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PATIENT RELATED OUTCOME MEASURES AFTER SPECIALIZED TREATMENT OF PERSISTENT CRITICAL ILLNESS – A PILOT STUDY ON FEASIBILITY

Author: Sofia Bråse

Supervisor: Eva Sundman

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Table of contents

Populärvetenskaplig sammanfattning

Patienter med akut livshotande sjukdom får livsuppehållande behandling på intensivvårdsavdelning. De flesta på detta sätt akut kritiskt sjuka blir bättre inom några dagar och kan lämna intensivvårdsavdelningen. Långvarigt kritiskt sjuka har ett fortsatt behov av intensivvård, men skiljer sig på många andra sätt från dem som nyligen insjuknat och deras behov är ofta svåra att tillgodose på en vanlig intensivvårdsavdelning.

I takt med att intensivvården har förbättrats har antalet långvarigt kritiskt sjuka ökat, eftersom fler överlever den akuta fasen. För att möta deras behov har specialiserade kliniker startats och resultaten rapporteras generellt bättre än äldre mycket pessimistiska rapporter. Det är dock fortfarande kontroversiellt hur denna patientgrupp ska omhändertas och om, eller när, man ska avbryta behandling.

REMEO är Sveriges enda klinik specialiserad på långvarigt kritiskt sjuka och startade 2018 ett kvalitetsuppföljningsprogram efter utskrivning. Denna pilotstudie har fokuserat på det första uppföljningstillfället, tre månader efter utskrivning, och undersökt om programmet är genomförbart och därmed lämpar sig för en större framåtblickande studie. Patienterna skattade själva sin hälsorelaterade livskvalitet och psykiska hälsa medan fysioterapeuter utvärderade fysisk funktion.

Studien visade att många patienter inte kunde genomföra uppföljningen tre månader efter utskrivning och endast 10 av 31 patienter kom till besöket. Orsakerna varierade, men genomförbarheten skulle sannolikt öka om besöket flyttades till sex månader efter utskrivning. Undersökningar och enkäter genomfördes och besvarades till 100%, talande för god genomförbarhet i detta avseende. Resultaten antyder god mental och emotionell hälsa trots stor variation i fysisk funktion där hälften av patienterna var självständiga i vardagliga aktiviteter. Detta överensstämmer med internationell forskning och indikerar bättre återhämtning än vad man tidigare trott är möjligt för denna patientgrupp.

Abstract

Aim

The aims of this pilot-study was to prove feasibility of a follow-up program for patients with persistent critical illness after treatment at a specialized clinic and to document patient related outcome measures and physical function after discharge.

Methods

Patients treated ≥14 days and discharged from the unit between December 2018 and August 2019 were included. Data from the three-month follow-up visit were analyzed for health related quality of life, depression, anxiety, activities of daily living, physical function and frailty using questionnaires and examinations by a physiotherapist.

Results and Conclusion

The selected questionnaires and evaluation instruments worked well with a 100% completion rate. However, many patients found the time too early after discharge and only ten of intended 31 patients came to the follow-up visit. The content of the follow-up program proved feasible and provided important information. The follow-up visit will be postponed until six months after discharge to reduce the number of patients lost to follow-up. The small number of patients followed up limits possible conclusions regarding patient related outcome measures, but we suggest that patients with persistent critical illness treated at a specialized unit may have good emotional outcome and mental health despite widely varying physical function.

Abbreviations

CFS – Clinical Frailty Scale

CPAx – The Chelsea Critical Care Physical Assessment

EQ-5D-5L – EuroQol 5 Dimensions 5 Line

FOIS – Functional Oral Intake Scale

GAD-7 – General Anxiety Disorder 7-item

HDU – High-dependency unit

HRQoL – Health related quality of life

ICU – Intensive care unit

Katz ADL – Katz Index of Independence in Activities of Daily Living

LTACH – Long term acute care hospital

MV – Mechanical ventilation

NIV – Non-invasive ventilation

p – Point

PHQ-9 – Patient Health Questionnaire-9

PMV – Prolonged mechanical ventilation

SIR – Swedish Intensive care Register

Introduction

The first intensive care unit (ICU) was established in Copenhagen in Denmark in 1958 and was defined as a ward where physicians and nurses observed and treated critically ill patients 24 hours a day[1]. The primary goal for the intensive care was to maintain and restore functions of vital organs to improve the chance of survival in critically ill patients defined as suffering from an acute, life-threatening condition requiring vital organ support to avoid imminent death[2].

About 5-10% of patients surviving acute critical illness transform into a condition of persistent or chronic critical illness[3]. When a patient is persistently critically ill, his or her illness is no longer related to the original reason for ICU admission but instead related to the patient's ongoing critical illness[4]. These patients require intensive care for prolonged periods of time, frequently weeks or even months. Main diagnoses vary widely and significant comorbidity is common. Patients who are chronically critically ill are often relatively stable but require extended time at the ICU, many of them with a prolonged need for mechanical ventilation (PMV)[5–7]. Iwashyna *et al* found in a study performed in Australia and New Zealand that patients with persistent critical illness accounted for 33% of ICU bed-days and 15% of hospital bed-days and only 47% were eventually discharged home[8].

With modern health care, we are able to save the lives of many critically ill, but the number of patients with persistent or chronic critical illness increase simultaneously. Critics have questioned how much resources should be put into this kind of care and if it is worthwhile to provide PMV when long-term outcome may be poor and the weaning process daunting to patients[9]. Some studies have found that many of these patients are in need of continuous care because of functional limitations and that most patients leaving the hospital have great deficiencies in physical function, cognitive status, or both[10]. Other conditions that might follow persistent or chronic critical illness are depression and post-traumatic stress disorder[11].

With a growing number of patients with persistent or chronic critical illness, units dedicated to specialized treatment, weaning from mechanical ventilation and rehabilitation, have been developed in many places around the world and better outcomes have been reported[12]. The staff-patient ratio may be lower than in a regular ICU, contributing to cost-effectiveness[13]. However, treatment differs in many ways from regular intensive care.

Jubran and coworkers suggested that the focus on weaning and individualized rehabilitation at a long term acute care hospital (LTACH) contributed to the improved results compared to patients treated in an ICU[9]. Health related quality of life (HRQoL) surveys answered by survivors from persistent or chronic critical illness usually report a higher level of social and emotional well-being than physical function or symptoms, implying that symptoms of depression and post-traumatic stress disorder may be possible to handle[14].

The only existing specialized unit for patients with persistent or chronic critical illness in Sweden is REMEO, located outside Stockholm. The unit was founded in 2013 and has developed into a national center of excellence for weaning and rehabilitation. Through a combination of intensive care and rehabilitation in multidisciplinary teams, patients are weaned from ventilatory support, decannulated and simultaneously rehabilitated.

