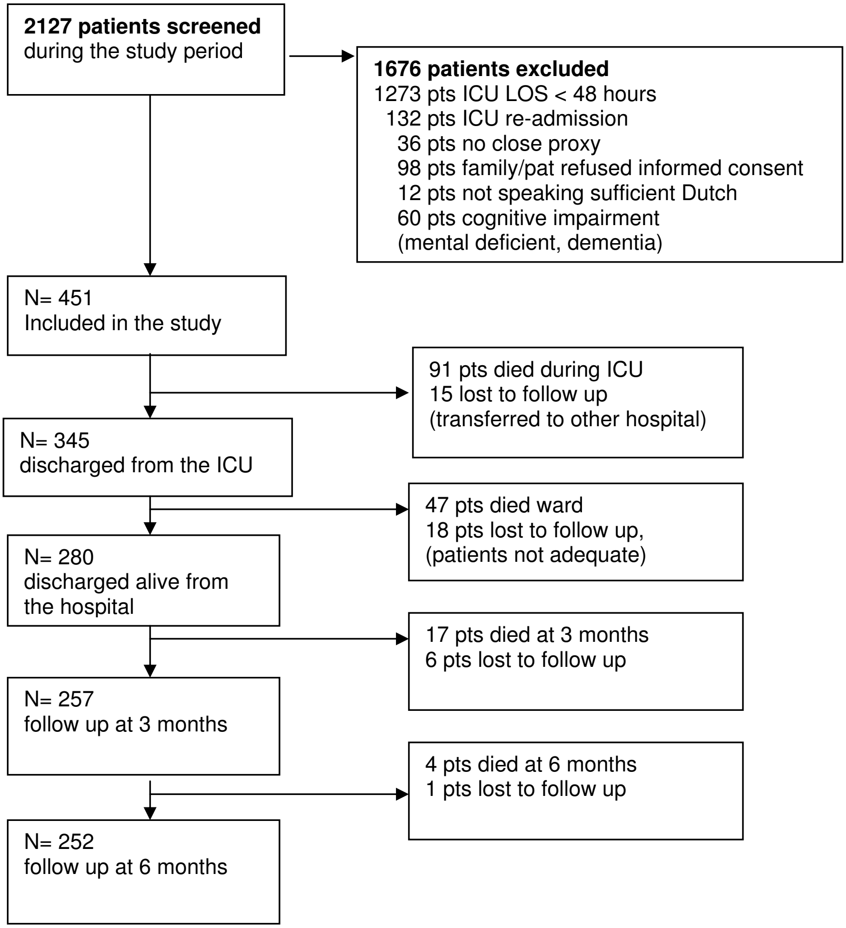
Pre-ICU admission HRQOL was measured within 48 h following ICU admission. Proxies were asked to assess the HRQOL of the patient 1 month before ICU admission. Proxies had to be in close contact with the patient on a regular basis. HRQOL was further measured at discharge from the ICU, at hospital discharge, and at 3 and 6 months following ICU discharge. At the time of discharge (from the ICU and the hospital), the patients were specifically asked to score their HRQOL according to their current situation. One investigator (JH) conducted all of the interviews to complete the questionnaire (average completion time, 15 to 20 min). During hospital admission, patients completed the questionnaire by personal interview. Post-hospital discharge patients were invited to come to the outpatient clinic for the personal interview, or the interview was conducted by phone. When needed, the investigator (JH) visited the patients at home. We used the Dutch language version (validated in 1998) (15) of the SF-36, which is a validated and reliable generic instrument (16) to measure HRQOL (17). This instrument contains eight multiitem dimensions (*ie*. physical functioning (PF), role limitation due to physical problems (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role limitation due to emotional problems (RE), and mental health (MH). Answers were transformed, weighed, subsequently scored (range 0 to100), and aggregated to summary measures according to pre-defined guidelines. The physical health summary score (PCS) reflects physical functioning, physical role, bodily pain and general health. The mental health summary scale (MCS) reflects vitality, social functioning, emotional role, and mental health (18).

4.3.2 *Statistical analysis*

X^2 tests were used to assess the demographic differences between ICU survivors and ICU nonsurvivors. Independent *t* tests were used to detect differences in the mean SF-36 scores in all dimensions at admission between ICU survivors and ICU nonsurvivors. Paired *t* tests were used to analyze the changes between two time points. To analyze individual changes over time, multivariate analysis of variance was used with Wilks' lambda as the multivariate test and

Bonferroni correction as the adjustment for multiple comparisons as we had more than one dependent variable with repeated measurements. The acute physiology and chronic health evaluation (APACHE) II score and patient's age were used as covariates in the multivariate analysis of covariance. Although age is a variable in the APACHE II score, the analysis showed that age proved to be predictive independent of the APACHE II score. To examine the relevance of the changes in HRQOL over time and between groups, effect sizes were calculated using the mean change of a variable divided by its baseline SD (19). An effect size of ≥ 0.20, ≥ 0.50, and > 0.80, respectively, were considered to be small, medium, and large (20). All data are expressed as the mean ± SD, unless otherwise indicated. The study received institutional review board approval, and proxies and, subsequently, all patients were asked for consent.

Figure 1. Flow diagram of the patients screened and included in the study.



4.4 Results

Of the 2127 patients screened, 1676 patients were excluded (Fig.1). Of these excluded patients, 179 died while in the ICU (10.7%) and 87 died while on the general ward (5.2%). In the 451 patients included in the study, HRQOL was measured on ICU admission, and in 252 patients at the 6 months follow-up. At that time,159 patients had died and 40 patients (9%) were lost to follow-up (Fig.1). The demographic and clinical characteristics of the patients lost to follow-up did not differ from the group analyzed in the study (data not shown). Demographic and clinical characteristics are shown in Table 1. About half of the patients were admitted to the ICU due to acute non-surgery-related illness. The majority of the surgical patients were admitted to the ICU following acute surgery. Pre-ICU admission HRQOL in patients >80 years of age was significantly lower in four dimensions (PF, p<0.001; RP, p<0.005; VT, p<0.05; SF, p<0.05; and PCS, p<0.001) compared with patients < 80 years of age, indicating that preadmission HRQOL was impaired in patients with advanced age. The nonsurviving patients were older, more severely ill, had a longer duration of mechanical ventilation and stayed in the ICU longer than the long- term survivors (Table 1).

Table 1. Demographic and clinical characteristics

Characteristics	All patients (*n*=451)	Long term survivors (*n*=252)	Non-survivors (*n*=159)
Age (yr)	69 ± 13	67 ± 12	74 ± 9 ŧ
Sex: M/F (%)	61/39	58/42	66/34
APACHE II score	19.2 ± 6.6	18.1 ± 6.1	21.5 ± 6.5 ŧ
ICU length of stay d	15 ± 19	13 ± 15	18 ± 22 Φ
Hospital length of stay d	33 ± 30	37 ± 33	27 ± 29 ŧ
Mechanically ventilated patients No.	420	226	156 Φ
Ventilation days No.	11 ± 17	9 ± 14	15 ± 20 ŧ
Renal replacement therapy No.	64	19	41 ŧ
Diagnostic groups %			
Cardiovascular pathology	27.9	29.6	27.0 ŧ
Respiratory pathology	30.2	28.0	32.7 Φ
Gastrointestinal pathology	34.8	38.0	31.4 ŧ
Neurologic pathology	3.3	0.8	6.9
Trauma	3.3	3.6	0.6 Φ
Others	0.4	0.0	0.4
Type of admission %			
Medical •	53.2	47.6	62.3 Φ
Elective surgical †	8.7	12.8	8.2 Φ
Acute surgical #	38.1	39.6	29.6 ŧ

* Values are given as mean ± SD, unless otherwise indicated; ŧ p<0.001 (long-term survivor vs. nonsurvivors);Φ p<0.01 (long-term survivor vs. nonsurvivors);• All nonsurgical hospital admissions not for elective or acute surgery;†Scheduled >24 h before surgery;# Scheduled <24 h before surgery

4.4.1 Changes of HRQOL Over Time

In surviving patients, all dimensions of the SF-36 changed significantly over time (p<0.001) (Table 2, Fig.2). Consequently, the PCS and MCS score also changed significantly. Age or APACHE II score did not influence these changes. At ICU discharge, the MCS showed a small but significant decrease from pre-ICU admission. However, at hospital discharge the MCS score had recovered to pre-ICU admission values and improved even further in the 6 months following ICU discharge (Table 2, Fig.2). ICU stay was associated with a sharp decline in HRQOL in almost all dimensions (except bodily pain) and summary scores (except the MCS score) followed by a significant improvement in HRQOL already during general ward admission that was maintained or further improved in the follow-up period (Table 2, Fig.2). Although at 6 months following ICU discharge HRQOL in the physical functioning, role-physical, general health, and social functioning dimensions were still significantly lower compared to pre-ICU admission values, the effect sizes were only small to medium (Table 2, Fig.3).

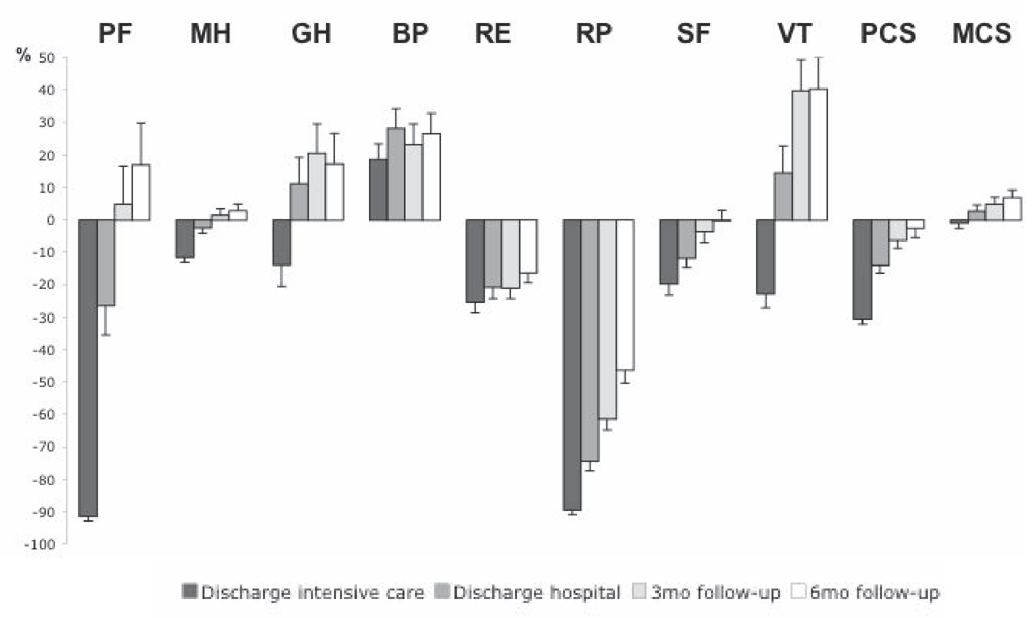


Figure 2. Diagram showing the changes from baseline values in the 252 patients surviving to 6 months following discharge. Pre-ICU admission scores are set to zero-level. Negative changes denote a decline in HRQOL in the dimension or component score. Data are expressed as the mean±SD. Differences between timepoints are given in Table 2.

Table 2. HRQOL in ICU survivor in the Period Between ICU admission and 6 months after ICU discharge

SF-36 dimensions	Pre-ICU admission		ICU discharge	Hospital discharge	3 months	6 months	Individual changes over time Wilks lambda	Pre-ICU admission vs 6 months	Healthy population	P value 6 months vs Healthy population
	All patients	ICU-survivors								
	(*n*=451)	(*n*=345)	(*n*=345)	(*n*=280)	(*n*=257)	(*n*=252)	(*n*=252)	(*n*=252)	(*n*=1742)	
PF	59.4±34.5	61.9±35.1	4.3±10.6	31.3±26.3	49.0±32.0	53.5±32.9	<0.001	<0.001 Φ	71.7±25.6	<0.001 ǂ
RP	48.4±47.0	51.9±47.6	7.4±23.3	20.3±36.2	28.9±40.9	38.9±44.6	<0.001	<0.001 ǂ	67.3±40.9	<0.001 ǂ
BP	80.5±25.4	79.9±24.8	78.3±25.7	85.6±21.3	83.1±23.4	84.8±23.2	0.014	0.16	70.5±24.6	<0.001 ǂ
GH	53.6±29.1	56.5±29.7	34.6±20.7	43.1±23.1	47.5±24.9	46.6±24.6	<0.001	<0.001 Φ	61.7±20.2	<0.001 ǂ
VT	53.8±25.3	55.8±25.7	31.0±16.8	45.0±19.6	56.4±23.0	58.6±22.8	<0.001	0.83	67.7±19.6	<0.001 Φ
SF	75.5±25.3	77.8±25.3	54.6±25.8	66.3±26.3	72.6±28.8	77.1±25.0	<0.001	0.02 Φ	82.0±24.6	0.002 Φ
RE	73.6±41.4	74.2±41.6	61.6±44.6	69.4±46.6	70.1±43.9	76.6±40.2	0.002	0.88	81.8±35.0	0.033 Φ
MH	67.6±17.1	69.2±16.8	57.8±17.7	65.1±13.6	68.2±16.4	69.3±16.0	<0.001	0.16	76.9±17.9	<0.001 Φ
PCS	41.6±13.5	42.6±13.6	26.2±5.9	33.4±9.0	37.5±10.5	38.9±11.2	<0.001	<0.001 Φ	-	-
MCS	48.8±10.9	49.5±10.6	46.7±10.0	49.1±9.9	50.2±11.4	51.2±10.1	0.014	0.38	-	-

Values are given as the mean ± SD, unless otherwise indicated; Ŧ Difference, 6 month vs healthy population; Φ Small effectsize (≥ 0.20);
ǂ Medium effect size (≥ 0.50)

4.4.2 Pre-ICU Admission Scores in Relation to Survival

Pre-hospital admission scores in seven of the eight dimensions were significantly lower in the nonsurvivors compared to the survivors (Table 3, Fig.4). The effect sizes were large (role-physical dimension) and medium (physical functioning, vitality, social functioning and mental health dimensions). Both survivors and nonsurvivors had a significantly lower pre-hospital admission HRQOL when compared to the age matched healthy control population (Table 3). The effect size of the differences for the survivors was however, small. In the nonsurviving patients, even more dimensions were significantly impaired (six of eight dimensions) than in the healthy population with small- to- medium effect sizes. In contrast to the nonsurviving patients, long term survivors had similar HRQOL in the social functioning and mental health dimensions, whereas the score on bodily pain was even better, when compared to the aged- matched healthy control population (Table 3, Fig.4).

Table 3. HRQOL in Long-term ICU Survivors and Non-survivors Compared to the healthy Dutch population

SF-36 Dimensions	Pre-ICU LT-Surv (*n*=252)	Pre-ICU NS (*n*=159)	LT-Surv vs NS	HP A (*n*=1742)	HP B (*n*=1742)	LT-Surv vs HP A	NS vs HP B
PF	66.3±33.6	47.7±32.1	<0.000 †	71.7±25.6	58.9±30.8	0.01 Φ	<0.001 Φ
RP	56.6±47.2	33.0±42.8	<0.001 •	67.3±40.9	56.9±44.0	<0.001 Φ	<0.001 †
BP	81.5±27.5	78.0±27.7	0.212 Φ	70.5±24.6	68.1±27.4	<0.001 Φ	<0.001 Φ
GH	58.5±29.2	45.3±28.1	<0.001 *	61.7±20.2	58.9±21.1	0.09 Φ	<0.001 †
VT	58.6±25.9	45.3±22.6	<0.001 †	67.7±19.6	61.8±23.6	<0.001 Φ	<0.001 †
SF	81.6±23.9	67.0±25.2	<0.001 †	82.0±24.6	75.6±27.0	0.82	<0.001 Φ
RE	76.7±41.1	67.9±42.2	0.039 Φ	81.8±35.0	74.5±38.2	0.05	0.051 Φ
MH	71.1±16.7	62.2±16.9	<0.001 †	76.9±17.9	73.0±19.9	0.08	<0.001 †
PCS	43.9±13.1	37.3±12.5	<0.001 †	-	-	-	-
MCS	50.4±10.5	46.7±11.1	0.001 Φ				

* Values are given as the mean ±SD, unless otherwise indicated. LT-Surv = patient alive at 6 months following ICU discharge; NS= nonsurvivors; HP= healthy population; HP A= subgroup 61-70 years of age; HP B= subgroup >70 years of age; Difference, LT surv vs NS;.Φ Small effect size (≥ 0.20); †Medium effect size (≥ 0.50); Large effect size (> 0.80).

4.5 Discussion

Both the change in HRQOL during ICU admission and its immediate recovery following ICU discharge have never been studied. This long-term prospective study evaluated the impact of critical illness on the perceived HRQOL in patients admitted to the ICU for >48 h and surviving up to 6 months following ICU discharge. Before ICU admission, HRQOL was already impaired when compared to the healthy population. This was even more pronounced in the nonsurvivors. Critical illness caused a significant drop in all HRQOL dimensions (except for bodily pain) and the component scores. Interestingly, the recovery of HRQOL during the general ward stay was the most significant improvement in HRQOL for the whole follow-up period of 6 months. At the end of the follow-up, the role- emotional and mental health dimensions had returned to pre-ICU admission values. However, physical functioning, role-physical, general health and social functioning dimensions remained lower than the pre-ICU admission values and the values for the healthy population.

Figure 3. Radar chart of the HRQOL in long term survivors at ICU admission and follow up compared to the healthy control population. Solid line with square= normal population; interrupted line with circle= survivors pre-ICU admission; interrupted line with triangle= survivors at 6 months following ICU discharge;$ = pre-ICU admission vs healthy population (significant difference, Table 3);* = pre-ICU admission vs 6- month follow-up (significant difference, Table 2);# = 6-month follow-up vs healthy population (significant difference, Table 2).

In this study, we used the SF-36 questionnaire to assess the quality of life. Other questionniares, like the EuroQol-5D, have been used in the ICU and would have required significantly less time to complete (8). However, the EuroQol-5D has not been clearly validated for ICU patients. In addition, the SF-36 covers much more domains and is more precise, although imbalances between the different domains in the SF-36 are present (21). We and others (5;14) have validated the use of proxies and found good agreement between proxy and patient. Although others reported (22) poor correlation when using substitute decision makers, a retrospective assessment at 3 months following ICU discharge of the pre-ICU admission HRQOL by the patient was used, and it was unclear whether the substitute decision makers were in close contact with the patient on a regular basis (23). In addition, we found that proxies, although in close contact, scored the HRQOL in patients with advanced age (*ie*, > 80 years of age) lower than in patients of younger age (*ie*, < 80 years of age).

Our follow-up occurred over 6 months following discharge from the ICU. The appropriate time for the assessment of HRQOL following ICU discharge has not been established. Cross-sectional studies of HRQOL in critically ill patients have been performed at 1 month (2), 3 months (24), 6 months (25;26) and 12 months after ICU discharge (27;28). A limited number of studies have retrospectively examined HRQOL over time and reported an improvement in HRQOL up to 6 months (26) and 12 months (24) following ICU discharge.

Like other studies (7;10), we also found that HRQOL at the time of discharge from the hospital was impaired and that a gradual improvement occurred during follow-up, in some cases to pre-admission hospital levels. However, we have shown, for the first time, that a major part of recovery was already accomplished on discharge from the hospital. This was especially true for the PCS score but also noticeable in all eight dimension scores and the other summary scores. It is important to recognize that we asked the patient to assess his actual HRQOL at the time of discharge from the ICU and just before hospital discharge. As the HRQOL measured by the SF-36 is subjective, we measured the HRQOL as perceived by the patient and thus did not use proxies. Joy over having survived the ICU admission or amnesia of the ICU admission may have caused this sharp increase in HRQOL despite the fact that many patients were still confined to the bed at the time of discharge from the ICU. This could also indicate that the patients developed active coping strategies during ICU recovery. This could be reflected by the observation that the MCS component score did not change from pre-hospital admission to hospital discharge and even significantly improved during follow-up in our patients. The hospital is situated in a region of the Netherlands were close communities of specific religions exist, and thus, the social network may be more advanced. As has been shown, (29) social support during the ICU stay, might improve post-ICU discharge HRQOL. In addition to the family, emotional support, and empathy, helpful accepting behaviour of the nurses and doctors could also have contributed to the development of these active coping strategies by the patients. In addition, a response shift, defined as the change in internal standards, values, or conceptualization of HRQOL (30), may have caused improvement in HRQOL during hospital admission. This could be because either the patients became accustomed to their illness or their expectations about their HRQOL had changed. As we did not study this, further studies would be needed to explore these mechanisms.

In our study, critically ill patients already had a lower pre-ICU admission HRQOL when compared to the healthy Dutch population. Others (2;9;26) have also reported decreased pre-ICU admission HRQOL in surviving patients. However, Cuthbertson et al. (7) showed that only pre-ICU admission physical scores were below values for the healthy population, whereas the mental scores were similar. Differences in inclusion criteria, case-mix, pre-ICU admission health status, comorbidity, social characteristics, individual coping capacity in patients from various geographical areas, and the assessment of pre-ICU admission HRQOL (prospectively vs retrospectively) may explain these differences (25;31).

In our study, these differences between critically ill patients and the healthy population were even more pronounced in the nonsurvivors, where they also had a significantly worse pre-ICU admission HRQOL when compared to survivors in all composite scores and all but one dimension score (bodily pain). One other study reported similar findings. Cuthbertson et al. (7) showed that the pre-ICU admission PCS was significantly lower in nonsurvivors when compared to survivors. Although the MCS score was also lower, this difference was not statistically significant. The definition of nonsurvivors was, however, very different from that in our study as these authors pooled all patients who died in the first year to the nonsurvivors group. The recovery of HRQOL was not complete at the end of follow-up at 6 months for physical functioning and general health. Others also have reported (2;9;26;27;32-35) significant decreased HRQOL at follow up. In contrast, other studies have reported (2) the full recovery of all health dimensions to pre-ICU admission levels 9 months following ICU discharge.

