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Functional recovery after critical illness

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CHAPTER 8

GENERAL DISCUSSION
With increased survival rates in intensive care unit (ICU) patients, the awareness of morbidity following intensive care treatment has been growing. With this, it has been recognized that the intensive support of these patients need to be continued after discharge from the ICU\textsuperscript{1,2}. A prerequisite for the development of adequate follow-up care is a thorough understanding of post-ICU sequelae and its potential determinants.

The aim of this thesis was to describe the course of functional recovery and its potential determinants of patients who stayed >48 hours in the ICU during the first year after discharge from the ICU. In the present chapter the results and the methodology of the studies are reviewed, clinical implications are discussed and recommendations for future research are made.

The outcomes in the previous chapters are categorized according to the World Health Organization’s (WHO) framework; the International Classification of Functioning, Disability and Health (ICF) for measuring health and disability. Within the ICF framework, disability is characterized as the outcome or result of a complex relationship between an individual’s health condition (e.g. disorder or disease) and personal factors, and of the external factors that represent the circumstances in which the individual lives.\textsuperscript{3} (Figure 8.1)

![Figure 8.1](image-url)
Since the studies in this thesis were initiated in 2000, literature on the quality of survival of ICU patients has increased steadily. Nevertheless, a thorough understanding of the course of functional recovery, and of long lasting impairments in functioning from an ICF perspective was not available.

**Main findings**

*High prevalence of impairments in body functions, limitations in activities and restrictions in participation during the first year following a critical illness*

*Impairments in body functions*

The results of the studies in chapter 2-7 were consistent with respect to the occurrence of a large variety of impairments in neuromuscular, and skeletal, cardiovascular, respiratory, mental, and digestive functions, in a substantial proportion of ICU survivors who were treated for at least 2 days in the ICU (*Chapter 2-7*).

During the first year following ICU, the prevalence of movement related impairments was remarkably high. The first week after ICU discharge, median grip strength was 50% lower than age-corrected and gender-corrected normative data (*Chapter 4*), and after one year, muscle strength was still reduced in 50% of the patients (*Chapters 6, 7*). Furthermore, joint mobility was limited in 46%, and physical endurance was reduced in 83% of the patients (*Chapter 6*).

Shortly after ICU discharge, cognitive functions such as concentration and short-term memory were impaired in 25% of the patients (*Chapter 4*). It is alarming that after 3 months, the prevalence of impairments in attention had raised to 70%, and in memory to 40%, and remained unchanged during the subsequent 9 months (*Chapter 6*). Furthermore, after one year, symptoms related to anxiety and depression were present in 14% of the patients, and 18% had symptoms related to post traumatic stress disorder (PTSD) (*Chapter 4*).

The assessment of metabolic status and adequacy of nutritional support are integrated in the intensive care treatment, and metabolic and nutritional interventions have improved outcome in ICU patients. Nevertheless, the high prevalence of impairments in weight maintenance and dietary intake after 3 months (50-70%, *Chapter 6*) suspect impaired nutritional status which may impede recovery.

We found a different course for the recovery of physical and psychological impairments, with significant improvement in physical functions, while impaired psychological functions persisted (*Chapter 6*). Moreover, the
course of recovery for grip-strength showed a substantial improvement during the first 3 months after discharge from the ICU, followed by a slight improvement over the subsequent 9 months (Chapter 7). In contrast, no effect of time was found for the mental functions anxiety and depression (hospital anxiety and depression scale; HADS) and symptoms of PTSD (and impact of events scale; IES), which were recorded additionally to the data on physical functions (unpublished data). In this prospective cohort of which the inclusion criteria and patient characteristics were in agreement with those as described in chapter 7, the median HADS and IES score did not change during the 12 months following discharge from the ICU (Figures 8.2 and 8.3). The number of patients with clinically significant symptoms of anxiety and depression (HADS > 19) was 2 (10%) after 3 months, and 3 (15%) after 6 and 12 months. The number of patients with PTSD-related symptoms (IES > 35) was 2 (10%) after 3 months, and 4 (20%) after, and 12 months.