Knowledge Gap

Quality of life and physical and mental function in patients surviving persistent or chronic critical illness have often been described as low[9]. However, very few studies describe outcome following treatment in a specialized unit. Quality of life may also be affected by the possibilities of support after hospital discharge, for example with activities of daily living, and how such support is financed. This is largely dependent on national and regional regulations, and thus outcome may differ between countries and regions. No Swedish data on patient related outcome measures or physical function after persistent critical illness have been presented previously. In 2018, a follow-up program was started at REMEO, to gain information on patients' HRQoL, experience of depression and anxiety, physical function and healthcare consumption after discharge from the unit. When designing a follow-up program several things need consideration. Patients with persistent or chronic critical illness have a recovery process lasting for a long time also after discharge from hospital care. They are usually easily fatigued and may require further rehabilitation as well as medical treatments though no longer in need of rehabilitation connected to intensive care. Thus, both timing and content of a follow-up program need to be carefully selected to provide the most comprehensible information on the patients' mental and physical well-being, while limiting extent to make it possible for patients to complete the program.

Aim

The primary aim of this pilot study was to investigate feasibility of the REMEO follow-up program in preparation for a larger prospective study. Are the questionnaires that are used relevant and do they

provide the information we are looking for? Will patients be able to follow the program? The secondary aim was to gain information on patient related outcome measures in patients with persistent critical illness three months after discharge from a specialized unit. How do they experience their heath related quality of life? What is their physical and mental function?

Materials and Methods

Study Design and Population

This was a single-center observational pilot study to prove feasibility of an intensive care rehabilitation follow-up program and to provide information on patient related outcome measures and physical function before starting a larger prospective study.

The REMEO clinic accepts patients with persistent or chronic critical illness referred from acute care hospitals in all parts of Sweden, for intensive care rehabilitation with simultaneous weaning from mechanical ventilation and decannulation. REMEO is a stand-alone unit located apart from other hospitals and provided at the time of the study eleven beds.

Starting in December 2018, all patients treated 14 days or more at REMEO were asked upon discharge if willing to participate in a follow-up program. The program was a part of the clinic's continuous quality improvement work. Patients were excluded if discharged to palliative care or if both patient and family were unable to communicate in Swedish or English. Patients willing to participate were scheduled for a visit at three and twelve months after discharge, to meet a physiotherapist for physical evaluation and to bring answers to questionnaires sent out beforehand. At six months after discharge questionnaires were sent out by mail, but no visit was scheduled. The data collected from questionnaires and follow-up visits were saved in a quality database. Data from the first follow-up visit, performed three months after discharge between March and October 2019, were analyzed in this study.

Measurements, Instruments and Questionnaires

Health Related Quality of Life

Health related quality of life refers to how an individual's health affects his or her ability to perform activities of everyday life and the perceived well-being in mental, physical and social domains. **RAND-36** is a validated, free and widely used instrument for measurement of HRQoL. RAND-36

reflects WHO's definition of health as physical, mental and social well-being and assesses eight domains, each providing a score ranging from 0 point (p) (worst, most limited) to 100 p (best, not limited)[15]. The domains are; physical functioning (ten questions), role limitations caused by physical health problems (four questions), pain (two questions), general health (five questions), energy/fatigue (four questions), social functioning (two questions), role limitations caused by emotional problems (three questions) and emotional well-being (five questions).

EQ-5D-5L is a standardized measure of health status[16]. It comprises five dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension has five levels, from "I have no problems" to "I am unable". Results from each dimension is presented as a mode value. EQ-5D-5L also comprise a visual analog scale (VAS) where the patient rates his or her health today where 100 p is the best health the patient can imagine and 0 p the worst.

Functional and Physical Status

Ability to perform activities of daily living was assessed using the **Katz Index of Independence in Activities of Daily Living** (Katz ADL). Katz ADL comprise six activities to assess the patient's functional status and his or her ability to perform activities of daily living independently[17]. The functions are; bathing, dressing, toileting, transferring, continence, and feeding where the patient scores "yes" or "no" for independence for each function. The patient gets one point for each activity performed independently. Six points indicates full independence in activities of daily living and two or fewer points indicate severe functional impairment.

The patient's physical status was assessed using **The Chelsea Critical Care Physical Assessment tool** (CPAx). CPAx includes ten components; respiratory function, cough, moving within the bed (e.g. rolling), supine to sitting on the edge of the bed, dynamic sitting, standing balance, sit to stand, transferring from bed to chair, stepping, and grip strength[18]. Each component has six levels. The patient can get 0-5 p for each component, where 0 p is completely dependent, and 5 p is complete independence with a total maximum score of 50. For grip strength a scale with expected strength for gender and age was used, where 0 p is "not able to assess" and 5 p is ≥80% of expected strength. A higher score indicates greater physical ability.

The patients' ability to swallow was assessed using the **Functional Oral Intake Scale** (FOIS). The scale has seven levels where 1-3 p reflects tube feeding, 4-5 p reflects oral feeding requiring food consistency changes, and 6-7 reflects oral feeding with no changes in food consistency[19].

Mental Health

Depression was assessed using the **Patient Health Questionnaire-9** (PHQ-9). It comprises nine items, each of which is scored 0-3 p where 0 p is "not at all" and 3 p is "nearly every day". This provides a 0 to 27 p severity score where scores of 5, 10, 15 and 20 p represent cutoffs for mild, moderate, moderately severe and severe depression[20].

The General Anxiety Disorder 7 (GAD-7) questionnaire was used to assess general anxiety. It comprises seven questions where the patient scores 0 p "not at all" to 3 p "nearly every day" for each question with a maximum of 21 p in total. The scale ranges from mild, to moderate and severe general anxiety disorder with cutoffs at 5, 10 and 15 p[21].

Frailty

The Clinical Frailty Scale (CFS) was used to assess the patients' frailty. The CFS is a widely used tool to evaluate patients' vulnerability in connection to anesthesia, surgery and intensive care treatment[22]. Evaluations of frailty provide a comprehensive summary of a patient's overall fitness and may help predict in-patient mortality. The scale has nine levels where 1 p is "very fit" and 9 p is "terminally ill"[23].

Health Care Consumption and Infectious Complications

To evaluate the need for healthcare after discharge from the unit, a four questions form was used. The questions were "have you been in touch with or visited a physician or nurse?", "have you visited the emergency department?", "have you been hospitalized?", "have you been treated with antibiotics for respiratory tract infection?"