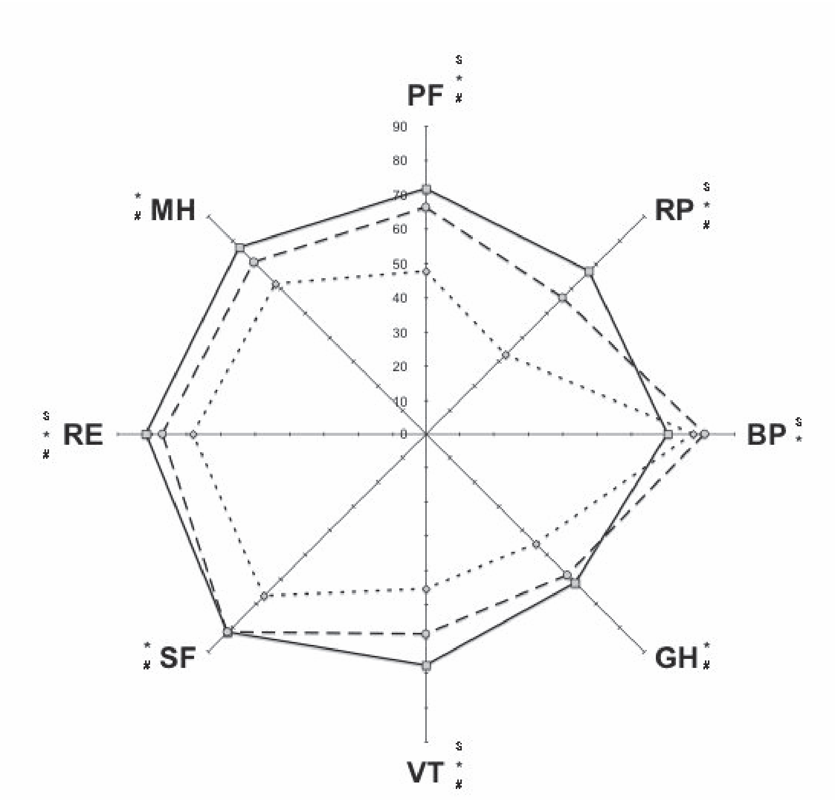


Figure 4. Radar chart of the HRQOL before ICU admission in long term survivors (n=252) and nonsurvivors (n=159) versus the healthy population. Solid line with square= healthy population; interrupted line with circle= survivors pre-ICU admission; interrupted line with diamond= nonsurvivors pre-ICU admission;$ =long term survivors pre-ICU admission vs healthy population (significant difference, Table 3);* = nonsurvivors pre ICU admission vs healthy population (significant difference, Table 3);# = pre-ICU admission long term survivors vs nonsurvivors at 6 month follow up vs healthy population (significant difference, Table 3)

This discrepancy may be explained by a different patient population (*ie*, in the study of Graf et al. (2) only 10 % of the patients received mechanical ventilation, whereas in our study 93 % of the patients received mechanically ventilation). Also, intermittent HRQOL assessments were not obtained, and temporal drops in HRQOL may have remained undetected in this study. This study is limited in that is was carried out in one hospital including only patients admitted for > than 48 h. Second, the interpretation of the results of ICU discharge and hospital discharge could have been biased, since the patients were specifically asked to score their HRQOL at the time of discharge from the ICU and hospital. Finally, the use of proxies to assess pre-ICU admission HRQOL has been questioned (22). Both patients and proxies may have encountered recall bias that could have limited the interpretation of the results. However, we and others (5;14;36) have validated the use of proxies when they were in close contact with the patient on a regular basis. In addition, all interviews were conducted in the same manner by only one person (JH).

In conclusion, this study demonstrates that critical illness, requiring ICU admission for > 48 h, has a strong impact on HRQOL. A sharp multidimensional decline occurred during ICU admission, followed by recovery towards normal functioning that started immediately following discharge from the ICU. Recovery was, however, not consistent in all dimensions of HRQOL. Before and after ICU admission, survivors of critical illnesses had lower HRQOL when compared to a healthy Dutch population. Also, nonsurvival was associated with a lower HRQOL on ICU admission. This study shows that the recovery of HRQOL already starts at ICU discharge so that rehabilitation programs should start early. As role limitations due to emotional and physical problems remained impaired at the 6-month follow up, specific interventions directed towards these dimensions of HRQOL may help to improve HRQOL following ICU discharge.

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Chapter 5.

The impact of severe sepsis on health related quality of life: a long term follow up study

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5.1 Abstract

Introduction *Severe sepsis is frequently complicated by organ failure and accompanied by high mortality. Patients surviving severe sepsis can have impaired health related quality of life (HRQOL). The time course of changes in HRQOL in severe sepsis survivors following discharge from the Intensive Care (ICU) and during a general ward stay has not been studied.*

Methods *We performed a long-term prospective study in a medical-surgical ICU. Patients with severe sepsis (n=170) admitted for >48 h were included in the study. We used the Short-form 36 (SF-36) to evaluate the HRQOL of severe sepsis patients before ICU admission, at discharge from the ICU and hospital and at 3 and 6 months following ICU discharge. Furthermore we compared the results for ICU admission and six months after ICU discharge with those of an age-matched general Dutch population.*

Results *At six months after ICU discharge 95 patients could be evaluated (8 patients were lost to follow up, 67 died). HRQOL showed a multidimensional decline during ICU stay and gradual improvement over six months following ICU discharge for the social functioning, vitality, role-emotional and mental health dimensions. However, six months after ICU discharge, scores for the physical functioning, role-physical and general health dimensions, were still significantly lower than pre-admission values. Physical (PCS) and mental (MCS) component scores changed significantly over time. In particular, MCS showed a small decline at ICU discharge but recovered rapidly and at six months after ICU discharge had improved to near normal values. In addition, these SF-36 scores were lower than those in a matched general population in six of the eight dimensions, except social functioning and bodily pain. Interestingly, the pre-admission HRQOL in surviving patients was already lower in three of the eight dimensions (role-physical, mental health and vitality) when compared to the general population.*

Conclusions *Severe sepsis patients demonstrate a sharp decline of HRQOL during ICU stay and a gradual improvement during the six months following ICU discharge. Recovery begins following ICU discharge to the general ward. Nevertheless, recovery is incomplete in the physical functioning, role-physical and general health dimensions at six months after ICU discharge compared with pre-admission status.*

5.2 Introduction

Severe sepsis is frequently complicated by organ failure that accounts for the persisting high mortality rate (1;2). Although survival is a primary goal of treatment in the Intensive Care Unit (ICU), health related quality of life (HRQOL) following discharge is an important issue for patients, relatives, and the physicians and nurses involved in the patient's treatment. Patients surviving severe sepsis might have impaired quality of life like survivors of Acute Respiratory Distress Syndrome (ARDS) (3). HRQOL is a complex outcome measure that can be measured by a generic instruments such as the Short-form 36 (SF-36). Heyland and coworkers showed that estimation of HRQOL with the SF-36 in ICU patients is possible and reliable (4). In particular, estimating patients' pre-admission HRQOL with the SF-36 appears to be a valid approach in spite of the fact that proxies frequently have to be used to fill out the questionnaire (5). Assessment of HRQOL can improve the answers given by doctors and nurses to patients and relatives about the prospects of their patients (23).

The purpose of this study was twofold: first, to describe the impact on HRQOL in patients with severe sepsis during the ICU and hospital stay, and until six months after ICU discharge, using the

SF- 36 and second, to compare HRQOL on admission and at six months after ICU discharge in survivors of severe sepsis with the general Dutch population.

5.3 Materials and methods

This study is part of a larger project aimed at the evaluation of HRQOL in critically ill patients. Patients eligible for this study were those admitted to the 10-bed closed-format mixed surgical-medical ICU of the Gelre Lukas hospital, a 654 -bed university affiliated teaching hospital in Apeldoorn, The Netherlands. Between September 2000 and April 2004 all admissions were screened for study participation. Patients admitted for the first time to the ICU with an expected length of stay for more than 48 h and fulfilling the criteria for severe sepsis were eligible for inclusion. The study was approved by the local ethics committee. Informed consent was given by proxies and later by patients before answering the HRQOL questionnaire. Patients with an impaired level of self-awareness or without the ability to communicate adequately at any time point during the study were excluded.

Severe sepsis was defined by the presence of infection or a likely focus of infection, two or more systemic inflammatory response syndrome (SIRS) criteria and dysfunction of one or more organ systems. Organ dysfunction was defined according to previous published criteria by Bone *et al*. (6). Patients' demographic data and severity of illness (Acute Physiology and Chronic Health Evaluation, APACHE II) of the patients were also collected.

5.3.1 Health related quality of life measurement

The Short-form 36 (SF-36 version 1; copyright 1993 Medical Outcome Trust), a generic widely used standardized health status questionnaire, was used to measure HRQOL. This measurement contains eight multi-item dimensions, i.e. physical functioning, role- physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. Answers to the 36 items were transformed and weighed according to earlier recommendations and subsequent scoring was performed according to predefined guidelines (7). Higher scores represent better functioning, with a range from 0 to 100. Furthermore, scores were aggregated to summary measures representing a physical component score (PCS, mainly reflecting physical functioning, physical role, pain and general health) and a mental component score (MCS, mainly reflecting vitality, social functioning, emotional role, and mental health) (8). Population scores on PCS and MCS have been standardized on 50 (SD10 representing 1) (8). The SF-36 has been validated in primary care, for members of the general population (9;10) and for assessing quality of life following critical illness (4;11). Translation, validation and norming of the Dutch language version of the SF-36 health questionnaire have been evaluated in 1998 in community and chronic disease populations (12).

We assessed the effects of critical illness and ICU treatment on HRQOL by using the SF-36 at admission (proxies), ICU discharge (patients), hospital discharge (patients), and three and six months after ICU discharge (patients). This evaluation period was predefined as earlier studies indicated that the changes are minimal among ICU patients after this period (13;14). As most ICU patients are not able to complete a questionnaire at the time of admission, proxies have to be used frequently. In this study, we assessed HRQOL in the four weeks before admission through proxies. This approach was validated in an earlier study by our group (15). Proxies had to be in close contact with the patient on a regular basis.

The first SF-36 questionnaire was completed within 48 h of admission. At time of discharge from the ICU and the hospital, the patients were specifically asked to score their HRQOL according to their current situation instead of their HRQOL in the past four weeks. During hospital admission patients completed the questionnaire by personal interview. All interviews were performed by the same investigator (JH). After discharge from the hospital the questionnaire was completed by personal interview or taken by phone. When needed the investigator (JH) visited the patients at home. The average time required to complete the questionnaire was 15-20 min. Presence or absence of delirium of the patients, especially at ICU and hospital discharge, was based on the opinions of the nurses, doctors involved in daily care of the patients, and close relatives. Patients suspected of delirious states or other incapacities were excluded from the study.

5.3.2 Statistical analysis

Paired T tests were used for evaluating changes between two time points. To analyze individual changes over time, a MANOVA test was used with Wilks' lambda as the multivariate test and Bonferroni correction as the adjustment for multiple comparisons, as we had more than one dependent variable with repeated measures. We studied APACHE II score and age by using them as covariates in multivariate analysis of covariance (MANCOVA). SF-36 dimensions of survivors were compared with normative data from the age-matched Dutch general population (12), using a one-sample t-test. To examine the relative magnitude of changes over time and between groups, effect sizes were used based on the mean change found in a variable divided by the baseline standard deviation (16). Effect sizes estimate whether particular changes in health status are relevant. Following Cohen (17), effect sizes of ≥ 0.20, ≥ 0.50, and > 0.80 were considered small, medium, and large changes, respectively. Data were analyzed using the Statistical Package for the Social Sciences (version 11.5). All data are expressed as means±SD where appropriate unless otherwise indicated. P<0.05 was considered to be statistically significant.

Table 1. Demographic and clinical characteristics in severe sepsis patients

Median (IQR)	Severe Sepsis (*n*=170)	Survivors six months (*n*=95)
Age (years)	70 (62-77)	66 (57-74)
Sex: M/F (%)	63.5/36.5	56.7/43.3
APACHE II	21(17-25)	20 (15-24)
Standard Mortality Ratio (SMR)	0.80	
ICU length of stay (days)	12 (7-22)	10 (7-18)
Hospital length of stay (days)	24 (16-48)	32 (20-56)
Ventilation days	10 (5-17)	8 (4-15)
Origin of sepsis (%)		
Respiratory	60 (35.5%)	38 (36.5%)
Abdominal tract	80 (47.1%)	46 (44.2%)
Urinary tract	12 (7.1%)	9 (8.7%)
Other	18 (10.6%)	11 (10.6%)
Type of admission (%)		
Non-surgical	58.2	57.7
Elective surgical	5.9	5.8
Emergency surgical	35.9	36.5

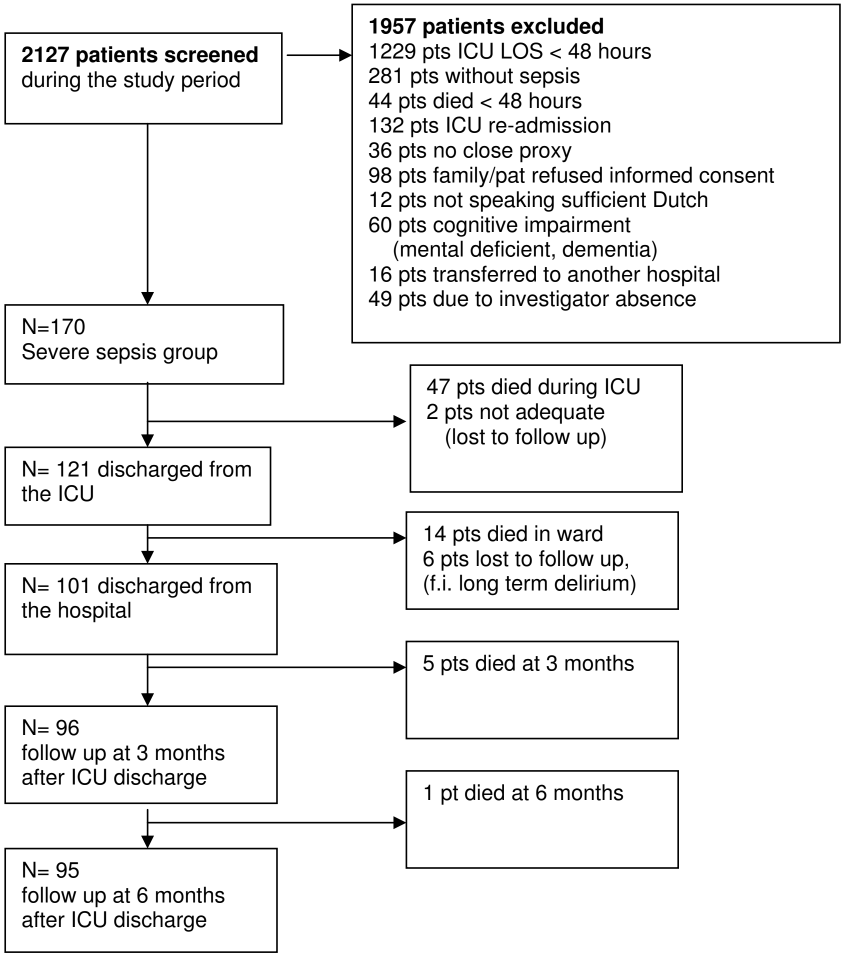
Elective surgical: ICU admission was planned within a 24-h period before surgery.
Emergency surgical: unplanned surgery.; Nonsurgical: all other admissions
APACHE-II: Acute Physiology and Chronic Health Evaluation; IQR: interquartile range

5.4 Results

5.4.1 Demographic and Clinical Characteristics

A baseline HRQOL was obtained from all 170 patients (63.5% male, 36.5% female) with severe sepsis. HRQOL was also measured at ICU discharge (*n*=121), hospital discharge (*n*=101) and at three (*n*=96) and six months (*n*=95) after ICU discharge. Mean age was 68 ±12 years. At six months, 67 severe sepsis patients had died (38.3%) and 8 patients were lost to follow up (Fig.1). The most frequent origins of severe sepsis were the abdomen (47.1%) and respiratory tract (35.5%). The type of admission was pre-dominantly medical (58.2%) or acute surgery (35.9%). Demographic and clinical characteristics of study patients are shown in Table 1.

Figure 1. Flow diagram of the patients screened and included in the study



5.4.2 Changes of HRQOL over time in survivors

During the study period a decrease was found in the physical functioning, role-physical, general health, vitality and social functioning dimensions. Scores were lower at ICU discharge and hospital discharge in comparison to baseline values (Table 2). These HRQOL aspects improved at three and six months after ICU discharge. There was a distinct pattern of a sharp multidimensional decline during ICU stay and gradual improvement in the six months following ICU discharge in all dimensions except for bodily pain and the mental component score. Nevertheless, six months after ICU discharge (*n*=95), average scores for the physical functioning, role-physical and general health dimensions were still significantly lower than baseline values (all P<0.05 ; Table 2; Fig.2). Effect size was medium for the role-physical (0.51) dimension and small for the physical functioning (0.37) and general health (0.41) dimensions. Bodily pain did not change at all during the study period. HRQOL decreased significantly over time in all dimensions in severe sepsis survivors except bodily pain (P<0.05; Table 2). Interestingly, the significant difference of the bodily pain dimension in sepsis survivors was based on a higher mean at six months compared with pre-admission (P< 0.002). The physical component score (PCS; P< 0.001) and mental component score (MCS; P<0.05) changed significantly over time (Fig. 3). The MCS showed a small but significant decline from ICU admission and had recovered to pre-ICU admission values at hospital discharge and improved even further when the situation at six months following ICU discharge was evaluated (Table 2). These changes over time were not influenced by age or admission APACHE II score.

5.4.3 *Comparison at six months: Severe sepsis survivors versus general population*

Patients who survived severe sepsis up to six months were compared with an age matched general population. The average SF-36 scores were lower than normal in six of the eight dimensions studied (all P <0.01) the exceptions being the social functioning and bodily pain dimensions (Table 2). Effect size was medium for the physical functioning, role-physical and general health dimensions (range:0.50-0.73). Average SF-36 scores of the bodily pain dimension was higher in the severe sepsis survivors, indicating less pain (Fig. 2, Table 2).

5.4.4 *Comparison of HRQOL before ICU admission with HRQOL in the general population*

The pre-admission HRQOL of severe sepsis survivors was compared to HRQOL in the general population. Three of the eight dimension scores (role-physical, mental health and vitality) were lower in the severe sepsis survivors (all P<0.001). However, effect sizes tended to be small (range: 0.13-0.28) (Table 3).

5.5 Discussion

This study is the first long term study evaluating the time course of changes in HRQOL for sepsis survivors during ICU admission following a general ward stay, and at six months after ICU discharge. Severe sepsis was associated with a sharp multidimensional decrease of HRQOL during ICU stay and gradual improvement in the six months thereafter. These changes over time were not influenced by age or APACHE-II score on admission, which was recently reported by others (18;19).

Table 2. HRQOL in survivors of severe sepsis in the period between ICU admission and six months after ICU discharge

SF-36 dimensions	Pre-ICU (All ICU Survivors)	ICU Discharge	Hospital discharge	3 months after ICU discharge	6 months after ICU discharge	Changes over time P value	Differences between pre-ICU (*n*=95) and 6 months after ICU discharge (*n*=95)		Differences between 6 months after ICU discharge with general population	
	(*n*=121)	(*n*=121)	(*n*=101)	(*n*=96)	(*n*=95)		Mean diff	95% CI	Mean diff	95% CI
Physical functioning	69.0 ±32.9	4.3 ±10.9	29.3 ±23.5	54.4 ±33.4	59.4 ±33.4	0.000	11.5	5.7-17.3*	-12.3	-19.0- -5.6**
Role-physical	56.4 ±47.4	3.9 ±15.4	13.1 ±29.9	27.0 ±40.0	39.2 ±44.4	0.000	20.4	8.8-32.0**	-28.1	-37.2- -18.9**
Bodily pain	81.3 ±28.5	82.8 ±24.0	89.4 ±17.7	86.1 ±21.6	83.1 ±25.2	0.002	-1.7	-9.7-6.4	12.7	7.5-17.9**
General health	58.1 ±30.5	31.6 ±19.7	39.3 ±19.5	44.0 ±24.5	46.9 ±24.1	0.000	12.0	4.9-19.1*	-14.8	-19.8- -9.8**
Vitality	58.9 ±25.2	30.2 ±16.2	45.0 ±19.2	57.2 ±22.0	59.8 ±21.5	0.000	1.0	-4.3-6.4	-7.8	-12.2- -3.4*
Social functioning	80.3 ±24.3	53.0 ±26.5	64.7 ±25.8	73.1 ±27.3	80.3 ±23.8	0.000	3.3	-2.1-9.4	-1.6	-37.2-3.3
Role-emotional	77.6 ±39.9	56.7 ±45.0	75.9 ±47.8	67.7 ±43.9	72.0 ±42.0	0.011	6.8	-4.0-17.6	-9.1	-6.5-3.3*
Mental health	69.7 ±16.6	57.1 ±11.4	65.3 ±13.3	68.0 ±16.5	69.8 ±15.4	0.000	1.8	-2.8-5.5	-7.0	-10.2- -3.8*
PCS	44.4 ±12.6	26.3 ±5.3	32.0 ±7.4	38.6 ±11.2	40.2 ±11.1	0.000	4.8	2.1-7.5	-9.5	-11.8--7.1***
MCS	49.8 ±9.6	45.7 ±9.5	50.0 ±9.1	49.3 ±11.2	50.8 ±10.0	0.018	-.05	-2.8-2.7	-1.2	-3.4-.91

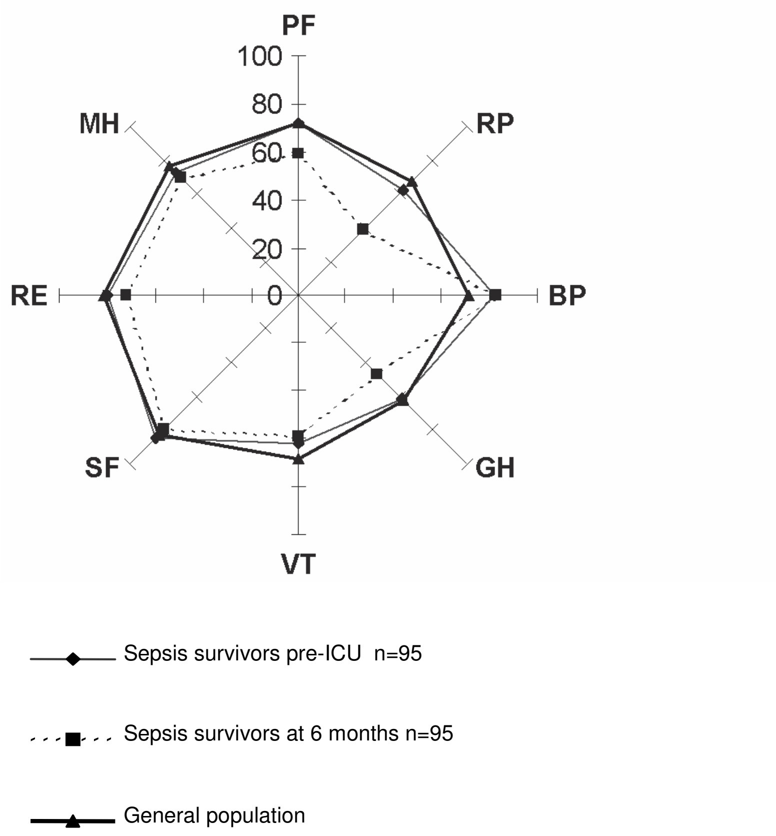
Effect size: * ≥ 0.20 small, ** ≥ 0.50 medium, *** > 0.80 large,
The mean age was 64.4 years in the study group and between 61-70 years in the age matched general population group
PCS: physical component score, MCS: mental component score ;Mean diff= Mean difference, 95% CI= 95% confidence interval
Mean ±SD general population Table 3;.Mean ± SD Pre-ICU long- term survivors (*n*=95) Table 3

Interestingly, the bodily pain dimension did not change at all during our study. A possible explanation may be a phenomenon called ‘response shift’, i.e. a change of one’s self evaluation resulting from changes in internal standards or values in patients confronted with a life-threatening disease or chronic uncurable disease (20). One could argue that ’response shift’ is more likely to occur in those dimensions which are prone to subjective influences such as pain. However, other studies in general ICU patients (18) and in ARDS patients (21) showed that the bodily pain dimension scores at 3 and 6 months after discharge were decreased.