Limitations in activities and restrictions in participation
During the first year after discharge from the ICU, the performance of daily activities improved (SIP68), but the prevalence of limitations in activities remained high. After one year, 54% of the patients were limited in the performance of daily activities; 22% had mild, and 32% had severe limitations (Chapter 4).

The first week after ICU discharge, 94% of the patients were dependent on the
help of others in the performing of basic activities of daily living (Chapter 5). Between 3 and 12 months following ICU, limitations in activities were predominantly found with respect to mobility, and domestic, and social life. Moreover, limitations in mobility were reported by 72% after 3 months and by 46% after 12 months. With this, walking stairs, hills, and distances were most frequently limited. In addition, the following limitations in activities related to domestic life were frequently reported after 3 and 12 months; acquisition of goods and services (52% and 24%), preparation of meals (28% and 30%), and doing housework (44% and 14%). Furthermore, 20-50% of the patients reported limitations with activities related to community life and recreation and leisure after 12 months (Chapters 5-6).

The recovery of the performance of physical, and psychological activities followed a different time course. Whereas the scores on the physical and social dimensions of the SIP68 decreased over time, indicating functional improvement, no significant effect of time was found on the psychological dimension (Chapter 6). Similar results were found for the different dimensions of the Medical Outcomes Study 36-item Short-Form General Health Survey (SF-36). Scores on the physical functioning dimension (SF-36 PF) increased substantially during the first 6 months, followed by a slight further improvement, while scores on the dimension mental health (MH) did not change following ICU admission (Chapter 7).

After one year, participation in major life areas such as employment was restricted in the majority (54%) of patients who were employed before ICU admission (Chapter 4).

**Limited predictive value of potential determinants of functioning after ICU**

**Health condition as a determinant of functioning**

In this thesis, the relation between health condition and functioning which is assumed within the ICF framework, after ICU was explored. The understanding of health condition in ICU patients is complex due to changes before, during, and after ICU treatment by which health condition varies widely over time between patients, as well as within the individual ICU patient.

**Relationship between preexisting conditions and diseases and post ICU functioning**

From studies on mortality, it has been known that preexisting factors such as chronic disease, comorbidity, age and quality of life before ICU, are related to survival.7-9 The literature on predictors of functional outcome is scarce, but the association between increased age and functional status after ICU has been reported previously.10 A priori, we hypothesized that a poor func-
tional status before admission is a predictor for poor functioning after ICU. To illustrate, we expected that the presence of pre-existing impairments would impede functional recovery after a critical illness. With this, we proposed that with a higher age, the risk for pre-existing impairments would increase, and therefore age, as a surrogate for preexisting conditions, was expected to be associated with functional recovery. Nevertheless, we did not found an association between pre-ICU health or age, with functioning one year after ICU (Chapters 4, 7).

**Relationship between the severity of illness and diagnosis at ICU admission, and post ICU functioning**

Severity of illness at ICU admission and ICU admission diagnosis are generally considered as important predictors of mortality in ICU patients.\(^7\)\(^-\)\(^9\) The relationship between these factors and functioning after ICU seems to be more complex. It has been shown that long-term functional health is related to the prognosis of the underlying disease process rather than to the severity of the acute episode necessitating the ICU admission.\(^10\) However, often, the ICU admission diagnosis is related to the pre-ICU health status. For example, this is the case in non-surgical patients with a chronic impaired health condition that becomes life threatening and requires admittance to the ICU. In elective surgery patients, the ICU admission diagnosis can also be related to pre ICU morbidity (for instance after a coronary artery bypass surgery). In contrast, in other sub groups of patients (surgical and non-surgical), the condition for admission to the ICU may be independent of pre-ICU health, but significantly impact on functional status after ICU. Common examples are head trauma with remaining brain injury, and myocardial infarction, resulting in left ventricular dysfunction and subsequent exercise intolerance.

In our cross sectional study, increased severity of illness at ICU admission, and acute admission to the ICU (together with increased length of stay in the ICU) were independently associated with poor functional health after one year. However, this relationship appeared to be of limited clinical value as these factors explained only 10% of the health status after one year (Chapter 4).