Data Collection

The patients were sent the questionnaires and the healthcare contact form by mail approximately three weeks before their scheduled follow-up visit. During the visit, the physiotherapist went through the answers with the patient. The physiotherapist performed the CPAx and assessed the FOIS and Katz ADL scores. All data collected were stored in a quality database from where the information to this study was extracted.

From the quality database information was collected on patients' age, gender, referring unit, number of days in hospital and in ICU before REMEO, tracheostomy when admitted to REMEO (deemed

permanent or not permanent before admittance), tracheostomy when discharged from REMEO, mechanical ventilation on admittance and discharge, use of noninvasive ventilation (NIV), length of stay at the unit, need of support after discharge and discharge destination.

Statistical Methods

For descriptive statistics medians and interquartile range was used to limit the effect of outliers for all data except EQ-5D-5L, PHQ-9 and GAD-7 where mode was used.

Ethical Considerations

The present study reported data from the continuous quality improvement work at REMEO and ethical permission was therefore not needed. All data were obtained from the quality database and there was no need for access to the patients' medical records. All data were analyzed and reported anonymously. However, when results on a very small number of patients are reported, there may still be a risk of individual patients being recognized. Therefore, information relating to only one patient have been limited in the report. An ethical permit (Dnr 2019-05294) has been obtained for future prospective studies including patient characteristics before and during care at the unit, detailed descriptions of the care provided, and outcome documented in the follow-up program.

Results

Inclusion of Patients and Their Characteristics

A total number of 36 patients were treated at REMEO for 14 days or more and discharged between December 2018 and July 2019 (figure 1). Two patients were excluded because of discharge to palliative care (n=2) and three for inability to communicate in Swedish or English (n=3). The remaining patients constituted the potential follow-up group (n=31). Of these, ten patients were followed up at the planned three-months visit. Reasons why the remaining 21 patients were not followed up are listed in figure 1. Characteristics of patients followed up at three months and patients lost to follow-up are listed in table 1. All patients had spent more than ten days in intensive care treatment before admission to REMEO and were considered persistently critically ill.

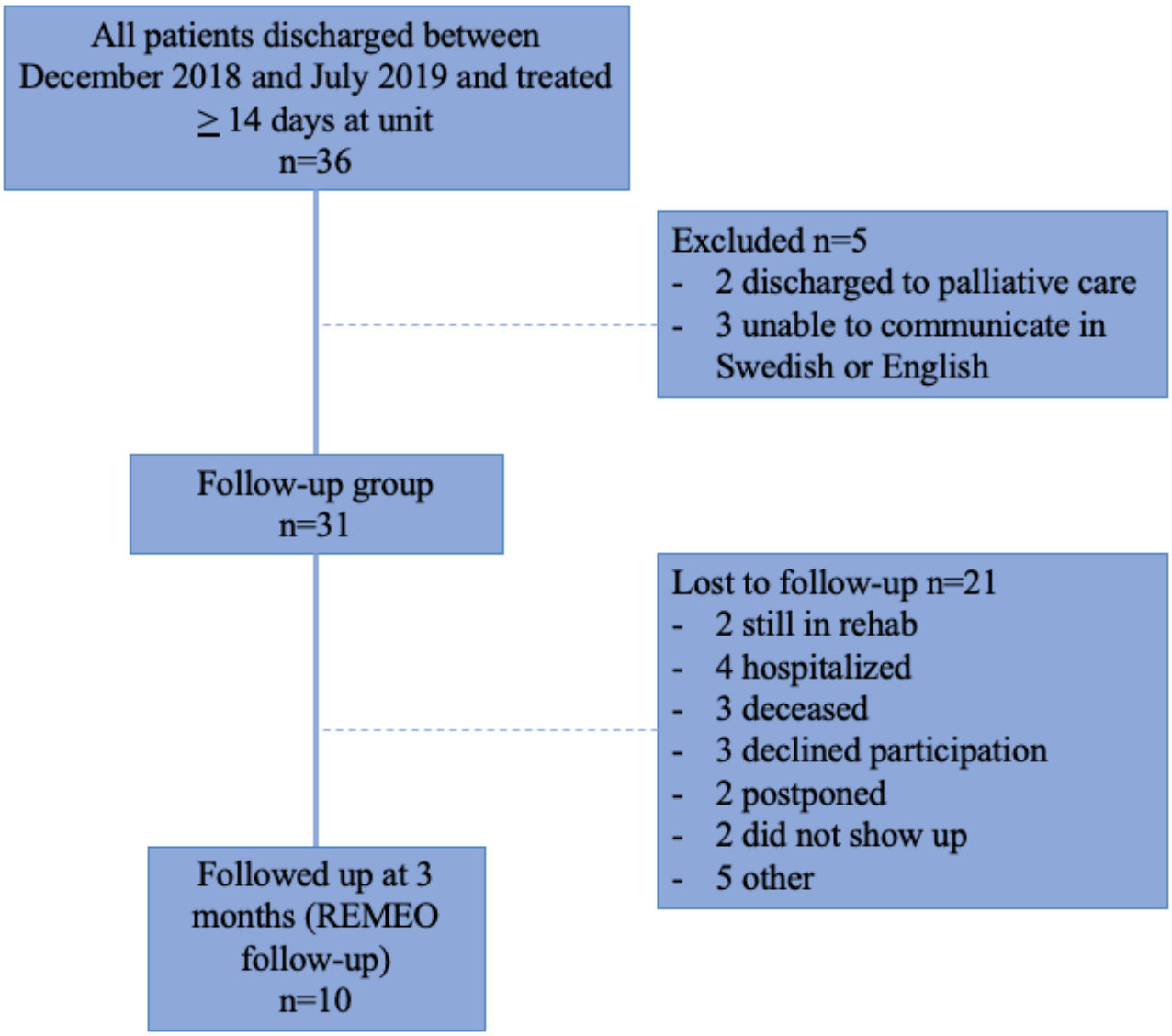


Figure 1 – Flowchart of patient inclusion. Ten patients of the intended 31 were followed up at three months after discharge. Twentyone patients were lost to follow-up for reasons listed.

Table 1- Characteristics of patients followed up three months after discharge and patients lost to follow-up. When not indicated otherwise, numbers are numbers of patients.