The observed temporal drop in HRQOL during critical illness, with gradual improvement over time, concurs with previous findings (22;23). Graf et al. used the SF-36 in medical ICU patients staying for > 24 hours and found that physical and role- emotional scores had deteriorated one month after ICU discharge but returned to baseline nine months thereafter. In addition, they showed that the mental summary scale did not change during the investigational period (22). Wehler et al. investigated patients with multiple organ dysfunction syndrome (MODS) and found that 83-90 % of the survivors had regained HRQOL at six months after ICU discharge, although persistent deterioration was especially noted in the physical health domains (21;24). Herridge et al. found that patients with acute respiratory distress syndrome (ARDS) have persistent functional limitation one year after being discharged from the ICU (21). In line with our findings, the latter studies showed no impact on mental health domains (21;24). Our study showed a temporal drop in most domains of HRQOL during ICU stay which was followed by recovery starting immediately following ICU discharge. Other investigators have demonstrated persisting disturbance in HRQOL after ICU stay. Using a different scoring method, the EQ- 5D, a study in sepsis survivors (not evaluating baseline values) showed that HRQOL of sepsis survivors was fair at six months after ICU discharge. Nevertheless, moderate to severe problems were reported at percentages ranging 24-46 % in the five dimensions of the EQ-5D, which was similar to the HRQOL of other critically ill survivors admitted without sepsis (25). Moreover, the significantly lower response rate for the sepsis group could have induced a response bias, whereby survivors from the sepsis group with a lower HRQOL may be under represented (25). In addition, using the EQ-5D, in pre-dominantly abdominal sepsis, no significant difference in HRQOL was found between sepsis and trauma patients two years following intensive care treatment. HRQOL was reduced to the same level, i.e. 82 % of the patients reported a problem (moderate or extreme) in at least one dimension, but most patients (74 %) reported no problems in self-care (26). Bosscha et al. determined HRQOL after severe bacterial peritonitis at least 1 year after discharge and found that about 75 % of patients regained a good HRQOL, while some patients, especially those who suffered from persistent polyneuropathy and mental disorders, showed persisting limitations in daily life (27). Another study in abdominal sepsis patients 15 months after ICU discharge showed that 75% of survivors were independent, ambulatory and capable of self care (28). None of the survivors became completely disabled.

However, in addition to the published literature, our study has shown that in severe sepsis survivors recovery already starts following ICU discharge to the general ward. While in the critical care environment, nursing care for patients can have a positive effect on psychological well-being of patients and relatives (29). In particular, the way doctors and nurses support the patient during critical illness and recovery-periods is seen as an important factor in the patients’ contentedness and perceived HRQOL after ICU discharge (30).

Figure 2. Comparison of severe sepsis survivors before ICU admission in comparison to six months after ICU discharge versus the Dutch general population



5.5.1 *Comparison of general population with sepsis patients at ICU admission*

The pre-admission HRQOL in our study of severe sepsis survivors showed that three of the eight dimension scores (role-physical, mental health and vitality) were already lower in the severe sepsis survivors compared to HRQOL in the general population. This concurs with the finding that HRQOL at admission was reduced in comparison with a matched general population in patients with MODS (24), but also in comparison with general ICU patients (22). In contrast to these findings, pre-ICU HRQOL was reported to be unimpaired in 70% of medical-surgical ICU admissions (31). These differences may be explained by differences in the way HRQOL was measured, but also by the geographical setting, with inherent differences in case mix. Nevertheless, the aforementioned data indicate that severe sepsis patients frequently have a lower HRQOL before critical illness occurs.

5.5.2 *Comparison of general population with sepsis patients at six months after ICU discharge*

Six months after ICU discharge, HRQOL in severe sepsis survivors was still lower compared to a general population. This impairment occurred particularly in the role-physical, general health and physical functioning dimensions. Heyland et al. also found that survivors of sepsis have significantly lower average scores in physical functioning and general health dimensions but exhibit no differences in the emotional component compared to the general population (4). A limitation of that study is the small sample of included patients (*n*=30), which also puts the study of Perl et al. in a different perspective. Perl et al. assessed the HRQOL of 38 patients who survived Gram-negative sepsis and found that septic patients scored poorly on domains within the SF-36 that measure perceived physical function when compared with the general population (32). Even stronger impairment in HRQOL was reported by Pettilla et al. who studied patients with MODS using the SF-36. They compared HRQOL one year after ICU treatment with HRQOL in a general population and reported impaired scores for ICU survivors in all eight domains (33). On balance, it would seem that severe sepsis survivors have reduced HRQOL especially pertaining physical health. Whether this outcome is a result of the severe sepsis or the underlying co-morbid illness is unknown.

5.5.3 *Strengths and limitations*

We conducted a long term, prospective study which measured HRQOL not only before and after hospital discharge, but also at ICU discharge and in a six month period after ICU discharge. It is possible that the follow up time of six months may be too short to evaluate final improvement in HRQOL in sepsis patients. However, this evaluation period of six months was predefined in view of some earlier studies that indicated that further changes are minimal among ICU patients after this period (13;22). Only patients on their first admission and admitted for more than 48 h on the ICU were included. Therefore, these results are not generalizable to the group of patients with a short ICU stay with a lower disease severity. Another limitation could be that we did not make a distinction between severe sepsis and septic shock.

It is also important to measure HRQOL before and after ICU discharge to examine the impact of the critical illness and ICU admission on HRQOL. On admission to the ICU, the emergency procedures and abnormal levels of consciousness limit the assessment of HRQOL by the patient. We chose to use proxies for pre-admission scores, instead of a retrospective assessment at ICU discharge (34) because the critical illness can influence the patients' recollection of their previous health. The approach of using proxies in this setting was validated in an earlier study by our group (15) and by other studies (34;35). However, some investigators have raised concerns about proxy estimations of HRQOL in populations with high disease severity (36). The same study suggested that predictions of poor ICU outcome may be exaggerated if proxies underestimate HRQOL (36). However, in contrast to the situation in our previous validation study, where patients and their proxies were interviewed within 72 h of ICU admission, those investigators interviewed patients 3 months after ICU discharge and their proxies at study entry. This makes it entirely possible that survivors of critical illness may overestimate pre-admission HRQOL.

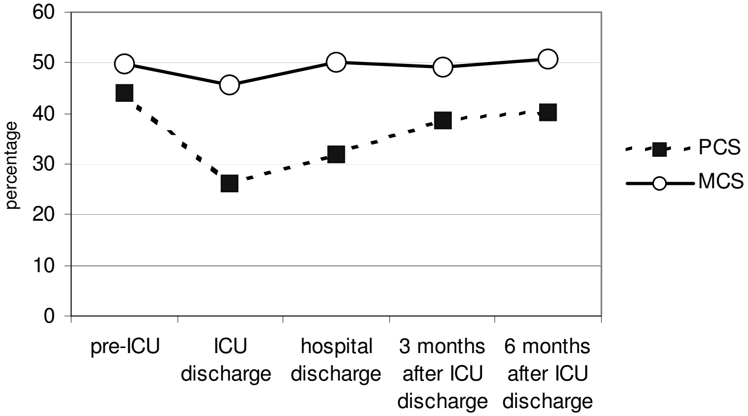
In our study, at the time of ICU and hospital discharge, the patients were specifically asked to score their HRQOL according to their current situation instead of their HRQOL in the last four weeks. This was necessary to avoid overlap between periods, but complicates the interpretation of the results at ICU discharge and hospital discharge. However, in our opinion this is a reasonable approach to gain insight into the patient's perception of their HRQOL at that time. Still, a direct comparison of different time points is hampered by the different recall periods and the use of both proxies and patients.

Table 3. Comparison of HRQOL in survivors of severe sepsis (*n*=95) at ICU admission and in the general Dutch population.

SF-36 Dimensions	Pre-ICU All sepsis patients	Pre-ICU long term survivors	General population (age subgroup: 61-70)	Differences between survivors and general population	
	(*n*=170)	(*n*=95)		Mean diff	95 % CI
Physical functioning	63.0 ±33.7	71.1 ±32.7	71.7 ±25.6	-6.0	-7.3-6.1
Role-physical	48.8 ±47.0	61.8 ±46.7	67.3 ±40.9	-7.8	-17.5-1.8*
Bodily pain	80.9 ±28.5	81.4 ±28.8	70.5 ±24.6	10.9	5.1-16.9*
General health	53.8 ±30.5	59.2 ±30.2	61.7 ±20.2	-2.5	-8.6-3.7
Vitality	55.6 ±25.0	60.8 ±25.8	67.7 ±19.6	-6.9	-12.1-1.6*
Social functioning	76.4 ±25.1	83.6 ±23.1	82.0 ±24.6	-1.6	-3.2-6.3
Role-emotional	75.6 ±40.3	78.2 ±40.6	81.1 ±35.0	-2.9	-11.4-5.4
Mental health	67.6 ±17.4	71.2 ±16.5	76.9 ±17.9	-5.7	-9.0-2.3*
PCS	42.2 ±13.2	45.1 ±12.4	49.7 ±9.3 #	-4.6	-7.2- -2.1**
MCS	48.1 (10.4)	50.7 ±9.4	52.1 ±9.6 #	-1.5	-3.4-.37

Effect size: * ≥ 0.20 small, ** ≥ 0.50 medium, *** > 0.80 large, Mean ± SD
The mean age was 68.0 in all sepsis patients and 64.6 in the long term survivors. Comparisons were made with an matching age group in the general population as indicated in the table.; PCS: physical component score, MCS: mental component score
PCS, MCS data (37);Mean diff.= Mean difference; 95 % CI = 95 % confidence interval

Figure 3. Mean physical (PCS) and mental (MCS) component scores of severe sepsis survivors before ICU admission up to six months after ICU discharge



In addition, the presence of delirium could have influenced the response, although we made an effort to screen out delirious patients. Another limitation may be a phenomenon called ‘response shift’, i.e. a change in patients’ evaluation of their HRQOL resulting from changes in internal standards or values in patients confronted with a life-threatening disease or chronic uncurable disease (20). One could argue that ’response shift’ is more likely to occur in those dimensions which are subjective (e.g. pain, interpersonal relationships like social functioning, mental health/emotional wellbeing) rather than objective dimensions (e.g. physical functioning, role performance) (20). Social functioning, for instance, could be perceived differently in the clinical setting because of the many visitors in the hospital and post cards received. Although we did not measure ‘response shift’ in the present study, dimension scores for bodily pain, social functioning and mental health at ICU and hospital discharge were higher than we expected. Future research should evaluate whether these effects are at least in part caused by ‘response shift’.

5.6 Conclusion

This study indicates that HRQOL in severe sepsis survivors showed a sharp multidimensional decline during ICU stay and a gradual improvement approaching normal values six months after ICU discharge, with recovery already beginning following discharge from the ICU to the general ward. This implies that intensive care treatment of severe sepsis is worthwhile. However in spite of survival, patients report incomplete recovery in the physical functioning, role-physical and general health dimensions at six months after ICU discharge compared with the situation before their ICU stay. A follow-up clinic for patients after ICU and hospital discharge could be a way of improving the speed and quality of long- term recovery from severe sepsis.

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Chapter 6.

Quality of life before ICU admission is a predictor of survival

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6.1 Abstract

Introduction *Predicting whether a critically ill patient will survive intensive care treatment remains difficult. The advantages of a validated strategy to identify those patients who will not benefit from intensive care unit (ICU) treatment are evident. Providing critical care treatment to patients who will ultimately die in the ICU is accompanied by an enormous emotional and physical burden for both patients and their relatives. The purpose of the present study was to examine if health-related quality of life (HRQOL) before admission to the ICU can be used as a predictor of mortality.*

Methods *We conducted a prospective cohort study in a university-affiliated teaching hospital. Patients admitted to the ICU for longer than 48 h were included. Close relatives completed the Short-form 36 (SF-36) within the first 48 h of admission to assess pre-admission HRQOL of the patient. Mortality was evaluated from ICU admittance until 6 months after ICU discharge. Logistic regression and receiver operating characteristics analyses were used to assess the predictive value for mortality using five models: the first question of the SF-36 on general health (model A); HRQOL measured using the physical component score (PCS) and mental component score (MCS) of the SF-36 (model B); the Acute Physiology and Chronic Health Evaluation (APACHE- II) score (an accepted mortality prediction model in ICU patients, model C); general health and APACHE-II (model D); and PCS, MCS and APACHE-II score (model E). Classification tables were used to assess the sensitivity, specificity, positive and negative predictive values, and likelihood ratios.*

Results *A total of 451 patients were included within 48 h of admission to the ICU. At 6 months of follow-up, 159 patients had died and 40 patients were lost to follow up. When the general health item was used as an estimate of HRQOL, area under the curve for model A (0.719) was comparable to that of model C (0.721) and slightly better than that of model D (0.760). When PCS and MCS were used, the area under the curve for model B (0.736) was comparable to that of model C (0.721), and slightly better than that of model E (0.768). When using the general health item, the sensitivity and specificity in model D (sensitivity 0.52 and specificity 0.81) were similar to those in model A (0.45 and 0.80). Similar results were found when using the MCS and PCS.*

Conclusion *This study shows that the pre-admission HRQOL measured with either the one item general health question or the complete SF-36 is as good at predicting survival/mortality in ICU patients as the APACHE-II score. The value of these measures in clinical practice is limited, although it seems sensible to incorporate assessment of HRQOL into the many variables considered when deciding whether a patient should be admitted to the ICU.*

6.2 Introduction

It is difficult for doctors to predict whether a critically ill patient will survive intensive care treatment. Mortality in patients admitted to intensive care units (ICU) remains high (1). An increasing number of in-hospital patients die in the ICU (2). The advantages of a validated strategy to identify those patients who will not benefit from ICU treatment are evident. Providing critical care treatment to patients who will ultimately die in the ICU is accompanied by an enormous emotional and physical burden for both patients and their relatives. Furthermore, ICU resources are scarce, and identifying those patients who will not survive intensive care treatment allows us to make better use of what resources are available (3). The available predicting tools, including the Acute Physiology and Chronic Health Evaluation (APACHE-II) score are based on a combination of pre-morbid factors and acute physiology items recorded during the first 24 hours after admission. The use of these systems in individual patients is limited because they have been validated at the group level. Consequently, ICU doctors must rely upon their clinical experience in their decision making. The predictive value of clinical experience in this regard is also limited (4). We hypothesized that the perceived health related quality of life (HRQOL) of patients also reflects components of ‘physiological reserve’ and could, as such, act as predictor of mortality.

The goal of the present study was to evaluate the predictive value for survival of the pre-admission HRQOL, alone and in combination with the APACHE- II score, in critically ill patients.

6.3 Materials and Methods

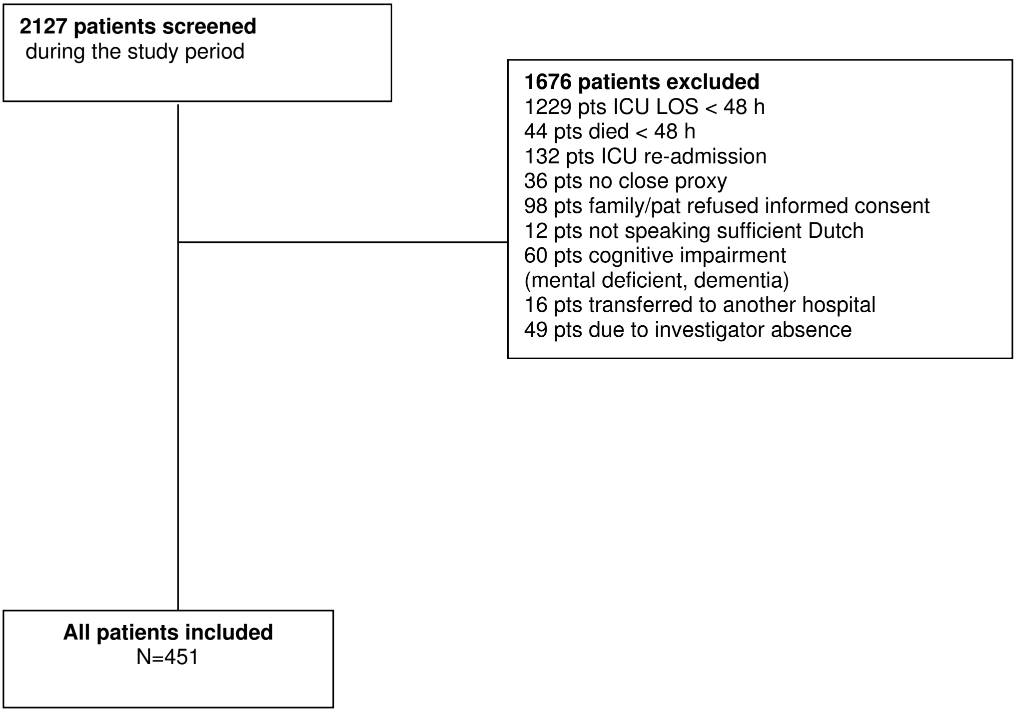
All patients admitted for more than 48 h to the 10-bed mixed surgical-medical ICU of the Gelre Lukas hospital in Apeldoorn (a 654-bed, university affiliated hospital in The Netherlands) were eligible for the study. We included only patients with a ICU stay of longer than 48 h, because we aimed to evaluate the sickest patients, hypothesizing that those patients were more likely to die. We felt that proxies of patients who would die during the first 48 h after ICU admission should not be burdened with study participation. Between September 2000 and April 2004, all admitted patients were screened for eligibility for study participation (Fig 1). The local ethics committee approved the study. Informed consent was given by a close relative and as soon as possible by the patient. Mortality was evaluated from ICU admittance until 6 months after ICU discharge. The severity of illness was routinely measured using the APACHE-II score (5). Physicians treating the patients were not aware of the pre-admission HRQOL.

6.3.1Health related quality of life measurement

The Short-form 36 (SF-36, version 1; © 1993 Medical Outcome Trust), a generic, widely used standardized health status questionnaire, was used to measure HRQOL. This measurement contains eight multi-item dimensions: physical functioning, role limitation due to physical problems, bodily pain, general health, vitality, social functioning, role limitation due to emotional problems, and mental health. Answers to the 36 items were transformed, weighed and subsequently scored according to predefined guidelines (6). Higher scores represent better functioning, with a range from 0-100. Furthermore, scores were aggregated to summary measures representing a physical component score (PCS; mainly reflecting physical functioning) and a mental component score (MCS; mainly reflecting social functioning and mental health) (7). Population scores on PCS and MCS have been standardized on 50 as population mean (SD 10 representing 1) (7). For the PCS, very high scores indicate no physical limitations, disabilities, or decrements in well-being, as well as high energy levels. Very low scores indicate substantial limitations in self-care and in physical, social and role activities; severe bodily pain, or frequent tiredness (7). For the MCS, very high scores indicate frequent positive effect, absence of psychological distress, and limitations in usual social/role activities caused by emotional problems. Very low scores indicate frequent psychological distress, and substantial social and role disability due to emotional problems (7).

Translation, validation and generating normative data of the Dutch language version of the SF-36 health questionnaire were evaluated in 1998 in community and chronic disease populations (8). Because most of the patients in our study were unable to complete a questionnaire at the time of admission, proxies had to be used as a surrogate approach. In proxies and patients the same method was used to complete the SF-36. The use of proxies to assess the patients’ HRQOL using the SF-36 in the ICU setting was validated in earlier studies conducted by our group (9) and others (10;11). HRQOL was measured within 48 h of ICU admission (estimation of HRQOL up to 4 weeks before admission). All interviews were performed by the same investigator (J.H.). The average time required to complete the questionnaire was 15 to 20 min. Consideration of multiple items has the advantage of allowing construction of a comprehensive profile of HRQOL, but it may burden the critically ill patient. We used the first question of the SF-36 as a primary approach to estimation of the patient's HRQOL. This is the single-item question pertaining general health status: "In general, would you say your health is excellent, very good, good, fair, or poor?" (12;13). The advantage of such a single item question are its simplicity and ease of application.

Figure 1.



Flow diagram of patients selection and inclusion.
Follow up was lost in 40 patients, usually because the patients did not live in the area of the hospital (they were on vacation). Characteristics of those patients did not differ from those of the group analyzed in the study (data not shown). A large group of patients (*n*=1229) were admitted to the intensive care unit (ICU) for under 48 h and hence were excluded from the final analysis. Patients who died within 48 h of ICU admission (*n*=44) were excluded. In some cases the patient had no close proxy (*n*=36). Patients re-admitted to the ICU were excluded (*n*=132) because it was possible that the first admission could have biased the proxy memories of the patients' pre admission health related quality of life (HRQOL). Proxies or the patients themselves refused informed consent (*n*=98) mainly because they felt study participation to be too great a burden at that stressful moment. Patients transferred to other hospitals (*n*=16) or with cognitive impairment (*n*=60) or who did not speak sufficient Dutch (*n*=12) were also excluded. Some patients were not included because of investigator absence (*n*=49). LOS, length of stay

6.3.2 Statistical analysis

A Pearson's X^2 test was used to assess demographic differences between ICU survivors and ICU non-survivors. The differences between scores for the single-item question were tested using the X^2 test for trend. We examined the relationship between the single-item question on HRQOL before ICU admission and mortality at 6 months after ICU discharge with multivariate logistic regression using the variables known on the first day of ICU admission (APACHE-II score) adjusted for age and sex. To analyze the potential of variables to predict mortality in patient subgroups, we used five statistical models. HRQOL was entered as the response to the single-item question, or as MCS and PCS. In the model A we included the general health item of the SF-36, age and sex. In model B we included both the PCS and MCS from the SF-36, age and sex. In model C we included APACHE-II score, age and sex. In model D we included the general health item of the SF-36, APACHE-II score, age and sex. In model E we included both the PCS and MCS from the SF-36, APACHE-II score, age and sex.