**Relationship between ICU stay and post ICU functioning**

There is increasing evidence that care delivered in the ICU, such as sedation, ventilation strategies, monitoring devices, and diagnostic tests, may have important effects on post-ICU disability\(^11\)\(^-\)\(^12\), including cognitive dysfunction\(^13\)\(^,\)\(^14\), and PTSD.\(^15\) For example, neuromuscular blockers and corticosteroids may contribute to critical illness abnormalities.\(^16\) Additionally, arisen complications in the course of the disease during ICU stay influences
outcome. For example, patients with sepsis may have ongoing decrements in functioning that seem to be a result of their critical illness rather than their underlying medical problems. To illustrate, we found severe restrictions in daily functioning in patients with critical illness polyneuropathy (CIP) one year after discharge from the ICU (Chapter 3). Taking into account the high mortality rate (Chapter 3), patients with CIP appear to be a subgroup of ICU patients with a highly increased risk for poor recovery. But as electromyography to establish the diagnosis CIP is not routinely performed in ICU patients, and the clinical management of patients with a diagnosis CIP does not differ from other ICU patients, we decided no longer to focus only on patients with CIP. Therefore the focus in the subsequent studies (Chapters 4-7) was expanded from patients with CIP to a larger population of ICU patients potentially at risk for poor functional outcome, i.e. patients who were mechanically ventilated for longer than 48 hours. In the cross-sectional study, length of stay (LOS) in the ICU was, together with severity of illness and admission category, identified as one of the prognostic factors for functional outcome after one year (Chapter 4). Remarkably, functional status at ICU discharge was not found to be related to functional outcome after one year in the prospective study (Chapter 7). Apparently, the recovery potential in patients after a critical illness, is determined by other factors than the severity of limitations at the beginning of the recovery process.

In conclusion, the weak relationship between initial health status and functional outcome does not allow an accurate prediction of functioning in individual patients after discharge from the ICU. With respect to the limited clinical prognostic value of the independent determinants related to health status (Chapter 4 and 7), we propose that the interaction of external factors and functional outcome, as it is assumed within the ICF (Figure 8.1), should be considered.

**External factors as potential determinants for functioning after ICU**

According to the ICF framework, environmental, and personal factors (i.e. external factors) interact with the components of Body Functions and Structures and Activities and Participation. The environmental, and personal factors represent the complete background of an individual’s life and living. From the previous chapters we can not infer the role of external factors on the performance of activities in patients after ICU. Nevertheless, the supportive network appears to be an important factor for the performance of daily activities and participation of patients who are discharged home, as they, to a large extent, rely on others for their activities of daily living (Chapter 6). Additionally, the role of personal factors on functional outcome in
patients after discharge from the ICU should be considered, as the relationship between personality and coping behavior and the course of recovery in various patient populations has been described.\textsuperscript{18,19}

**Methodological considerations**

The findings of the studies in this thesis may be criticized with respect to the small study sample sizes in combination with the heterogeneity of our populations. In the first place, this was due to the design of the studies in which limited numbers of patients were included, on the other hand, follow-up was impeded by high mortality and high post ICU morbidity. Due to severe functional restrictions, the majority of the patients was not able to attend the follow-up appointment in the hospital 3 months after ICU discharge. Nevertheless, the response rate in the prospective studies after one year was high (88-90%) and the findings of our studies with respect to quality of life were in agreement with previous international studies with large study populations. Therefore, the findings of the previous chapters can be considered as valid and representative for ICU patients who have been ventilated for more than 48 hours in an ICU.

In the previous chapters it was demonstrated that the majority of patients after discharge from the ICU had severe impairments in functions and restrictions in activities and participation. Due to the observational nature of the study, the patients in the studies were provided with usual care, comprising a wide range of physical therapies and multidisciplinary rehabilitation. Their effect on the functional outcome could not be determined and was not a focus of interest. Moreover, there was no relation between the extent of the impairments and whether or not patients received rehabilitation treatment. Apparently, the functional outcome of patients after one year from whom usual care was not withheld was poor.