	Patients followed up at three months (n=10)	Interquartile range	Patients lost to follow-up (n= 21)	Interquartile range
Age (median, years)	67	64-73	60	48-71
Gender				
- Men	9 (90%)		14 (67%)	
- Women	1 (10%)		7 (33%)	
Referring unit				
- ICU	6 (60%)		11 (52%)	
- HDU	3 (30%)		4 (19%)	
- Ward	1 (10%)		6 (29%)	
Days in hospital before REMEO (median)	40	30-55	50	36-61
Days in ICU before REMEO (median)	26	17-38	34	23-45
Tracheostomy when admitted to REMEO	10 (100%)		15 (71%)	
- deemed permanent	0 (0%)		1 (5%)	
Mechanical ventilation when admitted to REMEO	5 (50%)		7 (33%)	
decannulated before discharge (of not deemed permanent)	6 (60%)		10 (71%)	
Tracheostomy when discharged	4 (40%)		5 (33%)	
- without ventilator	2		3	
- with ventilator	2		2	
Days from admittance to REMEO to decannulation (median)	41	22-43	22	15-37
Use of NIV at some point while at REMEO	5 (50%)		6 (29%)	
NIV at discharge	2 (20%)		5 (24%)	
Days at REMEO (median)	70	63-103	50	30-66
Discharged to				
- Previous home	6 (60%)		4 (19%)	
- ICU	0 (0%)		1 (5%)	
- Ward (including rehab)	4 (40%)		16 (76%)	
Level of support for patients discharged to previous home				
- no assistance	3 (50%)		0 (0%)	
- limited help	1 (17%)		4 (100%)	
- personal assistance	2 (33%)		0 (0%)	

The three months follow-up meeting was performed within 80-100 days after discharge for seven patients. One follow-up meeting was performed 69 days after discharge, one 117 days after discharge and one was performed 122 days after discharge.

Data Collected at Follow-up Visits

All patients completed all questionnaires and all tests were carried out according to plan.

Health Related Quality of Life

Median HRQoL scores measured by RAND-36 are displayed in figure 2. Higher scores indicate better perceived function in the domain. The *Physical functioning* median score was 10 p (IQR 5-59). However, six patients scored ≥70 p. The *Role limitations caused by physical health problems* median score was 0 p (IQR 0-81), though three patients scored the maximal 100 p. The median score for *Pain* was 56 p (IQR 32-77). The *General health perception* median score was 43 p (IQR 33-73). The *Energy/fatigue* median score was 63 p (IQR 46-86). The *Social functioning* median score was 37 p (IQR 25-100), while four patients scored the maximal 100 p. The *Role limitations caused by emotional problems* median score was 83 p (IQR 8-100) and five patients scored 100 p. *Emotional well-being* median score was 80 p (IQR 54-97).

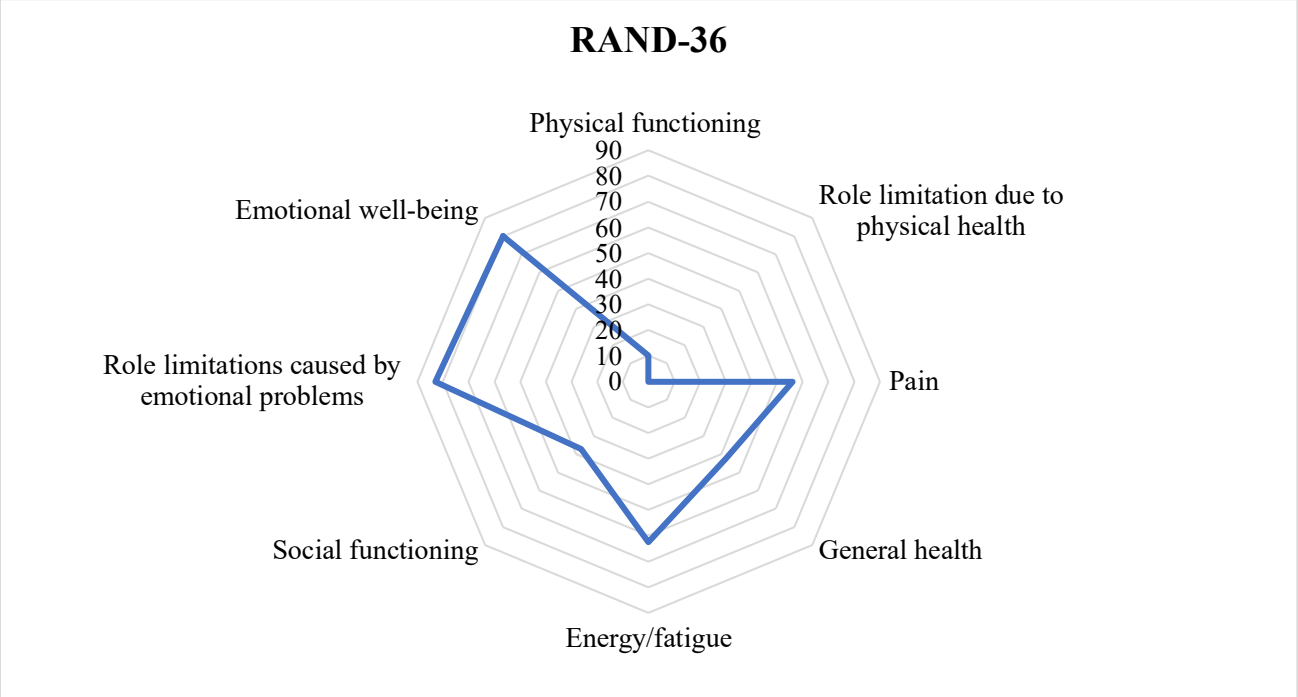
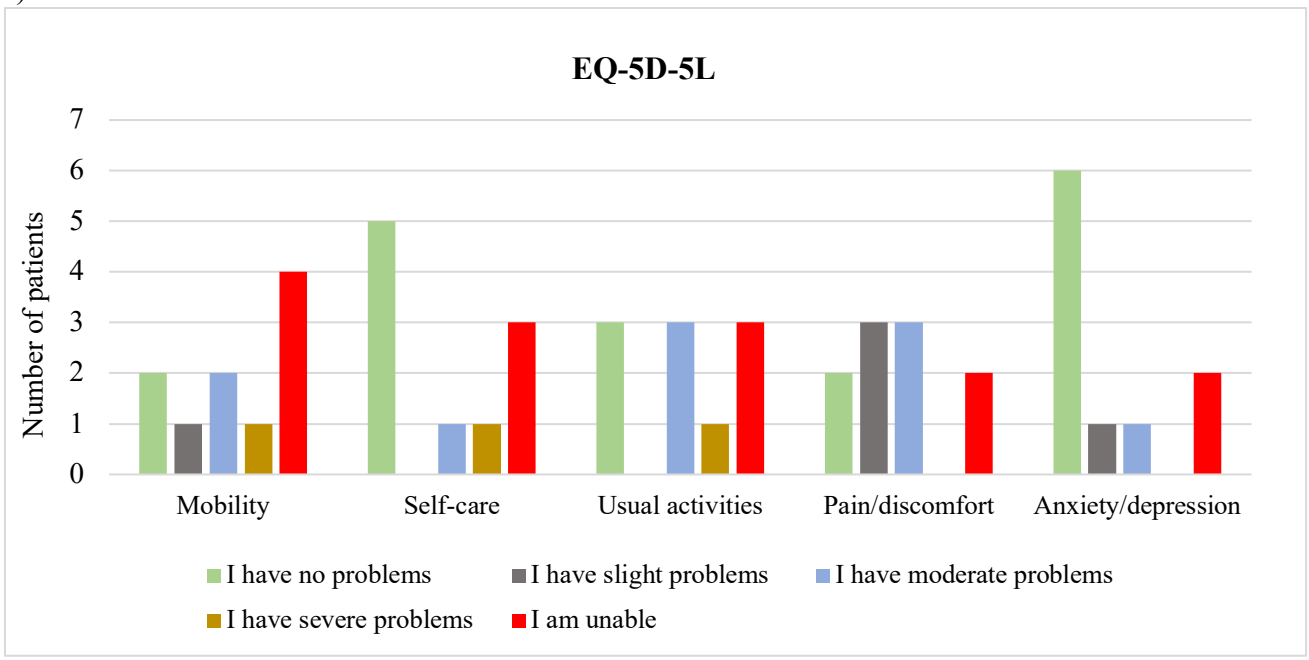