To estimate the ability to discriminate between survivors and non-survivors, odds ratios were calculated, receiver operating characteristic analysis was performed and the area under the curve (AUC) was calculated. Classification tables were used to assess the sensitivity for observed deaths being labeled by the models as predicted deaths, specificity for a predicted death being an observed death, and positive and negative predictive values and likelihood ratio. Data were analyzed using SPSS (version 11.5; SPSS Inc., Chicago, IL, USA). All data are expressed as median (interquartile range), unless indicated otherwise. $P<0.05$ was considered statistically significant.

6.4 Results

During the study period, 451 patients (61.2% male and 38.8% female) were included. At 6 months after ICU discharge, 159 patients had died. Forty patients were lost to follow up (Fig.1). Demographic and clinical characteristics are shown in Table 1. Of the 451 included patients, in a small portion of patients (*n*=23) pre-admission HRQOL was derived from the patients themselves, whereas all other SF-36 scores were obtained from proxies.

Table 1. Demographic and clinical characteristics

Characteristics	Included patients (*n*=451)
Age (years) [a]	71.0 (63 to 71)
Sex: Male/ female (%)	61.2/38.8
APACHE-II score [a]	19.0 (15 to 23)
ICU length of stay (days) [a]	8.0 (5 to16)
Hospital length of stay (days) [a]	23.0 (14 to 40)
Ventilation days +	6.0 (3 to13)
Type of admission (%)	
Nonsurgical [b]	53.2
Elective surgery [c]	8.7
Acute surgery [d]	38.1

[a] Median (interquartile range) [b] All admissions other than surgical.
[c] Intensive Care unit (ICU) admission was planned within a 24-h period before surgery.
[d] Unplanned surgery; APACHE-II: Acute Physiology and Chronic Health Evaluation.

6.4.1 Prediction models

Using the single-item question on HRQOL as a potential predictor of survival, the AUC for model A (0.719) was comparable to that for the APACHE-II score (model C; 0.721) and slightly better than that in model D (AUC=0.760) in which both factors were combined (Table 2 and Fig.2). Comparable results were obtained when calculating odds ratios (Table 3) and with analysis using MCS and PCS in models B and E. The sensitivity and specificity in model D (sensitivity 0.52 and specificity 0.81) were similar to those in model A (0.45 and 0.80). Similar results were found when using PCS and MCS. In ICU patients (*n*=451), sensitivity improved from 0.44 (model C; APACHE-II score only) to 0.56 (model E; APACHE-II score and PCS and MCS), respectively. Results for specificity were similar, improving from 0.84 (model C; APACHE-II score only) to 0.82 (model E; APACHE-II score, and PCS and MCS). Similar results were also found when using the general health item (models A and D; Table 2). The negative and positive predictive values and likelihood ratios are shown in Table 2.

The scores on the single-item question pertaining to general health status before ICU admission were higher in survivors than in the patients who died (P<0.001), with respect to all, that is: excellent (3.6% of survivors versus 1.9% of those who died), very good (5.6% versus 4.4%), good (41.3% versus 18.9%), fair (38.1% versus 50.9%), or poor (11.5% versus 23.9%). Other possible relevant variables such as the presence of severe sepsis, length of ICU and hospital stay, and ventilation days were included in the logistic regression analysis. However, because these variables did not contribute significantly to the prediction models, they were omitted from the final models, as described above.

Table 2. Statistical characteristics of mortality prediction models in ICU patients

Characteristic	Model A	Model B	Model C	Model D	Model E
Sensitivity	0.45	0.50	0.44	0.52	0.56
Specificity	0.80	0.81	0.84	0.81	0.82
PPV	0.58	0.62	0.63	0.63	0.66
NPV	0.70	0.72	0.70	0.73	0.75
AUC	0.719	0.736	0.721	0.760	0.768
LR +	2.24	2.59	2.71	2.69	3.07
(95% CI)	(1.66 to 3.02)	(1.93 to 3.48)	(1.95 to 3.77)	(2.00 to 3.60)	(2.28 to 4.12)
LR -	0.69	0.62	0.67	0.59	0.54
(95% CI)	(0.59 to 0.80)	(0.52 to 0.73)	(0.58 to 0.78)	(0.50 to 0.71)	(0.45 to 0.65)

Model A included the general health item of the 36-item Short-form 36 (SF-36), age and sex. Model B included the physical component score (PCS), mental component score (MCS), age and sex. Model C included the Acute Physiology age and Chronic Health Evaluation (APACHE-II score), age and sex. Model D included the general health item of the SF-36, APACHE-II score, age and sex. Model E included PCS, MCS, APACHE-II score, age and sex. AUC, area under the curve; CI, 95% confidence interval; HRQOL, health related quality of life; ICU, intensive care unit; LR, likelihood ratio (+positive, -negative); NPV, negative predictive value; PPV, positive predictive value.

6.5 Discussion

We demonstrated that HRQOL before ICU admission can be used as a predictor of mortality in patients admitted to the ICU for longer than 48 h. The mortality prediction ability of the pre-admission HRQOL estimated from the single-item question on the SF-36 was equal to those of the SF-36 (PCS and MCS) and the APACHE-II score. Incorporating HRQOL into prediction models does not improve the predictive capacity of established models such as APACHE II and is not useful in clinical practice for making decisions in individual cases.

Mortality is difficult to predict for an individual patient, because many factors determine survival from critical illness, such as age, sex, acute physiological deterioration and underlying illnesses. Several scoring systems aimed at predicting mortality have been developed that incorporate these factors. The APACHE-II and III scores (5;14), the Mortality Probability Model (15) and the Simplified Acute Physiology Score (16) are established examples. When these systems were compared (17) their predictive ability, as judged by the AUC of the receiver operating characteristic curve, was around 70%, which is comparable to our findings. However, these scoring systems are only available after 24 hours of ICU admission, and they are highly specific (able to predict survival [specificity 90%]) but not very sensitive (less accurate in predicting death [sensitivity 50 to 70%]) (4). The advantages of using pre-admission HRQOL as a predictor of mortality are that it is easily obtained and available as soon as the patient, or a proxy (close family member), in the case of incapacity, can be questioned. In particular, a single-item like the first question of the SF-36 is advantageous because of its simplicity and ease of administration in seriously ill patients. However, this benefit may be obtained at the cost of detail in the information provided. Multiple-item scoring systems such as the SF-36 have the advantage of providing a complete profile of HRQOL, although they are more laborious and carry the risk of asking potentially irrelevant questions (13). These two types of items (multiple and single) could be used together in the clinical setting.

Can HRQOL be used as an indicator of final outcome? Several studies have addressed this question in dialysis patients (18-20), coronary artery bypass graft surgery patients (21), patients with congestive heart failure (22) and those with advanced colorectal cancer (23). Currently, HRQOL surveys are rarely used in ICU clinical practice, and they predominantly address the impact that critical illness has on HRQOL after ICU survival. Only a few studies have focused on the association between pre-admission HRQOL and survival in critically ill patients (24-26). Yinnon and coworkers (24) analyzed HRQOL in a 1-week period preceding ICU admission using the linear analogue self assessment (LASA) score. Mortality was higher in patients with lower LASA scores, indicating worse HRQOL, than in those with higher LASA scores, indicating a good HRQOL. However, the LASA was developed for application in cancer patients receiving chemotherapy, and it has not been validated for use in critically ill patients. In addition, the period of 1 week preceding ICU admission may be rather short to conduct an adequate evaluation of HRQOL pre -emptively.

More recently, Welsh and coworkers (25) found that baseline patient functional status, as assessed by care providers, is correlated with mortality after ICU admission. However, that study is hampered by several drawbacks. Although the investigators also focused on patients with an expected ICU stay longer than 48 h, they included only 9% of all ICU patients, which may indicate at least some form of selection bias. In addition, it may be questionable to correlate HRQOL scores directly with APACHE-II scores without making any attempt to correct for confounding by multivariate analysis. Also, hospital deaths were not included in their analysis, which makes it difficult to understand the relation between HRQOL before ICU admission and mortality during or after critical illness. The most recent work on this issue is that reported by Rivera-Fernandez and coworkers (26), who demonstrated in a multi-centre study that HRQOL before ICU admission is related to ICU mortality, but that it contributes little to the discriminatory ability of the APACHE-III prediction model and has little influence on ICU resource utilization, as indicated by length of stay in the ICU or therapeutic interventions (26).

Table 3. Logistic regression models: odd ratios with 95% confidence intervals

	OR	95% CI	P value
Model A			
Sex	1.61	1.03 to 2.52	0.037
Age	1.06	1.04 to 1.09	<0.001
GH [a]	0.62	0.49 to 0.77	<0.001
Model B			
Sex	1.69	1.07 to 2.68	0.026
Age	1.07	1.04 to 1.09	<0.001
PCS	0.97	0.95 to 0.99	<0.001
MCS	0.96	0.94 to 0.98	<0.001
Model C			
Sex	1.74	1.11 to 2.74	0.016
Age	1.06	1.04 to 1.09	<0.001
APACHE-II	0.09	1.05 to 1.13	<0.001
Model D			
Sex	1.80	1.13 to 2.86	0.013
Age	1.06	1.04 to 1.09	<0.001
GH [a]	0.60	0.48 to 0.76	<0.001
APACHE-II	1.09	1.06 to 1.14	<0.001
Model E			
Sex	1.89	1.17 to 3.05	0.009
Age	1.06	1.04 to 1.09	<0.001
PCS	0.97	0.95 to 0.99	<0.001
MCS	0.96	0.94 to 0.98	0.001
APACHE-II	1.09	1.05 to 1.13	<0.001

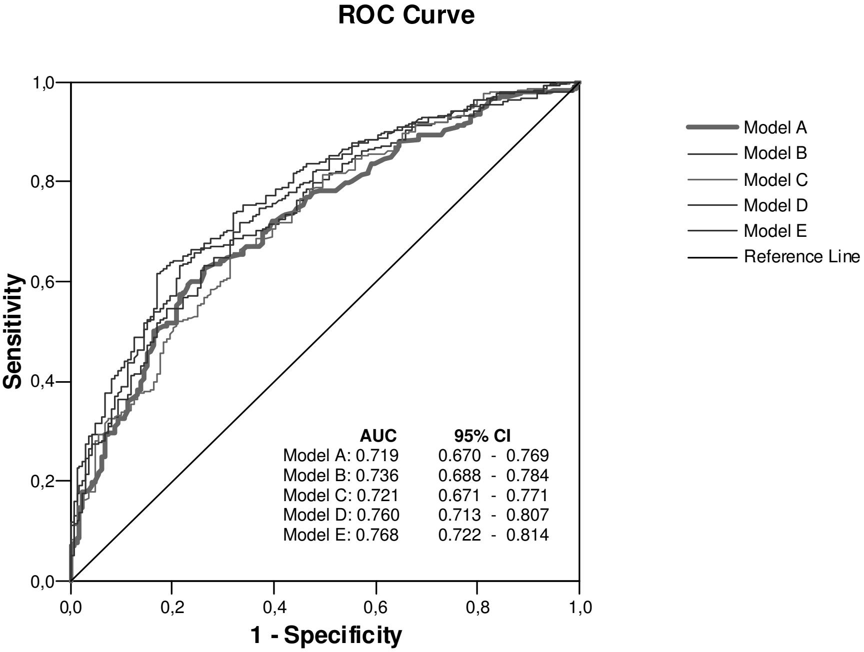
[a] General Health (GH) is item 1 from the SF-36: range 1 (poor) to 5 (excellent). The ranges for PCS and MCS are both 0 to 100. Model A included the general health item of the 36-item Short-form 36 (SF-36), age and sex. Model B included the physical component score (PCS), mental component score (MCS), age and sex. Model C included the Acute Physiology and Chronic Health Evaluation (APACHE-II score), age and sex. Model D included the general health item of the SF-36, APACHE-II score, age and sex. Model E included PCS, MCS, APACHE-II score, age and sex. CI, confidence interval; OR, odds ratio.

However, the cohort they evaluated is not comparable with our patients, because at least 25% of the patients were admitted with a cardiac diagnosis, probably because coronary care units also participated in the study. Consequently, the number of surgical patients was only 24%, which is much lower than in a general ICU. In addition, the APACHE-III score was used and related to a self-developed HRQOL questionnaire. Despite the differences that exist between these previous reports and ours, their findings are generally in accordance with ours and indicate that estimation of HRQOL before ICU admission deserves more attention by those caring for critically ill patients.

We conducted a long-term prospective study, which is an important strength of the data presented. Nevertheless, several limitations of our study should be mentioned. First, potential selection bias might have been present, because the HRQOL assessment could have influenced the decision to admit a patient to the ICU. However, we do not believe that this factor is important because the research nurse conducting the study did not communicate HRQOL findings to attending ICU physicians. Second, the APACHE -II system was intended to be used to predict in-hospital mortality, not long-term mortality at 6 months or even later. However, repeating the analysis when omitting those patients who died after hospital discharge did not alter the results.

A third limitation of our study was the necessary use of proxies to evaluate pre-admission HRQOL instead of a retrospective assessment at ICU discharge could also have hampered results. We believe that this approach did not affect the final results, in view of the findings of previous validation studies (9-11). Moreover, the use of proxies appears to be sensible, because critical illness itself could have influenced patient's recollections of their pre-admission health status. However, other groups have raised concerns about proxy estimations of HRQOL in populations with greater disease severity (27). The same study suggested that predictions of poor ICU outcome may be exaggerated if proxies underestimate HRQOL. However, in contrast to the situation in our previous validation study, in which patients and their proxies were interviewed within 72 h of ICU admission, these investigators interviewed patients 3 months after ICU discharge, and their proxies at study entry. This makes it entirely possible that survivors of critical illness may overestimate pre-admission HRQOL.

Figure 2



	AUC	95% CI
Model A:	0.719	0.670 - 0.769
Model B:	0.736	0.688 - 0.784
Model C:	0.721	0.671 - 0.771
Model D:	0.760	0.713 - 0.807
Model E:	0.768	0.722 - 0.814

Receiver operating characteristic analysis of pre-admission HRQOL and APACHE-II scores in relation to mortality. A total of 451 critically ill patients were included in the analysis. Model A included the general health item of the 36-item Short-form 36 (SF-36), age and sex. Model B included the physical component score (PCS), mental component score (MCS), age and sex. Model C included the Acute Physiology and Chronic Health Evaluation (APACHE-II score), age and sex. Model D included the general health item of the SF-36, APACHE-II score, age and sex. Model E included PCS, MCS, APACHE-II score, age and sex. CI, confidence interval, HRQOL, health-related quality of life, ROC, receiver operating characteristic**.**

A fourth limitation is that we only included patients with an ICU stay longer than 48 h, because we aimed to evaluate in particular the sickest patients surviving critical illness. Clearly, this selection makes definite conclusions regarding HRQOL as a predictor of mortality impossible. Nevertheless, the combination of the APACHE-II score with HRQOL scores improved the correct prediction of survival. A final potential limitation of the study is that this was a single centre study and the results may not be generalizable to other ICU populations with different patient populations or staffing situations.

6.6 Conclusion

Pre-admission HRQOL, as estimated using a single-item question, in critically ill patients is as good at predicting survival/mortality as the APACHE-II score. Initial evaluation of HRQOL can be done with the single-item question, because the SF-36 (PCS and MCS) yielded comparable results.The value in clinical practice of using the pre-admission HRQOL (PCS, MCS and general question) and the APACHE II score to provide useful predictive information in order to inform decision making appears to be limited, because of limitations in these models' abilities to predict survival/mortality in individual cases. Incorporating HRQOL into prediction models does not improve the predictive capacity of established models such as the APACHE II score. Nevertheless, it appears sensible to incorporate assessment of HRQOL into the many variables that may be considered when deciding whether a patient should be admitted to the ICU.

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Chapter 7.

Experiences of critically ill patients in the ICU

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7.1 Abstract

Introduction *Experiences of critically ill patients are an important aspect of the quality of care in the Intensive Care (ICU).*

Objective *The aims of the study were firstly, to evaluate the perceptions of patients regarding nursing care in the ICU, and secondly, to explore patients' perceptions and experiences of ICU stay.*

Method *A qualitative approach using a semi-structured focused interview in 11 patients was used (phase 1), followed by a quantitative approach using a self-reported questionnaire in 100 patients, 62 were returned and 50 could be evaluated (phase 2).*

Results *A number of themes emerged from the interviews (phase 1), although support dominated as an important key theme. This was experienced as a continuum from the feeling being supported by the nurse to not being supported. This key theme was central to each of the three categories emerging from this data pertaining to: (1). providing the seriously ill patient with information and explanation, (2). placing the patient in a central position and (3). personal approach by the nurse. The responders to the subsequent questionnaire (phase 2) predominantly experienced sleeping disorders (48%), mostly related to the presence of noise (54%). Psychological problems after ICU stay were reported by 11% of the patients, i.e. fear, inability to concentrate, complaints of depression and hallucinations.*

Conclusions *Although the nurses' expertise and technical skills are considered important, caring behaviour, relieving the patient of fear and worries were experienced as most valuable in bedside critical care.*

7.2 Introduction

Experiences of critically ill patients are an important aspect of the quality of care in the intensive care unit (ICU) and a consistent theme in research findings from 1970 to 2007 (1-6).The goal of intensive care is not only to save lives, but also to support patients and their relatives during critical illness (7). Intensive Care stay may have implications for the patients' psychological well-being, both in the ICU, but also after ICU discharge (7). The current treatment preference for patients requiring mechanical ventilation is to use minimal sedation levels whenever feasible (8). Due to this regime with a decreasing prescription of sedatives and the use of a daily wake- up call when sedated, memories of patients' experiences in the ICU are increasing. Stein-Parbury and McKinley (2000) reviewed 26 studies that used either qualitative or quantitative approaches to examine patients' experiences (9). Of the reviewed papers many patients recalled their time in the ICU, sometimes in vivid details (10). Patients recalled not only experiences that were negative but also ones that were neutral and even positive. Positive experiences included a sense of safety and security promoted especially by nurses (2;11). Negative experiences included impaired cognitive functioning and discomforts such as problems with sleeping, pain and anxiety (11;12). In a study of Russell (1999) some actions of ICU staff were not only remembered by ICU patients and their families but also continued to affect patients 6 months after their ICU discharge (6). Patients' memories of the ventilation period are especially related to the difficulty in accepting an inability to speak. Communication between patient and nurse is important. Consequently, impaired communication possibilities are related to feelings of anger and low mood, which may lead to a disturbed rehabilitation process (4). Both verbal and non-verbal communications have a major impact on the patient's emotional stability and perceived care (5;8;13;14). Memories of hallucinations are a source of discomfort recalled by patients even after discharge.

These experiences, also known as delusional memories, can be a sign of the so called ICU syndrome/delirium, that is a predictor of mortality (15). Furthermore, delusional memories may be related to the development of post traumatic stress disorder (PTSD) (16). Nursing care for patients while in the ICU can have a positive effect on psychological well-being (7). In a study of Granberg et al*.* interviewing 19 patients who had been ventilated, the caring relationship was perceived as the provision of an important degree of security and comfort. Nursing actions can therefore be seen as vital factors in patients overcoming ICU experiences (17). In a study evaluating factual memories 2 years after ICU discharge, the need for continued patient information, re-assurance and optimised comfort was stressed (18). However, exploration of the experiences of critically ill patients in the Netherlands is limited. Therefore, we decided to conduct a study exploring patient experiences during ICU stay with specific attention to the perceptions of patients regarding nursing care, support and psychological problems.

The aims of our study were twofold: firstly, to evaluate the perceptions of patients regarding nursing care in the ICU, and secondly, to explore patients' perceptions and experiences and possible psychological problems related to ICU stay.

7.3 Patients and methods

This study was part of a larger investigation examining the experiences of ICU patients. Patients admitted to the ICU (medical or surgical) of the Gelre Hospitals (Lukas site, Apeldoorn, The Netherlands) staying >48 h were selected in a 6-month period. The local ethics committee approved the study. The study was conducted in two phases. A qualitative approach using a semi-structured focused interview with a list of topics (phase 1), followed by a quantitative approach using a self-reported questionnaire (phase 2). This combined approach was chosen because we expected that this could increase our understanding about the emotional and psychological phenomena that influence patients' experiences. Disorientation was measured by checking the presence or absence of delirium in the patients. This was assessed by asking the opinions of the nurses, doctors and especially close relatives. Patients suspected as having delirious states or other incapacities were excluded from the study. When patients asked for help regarding problems, for instance psychological problems, we provided professional help.

7.3.1 Phase 1. Qualitative approach

In the first part of the study we aimed to evaluate the perceptions of patients regarding nursing care in the ICU**.** Patients who had been ventilated for at least one day, and were admitted to the ICU for the first time were eligible for the study. Patients who were disoriented during mechanical ventilation; patients with cerebral neurological diseases; and patients who could not remember their stay in the ICU were excluded. We used the nursing tasks listed in the Dutch Nursing Profile as a theoretical framework, by using a topic-list, based on the tasks referred to in the profile. The National Council of Public Health published the Nursing Profile in 1988. This Nursing Profile sketches the profile of the professional practising nurse and is based on the definition of the American Nurses Association (1980). By using this profile, a clear description of the specific components of nursing care emerges. We chose to use a qualitative approach through interviews so that information regarding personal experience could be obtained. Initially, we considered a phenomenological approach because the purpose of phenomenology is to describe the perceptions of the people, trying to understand the total subjective and objective perceptions as an individual. However, we wished like to know more about a number of aspects concerning the perception of nursing care. Since too much structure and redirecting was necessary to use the phenomenological approach, we decided to apply Maso's approach, in which data-collection, analysis and creating relations of possible theoretical insights exchanging among each other, seemed well suited (19). Finally, a qualitative approach was chosen using a semi-structured focused interview with a list of topics (Table 1). These interviews took place 6-14 days after transfer from the ICU to the ward. This time window was deliberately chosen because earlier interviewing might have been influenced by critical residual illness. A purposive sampling technique was employed, and inclusion and exclusion criteria were identified (20). The interviews were recorded on tape and fully transcribed. Accordingly, the analysis (19) was conducted on two levels. Maso (1989) used the working methods of Becker and Geer (1960), and of Hyckner (1985) as sources of inspiration for the elaboration of an analytical procedure (21;22). The primary analysis consisted of six steps, and the secondary analysis takes place in four steps (Fig. 2). Accordingly, the collection of accumulating data with every subsequent patient was repeatedly analysed and related to possible theoretical insights (19) (Fig. 2). This procedure of analysis was used alternately after 3, 6, 9 and ultimately after 11 interviews. Since no more new findings emerged from the data and the saturation point was reached, further interviews would not yield additional information (19).