Physical improvement occurred predominantly within the first 6 months, followed by only a slight progress, while psychological functioning did not change within one year following ICU discharge. Because the follow-up was limited to the duration of one year after ICU discharge, we do not know whether optimal recovery was achieved within one year, or whether further improvement is to be expected. Nevertheless, the high prevalence and severity of impairments and restrictions during the first year necessitates interventions aiming at the improvement of functional outcome of patients after discharge from the ICU.

In the studies within this thesis, patients who stayed >48 hours in the ICU were included with the assumption that in this way patients who were most at risk for a poor functional outcome would be studied. Apparently, in view of
the severity of impairments in functions, limitations in activities and restrictions in participation in our study population, the cut-off of 48 hours was adequate. Nevertheless, with respect to the limited predictive value of prolonged ICU LOS for poor outcome (Chapter 4), it is likely that functional restrictions will also be found in patients after a shorter duration of ICU stay.

**Clinical implications**

*Structured multidisciplinary ICU follow-up care is urgently warranted*

The high prevalence and the severity of impairments in physical and mental functions, and the restrictions in activities in survivors of a critical illness, need appropriate multidisciplinary interventions for ICU patients. The early identification of rehabilitation needs can help to prevent chronic disability, and can reduce healthcare costs as well as economic costs due to limited job participation.

Obviously, rehabilitation should not start after discharge from the ICU, but should be initiated during the stay in the ICU in order to reduce deconditioning and related complications, and to optimize respiratory condition. Active or passive mobilization, muscle training, and muscle stretching are some preventive measures during the stay in the ICU which are promising with respect to the reduction of physical decline.\(^2\,20,\,21\) With respect to the prevention of PTSD during ICU stay, the administration of the stress hormone cortisol, and the provision of an ICU diary has been suggested to reduce the level of symptoms of PTSD.\(^22,\,23\)

We propose that structured multidisciplinary follow-up of ICU patients should be established. Intensive care need to be regarded as a phase in a health care process that also includes functional recovery. To date the follow-up of ICU patients is usually performed by physicians who are involved with the initial diagnosis for which the patient was admitted to the ICU. This often means that follow-up is in terms of the admission diagnosis and might not reflect upon the problems that develop as a consequence of the ICU stay. As a consequence, restrictions in physical and psychological functioning, or specific problems that need the attention during rehabilitation after ICU, often remain unrecognized.\(^24\) To illustrate, we found that after one year, only half of the patients with residual physical impairments or restrictions, had physical therapy, and that only a quarter of the patients with psychological distress received treatment from a psychiatrist or psychologist. Structured follow-up will help to identify problems and serve to facilitate referrals to rehabilitation and other specialties.

With respect to the recovery course, the heterogeneity of the population, the
variety of outcomes, and the lack of early clinical predictors of functional outcome, we propose a multidisciplinary stepped care approach with different degrees of therapeutic intervention depending on the patient’s individual needs.

Already at discharge from the ICU, patients and their relatives can be informed about the possible sequelae after discharge from the ICU. This will help to recognize ICU related symptoms, and may help in accepting, and anticipating a slow course of functional recovery. Four weeks after ICU discharge, patients should be screened for the presence of symptoms related to acute PTSD as the early identification of symptoms indicative of later PTSD would allow timely intervention. Several short screening tools have been validated for ICU patients to identify those patients in need of referral to specialist psychological services, but these have not yet been translated and validated for the Dutch ICU population.25

Three months following ICU discharge, patients should be invited for an ICU follow-up appointment. During this visit, patients should be reassessed regarding the original condition that necessitated the ICU admission, and the specific problems they acquired during and after their critical illness. The patient could also debrief about their experience in the ICU. In this way, the ICU follow-up visit can provide an opportunity to alert patients and families of the chance of developing sequelae so that early recognition and necessary treatment can be offered.

In order to adequately refer patients to the appropriate specialties, a screening tool to elicit and record information on the functioning and disability of each individual patient is necessary. The ICF checklist for measuring disability is useful, as it focuses on the consequences of morbidity rather than on the disease itself. Furthermore, the dimension ‘physical functioning’ of the SF-36 can be used for the identification of patients at increased risk for limitations in physical activities by applying a cut-off value of 60 points (Chapter 7). In addition, the presence of symptoms related to PTSD need to be evaluated again to identify new cases of PTSD, since we observed that symptoms related to PTSD can develop after 4 weeks following ICU.