Figure 2 - Median scores of the domains in RAND-36 displaying the patients' perceived health related quality of life. Higher scores indicate better perceived function in the domain.

Health related quality of life was also evaluated using EQ-5D-5L (figure 3). The mode for *Mobility* was "I am unable" while the mode for *Self-care* was "I have no problems". For *Usual activities,* the answers "I have no problems", "I have moderate problems" and "I am unable" were equally common illustrating the wide variability in physical function. For *Pain/discomfort* the answers "I have slight problems" and "I have moderate problems" were equally common. The mode for *Anxiety/depression* was "I have no problems". EQ-5D-5L also comprise a Visual Analog Scale (translated into 0-100 p) with the question "your health today" (figure 3). The median score was 50 p (IQR 31-74).

a)



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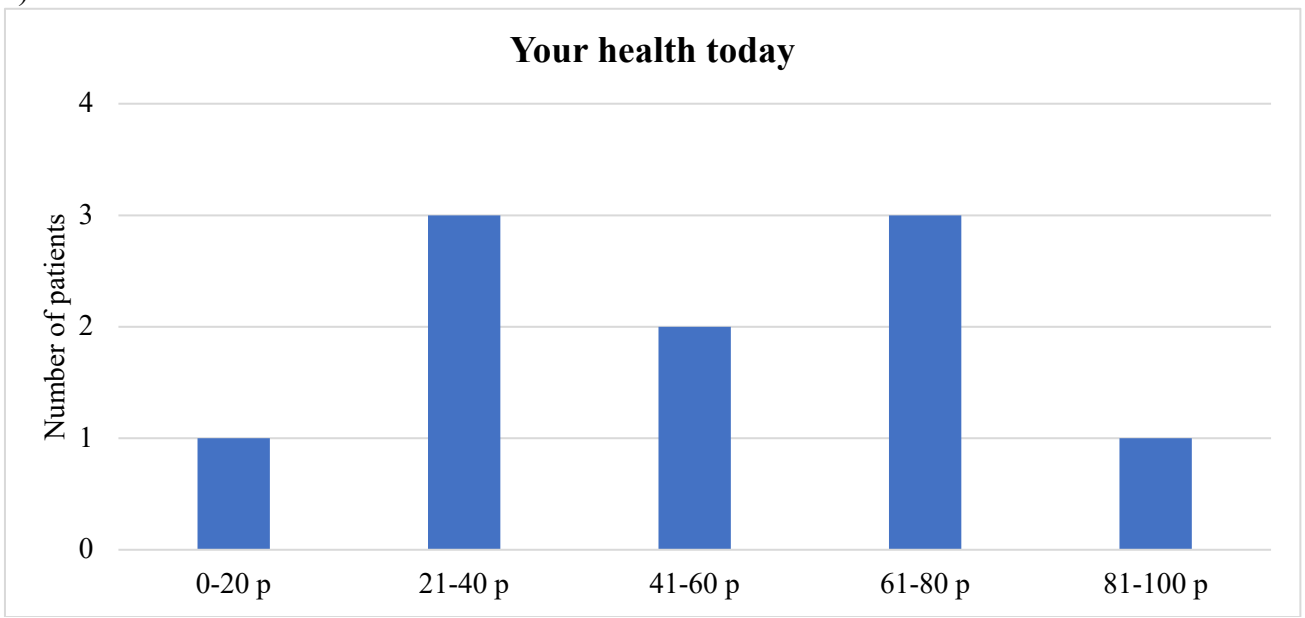
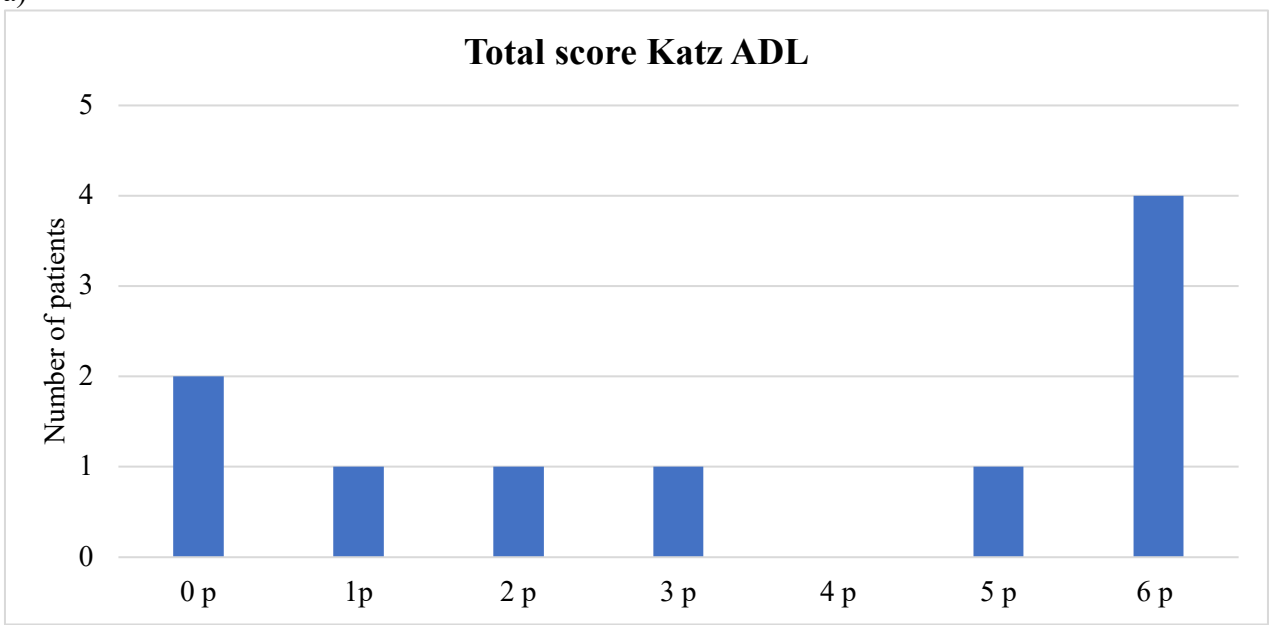


Figure 3 – Patients' perceived health related quality of life as measured by EQ-5D-5L. a) The number of patients giving each answer in the respective domains in the EQ-5D-5L. b) Answers to the question "your health today". 0 p is "the worst health you can imagine" and 100 p is "the best health you can imagine".