Reliability of the topics list was investigated by evaluating personal feelings or prejudices by other investigators in line with Maso (1989). Lincoln and Guba (1985) suggested that four factors can be used to assess the rigor of the qualitative study: creditability, transferability, dependability, and confirmability (23). The credibility of the data (validity) was studied by "peer debriefing", which is the comparison of insights obtained by the investigator with the insights of colleagues not involved in the study. Also by showing the transcribed interviews to four patients they indicated that the interpretation of the information they had provided was correct. Transferability of the data was studied by the use of thick descriptions relating to the context of the data collected. Dependability (reliability) and confirmability were studied through independent inquiry audits by external auditors.

7.3.2 Phase 2. Quantitative approach

In the second part of the study we aimed to explore patients' perceptions and experiences of their ICU stay and possible psychological problems related to this. Following a pilot study in 10 patients, subsequently, all patients in a 6-month period who stayed in the ICU > 48 h and survived hospital stay were included in the study using a quantitative approach (n=100). Additionally, in this part of the study we were interested in the experiences of all patients admitted at our ICU and not only patients who were ventilated (phase 1). All patients received a questionnaire 3 months after hospital discharge for retrospective evaluation of their experiences that was returned anonymously. Validity of the items used in the questionnaire was sought by using the data collected in the interviews (phase 1), the literature and the results after consultation with the ICU nurses. After analysing the data, definite questions were formulated, which were understandable for the patients and mentioned by the patients as an important issue for them in the ICU. Cronbach's α coefficient was calculated for evaluating the internal reliability of the items of the questionnaire.

The patients were asked about preparation for their ICU admission and support during their stay together with recollections of their stay and time on respiratory support. The questionnaire was divided in three domains i.e. preparation and support of the patient by the ICU staff, recollection of their stay, recollections during mechanical ventilation in addition to an open-ended question (Table 3). Data were analyzed using the SPSS version 11.0 programme.

Categorical data were compared using X^2 test. SPSS was also used for the documentation of responses of the open-ended question by using frequency testing.

Table 1. Perception of nursing care: list of topics, used during the interview

(1) What happened when tasks were undertaken concerning you? (Such as washing, making the bed). In what way was this done, and was there anything, that had a special significance to you? How did you experience the information given?

(2) Did the nurses talk to you? If yes, what did they talk about?

(3) Can you describe, what the nursing staff did for you, which gave you the feeling they cared for you?

(4) What did the nursing staff do while performing technical duties, such as given medicine, handling the mechanical ventilator, or the ECG monitor?

(5) What did you think of while being attached to all the machinery? What did you think about being dependent on this machinery?

(6**)** What is your perception of the shift changeover of nursing staff (the handover and reporting) between nurses?

(7) If there was a nurse at your bedside (like making the bed, and taking care of the feeding) what do you value about this?

(8) What did you perceive as positive and what did you perceive as negative?
(What was good en what was bad about this?)

7.4 Findings

7.4.1 *Phase 1: Qualitative approach*

A total of 11 patients were interviewed: 8 surgical and 3 non-surgical patients. Characteristics of those patients are shown in Table 2 panel A. The primary analysis according to Maso (1989) was carried out first and yielded the following 10 categories: appreciation of the nurse; information and explanation given by the nurse; talking with the nurse; being attached to machines; technical performances of the nurse; basic care given by the nurse; transfer of shifts between the nurses; noise caused by the nurse and machinery; dreams and hallucinations; common organisational perceptions. A number of themes seemed to emerge from these categories, which narrowed down to one key theme. This key theme was support and was seen as a continuum from feeling supported by the nurse to not being supported with movement back and forth along the continuum. This key theme was central to each of the three categories emerging from this data. In the secondary analysis, 3 of the 10 categories were related to existing theoretical insights, i.e.
1. providing the seriously ill patient with information and explanation (24), 2. placing the patient in a central position (25) and 3. personal approach by the nurse (26).

7.4.2 *Providing the seriously ill patient with information and explanation*

When providing patients with information and an explanation, patients were more aware of what was going to happen so that they could focus on feeling more relaxed and better able to handle the stress:

……*'Certainly, then you know what you're dealing with. Yes, and I find that one can prepare oneself. Yes, I do feel more relaxed because of that, and I am able to handle stress much better' (patient 1).*

Figure 1 Annoying experiences in patients who were mechanically ventilated (%)
(Multiple answers possible)

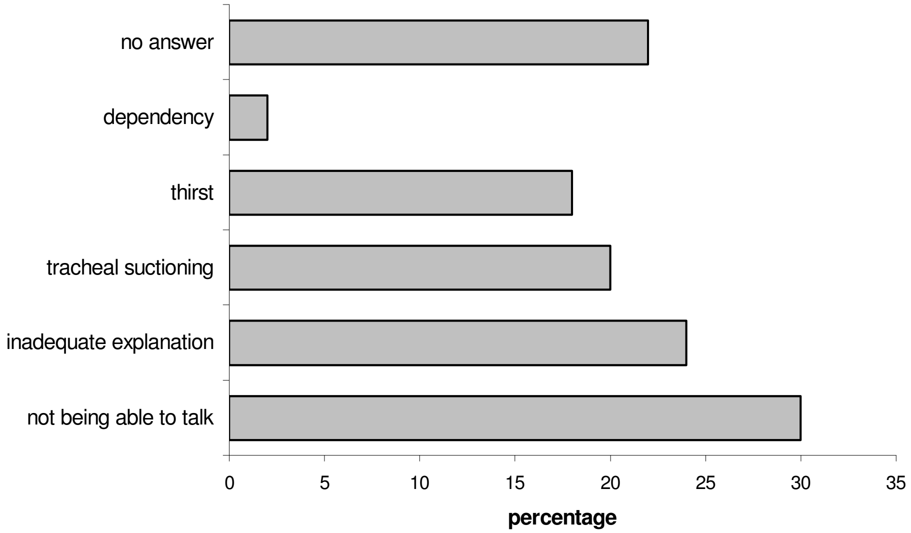


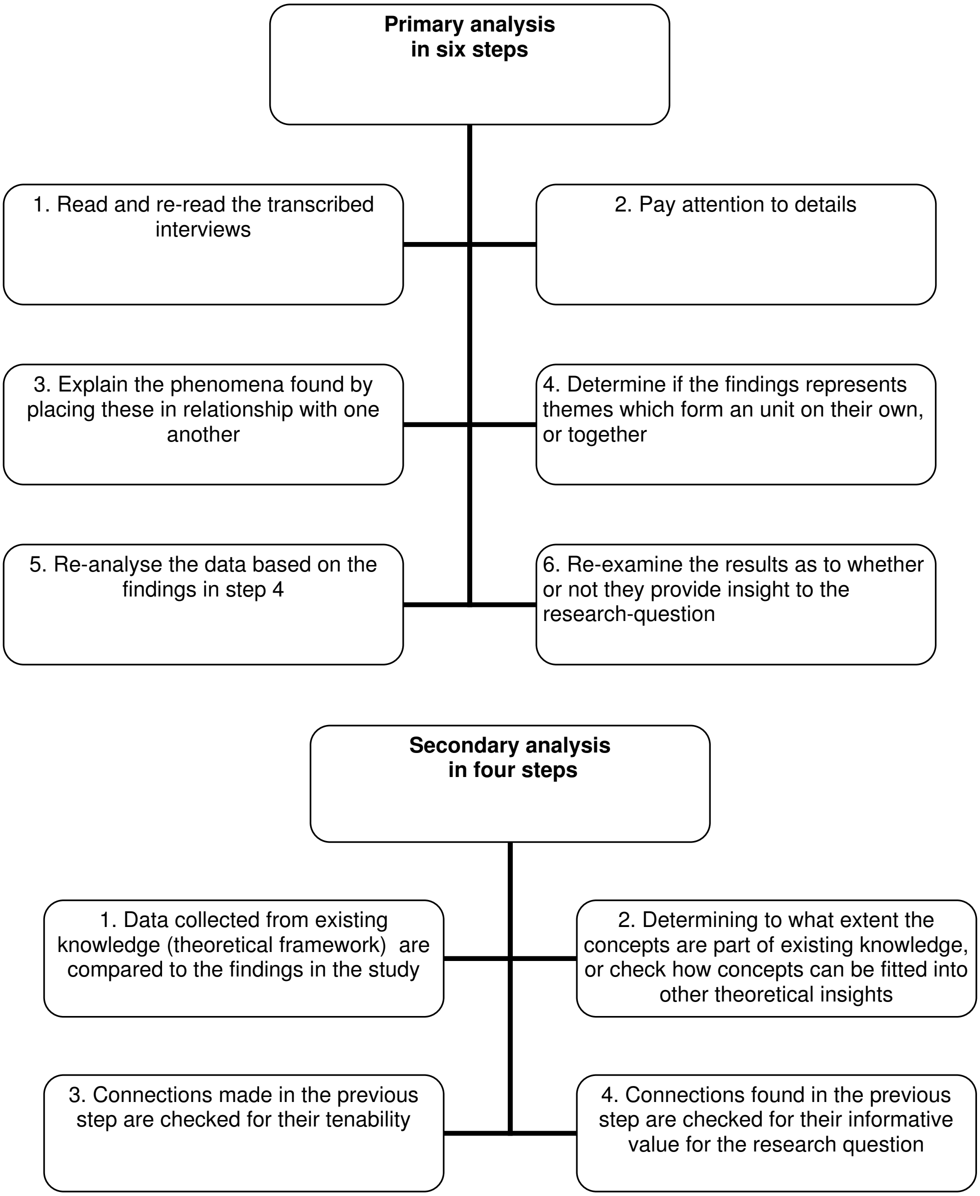
Table 2. Panel A Perception of nursing care: characteristics of the patients (*n*=11)

Patient	Interview time after transfer ICU (days)	Diagnosis	Age (years)	Gender	ICU length of stay (days)	Ventilation (days)
1	7	Abdominal aortic aneurysm	67	Male	11	8
2	8	Exacerbation chronic demyelinating neuropathy	65	Male	8	4
3	7	Abdominal aortic aneurysm	67	Male	13	11
4	13	Pancreatitis	54	Male	21	14
5	11	Small bowel perforation	70	Female	6	4
6	8	ileus, renal dysfunctions	68	Female	6	4
7	6	Abdominal aortic aneurysm	60	Female	5	4
8	7	COPD	61	Female	20	20
9	6	Ruptured abdominal aortic aneurysm	73	Male	7	5
10	8	ileus, shock	68	Male	16	14
11	7	Pneumonia	66	Male	7	6

Table 2. Panel B Experiences of ICU stay: characteristics of the patients (*n*=100)

Mean± SD	*n*=100
Age	69.1±13.0
ICU length of stay	15.0±18.5
Apache II score	18.6±7.0

Figure 2. Schematic description of the analysis, following the principles of Maso (1989)



The explanations and the instructions during the ventilation were perceived as being reassuring, resulting in less fear and insecurity:

……*'Yes, they explained everything well. And if the ventilation machine next to me stopped for a moment they told me about it. Or when they were trying out something else. You knew that they would explain what they were doing first. Yes, in my opinion you'd worry less about things' (patient 6).*

Information concerning their illness and the course of the illness should be complete and honesty was perceived as important. Knowing 'why' was supportive and reduced fears:

…… *' I did say that I wanted honest information. And even they couldn't know everything that was going to happen, naturally, but that the way things were at that time looked very promising. They told me that it was no use to think about things that "could" happen. Yes and then I thought: well, they are right. Yes and then it felt like a weight dropping off my shoulders. Yes, I appreciated that very much' (patient 5).*

7.4.3 *Placing the patient in a central position*

Important to patients is the fact that nurses try to keep seeing them as a human being and as the centre of their attention in the ICU. Especially putting them central, meaning the humane care is crucial:

…… *'Yes, there was a nurse who held my hand, came to sit with me on my bed and she stayed until I felt more relaxed again. Now, I feel that it helped me very much. I told my wife about that later on, and even now I still know who the nurse was. I was thinking then, gosh I wish the nurse who was there the other night did the same. I think I would have had a far better night' (patient 2).*

Not only the amount of technical equipment, but also encouragement, providing care and "cheering" them up was perceived by patients as being lifesaving factors. When talking was not possible the aid of nurses in pointing out letters and writing was perceived as stress relieving:

…… *'Yes, and what was very annoying of course was that you couldn't talk. You just let things wash over you sort of. But I have to say that it makes you feel kind of scared, I mean, trying to talk and not being able to… You can't say what's bothering you or anything, and you can't ask for anything. Anyway, then the nurse said: I'll get a paper and then you write it down. But I don't write much even at home, so I just hoped it would work… Well, it was really difficult, it seemed as though my hand was too weak or something… Then they tried by pointing out letters, which was quite hard at first, but that worked eventually. Yes, the nurses try their best to help you out… You truly appreciate it then, I think it reduces the stress' (patient 9).*

From these interviews, it was clear that not only technology and the expertise of the nurses were important to patients, but that human aspects including compassion, encouragement, attention, giving comfort, relieving fear and creating security were also important.

The most vital aspect of nursing care as experienced by patients was support. Patients viewed their ICU stay as a situation that they had to get through and non-supportive care was found to hinder their recovery. If the nurses responded very slowly when patients rang the bell, this caused feelings of helplessness, hurt, powerlessness and dependency:

……*'Yes and then you have rung the bell and no one shows up. And sure, there are emergencies, and I understand that completely, but waiting on the bedpan for half an hour isn't exactly fun either. But it could have been that they thought: just wait for a while. Yes, I had that feeling. I mean, you could see them having coffee together and no one came. You know, it made me feel helpless, and powerless. It's hard to describe. You feel, what can I say, you feel hurt and you could easily start to cry. Yes and then I thought oh please let someone come, don't let a person who is so dependant wait so long. That is important, right? I mean, I know that on such a ward they also look after the other things such as the equipment and so on. And there are very ill people there too, but surely they should pay some attention to what's going on? For a patient it's very important I can tell you…' (patient 8).*

When nurses did not take a patient seriously or even reacted aggressively to hallucinations or dreams this caused feelings of not being understood, anger, fear, feeling ill at ease, not understanding what was going on and also the feeling of not being treated as a human being:

…… *'Well, that he didn't take me seriously I mean, and they didn't tell me what was going on. They didn't have much experience with it I guess. I um.. I mean, they could have coped with it better than that… Yes I mean they just reacted aggressively when I told them I was seeing things. They said: "Well, sir… listen up" and in such a tone of voice… I mean, it's just no attitude. I know I saw things that weren't there, but that's no reason to react that way. No, I want to share that. I can't keep that to myself. I was angry because of that, and not just angry but sad too. Yes, I mean you want to be treated as an adult instead of a child, right? Yes, I mean I'm not an engine that needs to be fixed, I mean, I'm a human being… And well, I just don't think that's the right way to deal with people' (patient 10).*

Most patients also reported discomfort due to the noise of loud voices and conversations between nurses. When the personnel made a lot of noise during conversations by talking too loudly and wearing clogs, the patients often got the feeling that they were not improving. The fear of not clinically improving combined with the noise caused the participants to feel tired and unable to handle the situation adequately:

……*'Yes then I thought, please be a bit quieter. I can hear all of it. Yes it's hard to explain but if you can't sleep, can't shut yourself down so to speak, and being afraid of all that may happen makes you scared. Yes all that makes you feel that you can't handle things anymore, you think: I can't hang on anymore' (patient 11).*

7.4.4 *Personal approach by the nurse*

Treatment was perceived as comforting, giving a safe feeling. It was judged important how the nurse dealt with them as a person; this was often not described directly as ‘behaviour’:

……*‘I was very scared and insecure in the beginning. However when the nurse is kind to you and gives you the feeling they sympathise, it is a very comforting feeling’ (patient 4).*

Certain types of approach resulted in patients being reluctant to ask the nurse questions:

…… *‘I remember nurses who always looked angry. I did not dare to tell them while they were at work checking on the pumps and everything that I was so thirsty. I would rather have had someone who looked nice and who did not run off immediately but asked me if I needed anything instead’ (patient 7).*

7.5 Results

7.5.1 Phase 2: Quantitative approach

During the study period (6 months) 308 patients were admitted. One hundred patients stayed in the ICU for more than 48 hours. Following the interviews, we sent questionnaires to all of those patients. Characteristics of those patients are shown in Table 2 panel B (*n*=100). Categorical data were compared on differences using the X^2 test. However, the differences were not significant. Internal reliability was measured computing Cronbach’s α which was reasonable and varied between 0.73-0.78. Sixty-two questionnaires were returned anonymously. Twelve patients had no recollection of their stay in the ICU, or had already died at home, leaving 50 questionnaires for evaluation. Most of the patients were acute admissions to the ICU (60%). Sixty percent of all patients and 52% of the patients who were ventilated were not prepared for their admission to the ICU. Half of the patients had only fragmentary recollections of their stay. Pain (46%) and noise (40%) (Table 3) were the most frequent complaints. Of the patients experiencing sleeping disorders (48%), 54% of them associated this with the presence of noise (Table 3). Most annoying procedures and events during admission were not being able to talk, tracheal suctioning, thirst, and inadequate explanation of actions taken by the ICU staff (Fig.1). Eleven patients (22%) had psychological problems after hospital discharge, which were related to fear, the inability to concentrate, depression, hallucinations and a bad memory Seven patients would have appreciated professional help (family doctor or psychologist) (Table 3).

7.6 Discussion

A number of themes emerged from the interviews with patients pertaining to their experiences, although one key theme, support, dominated. This was seen as a continuum from the feeling of being supported by the nurse to not being supportive. This key theme was central to each of the three categories emerging from this data: 1.providing the seriously ill patient with information and explanation, 2. placing the patient in a central position and 3. personal approach by the nurse (phase 1). The responders to the questionnaire experienced sleeping disorders (48%), mostly related to the presence of noise (54%). Psychological problems after ICU stay were reported by 11% of the patients, i.e. fear, inability to concentrate, depression and hallucinations (phase 2).

Table 3. Experiences of ICU stay: self-report questionnaire in three domains

Panel A: Preparation and support of the patient by the ICU staff

Were you prepared for the admission at the ICU?

	(*n*)	(%)
Yes	20	40
No	30	60
Other	0	0
If yes, how did you perceive this?		
Excellent	10	50
Good	6	30
Poor	4	20
Bad	0	0
How did you perceive the first help at the ICU ?		
Excellent	0	0
Good	28	56
Poor	6	12
Very poor	4	8
No answer	12	24
Did you get enough information about what you could aspect in the ICU?		
Yes	20	40
No	15	30
Don’t know	10	20
No answer	5	10
Did you understand the given information?		
Yes	25	50
No	11	22
Don’t know	0	0
No answer	14	28
How did you perceive the support during your stay in the ICU?		
Excellent	18	36
Good	17	34
Poor	8	16
Bad	0	0
No answer	7	14
How did you perceive the attitude of the nurse? (Multiple answers possible)		
Calmly	27	54
Hurried	4	8
Interested	28	56
Not interested	1	2
No answer	0	0
How did you perceive the attitude of the doctor? (Multiple answers possible)		
Calmly	33	66
Hurried	2	4
Interested	24	48
Not interested	0	2

Table 3 (Continued) Panel B Recollection of their stay

Do you have memories of your stay in the ICU? If yes, describe these memories		
	(n)	(%)
Yes	17	34
No	13	26
A little	19	38
No answer	1	2
If yes, are these memories		
Pleasant	19	53
Unpleasant	10	28
Very unpleasant	7	19
Did you experience pain in the ICU? Did you get enough medication ?		
Yes	23	46
No	17	34
I don't know	10	20
Did you get enough medication ?		
Yes	32	64
No	11	22
Other	7	14
Did you experience noise in the ICU and if yes, how much did it disturb you?		
Yes	20	40
No	25	50
Other	5	10
If yes:		
Much	13	65
Little	3	15
Very much	4	20
Did you have sleeping problems while in the ICU ? If yes, what was the most common cause of this?		
Yes	24	48
No	26	52
If yes:		
Noise	13	54
Fear	6	5
Pain	5	21
Other	0	0

What were annoying experiences for you when admitted in the ICU? (Multiple answers possible**)**

Table 3 (Continued)

	Great burden		Small burden		No burden		No answer	
	(n)	(%)	(*n*)	(%)	*(n)*	(%)	*(n)*	(%)
Shortness of sleep / rest	13	26	7	14	13	26	17	34
Thirst	7	14	6	12	10	20	27	54
Stomach tube	4	8	7	14	8	16	31	62
Oxygen mask or tube	6	12	3	6	7	14	34	68
Tracheal suctioning	6	12	5	10	8	16	31	62
Noise of machines	5	10	6	12	10	20	29	58
Being ventilated by a machine	6	12	4	8	10	20	30	60
Conversations in the ICU	6	12	9	18	15	30	20	40
Physical-therapy	0	0	4	8	14	28	32	64

Table 3 (Continued)

Panel C: Recollections during mechanical ventilation

When you were mechanically ventilated were you prepared for this?

	(n)	(%)
No, not at all	16	32
Not possible due to time	10	20
Good	3	6
Fair	5	10
Poor	5	10
No answer	11	22

Did you have psychological problems after hospital discharge?

If yes, was this? (Multiple answers possible)

If yes, would you appreciated professional help (family doctor or psychologist)?

	(n)	(%)
Yes	11	22
No	39	78
I don't know	0	0
If yes:		
Fear	8	50
Concentration disturbances	2	12.5
Hallucinations	2	12.5
Depressions	2	12.5
Forgetful	2	12.5
If yes: would you appreciated professional help (family doctor or psychologist)?		
Yes	7	64
No	1	9
I don't know	3	27

Table 3 (Continued)

Panel D: Open-ended question (Multiple answers possible)

Did you have other experiences in the ICU who were important to you?

If yes, would you describe this experiences?

	(n)
Relatives need more information and preparation	3
Nurses and doctors have to realise that some patients are conscious (anxiety, disturbing)	2
To short of rest/ sleep	6
Hallucinations and dreams were not taken seriously by nurses and doctors	5
Communication with the nurse was very difficult when on the ventilator	8
Hurrying while busy with washing	3
Complete and honest information concerning illness	4
Compassionate, sympathy, perceived as very important	4

Furthermore, results of both studies demonstrated that the attitude of the staff (nursing and doctors) was significant. This included the importance of explanation when mechanically ventilated and taking psychological problems seriously. Patients experienced these perceptions in both studies as supportive or non-supportive.