The follow-up of ICU patients should be a shared responsibility of the ICU staff and rehabilitation medicine

The intensivists and ICU nurses need to understand the outcome of their patients to develop and improve the care of patients within the ICU. An increased awareness of post-ICU disability may have the advantage of facilitating communication with family members.
Rehabilitation medicine may play an important role, as it already has expertise in aiding recovery and regaining or maximising functional status in a wide variety of conditions. A carefully planned multidisciplinary rehabilitation program may help patients to improve functional independence and return to work or to activities of daily living. However, to date the effectiveness of any follow-up interventions such as either psychiatry, physiotherapy, or occupational therapy during the course of recovery after a critical illness has not been systematically investigated. Finally, a structured follow-up offers the infrastructure to conduct intervention studies to improve ICU outcome.

**Considerations for future research**

Based on the findings of the thesis and the methodological and clinical considerations, some recommendations for future research can be made.

**Intervention studies are needed**

Now we have a clear picture of the implications of the problems encountered by ICU survivors, randomized controlled trails for the evaluation of effects of any of the after-care interventions for ICU patients are needed. It should be investigated whether functional outcome can be improved by interventions which are tailored to the specific ICU sequelae. Obviously, whereas the positive effects of individualized exercise programs are promising in a diversity of patient populations such as after cardiac surgery\(^{26}\), diabetes\(^ {27}\), and chronic obstructive pulmonary disease\(^ {28}\), the effect on patients after an ICU stay has not yet been investigated. Furthermore, future research should determine the optimal timing and the effects of psychological interventions in ICU populations. Whereas cognitive behavioural therapy has been proven to be effective at reducing traumatic stress symptoms in individuals with PTSD\(^ {29}\), the effect in ICU patients has not been investigated.

**Studies on outcomes at the ICF levels of body functions and structures, activities, participation and external factors are needed**

As patients are admitted to and discharged from the ICU as a heterogeneous group, there is a need for generic outcome measures, which can be used across a wide range of medical and surgical conditions and enables between study comparisons. The questionnaires SF-36 and the EQ-5D are recommended as standard questionnaires to evaluate QoL and utilities for quality adjusted survival in ICU patients.\(^ {30}\) In our opinion, the evaluation of ICU survivors should be structured according to the ICF distinguishing the level of body functions and structures, activities, participation, and also include...
personal and environmental factors. Although this thesis provides important information on functioning of ICU survivors on the different levels of the ICF, for the development of optimal rehabilitation care, physical capacity, and physical endurance as well as the influence of coping strategies and informal care providers need further investigation.

**Development of an ICF Core Set for the ICU population**

An ICF Core Set should be developed for ICU populations. ICF Core Sets, are short lists of ICF categories relevant for specific conditions, and serve as practical tools for clinical practice and standards for health information and research. In the ICU population, an ICF Core Set may facilitate adequate referral to different specialties, by generating profile of patients using the most important ICF categories. In one of the studies in this thesis (*Chapter 6*), a selection of 36 (of 123) components of the ICF checklist was used to describe the frequency of specific patient problems. Eighteen (50%) of the components reached a prevalence of 30% or more, with the most frequently reported problems in the categories mental, sensory, respiratory, neuro-musculoskeletal and movement related functions, and mobility, major life areas and community, social and civic life.

**Methodological issues for future research**

Finally, future research should account for the specific difficulties of the follow-up of ICU patients. Regarding the high mortality rate and the heterogeneity, studies should be sufficiently large to allow meaningful interpretation of subgroup data. Follow-up should exceed one year post ICU, and should include functional capacity measures which can not be evaluated only with questionnaires, but requires physical examinations. Additionally, follow-up should be extended to patients with an ICU LOS of less than 48 hours, to investigate the prevalence of impairments in body functions, limitations in activities and restrictions in participation during the fist year following an admission to the ICU in this specific sub-group.

In conclusion, although there is considerable need for further research, there is enough empirical evidence to support changing practice today.

**References**