Functional and Physical Status

Activities of daily living: The result from Katz ADL is shown in figure 4. The total median score was four out of six. Four patients had a severely impaired function with scores of two or less. Four patients were independent in all their activities of daily living with Katz ADL scores of six. Half of the patients were independent in *bathing, dressing* and *toileting*. Six patients were independent in *transferring* and seven in *continence* and *feeding.*

a)



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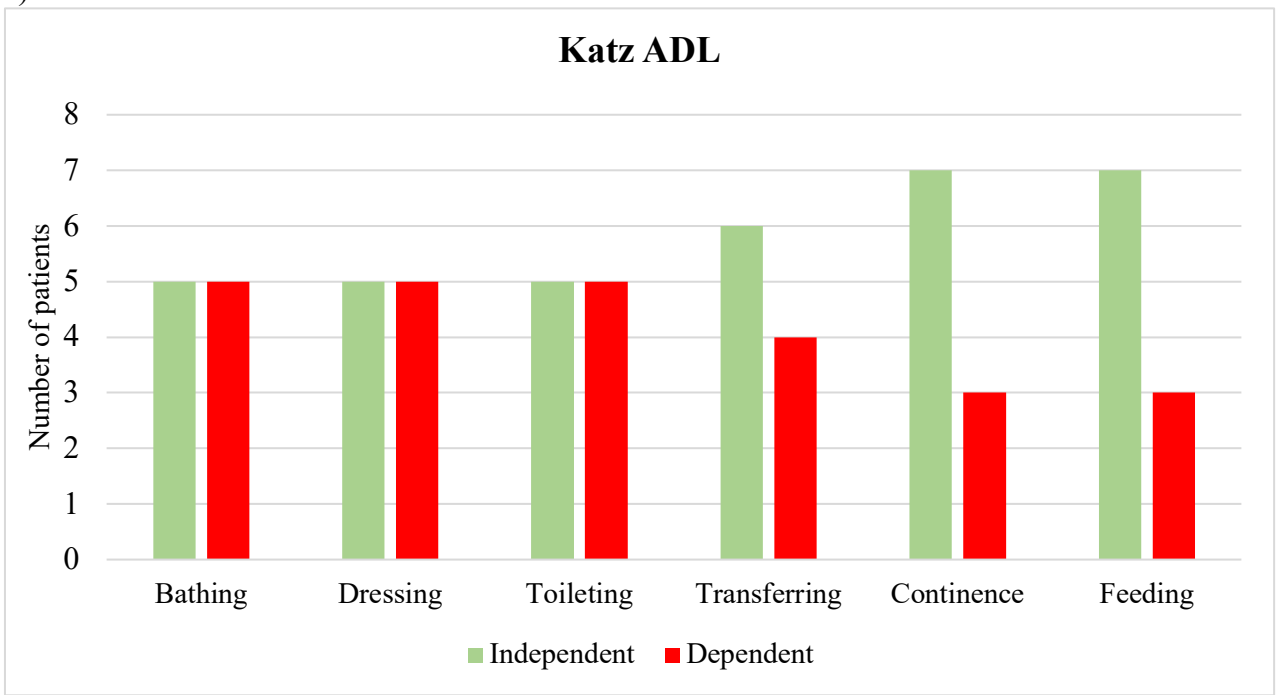
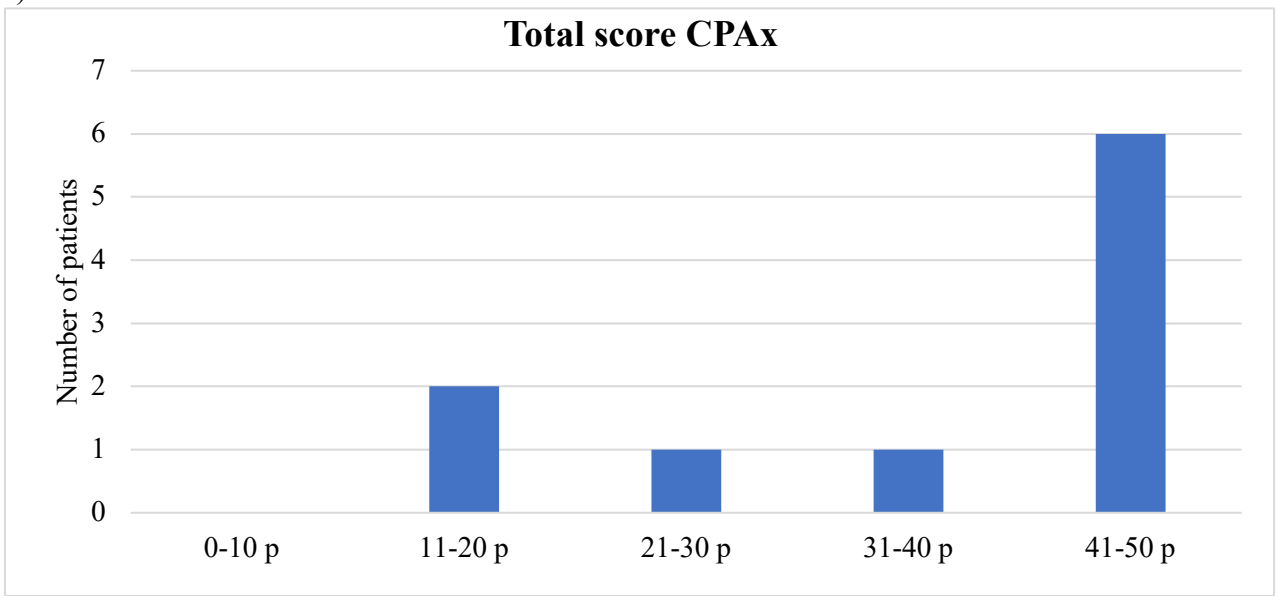


Figure 4 –Katz Activities of daily living (Katz ADL) was evaluated by the physiotherapist at the follow-up visit. a) The number of patients with each Katz ADL score. 0 p is completely dependent, and 6 p is completely independent. b) The number of patients independent and dependent in each domain.