7.6.1 *Providing the seriously ill patient with information and explanation*

Patients especially perceived that complete information and clear explanation was an important concept in the interviews as well as in the questionnaires. In addition, patients perceived clear explanations that were given to the family as being supportive and gave the feeling of being cared for, thus enhancing feelings of confidentiality and security, which confirms previous data (1;2;6). In contrast, patients may state that personal needs should be considered and that they should be asked whether or not they wish to receive detailed information (24). This is in accordance with our data, since some patients indicated that the process of being shown the ICU beforehand had been helpful in being able to prepare better or to reduce fear and nervousness. Previous studies concur with this finding, i.e. giving careful information and explanation of procedures beforehand relieved discomfort and distress, disappointment and insecurity for the patient (3;10;12;27;28)**.** Moreover, talking, giving instructions, explanations and encouragement prepared the patient for a specific procedure thus potentially reducing complications (29). Finally, ICU patients frequently wish to talk about their experiences. This emphasizes the necessity of some form of follow up (30).

7.6.2 *Placing the patient in a central position*

Communication is important to critically ill patients (31;32). Our findings showed that feelings of fear were reduced during the weaning period of mechanical ventilation if nurses took time to communicate with the patient, thus enhancing the weaning process. Help with writing and pointing out letters during the ventilation period was perceived as safe and supportive. However, when the nurses did not adequately attempt to understand example the patient may feel that nurses do not care enough. This makes patients angry and sad, which confirms previous data (4;33-37).

In our study, patients reported that the fact that they were being taken seriously when having hallucinations or disturbing dreams gave feelings of security and comfort. In contrast, when patients had the feeling not being taken seriously or were approached with aggressive behaviour by the attending nurse, they reported feelings of fear, not being understood, not knowing what was happening, or inhumanely treated. Also a feeling of embarrassment due to loss of self-control was described. This confirms previous data reporting the importance of communication in relation to psychological function (29;38-40). In situations where nurses asked colleagues to look at the patient they were attending without informing the patient, or when other personnel often came in during washing, this induced the feeling of being “just a case” with a lack of personal interest and a feeling of lack of control. This feeling of powerlessness was also reported in other studies (32;41). Investigating patient empowerment in an ICU situation using open-ended interviews in 11 ICU patients, showed that a positive environment that encouraged feelings of value and motivation and in which the patient felt safe, received additional care and participated as the patient wished had a positive influence and reduced feelings of powerlessness (42).

7.6.3 *Personal approach by the nurse*

The personal approach and the actions of the nurse in this study was perceived as being comforting, relaxing with feelings of compassion. When the personal approach by the nurse was positive, this was considered a first step in recovery. Sometimes patients described the personal approach as negative: “she looked mad”, “she looked angry”. That caused patients to be reluctant to ask questions of the nurse and reduced confidence. ICU patients are very sensitive to the attitudes and behaviour of staff, who may either increase patient’s anxiety and vulnerability or make them feel more safe and confident (2;5;10;11;28;43;44). Some patients in our study indicated that the caring behaviour of the nurse and their continuous support relieved their fears and worries in a way that they could concentrate on their recovery and rehabilitation. Caring behaviour was also described as sweet, nice, compassionate, showing personal interest in the patient as well as the family as confirmed in other studies (2;45;46).

7.6.4 *Hallucinations, noise, sleeping problem, psychological problems*

Patients had only fragmentary memories after ventilator treatment and discharge, confirming previous data (12;30). In our study, patients experienced sleeping disorders related to the presence of noise and complained of psychological problems after ICU stay. Most of these patients complained of fear, other problems were related to the ability to concentrate, depression and hallucinations. Turner et al. (1990) interviewed 100 patients within 48 h following ICU discharge (12). In accordance with our data, when asked about recollections regarding procedures and events only 50% percent of the patients had memories of their stay in the ICU. Although tracheal suctioning was generally considered unpleasant, careful explanations of procedures were considered important to relieve discomfort. Sensory overload, anxiety, and pain were also reported in other studies (10;41;47).Previous studies demonstrate both differences and comparable findings. Adamson *et al* (2004) reported three themes that differ from our findings: recollection, responses and comfort/discomfort. However, in contrast with our study (performed 6-14 days after ICU transfer) the interviews were undertaken 6 months after hospital discharge. It is possible that the difference in time influenced the memories of the patients (45). In contrast, Russell found similar findings to our study, interviewing 86 patients 6 months after discharge (6).

Differences between study findings may be related to differences in ethnic, socio-economical and theological background. However, all in all, our findings do not suggest that things have changed much during the past two decades concerning patient experiences of nursing care, as our findings were consistent with those of studies performed from 1970 to 2007 (3;4). Therefore, our findings may reflect a universal nursing phenomenon in relation of the nursing care provided in the ICU.

7.7 Limitations

This is a single centre study in the Netherlands, which implies that the perceived experiences of patients elsewhere may be different due to differences in case mix, staffing, but also ethnic, socio-economical and theological background. Previous data showed both parallel findings and differences (6;45). Also, the mean age of patients was 69**,** reflecting the average ICU population in our setting. It is possible, that perceptions of younger patients are somewhat different. Moreover, the interviews were taken while the patients were still in the hospital. Their perceptions may have influenced by the fact that they had not physically recovered completely. In addition, the interview was taken retrospectively and not at the time the patient received nursing care in the ICU. A further limitation is the lack of assessment of delirium by specific scores, however we checked the presence or absence of delirium in the participants, by asking the opinions of the nurses and doctors involved in the daily care of the patients, and included information from close relatives. Another potential drawback is the fact that only 50 of the 100 questionnaires could be evaluated. Finally, half of the patients had only fragmentary recollections of their stay.

7.8 Conclusions

Taking care of the patient is an important part of the treatment of critically ill patients. Although the nurses' expertise, technical skills and medical equipment are perceived as important by patients, as they are part of the necessary life saving interventions, caring behaviour, relieving the patient of fear and worries, may help them to concentrate on their recovery, and is regarded as most valuable. Nurses should be aware that patients sometimes perceive that increased attention to technical equipment decreases the patients' trust. Careful and adequate information to patients is an important factor to improve the patient-nurse relationship. The importance of these findings for the clinical practice may be, that being aware of this, we can improve the quality of care in the ICU.

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Chapter 8.

Measurement properties of health-related quality of life questionnaires used in critically ill patients from 1998-2007

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8.1 Abstract

Introduction *Traditionally the assessment of critical care has focused largely on mortality. However in the last years there is more attention for the quality of that survival. Health related quality of life (HRQOL) is an important issue for both patients and family. We performed a review from 1998-2007 of measurement properties of instruments that have been used in adults with critically illness, before and after discharge from the intensive care unit (ICU).*

Measurements *Medline, CINAHL, Embase, the Cochrane Library, and reference lists from relevant articles were searched. We reviewed the existing literature from 1998-2007 on measurement properties of HRQOL instruments used in critically ill adults using the explicit criteria proposed by Terwee and coworkers (1). Studies were selected for review if they met the following criteria: 1. representative population of adult ICU survivors (16 year and older), 2.data from before and after ICU discharge, 3.only instruments that were used in 2 or more studies were evaluated.*

Results *While instruments as the Nottingham Health Profile (NHP), Sickness Impact Profile (SIP), and self developed instruments were still used, especially the Short-form 36 (SF-36) and the EuroQOL-5D (EQ-5D) are the most frequently used instruments in the time period under evaluation. Content validity was well documented in part, but evidence for further measurement properties are poor.*

Conclusions *Depending on the research questions and definition of the concept being measured, it is important to choose an instrument or combination of instruments (generic, disease specific, domain specific) that is most suitable. The SF-36 and EQ-5D are currently the most used instruments to assess the HRQOL of critically ill patients. The EQ-5D requires significantly less time to complete compared with the SF-36. The SF-36 covers more domains and is more precise. However, both questionnaires show a lack of focus on disease specific issues and may lack sensitivity to detect HRQOL issues relevant to adults with critically illness.*

8.2 Introduction

Traditionally the assessment of critical care has focused largely on survival. Indeed, mortality in ICU patients remains high (2). However, there is more attention for the quality of that survival in the last years, which is an important issue for the patients and their family (3;4). Patients recovering from critical illness may show impaired functional status with an associated reduced HRQOL. In addition, the focus of doctors and nurses about people's feelings in relation to prolonging patient lives is rising. The ideal outcome for the patient is to return to their preexisting functional and psychological status or a status acceptable for the patient (5), whereas the ideal outcome for society is the efficiency of care (6). Nevertheless, the long term impact for the patient and his family of ICU admission is increasingly recognized (7).

Furthermore, as ICU patients have different admission diagnosis, there is a need for generic outcome measures that can be used across medical and surgical critically ill patients, as well as disease -specific ones (8). Black and coworkers published a literature review over the period up from 1970 to August 1998 and concluded that due to the poor current state of knowledge of appropriate outcome measures for adult critical care survivors at that time, it was impossible to make clear recommendations as to which particular measures should be used and when and how they should be administered (8). Additionally, Black and coworkers stated that there was an urgent need for rigorous assessment of the measurement properties being used in critical care research. In this paper we make a follow-up to that paper by reviewing the literature over the period 1998-2007 using explicit quality criteria for measurement properties (1). For this review, we focused on adult critical care, which was defined as care given to patients of at least 16 years of age in a general ICU (surgical and medical) or high-dependency unit. A systematic review of outcome measures for adult critical care can include impairment, physical functional status, mental functional status, neuropsychological function, measures of recovery and HRQOL. In a study regarding quality criteria for measurement properties of health status questionnaires Terwee and coworkers concluded that, when applying explicit criteria, several measurements properties are often not properly assessed or analyzed, nor clearly reported (1).

The objectives of our study were to perform a review from 1998-2007 of measurement properties (content validity, internal consistency, criterion validity, construct validity, reproducibility, responsiveness, floor and ceiling effects, interpretability) of instruments related to HRQOL that have been used in critically ill patients.

8.3 Material and methods

We performed a MEDLINE, CINAHL, Embase and a Cochrane Library search with specific focus on the description of measurement instruments commonly used in the ICU. To identify studies eligible for the systematic review of measurement instruments in critical care from 1998-2007, the following search terms were used with all terms mapped to the appropriate MeSH subject headings: “quality of life” OR “health related quality of life” OR “health status”, OR “Short form 36”, +SF36 + SF-36 OR “EuroQOL-5D” +EQ-5D +EQ5D +Euroqol OR “NHP” OR “Nottingham Health Profile” OR “Sickness Impact Profile” AND “intensive care” OR “critical care” OR “critical illness”, OR “sepsis” OR “severe sepsis” OR “acute respiratory distress syndrome” OR “organ failure” were used. Additionally, the references of the selected articles were examined for possibly relevant articles. Overall 933 potentially relevant articles were identified and their abstracts obtained. Studies were selected for review if they met the following criteria: 1. representative population of adult ICU survivors (16 year and older), 2. data from before and after ICU discharge, 3. only instruments that were used in 2 or more studies were evaluated. We excluded special units such as coronary care, cardiac surgery and neurosurgery.

Of the 933 articles, 72 met the inclusion criteria using 8 questionnaires. From 3 questionnaires there was only one reported use. The remaining 5 questionnaires were used on at least two occasions and these formed the basis of the review. We focused on explicit criteria, and evidence was sought for each outcome measure, for the following measurement properties as proposed by Terwee and coworkers (1), 1. content validity, 2. internal consistency, 3. criterion validity, 4. construct validity, 5. reproducibility, 6. responsiveness, 7. floor and ceiling effects, 8. interpretability.

8.4 Results

8.4.1 Methods and description of measurement instruments used in critically ill patients

HRQOL measures in critically ill patients can be made longitudinally or cross-sectionally with a focus on specific dimensions of health or disease, on economic utility, or on general health domains (9). Discriminative instruments are used for cross-sectional differences in quality of life between patients at a point in time. Evaluative instruments are suitable for assessing longitudinal changes in HRQOL within patients. A good measure is valid and reliable; it will measure what it aims to measure, the measure is consistent, it minimizes random errors, and the scale reflects the changes in its domains (18). Instruments to measure HRQOL in critically ill patients can be divided in three groups: generic, disease-specific and domain-specific questionnaires (10). Generic instruments measure HRQOL relevant for each human been independent of the clinical diagnosis. These instruments contain the physical, psychological and social domains and can be used in patients with different diagnoses, disease stages and treatments. This facilitates the comparison between clinical groups or with the general population. One can distinguish disease specific instruments that measure the consequences of a specific disease on quality of life. Domain-specific instruments measure the consequences of one part of health. These questionnaires are mostly used as a complementary to the generic and disease-specific instruments. Before a generic HRQOL instrument can be appropriately used, it should have undergone a cross-cultural translation, adaptation and validation process in a sample of the general population of the country in question. In this process, the questions and statements are examined to get the exact meaning of each dimension. In 2002 a consensus conference recommended the SF-36 and EQ-5D as the most appropriate instruments for future research (11).

In this review we discuss the use of the SF-36 (12), the EQ-5D (13), the Sickness Impact Profile (14), the Nottingham Health Profile (15), because especially the first two instruments are the most commonly used in critically ill patients.

8.4.2 What makes a good HRQOL instrument in critically ill patients?

Several instruments measuring HRQOL have been used in ICU populations both during and after ICU stay. The more global or generic instruments can be used, but may be less responsive to changes in specific conditions (16). As ICU patients have different admission diagnosis, there is need for generic outcome measures that can be used across medical and surgical critically ill patients, as well as condition-specific ones (8). Several characteristics are identified (Table 1). An ideal generic instrument in ICU patients should be easy to administer, not present too great a burden for the patient, and yet be sensitive to modest changes in quality of life (17). The SF-36 is currently one of the most widely used generic questionnaire in critical care and may be appropriate for critical care patients (17-20). The SF-36 has been used in a variety of patient populations and validated in community and chronic disease populations (21). The SF-36 is a questionnaire with 36 questions which comprise eight dimensions: physical functioning (ten items); social functioning (two items); role limitation due to physical problems (four items); role limitations due to emotional problems (three items), general mental health (five items); energy/vitality (four items); bodily pain (two items); general health perceptions (five items). Item scores for each dimension are summated and transformed using a scoring algorithm into a scale ranging from 0 (poor health) to 100 (good health) (12). The physical health summary scale (PCS) reflects physical functioning, physical role, pain and general health. The mental summary scale (MCS) reflects vitality, social functioning, emotional role; and mental health (22). The shortened version of the SF-36, the SF-12 gives only the PCS and MCS, not the individual domains (23). The shorter SF-12 improves efficiency in critically ill patients and lower costs. However the SF-12 yields less precise scores compared with the SF-36. For large group studies, these differences are not as important, because confidence intervals for group averages in health scores are largely determined by sample size (23) . Another generic questionnaire designed to measure health outcomes and which is used in critically ill patients, was developed at European level: the Euroqol (24). The Euroqol is a simple instrument comprising two parts: the EQ-5D self-classifier, a self-reported description of health problems according to a five dimensional classification, i.e. mobility, self-care, usual activities, pain/discomfort and anxiety/depression; and the EQ-VAS, a self-rated health status using a visual analogue scale (VAS) to record perceptions of the participant’s own current overall health (25).

Table 1. Description of health related quality of life instruments used in critical care 1998-2007

Instrument	Purpose	Description	Concepts measured
Short form 36 (SF-36)	To measure general health status	36 items, grouped into 8 scales and physical and mental summary scores	Physical: functioning, role limitations, pain, general health Mental: vitality, social, role limitations, mental health transition
Euroqol 5-D (EQ-5)	To assess state of health and preferences for 14 hypothetical health states	5 items assessed at 3 levels	Mobility, personal care, usual activities, pain/discomfort, anxiety/depression
Sickness Impact Profile (SIP)	To measure health related dysfunction	136 items, grouped into 12 categories	Physical: body movement, mobility, ambulation Psychosocial: intellectual, social interaction, emotional behaviour, communication Other: sleep and rest, daily work, household, leisure and recreation
Nottingham Health Profile (NHP)	To measure perceived physical, social and emotional health	First part: 38 items Second part: 7 items	Sleep, physical mobility, energy, pain, emotional reactions, social isolations. Employment, looking after the home and social life, sex life, hobbies and holidays
Self developed questionnaire Fernandez Questionnaire	To measure physiological activities, normal daily activities and emotional state	Fifteen items grouped into three subscales	Physiological activities, normal daily activities, and emotional state

It was recently recommended that either the EQ-5D or the SF-36 should be used in critical care outcomes studies, on the grounds that they are best suited to this setting (11). Older questionnaires used until about the year 2000 in critical care include the SIP and the NHP. The Sickness Impact Profile (SIP) is a multidimensional generic health index that evaluates all areas of sickness-related behaviour. However, the SIP was developed 30 years ago with the final version published in 1981 (14). Since then health perceptions or expectations may have changed(14). The SIP was developed as a measure of perceived health status across a wide number of health problems and diseases. It consists of 136 yes/no type questions divided in twelve categories. It provides an absolute measure of functional health status and is appropriate for use when comparing outcomes for different diseases, and does not require a value prior to the illness for its validity in documenting current health status. However, the SIP is so comprehensive that it is laborious for critically ill patients (26). Furthermore, the SIP is known to be rather insensitive to change (26).

The Nottingham Health Profile (NHP), also used in critically ill patients, was developed in the UK and is based on lay perceptions of functional status and quality of life. The NHP was designed to measure the experience of ill health, and consists of 38 items in the first part and 7 items in the second part (15). The 38 items of the first part are measuring sleep, physical mobility, energy, pain, emotional reactions, and social isolation. The 7 items of the second part are measuring: employment, looking after home and social life, sex life, hobbies and holidays. Both the NHP and the SIP are extensive and time consuming. They combine the measurement of physical, psychosocial, and several independent categories related to daily living (27). Especially the SIP is more comprehensive, reliable and acceptable in determining specific quality of life abnormalities but the SF-36 is easier to administer and correlates well at baseline and 1 year in patients with prolonged critical illness (26).

8.5 Measurement properties

We determined the measurement properties of the above mentioned measures (Table 2) used with the survivors of critical care from 1998-2007. Following Terwee, we searched for data on content validity, criterion validity, construct validity, internal consistency reproducibility, responsiveness, floor and ceiling effects, and interpretability of the measures (1). For each measurement property a criterion was defined for a positive, negative or indeterminate rating. The quality criteria from Terwee and coworkers are reproduced in Table 2. A summary of the assessment of the measurement properties in HRQOL questionnaires used for validating in critically ill patients and used in at least two studies from 1998-2007 are shown in Table 3.

The Short-form 36 was used in four studies (6;17-19). Content validity by a clear description provided of the measurement aim and target population, items selected and concepts that are being measured was reported in two papers (17;19), and content validity partly in one paper (18). Internal consistency by measuring Cronbach's alpha between 0.70 and 0.95 was measured in three papers (17-19). Criterion validity by reporting a gold standard was not found. Construct validity by testing pre-defined hypothesis was only mentioned in one study (17). Reproducibility by agreement was not reported, reliability by measuring intraclass correlation (ICC) or weighted kappa was reported in two studies (17;18). Responsiveness by detecting clinically important changes was not found. Floor and ceiling effects by the number of respondents who achieved the lowest or highest possible scores were only mentioned in two studies (6;19). Interpretability was mentioned in two studies (intermediate and positive) (6;18).

The Euroqol was used in two studies (6;28). In one study, content validity by a clear description of the measurement aim and target population, items selected and concepts that are being measured was partly reported and floor and ceiling effects were mentioned (6). No information was found concerning the other measurement properties. The Sickness Impact Profile was used in three studies (26;27;29). Internal consistency by measuring Cronbach's alpha, factor analysis and construct validity by predefined hypothesis was intermediate reported (26). With respect to the Nottingham health profile: we could not find a validation study of the measurement properties of the NHP in critically ill patients. Finally, the Fernandez's questionnaire was used (30). Construct validity by a clear description of the measurement aim and target population, items selected and concepts that are being measured was reported intermediate. Internal consistency measured by a Cronbach's alpha of 0.85 and predefined hypothesis testing was reported intermediate (30). We conclude that for HRQOL questionnaires used in critically ill patients the content validity was well documented, as the construct validity and reliability, but evidence on other measurement properties in ICU populations was poor. In addition, in general, as well ass using the SF-36, personal interviews, phone interviews or computer administration ensures compliances, decreases errors and decreases missing items compared with self administered questionnaires which are less expensive but increase the number of missing subjects and increases missing responses (31).

A total of 72 studies in critically ill patients were found using the SF-36 (3;18;19;32-63), the EQ-5D (6;28;64-72), the NHP (73-76), the SIP (27;77-80), and a self developed questionnaire (81-83). Some studies used a combination of questionnaires, such as the SF-36 and EQ-5D (6;84-88), the SF-36 and SIP (89;90), the SF-36 and ADL questionnaire (91), the SF-36 and St. George respiratory questionnaire (92), the NHP and Modified Perceived Quality of life scale (93), the Quality of Well being scale and the Karnofsky scale (94). Of these 72 papers only 4 mentioned a definition of HRQOL. Four health related quality of life measures and one self developed questionnaire have been used to assess outcome of critical care survivors from 1998-2007. For the five quality of life measures (Table 1), data providing some evidence of content validity was available in 70 of the 72 papers. However, using the criteria of Terwee et al. the 70 studies reported only partly of the 5 content validity criteria. Construct validity by testing pre-defined hypothesis was partly reported in 6 studies. Internal consistency by testing Cronbach's alpha was reported in 11 of the 72 papers. Only 2 studies reported some evidence of reproducibility by test-retest measures. Reliability was partly mentioned in 2 studies. Responsiveness was not mentioned, and floor or ceiling effects only in 1 study. Finally interpretability was partly mentioned in 23 studies.

We **conclude** that content validity for several generic HRQOL instruments is partly well documented but evidence on other measurement properties in ICU populations is poor.

8.6 Points to consider

The most commonly used instruments in ICU patients i.e. SF-36, EQ-5D, SIP and NHP are measuring the physical, psychological and social dimensions. However, special problems in patients after ICU discharge may be: cognitive dysfunction, severe physical problems, neuropathy or psychological problems like anxiety, depression, memory and concentration disturbances. It is important to make a choice, depending on the research questions and definition of the concept to be measured, which instrument (HRQOL) or combination of instruments (generic and disease specific) or if a special instrument covering the specific problems of critically ill patients and HRQOL may be needed. The SF-36 and EQ-5D are currently the most frequently instruments to assess the HRQOL of critically ill patients. The EQ-5D requires significantly less time to complete compared with the SF-36. The SF-36 covers much more domains and is more precise. The SF-12 may be an alternative, as it is short, and gives information about the most relevant domains. However, both questionnaire systems show a lack of a focus on disease specific issues and may lack sensitivity to detect HRQOL issues in critically ill patients. Consequently, they will not detect key issues in critically ill patients, such as cognitive dysfunction or severe physical problems like patients with critical illness neuropathy or psychological problems such as anxiety, depression, memory and concentration disturbances. A generic instrument including these key problem areas is needed to assess the full impact of critical illness on health related quality of life. However to communicate with the scientific community we used the instrument which is most common: the SF-36.