Physical status evaluated using CPAx revealed a total median score of 43.0 p of 50 (IQR 26.0-46.5) (figure 5). Six patients scored 41-50 p which indicate a high function. The *Respiratory function* and the *Cough* median scores were 5.0 p (IQR 5.0-5.0, and 4.0-5.0 respectively). *Moving within the bed* median score was 4.0 p and *Supine to sitting on the edge of the bed* median score was 4.5 (IQR 2.5-5.0 both components). *Dynamic sitting* median score was 5.0 p (IQR 4.5-5.0). *Standing balance median* score was 4.0 p and *Sit to stand* median score was 4.5 p (IQR 2.5-5.0, and 2.0-5.0 respectively). *Transferring from bed to chair* and *Stepping* median scores were 5.0 p (IQR 2.0-5.0 both components). *Grip strength* median score was 2 p (IQR 1.0-3.0).

a)



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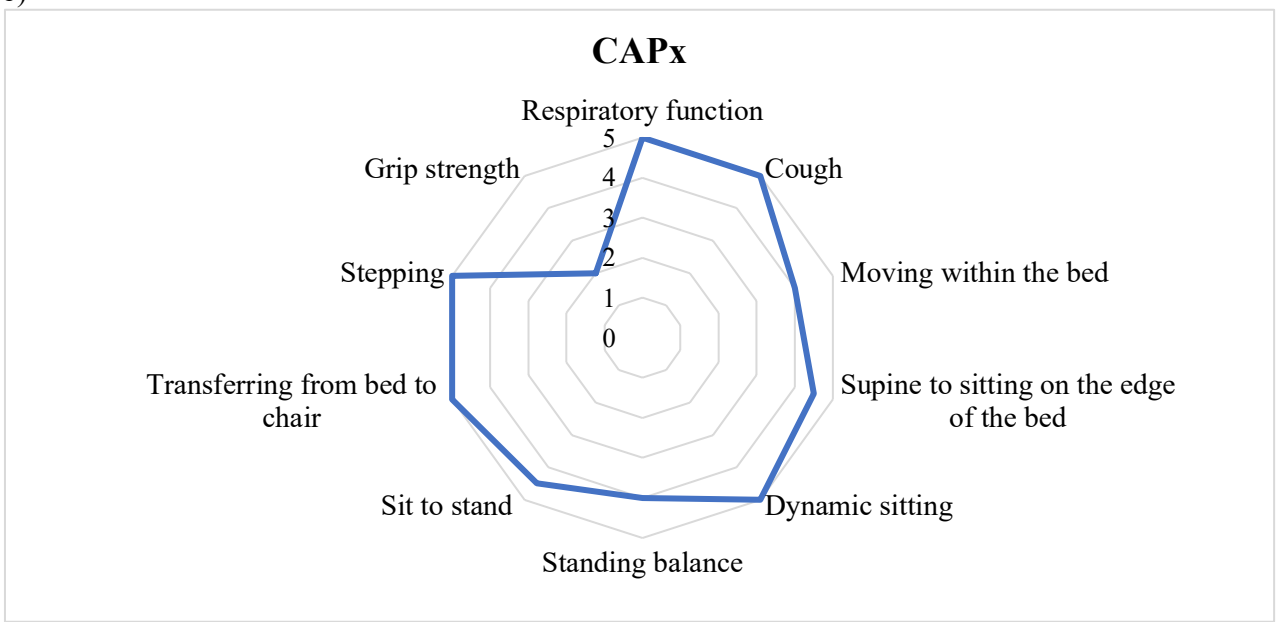

Figure 5 – Physical function as evaluated by the physiotherapist using The Chelsea Critical Care Physical Assessment (CPAx). a) Patients were divided into groups based on their physical function according to CPAx. Maximum score is 50 p. A higher score indicates higher level of ability. b) The scale ranges from 0 to 5 p for each component, where 0 p is completely dependent, and 5 p is completely independent.

Functional oral intake was evaluated using FOIS and the median score was 6 p (figure 6). Four patients had a severely impaired oral intake with FOIS scores of two or less. Six patients managed full oral intake with no special preparations and had FOIS scores of six or more.

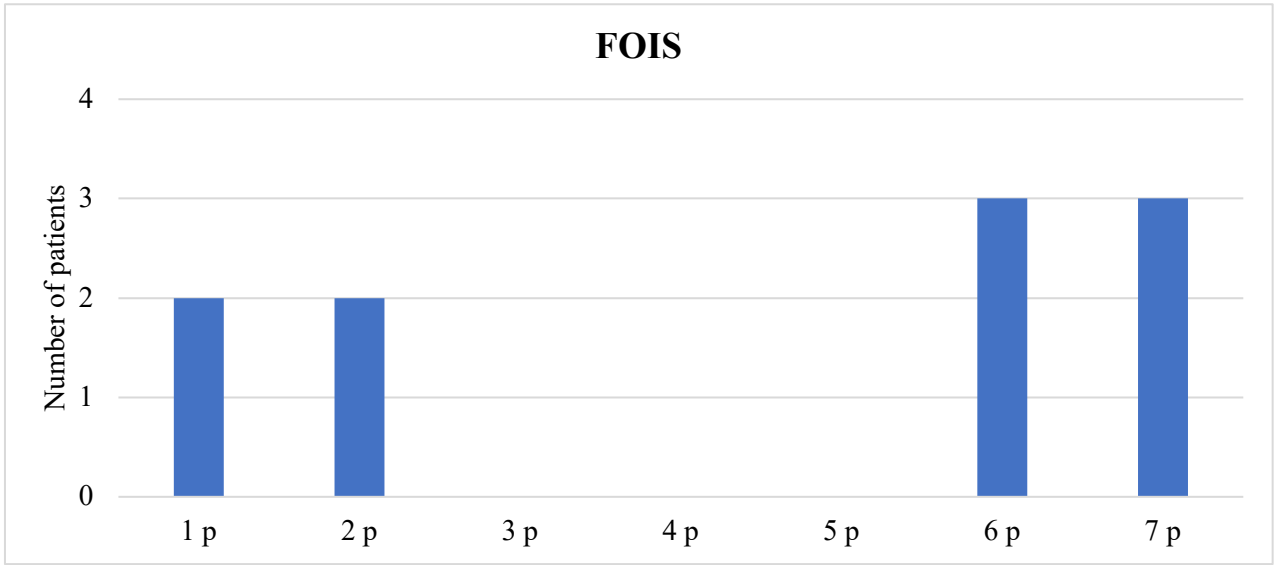

Figure 6 – Ability of oral food intake according to the Functional Oral Intake Scale (FOIS). 1 p is "no oral intake" and 7 p is "total oral intake with no restrictions".