8.7 Conclusions

When investigating measurement properties, content validity of HRQOL measures in ICU patients is partly well documented, but evidence for further measurement properties is poor. Finally, on the basis of our findings we suggest that there is need to develop a HRQOL instrument especially for critically ill patients, which covers all relevant domains, is still short and simple and can be administered to both patients and proxies.

Table 2. Quality criteria for measurement properties of health status questionnaires

Property	Definition	Quality criteria
1. Content validity	The extent which domain of interest is comprehensively sampled by the items of the questionnaire	+ A clear description is provided of the measurement aim, the target population, the concepts that are being measured, and the item selection AND target population and (investigators OR experts) were involved in item selection; ? A clear description of above-mentioned aspects is lacking OR only target population involved OR doubtful design or method - No target population involvement 0 No information found on target population involvement.
2. Internal consistency	The extent to which items in a (sub) scale are inter-correlated, thus measuring the same construct	+ Factor analysis performed on adequate sample size (7 *# items and ≥ 100) AND Cronbach's alpha (s) between 0.70 and 0.95; ? No factor analysis OR doubtful design or method; - Cronbach's alpha(s) < 0.70 or > 0.95, despite adequate design and method; 0 No information found on internal consistency.
3. Criterion validity	The extent to which scores on a particular questionnaire relate to a gold standard	+ Convincing arguments that gold standard is "gold" AND correlation with gold standard ≥ 0.70; ? No convincing arguments that gold standard is "gold" OR doubtful design or method; - Correlation with gold standard < 0.70 despite adequate design and method; 0 No information found on criterion validity.
4. Construct validity	The extent to which scores on a particular questionnaire relate to other measures in a manner that is consistent with theoretically derived hypotheses concerning the concepts that are being measured	+ Specific hypothesis were formulated AND at least 75 % of the results are in accordance with these hypotheses; ? Doubtful design or method (e.g., no hypothesis); - Less than 75 % of hypotheses were confirmed, despite adequate design and methods; 0 No information found on construct validity.

* Based on Terwee et al. 2007

MIC= minimal important change; SDC= smallest detectable change ; LOA= Limits of agreement ; ICC= Intraclass correlation ; SD= standard deviation.[a] + = positive rating; - = negative rating; ?= indeterminate; 0= no information available

[b] Doubtful design or method= lacking of a clear description of the design or methods of the study, sample size smaller than 50 subjects (should be at least 50 in every (subgroup) analysis), or any important methodological weakness in the design or execution of the study.

Continued Table 2. Quality criteria for measurement properties of health status questionnaires

Property	Definition	Quality criteria
5. Reproducibility 5.1 Agreement	The extent to which the scores on repeated measures are close to each other (absolute measurement error)	+ MIC < SDC or MIC outside the LOA OR convincing arguments that agreement is acceptable; ? Doubtful design or method OR (MIC not defined AND no convincing arguments that agreement is acceptable); - MIC ≥ SDC OR MIC equals or inside LOA, despite adequate design and method; 0 No information found on agreement.
5.2 Reliability	The extent to which patients can be distinguished from each other, despite measurement errors (relative measurement error)	+ ICC or weighted Kappa ≥ 0.70; ? Doubtful design or method (e.g. time interval not mentioned); - ICC or weighted Kappa , 0.70. despite adequate design and methods; 0 No information found on reliability.
6. Responsiveness	The ability of a questionnaire to detect clinically important changes over time	+ SDC or SDC < MIC OR MIC outside the LOA or RR > 1.96 OR AUC ≥ 0.70; ? Doubtful design or method; - SDC or SDC ≥ MIC OR MIC equals or inside LOA OR RR ≤ 1.96 or AUC < 0.70, despite adequate design and methods; 0 No information found on responsiveness.
7. Floor and ceiling effects	The number of respondents who achieved the lowest or highest possible score	+ ≤ 15 % of the respondents achieved the highest or lowest possible scores; ? Doubtful design or method; - > 15% of the respondents achieved the highest or lowest possible scores, despite adequate design and methods; 0 No information found on interpretation.
8. Interpretability	The degree to which one can assign qualitative meaning to quantitative scores	+ Mean and SD scores presented or at least four relevant subgroups of patients and MIC defined; ? Doubtful design or method OR less than four subgroups OR no MIC defined; 0 No information found on interpretation.

* Based on Terwee et al. 2007

MIC= minimal important change; SDC= smallest detectable change ; LOA= Limits of agreement ; ICC= Intraclass correlation ; SD= standard deviation.[a] + = positive rating; - = negative rating; ?= indeterminate; 0= no information available

[b] Doubtful design or method= lacking of a clear description of the design or methods of the study, sample size smaller than 50 subjects (should be at least 50 in every (subgroup) analysis), or any important methodological weakness in the design or execution of the study.

Table 3. Summary of the assessment of the measurement properties in HRQOL questionnaires used for validating in critically ill patients and used in at least 2 studies from 1998-2007

Study/Questionnaires	Content validity	Internal consistency	Criterion validity	Construct validity	Reproducibility		Responsiveness	Floor/ Ceiling effect	Interpretability
					Agreement	Reliability			
Short-form 36 (SF-36)									
(17)(19)(6)(18)	+	+	~	+		+			~
	+	+		~		~		+	~
	-							+	-
	~	+		~		+		~	+
EuroQol (EQ-5D)									
(6) (28)	-			-				+	-
	~								
Sickness Impact Profile									
(SIP) of FLP		-							
(29) (26) (27)	-	+	-	~	-	-	-	-	~
	-		-				~		
Fernandez's questionnaire	~	~		+		+	~		
(30;82)									

Rating + = positive; - = poor; ~ = intermediate; empty = no information available

8.8 Reference List

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Chapter 9.

Summary and discussion
Clinical relevance of the study

Summary and discussion

Introduction

This thesis describes the impact of critical illness on perceived health related quality of life (HRQOL).The time course of HRQOL during Intensive Care Unit (ICU) treatment, hospital stay, and after hospital discharge is described for ICU survivors, and for a subgroup of survivors of severe sepsis. Furthermore, we investigated whether proxies can assess the patients' HRQOL on admission to the ICU using the Short-Form 36 questionnaire(1). We examined if pre-admission HRQOL can be used as a predictor of mortality, as a substitute for or addition to other predictors. Finally, we studied patient experiences during ICU stay with specific attention to the perceptions of patients regarding support and nursing care.

9.1 The general introduction and aims of the study are described in **Chapter 1.** The main reason for HRQOL research described in this thesis is the lack of knowledge about the outcome of HRQOL in critically ill patients admitted to an ICU. Especially, the time course of changes in HRQOL following discharge from the ICU and during a general ward stay has not been studied. Furthermore, in general there is a lack of clear framework for defining and describing HRQOL in HRQOL studies in- and outside the field of critical care. One of the difficulties in HRQOL research is defining what one means by health related quality of life: there is no universally accepted definition. QOL, health status, functional status, and HRQOL are often used interchangeable in the literature. Yet each of these terms may reflect different aspects of an individual's well-being. This also may lead to different measurement approaches, leading to different results. Quality of life is described as "unique personal perception" (2), and influenced by social, psychological, cultural, familial, relational and individual factors. The World Health Organization defines health as not only the absence of infirmity and disease but also as a state of physical, mental and social well-being (3). Accordingly, an assessment of health related quality of life should reflect the patients' physiological and psychological status, social functioning and perception of health. The quality of life related to health, or HRQOL, takes into account not all dimensions of the quality of life, but those that are influenced by the disease or its treatment. If specific populations in the ICU are examined such as cardiac patients, a disease-specific instrument can be used to give information and comparisons. However, within the ICU patients with different diagnoses are treated, so in the ICU there is a need for generic outcomes that can be used across medical and surgical critically ill patients, as well as condition-specific ones (4). Black et al. published a literature review over the period up to 1997 and concluded that the poor state of knowledge of appropriate outcome measures for adult critical care survivors at that time meant that it was impossible to make clear recommendations as to which particular measures should be used and when and how they should be administered (4). Additionally Black et al. stated that there is an urgent need for rigorous assessment of the measurement properties being used in critical care research (4). In 2002 a consensus conference recommended the Short-Form 36 (SF-36) and EuroQol-5D (EQ-5D) as the most appropriate instruments for future research (5). The EQ-5D requires significant less time to complete compared with the SF-36. However, we used the SF-36 because compared with the EQ-5D the SF-36 covers much more domains and is more precise, although imbalances between the different domains in the SF-36 are present.

9.2 Conceptual issues specifically related to HRQOL in critically ill patients

We evaluated several conceptual issues related to HRQOL in critically ill patients, described in **Chapter 2.** Specifically conceptual issues were discussed such as "why HRQOL should be measured?”, “ how to define and standardize definition domains of HRQOL?”, “what utility measures are used pertaining critically ill patients?”, “can proxies provide useful information of HRQOL?” , “does response shift occur in critically ill patients?” and “do post- traumatic stress disorders occur in critically ill patients?”. Evaluating these specifically conceptual issues did not yield conclusive results. Some studies reported moderate agreement between patients and their proxies, although lower levels of agreement may be reported for psychological or physical functioning. Vigilance for symptoms of Post traumatic stress disorders (PTSD) is needed and early interventions to prevent PTSD implemented. Nursing care while in the ICU and intensive care follow-up may have an important role in recognizing and treatment of psychological problems after hospital discharge. Furthermore, response shift seems an important phenomenon and likely to be present, but is seldom measured when estimating HRQOL in critically patients.

9.3 Outcome of validation study patient/proxies

In critically ill patients, due to the emergency procedures and abnormal levels of consciousness, the possibility of assessing by the patient is small. Is the use of proxies, defined as relatives in close contact with the patient, valid and reliable?. **Chapter 3** of this thesis describes whether the Short-Form 36 questionnaire can be used to assess the patient’s HRQOL on admission to the ICU by use of proxies, studied in 112 patient/proxy pairs. This study includes patients/proxies before major elective surgery (*n*=55) or following emergency admissions (*n*=57). We chose to use proxies for pre-admission scores instead of a retrospective assessment at ICU discharge because the critical illness can influence the recollection of the patients previous health status. We performed a prospective study to examine whether the SF-36 can be used to assess the patient’s HRQOL on admission to the ICU involving direct interviews of patients and relatives before or during ICU stay. Patients and proxies completed a health questionnaire in the first 72 h following emergency admission or the day before a scheduled admission to the ICU. On all dimensions a significant correlation was found between the patient and their proxy. In general, proxies underestimated the patient’s HRQOL although the differences were small (less than 5%). On most items a good to very good agreement was found. Quality of life assessment was not affected by the admission status of the patient (acute or elective admission and surgical or medical diagnosis). This study shows that relatives in close contact with the patient can adequately reflect the patient’s quality of life on admission to the ICU. The proxy best reflected the patient’s functional quality of life. We found no differences in the agreement between patients and proxies between elective and emergency patients. Many of the seriously injured patients and critically ill patients had to be excluded from our study, as these patients were not able to fill out questionnaires. These results are limited, as the results from our emergency patients cannot be readily generalized to all emergency admissions.

9.4 Assessing the impact of critical illness on HRQOL in ICU patients

Patients recovering from critical illness may show persisting organ dysfunction that could impair functional status with an associated reduced HRQOL. Since ICU treatment is scarce and expensive, better insight is required for patients, families, and health care providers in the way this service affects the health an wellbeing of its survivors. The focus on concerns of doctors and nurses about people’s feelings in relation to prolonging patients lives is increasing. Assessment of HRQOL in critically ill patients is complex and is usually only measured after ICU discharge.

However, to assess the effects of critical illness and ICU stay on HRQOL, measurements should ideally be taken on ICU admission. The question of how the impact is of critical illness on HRQOL in ICU patients is addressed in **Chapter 4**. Patients admitted in the ICU for > 48 hour were included in the study. Proxies completed the Short-Form 36 in the first 48 hours of admission to assess HRQOL in the pre-ICU period. Patients completed this questionnaire at ICU discharge, hospital discharge, and three and six months after ICU discharge. At time of ICU and hospital discharge, the patients were specifically asked to score their HRQOL according their current situation instead of their HRQOL up to four weeks, which is the usual recall period. This was necessary to avoid overlap between periods, but complicates the interpretation of the results at ICU discharge and hospital discharge. Of the 451 included ICU patients 252 could be evaluated six months after ICU discharge. HRQOL decreased significantly in all dimensions of the SF-36 during ICU stay with a gradual improvement near to normal functioning at six months after ICU discharge. Nevertheless, at six months after ICU discharge, physical functioning, general health and social functioning were still lower as compared to baseline values, while all dimensions except bodily pain remained lower than in the age-matched general population. Pre-admission SF-36 scores of ICU survivors were higher compared with ICU non-survivors for seven of the eight dimensions. Moreover, HRQOL in ICU patients before ICU admission was already lower than in the general population. We found a gradual improvement of HRQOL. This improvement was larger than we expected and might be explained by a phenomenon called “response shift”. Response shift is the change in internal concepts, standards or values, and consequently in the perception of HRQOL (7). This means that most patients perceive their HRQOL as being better than expected at six months after ICU discharge. This could be either because patients become accustomed to their illness or chronic disease or because their expectations about their HRQOL have changed. Although this is a probable limitation of our study, we did not measure ‘response shift’.

9.5 Impact of severe sepsis on HRQOL

Severe sepsis is frequently complicated by organ failure that accounts for the persisting high mortality rate (8;9). Patients surviving severe sepsis might have impaired quality of life. In this study we examined the impact of severe sepsis on HRQOL in comparison with an age matched normal Dutch population. Patients admitted in the ICU for >48 h were included in the study. Proxies completed the Short-form 36 in the first 48 h of admission to assess HRQOL in the pre-ICU period. Patients completed this questionnaire at ICU discharge, hospital discharge, and three and six months after ICU discharge. Of the 170 patients with severe sepsis, 95 could be evaluated six months after IC discharge. In **Chapter 5** we found a sharp decrease of HRQOL during ICU treatment in sepsis patients and gradual improvement in the six months thereafter. Nevertheless, SF-36 average scores for the physical functioning, role physical and general health dimensions at six months were significantly lower compared with baseline values. Pre-admission HRQOL was already lower in severe sepsis survivors than in the normal population. HRQOL changed significantly in all dimensions of the SF-36. Only patients on their first admission and admitted for more than 48 h on the ICU were included. Therefore, these results are not generalizable to the less severe group of patients with a short ICU stay.

This study indicates that HRQOL in severe sepsis survivors showed a sharp multidimensional decline during ICU stay with recovery already beginning following discharge from the ICU to the general ward. This implies that intensive care treatment of severe sepsis is worthwhile. However in spite of survival, patients report incomplete recovery in the physical functioning, role-physical and general health dimensions at six months after ICU discharge compared with the situation before their ICU stay. A follow-up clinic for patients after ICU and hospital discharge could be a way of improving the speed and quality of long- term recovery from severe sepsis.

9.6 Health related quality of life (HRQOL) as a prognostic factor

Improved strategies for identifying those patients who have a greater chance not to survive the ICU, allows us to make better use of the available resources. HRQOL before Intensive Care admission may have a relation to subsequent mortality. In **Chapter 6** we examined patient's HRQOL before ICU admission and evaluated the predicting ability with survival at six months after ICU discharge in comparison with the Acute Physiology And Chronic Health Evaluation (APACHE II score). Patients admitted in the ICU for > 48 h were included. Close relatives completed the SF-36 in the first 48 h of admission to assess HRQOL in the pre-ICU period. 451 patients were included at admission ICU. At six months follow up, 159 patients had died, and 40 patients were lost to follow up. In the analysis we used five statistical models. The first question of the SF-36 on general health, age and gender (model A); HRQOL measured using the physical component score (PCS) and mental component score (MCS) of the SF-36, age and gender (model B); the Acute Physiology and Chronic Health Evaluation (APACHE) II score (an accepted mortality prediction model in ICU patients); age and gender (model C); general health and APACHE II score age and gender (model D); and PCS, MCS and APACHE II score, age and gender (model E). We demonstrated that the pre-admission HRQOL measured with the SF-36 is as good at predicting survival/mortality in ICU patients as the APACHE II score. Initial evaluation of HRQOL can be done with the single-item general health question as this yielded comparable results to using the PCS and MCS, i.e. the total SF-36.

The value in clinical practice of using the pre-admission HRQOL (PCS, MCS and general question) and the APACHE II score to provide useful predictive information in order to inform decision making appears to be limited, because of limitations in these models' abilities to predict survival/mortality in individual cases. It was necessary to use close relatives for evaluating pre-admission HRQOL. We think that this approach is not affecting the final results in view of previous validation studies (1;10;11). Moreover, this seems a sensible approach, because when using a retrospective assessment at ICU discharge, critical illness itself could have influenced the recollection of their previous health status. Furthermore we only included patients with an ICU stay >48 h, because we aimed particularly on the sickest patients. Concluding, the pre-admission HRQOL (general health question or PCS, MCS) is as good at predicting survival/mortality in ICU patients as the APACHE II score and it appears sensible to incorporate assessment of HRQOL into the many variables that may be considered when deciding whether a patient should be admitted to the ICU.

9.7 Experiences of critically ill patients

Experiences of critically ill patients are an important aspect of the quality of the care in the Intensive Care. Nursing care for patients while in the critical care environment can have a positive effect on psychological well-being. In particular, the way the ICU nurse supports the patient during critical illness and subsequent recovery-periods is seen as an important factor in the patients' contentment and perceived HRQOL post discharge. The current treatment preference for patients requiring mechanical ventilation is to have patients non-sedated whenever feasible. Due to this non-sedation regime and the currently more often used daily wake-up call when sedated, memories of patients' experiences in the ICU are increasing. In **Chapter 7** we explored the perceived nursing care of ICU patients and evaluated the patients' experiences of their stay in the ICU. A qualitative approach using a semi-structured focused interview with a list of topics (N=11) was used in addition to a quantitative approach using a self-reported questionnaire (N=100). The key theme in the interviewed patients was the feeling of being supported during ICU stay. Three perceptions of care from patients emerged: "providing the patient with information and explanation", "giving the patient a central position", and "personal approach by the nurse". From these interviews, it was clear that not only technology and the expertise of the nurses were important to patients, but that human aspects including compassion, encouragement, attention, comforting, relieving fair and creating security were also judged as important. The most valued aspect of nursing care experienced by patients was support.

Furthermore, we sent questionnaires to 100 patients. Sixty-two anonymous questionnaires were returned. Twelve patients had no recollection of their stay in the ICU, or had already died at home, leaving 50 questionnaires for evaluation. The results showed that half of the patients had only fragmentary recollections of their stay in the ICU. Pain (46%) and noise (40%) were the most frequent complaints. Of the patients experiencing sleeping disorders (48%), 54% of them associated this with the presence of noise. Most annoying procedures and events during admission were not being able to talk, tracheal suctioning, thirst, and inadequate explanation of actions by the ICU staff. Eleven patients (22%) had psychological problems after discharge from the hospital like fear, inability to concentrate, depression, hallucinations and a bad memory. Taking care for the patient is an important part of the treatment of critically ill patients. Although the nurses' expertise and technical skill and the medical equipment are perceived as important, as they are part of the necessary life saving interventions, caring behavior, relieving the patient of fear and worries, may help them concentrate on their healing, and is regarded as most valuable. Careful and adequate information to patients is an important factor to improve the patient-nurse relationship and the quality of ICU care. The interviews were taken while the patients were still in the hospital. It is possible that their perceptions were influenced by the fact that they had not physically recovered yet. Furthermore it is a single centre study in the Netherlands, which implies that the perceived experiences by patients may be different in case mix, staffing, but also ethnic, socio-economical and theological background. Another potential drawback is the fact that only 50 of the 100 questionnaires could be evaluated.

9.8 Measurement properties of health-related quality of life questionnaires used in critically ill patients from 1998-2007

We performed a review from 1998-2007 of measurement properties of instruments that have been used with adults in critically ill patients admitted and after discharge from ICU, described in **Chapter 8.** Attempts are made to determine the properties of any of the measures when used with the survivors of critical care from 1998-2007. Content validity, criterion validity, construct validity, internal consistency, reproducibility, responsiveness, floor and ceiling effects and interpretability of the measures were sought for each outcome measure (6). When investigating measurement properties content validity is partly well documented but evidence for further measurement properties is poor. An ideal generic instrument in ICU patients should be easy to administer and not present too great a burden for the patient; it should be have wide application and yet be sensitive to modest changes in quality of life. It seems important to make a choice, depending on the research questions and definition of the concept to be measured, which instrument (HRQOL) or combination of instruments (HRQOL and disease specific) or if a special instrument covering the specific problems of critically ill patients and HRQOL may be needed. The SF-36 and EQ5-D are currently the most used instruments to assess the HRQOL of critically ill patients. The EQ5-D requires significant less time to complete compared with the SF-36. The SF-36 covers much more domains and is more precise. Both questionnaires show a lack of a focus on condition-specific issues and may lack sensitivity to detect HRQOL issues in critically ill patients. Consequently, they will not detect key issues in critically ill patients, such as cognitive dysfunction or severe physical problems such as critical illness neuropathy or psychological problems such as anxiety, depression, memory and concentration disturbances. Finally, on the basis of our findings we suggest that there may be the need in the future, to develop a HRQOL instrument especially for critically ill patients, which is covering more domains, still is short and simple and can be administered to patients or patients surrogates.

Clinical relevance of the study

The demand for intensive care is on the rise and is expected to grow dramatically in the future. This increase is partly caused to a growing proportion of elderly in the Netherlands. Recent advances in ICU medicine have resulted in a remarkable increase in the chance of survival for the critically ill patient admitted into an ICU. As a result, the traditional goal for ICU doctors and nurses to achieve a reduction in short-term mortality has been challenged. Evaluating HRQOL in patients surviving the ICU may lead to reflection of global care, public health, psychological consequences of ICU treatment, and medical ethics. Assessment of HRQOL can improve the answers given by intensivists and nurses to patients and relatives about the prospects of their patients. To get insights in these issues regarding the impact of ICU treatment on HRQOL we should incorporate not only short-term outcomes, e.g. length of stay and mortality, but also long-term outcomes, measured using HRQOL for physical and psychological factors, functional status and social interactions. It is important to help patients to cope with their experiences and physical and psychological complaints after ICU ultimately, influencing the perceived HRQOL. A follow up clinic following their discharge from hospital can be improving the speed and the quality of recovery from critical illness and can help relatives to cope with symptoms of stress, anxiety and depression.

Future research could be focused on improvement in long-term outcome measures and in methods of reducing long-term poor outcomes in patients discharged from ICU.

9.9 Reference List

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Nederlandse samenvatting

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1. Inleiding

In de geneeskunde en verpleegkunde is het streven van de behandeling ziekte te voorkomen of te genezen, en als dat niet meer mogelijk is de schade te beperken en het lijden te verlichten. Op de Intensive Care (IC) is de aandacht lang alleen gericht geweest op sterfte. Pas recent is er meer belangstelling naar andere uitkomsten vanuit het perspectief van de patiënt, zoals gezondheidsgerelateerde kwaliteit van leven (KvL). Intensive care behandeling is schaars, duur, en ook zeer belastend voor patiënt en familie. Een beter inzicht is daarom vereist in de uitkomsten van deze behandeling voor patiënten, familie, artsen en verpleegkundigen. Het is bijvoorbeeld mogelijk dat behandeling op de IC slechts tot een kleine toename van de levensverwachting leidt, waarbij sprake kan van zijn van een zeer slechte KvL en gepaard gaande met zeer hoge kosten. Het meten van KvL bij ernstig zieke patiënten is moeilijk en wordt daarom vaak pas verricht bij ontslag van de Intensive Care of bij ontslag uit het ziekenhuis. Echter, om de effecten van de ernstige ziekte en Intensive Care opname te beoordelen zouden KvL metingen ook bij opname plaats moeten vinden. Aangezien de meeste patiënten op het moment van opname zo ziek zijn dat zij geen vragenlijsten kunnen beantwoorden, wordt er vaak gebruik gemaakt van familieleden.

Dit proefschrift beschrijft de impact van ernstige ziekte op KvL. De KvL op het moment van ontslag van de IC, gedurende verblijf op een algemene afdeling en na ontslag ziekenhuis bij intensive care patiënten is bestudeerd. De groep patiënten met ernstige bloedvergiftiging (sepsis) is tevens apart bestudeerd. Een derde vraag was of KvL vóór opname IC aan naaste familie gevraagd kan worden met de veelgebruikte Short-form 36 (SF-36) vragenlijst. De SF-36 is een algemene KvL vragenlijst die gebruikt kan worden bij IC patiënten met verschillende opnamediagnoses. Ook hebben wij onderzocht of KvL vóór opname op de IC gebruikt kan worden als een voorspeller van mortaliteit. Tenslotte is onderzocht hoe patiënten hun IC opname hebben ervaren. Waarbij met name is gevraagd naar de ervaringen wat betreft ondersteuning en verpleegkundige zorg.

De algemene introductie en onderzoeksvragen van de studie worden beschreven in **Hoofdstuk 1.**

2. Conceptuele punten specifiek gerelateerd aan KvL bij ernstig zieke patiënten

De definitie en domeinen van gezondheidsgerelateerde kwaliteit van leven worden besproken in **Hoofdstuk 2.** Enkele conceptuele punten specifiek belangrijk bij KvL van ernstig zieke patiënten worden besproken zoals: “waarom KvL meten bij ernstig zieke patiënten?”, “definitie en domeinen van KvL”, “beschrijving van de gebruikte meetinstrumenten”, “bruikbaarheid van de KvL instrumenten”, “of naaste familieleden betrouwbare informatie kunnen geven over KvL”, “aanpassing en verschuiving in beleving (response shift) bij ernstig zieke patiënten” en “post-traumatische stres stoornis (stagneren van verwerking traumatische gebeurtenis) bij ernstig zieke patiënten”. Sommige studies laten een goede overeenkomst zien tussen de beoordeling van KvL door de patiënten zelf en de familieleden, alhoewel het niveau van overeenkomst lager is bij psychosociale onderdelen. Waakzaamheid wat betreft symptomen van het post- traumatische stres stoornis (PTSS) en vroege interventies ter voorkoming ervan zijn nodig. Verpleegkundige zorg tijdens de IC opname en nazorg in een post IC poli kunnen een belangrijke rol spelen in het herkennen en behandelen van psychologische problemen na ziekenhuis ontslag. Een belangrijk concept in KvL onderzoek is dat ernstige ziekte of chronische ziekte kan leiden tot aanpassing en een verschuiving in de beleving van de ziekte (ook wel response shift) genoemd. Een dramatische gebeurtenis (zoals intensive care opname) kan de waarneming van de klachten beïnvloeden ofwel kan klachten overschaduwen. Patiënten geven soms aan dat in de loop van de behandeling hun KvL toeneemt, terwijl objectief gezien het lichamelijke functioneren vermindert. In feite is de patiënt een “zwarte doos” met “niet te meten” interne standaarden die de uitkomst van kwaliteit van leven beïnvloeden. Bij de evaluatie van de conceptuele punten komt de aanpassing en verschuiving in beleving (response shift) naar voren als een belangrijk fenomeen, waarschijnlijk aanwezig, maar zelden gemeten bij ernstig zieke patiënten.

3. Kwaliteit van leven bij opname op de IC: kunnen we dit vragen aan naaste familieleden?

De resultaten van het onderzoek, kan KvL vóór opname IC gemeten worden door dit te vragen aan naaste familieleden, zijn beschreven in **Hoofdstuk 3.** In totaal hebben 112 patiënten met hun naaste familieleden deel genomen aan dit onderzoek. Dit zijn patiënten en familieleden vóór grote geplande operaties (*n*=55) of na een acute opname (*n*=57). Patiënten en familieleden is gevraagd de SF-36 vragenlijst te beantwoorden in de eerste 72 uur na acute opname of de dag vóór de geplande opname op de IC. Bij alle onderdelen van de SF-36 vragenlijst is er een significante correlatie (samenhang) gevonden tussen de beoordeling van de KvL door de patiënt zelf en van diens familie. In het algemeen onderschatten de familieleden de KvL van de patiënt, hoewel de verschillen klein zijn. Bij de meeste vragen is een goede tot zeer goede overeenkomst gevonden. De KvL wordt niet beïnvloed door het type IC opname van de patiënt (acuut of gepland, chirurgisch of niet-chirurgisch). Opvallend is dat familieleden met name de lichamelijke onderdelen van de KvL goed kunnen beoordelen.

4. Het meten van de impact van ernstige ziekte op kwaliteit van leven

In **Hoofdstuk 4** is ingegaan op de impact van de ernstige ziekte op KvL bij IC patiënten. Vooral het tijdsverloop van veranderingen in KvL na ontslag Intensive Care, gedurende verblijf op een algemene afdeling en na ontslag ziekenhuis is bestudeerd. Alle patiënten langer dan 48 uur opgenomen op de IC zijn ingesloten in het onderzoek. Bij opname op de IC is aan naaste familieleden gevraagd te beoordelen hoe de patiënt zelf zijn kwaliteit van leven zou hebben aangegeven in de periode van 4 weken vóór de ernstige ziekte. Aan de patiënt zelf is gevraagd om de SF-36 in te vullen bij IC ontslag, ziekenhuis ontslag en drie en zes maanden na IC ontslag. Vanaf september 2000 tot april 2004 zijn 451 patiënten ingesloten in het onderzoek. KvL vóór IC opname is afgenomen bij alle 451 patiënten (gevraagd aan familieleden). Zes maanden na IC ontslag is door 252 patiënten de vragenlijst beantwoord, 40 patiënten konden niet meer worden opgespoord, 159 patiënten waren overleden. Alle onderdelen van de SF-36 veranderden significant (aanmerkelijk) in de tijd. Er is een patroon gevonden in de verschillende SF-36 dimensies, gekenmerkt door een scherpe daling tijdens de IC- periode en geleidelijke verbetering op drie en zes maanden na IC ontslag. De gemiddelde SF-36 scores zijn echter in vijf dimensies lager na 6 maanden vergeleken met de uitgangssituatie vóór IC opname (lichamelijk functioneren, lichamelijke rolbeperking, algemene gezondheid, sociaal functioneren en mentale gezondheid). Zes maanden na IC ontslag zijn de gemiddelde scores van alle SF-36 dimensies, behalve lichamelijke pijn, significant lager bij IC overlevenden in vergelijking met een algemene Nederlandse bevolkingsgroep met dezelfde gemiddelde leeftijd.

Scores vóór IC opname (n=252) bij patiënten die overleefden zijn lager in drie van de acht SF-36 dimensies vergeleken met een steekproef van een algemene Nederlandse bevolkingsgroep (lichamelijk functioneren, lichamelijke rolbeperking en vitaliteit). Interessant is dat de gemiddelde scores van de pijndimensie hoger zijn (dit betekent minder pijn) bij de patiënten die de IC opname overleefden vergeleken met de gezonde controle groep. De KvL vóór IC is significant lager in zes van de acht dimensies (lichamelijk functioneren, lichamelijke rolbeperking, algemene gezondheid, vitaliteit, sociaal functioneren en mentale gezondheid) vergeleken met een algemene Nederlandse bevolkingsgroep. Reeds bij opname zijn de scores van zeven van de acht dimensies (pijn uitgezonderd) significant lager bij patiënten die dood gingen vergeleken met de IC overlevenden. In het licht van deze bevindingen lijkt het cruciaal de KvL van de patiënt te meten, zoals deze was vóór de ernstige ziekte, om zo de definitie wat betreft grenzen aan de IC behandeling te verbeteren. Speciale interventies zoals een post IC poli kunnen de KvL van ex IC patiënten mogelijk verbeteren als ook de individuele patiëntenzorg.

5. Impact van ernstige sepsis op kwaliteit van leven

De impact van ernstige bloedvergiftiging (sepsis) op KvL is geëvalueerd in **Hoofdstuk 5.** Ernstige sepsis wordt vaak gecompliceerd met orgaan falen wat zou kunnen leiden tot een zeer beperkte KvL. In deze studie is gekeken naar de impact van ernstige sepsis op KvL in vergelijking met een qua leeftijd gelijke algemene Nederlandse bevolkingsgroep. Van de 170 patiënten met ernstige sepsis, konden er 95 worden geëvalueerd zes maanden na IC ontslag. Er is een scherpe daling gevonden van de KvL gedurende de periode in de IC waarna een geleidelijke verbetering in de zes maanden erna optreedt. Echter, gemiddelde scores wat betreft lichamelijk functioneren, lichamelijke rolbeperking en algemene gezondheid dimensies zijn zes maanden na ontslag significant lager vergeleken met waardes vóór IC opname. KvL vóór IC opname was al lager in de sepsis overlevenden vergeleken met de algemene Nederlandse bevolkingsgroep.

De conclusie is dat ondanks een beperkt herstel in de fysieke en algemene gezondheid dimensies zes maanden na IC, de behandeling van patiënten met ernstige sepsis de moeite waard is. Daarbij kan een IC poli voor patiënten na ontslag IC en ziekenhuis de snelheid en kwaliteit van dit herstel bevorderen.

6. Kwaliteit van leven als een voorspellende factor

Het is bekend dat KvL voorspellend is voor overlijden bij een aantal verschillende aandoeningen. In **Hoofdstuk 6** is onderzocht of dat ook geldig is voor IC patiënten. Onderzocht is of de KvL van de patiënt vóór de IC opname voorspellend is voor de overleving zes maanden na IC ontslag. Dit is vergeleken met een geaccepteerd model op groepsniveau om de overleving van IC patiënten te voorspellen; de zogenaamde APACHE II score (Acute Physiology, Age and Chronic Health Evaluation). 451 patiënten zijn bij IC opname ingesloten in het onderzoek. In de analyse hebben wij vijf statistische modellen gebruikt: de eerste vraag van de SF-36 (algemene gezondheid), leeftijd en geslacht (model A). KvL onderverdeeld in de lichamelijke component score (PCS) en de mentale component score (MCS) leeftijd en geslacht (model B), de APACHE II score (model C), algemene gezondheid, APACHE II score, leeftijd en geslacht (model D), PCS en MCS, APACHE II score, leeftijd en geslacht (model E). We hebben laten zien dat KvL vóór IC opname gebruikt kan worden als een voorspeller van sterfte bij patiënten die langer dan 48 uur op de IC zijn opgenomen. De effectiviteit in het voorspellen van sterfte van het algemene gezondheids item van de SF-36 (model A) was gelijk aan de complete SF-36 (model B) en de APACHE II score (model C). De modellen met APACHE II score én KvL (modellen D en E) waren marginaal beter dan de aparte modellen.

Concluderend kunnen we stellen dat de KvL vóór IC opname net zo goed is in het voorspellen van overleving/sterfte als de APACHE II score. Evaluatie van KvL kan worden verricht met de SF-36 of zelfs met alleen de eerste vraag van SF-36 (hoe vond u uw algemene gezondheid de laatste tijd: "uitstekend, goed, redelijk, matig, slecht ") aangezien dit vergelijkbare resultaten geeft. Vooral bij ernstige zieke patiënten is de eenvoud en gemak van de één enkele vraag aantrekkelijk. Dit kan helpen bij het proces van beslissen welke patiënten potentieel voordeel hebben van IC behandeling.

7. Ervaringen van ernstig zieke patiënten

Het belang van KvL is geïllustreerd door de ervaringen van patiënten wat betreft hun opname op de IC in **Hoofdstuk 7**. Ervaringen van patiënten geven informatie over de kwaliteit van de zorg in de IC. Verpleegkundige zorg kan een positief effect hebben op het psychologisch welzijn van patiënten opgenomen op de intensive care. De manier waarop verpleegkundigen patiënten ondersteunen gedurende de ernstige ziekte en de periode van herstel is een belangrijke factor in hoe tevreden patiënten zijn en de ervaren KvL na ontslag. Negatieve ervaringen van patiënten is een risicofactor voor het ontstaan van posttraumatische stress. Een kwalitatieve studie is verricht door gebruik te maken van een semi-gestructureerd interview met een lijst van relevante onderwerpen bij 11 patiënten. Daarnaast is een kwantitatieve studie uitgevoerd bij 100 patiënten. Uit deze studies komt één centraal thema van zorgervaringen naar voren: ondersteuning. Deze zorgervaringen zijn: patiënt geïnformeerd door uitleg en instructies, het centraal zetten van de patiënt en de bejegening door de verpleegkundige. Uit de interviews komt verder naar voren dat niet alleen de technologie en de deskundigheid van de verpleegkundigen als belangrijk wordt ervaren door patiënten maar dat ook medeleven, bemoediging, aandacht, verminderen van angst en zorgen voor veiligheid wordt gezien als belangrijk. Het meest gewaardeerde aspect van de verpleegkundige zorg is ondersteuning. Een kwantitatieve studie is verricht door het versturen van een zelf- ontwikkelde vragenlijst. De vragenlijst werd ontwikkeld op basis van de interviews. Van de 100 verstuurde vragenlijsten zijn 62 anoniem ingevuld. Twaalf patiënten hadden geen enkele herinnering aan hun verblijf op de IC of waren overleden. Daardoor bleven 50 vragenlijsten over voor onderzoek. De resultaten laten zien dat ongeveer de helft van de patiënten slechts een fragmentarische herinnering had aan de opname op de IC. Pijn (46%) en lawaai (40%) zijn klachten die het meest werden vermeld. Van de patiënten die slaapproblemen hadden relateerde 54% dit aan lawaai. De meest onaangename procedures en gebeurtenissen tijdens de IC opname zijn: het niet kunnen praten wanneer beademd, bronchiaal toilet, dorst en onvoldoende uitleg. Elf patiënten vermelden psychologische problemen na ontslag uit het ziekenhuis zoals: angst, niet goed kunnen concentreren, depressie, hallucinaties en een slecht geheugen. Hoewel de deskundigheid en de technische bekwaamheid van de verpleegkundige is ervaren als belangrijk, omdat zij een onderdeel vormen voor de noodzakelijke levensreddende interventies, wordt het zorggedrag en het verminderen van pijn en zorgen, ervaren als belangrijk om te kunnen concentreren op het herstel. Zorgvuldige en adequate informatie aan patiënten is een belangrijke factor voor het verbeteren van de patiënt- verpleegkundige relatie en de kwaliteit van de zorg op de IC.

8. Eigenschappen van KvL meetinstrumenten gebruikt bij ernstig zieke patiënten van 1998 tot 2007

De meetinstrumenten en methoden gebruikt bij ernstig zieke patiënten van 1998 tot 2007 zijn geëvalueerd in **Hoofdstuk 8**. Gezocht is in hoeverre de domeinen die van belang zijn worden gedekt door de vragenlijst (inhoudsvaliditeit), of het instrument is vergeleken met een gouden standaard (criteriumvaliditeit), of het instrument zich gedraagt zoals het zich op grond van verwachtingen moet gedragen (begripsvaliditeit), in hoeverre de items samenhangen (interne consistentie), of er een test- hertest meting is verricht (reproduceerbaarheid), de verdeling van antwoorden over de antwoordschaal, en verklaarbaarheid van elk meetinstrument. Bij evaluatie van de eigenschappen van de gebruikte meetinstrumenten blijkt dat de inhoudsvaliditeit van KvL-instrumenten die bij ernstig zieke patiënten worden gebruikt, gedeeltelijk goed wordt vermeld maar dat verdere meeteigenschappen zeer beperkt worden vermeld. Een ideaal meetinstrument bij IC patiënten moet eenvoudig zijn en makkelijk in te vullen, niet een te grote belasting vormen voor ernstig zieke patiënten, het moet een brede toepassing hebben en toch gevoelig blijven voor kleine veranderingen in KvL. Afhankelijk van de onderzoeksvraag is het belangrijk een keuze te maken welk meet instrument (KvL) of combinatie van instrumenten (KvL en ziekte- specifiek) het beste kan worden gebruikt of dat er een speciaal meetinstrument nodig is die de speciale problemen van ernstig zieke patiënten omvatten. De Short-form 36 (SF-36) en de Euroqol 5D (EQ-5D) zijn momenteel de instrumenten die het meest worden gebruikt om KvL te meten bij ernstig zieke patiënten. De EQ-5D kost minder tijd om in te vullen dan de SF-36. Echter, de SF-36 omvat meer domeinen en is preciezer. Beide vragenlijsten omvatten onvoldoende een aantal onderwerpen die relevant zijn voor ernstig zieke patiënten. Als gevolg hiervan worden belangrijke zaken als ernstige lichamelijke problemen zoals spierzwakte bij ernstige ziekte, of psychologische problemen zoals angst, depressie, geheugen en concentratie stoornissen niet gemeten. Uiteindelijk op basis van onze bevindingen stellen wij voor om een KvL meetinstrument te ontwikkelen speciaal voor ernstig zieke patiënten. Dit instrument moet meer relevante domeinen omvatten, toch kort en simpel zijn en beantwoord kunnen worden door zowel patiënt als familie.

Dankwoord

Dankwoord

Aan de totstandkoming van dit proefschrift hebben veel mensen bijgedragen. Op de eerste plaats waren dit alle patiënten en hun familieleden. Velen van hen deden dit met enthousiasme, vooral omdat ze hun verhaal kwijt konden. Anderzijds was het voor sommigen ook een belasting. Toch hebben zij belangeloos hun medewerking verleend en zo dit onderzoek mogelijk gemaakt.
Dank hiervoor.

Mijn promotoren en initiators van het onderzoek, Jan Bakker en Guus Schrijvers, hebben mij zowel voor als tijdens dit onderzoek met veel enthousiasme begeleid en waren bereid om mij de tijd te geven voor dit onderzoek. Ook Hans Rommes, intensivist, en alle intensive care verpleegkundigen hebben mij vanaf het begin gesteund en van goede raad voorzien.

Het maakt het voor mij wel bijzonder dat dit onderzoek begonnen is met Jan Bakker als copromotor (toen werkzaam als intensivist in Apeldoorn) en Guus Schrijvers als promotor. Doordat Jan Bakker Hoogleraar Intensive Care in het Erasmus Medisch Centrum te Rotterdam is geworden eindigt dit onderzoek met Jan als promotor samen met Guus Schrijvers.

De inhoudelijke bijdragen van Henk van Stel en Peter Spronk als copromotoren hebben mede dit boekje opgeleverd. De bijdragen van Henk van Stel zowel op het gebied van statistiek en ook als “kwaliteit van leven” specialist waren van doorslaggevend belang. Van Peter Spronk heb ik veel geleerd, hij was dagelijks aanwezig wanneer ik problemen of inhoudelijke vragen had. Ook al was hij druk, toch was hij altijd bereid om tijd voor mij vrij te maken of mij van goede raad te voorzien. Zijn gedrevenheid en enthousiasme voor dit onderzoek, als wel voor onderzoek in het algemeen, waren voor mij erg belangrijk, zeker op momenten als ik het even moeilijk had.

De bijdrage van Albertine van Horssen (bibliothecaresse) bij het bedenken van de juiste zoektermen voor het review heb ik als erg waardevol ervaren, bedankt hiervoor. Peter Beelen wil ik bedanken voor zijn hulp bij de vormgeving van de omslag van dit proefschrift.

Ook de leden van de kleine commissie, Prof. dr. D. Tibboel, Prof. dr. I.D. de Beaufort en Prof. dr. J.F. Bion wil ik bedanken voor het beoordelen van dit proefschrift.

Zeker niet in de laatste plaats wil ik mijn familie en vrienden bedanken, die mijn verhalen moesten aanhoren. Vooral mijn ouders (inmiddels beiden overleden) zouden erg trots op mij zijn geweest en het voelt als een groot gemis dat zij hier nu niet bij aanwezig kunnen zijn.

Curriculum Vitae

José Hofhuis werd in 1955 geboren te Raalte. Na afronding van haar middelbare schoolopleiding startte zij in 1974 met de inservice opleiding tot verpleegkundige te Deventer en was werkzaam als leerling verpleegkundige in de Deventer Ziekenhuizen. In 1978 behaalde zij het diploma Verpleegkundige A aan de School de “Zuysel” te Deventer. In het zelfde jaar startte zij met de brede basis Intensive Care opleiding in het Lukas Ziekenhuis te Apeldoorn. Na het behalen van het diploma heeft zij gedurende enige jaren afwisselend op de Hartbewaking en de Intensive Care afdeling gewerkt, en daarna volledig op de Intensive Care afdeling. In 1994 startte zij met de functie researchverpleegkundige op de Intensive Care van Gelre Ziekenhuizen lokatie Lukas, en volgde de Post-HBO opleiding praktijk gericht onderzoek aan de Hogeschool te Utrecht met succes. In 1995 begon zij aan de opleiding Master of Sience Degree in Nursing van de Universiteit van Wales. Begin 1998 heef zij deze afgerond. Daarna kreeg ze de mogelijkheid om een promotie onderzoek te doen naar kwaliteit van leven bij Intensive Care patiënten te Apeldoorn.