Mental Health

The mode for all domains on PHQ-9 was "not at all" (figure 7) and the median score was 0 p. Six patients scored 0-4 p (no depression) and two patients 5-9 p (mild depression). One patient scored 15-19 p (moderately severe depression) and one patient 20-27 p (severe depression).

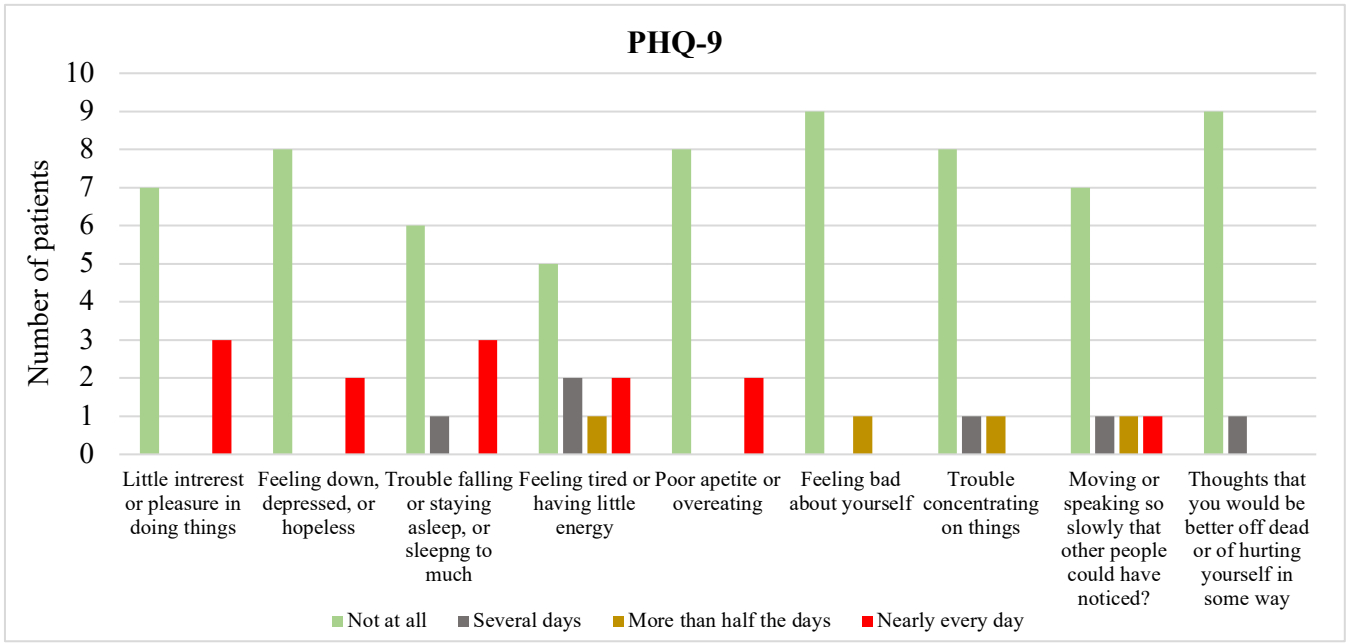

Figure 7 – Patients' perceived mental health was evaluated by the 9 item Patient Health Questionnaire (PHQ-9). Patients answered the question "over the last 2 weeks, how often have you been bothered by the following problems…?" and the number of patients giving each answer is displayed for each domain.

Most patients did not suffer from general anxiety and the mode for all domains of GAD-7 was "not at all" (figure 8). The median score was 0,5 p. Eight patients scored 0-4 p (no GAD) and one patient 5-9 p (mild GAD). One patient scored 15-21 p (severe GAD).

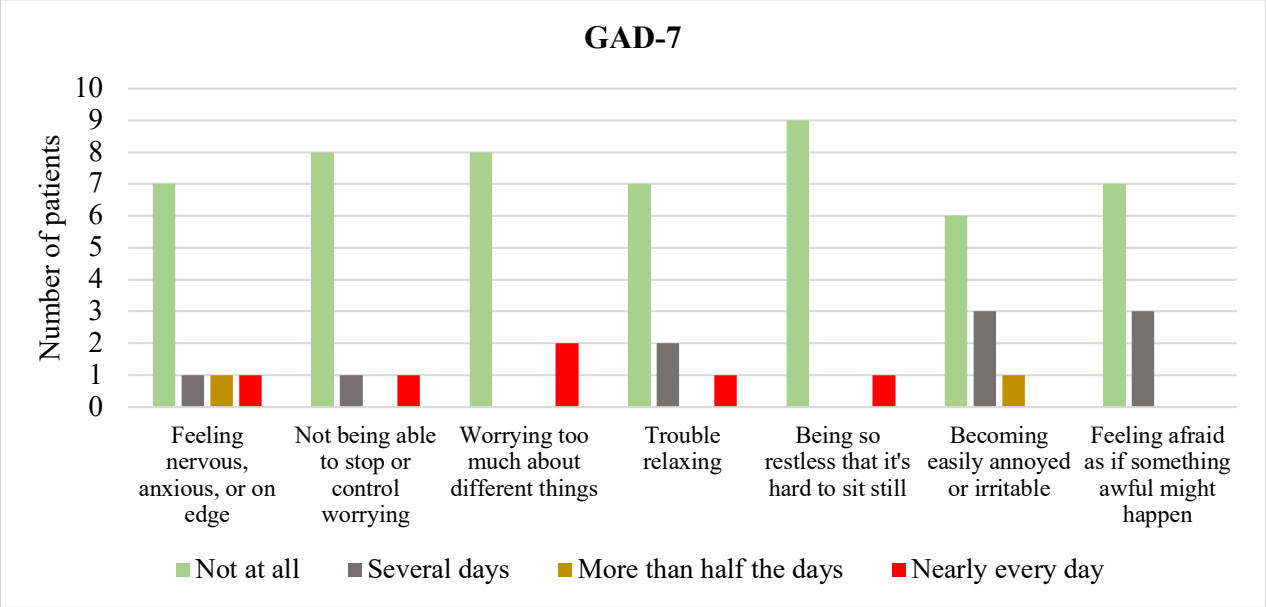

Figure 8 – General anxiety as perceived by the patients was measured by the 7 item General Anxiety and Depression scale (GAD-7). Patients answered the question "Over the last 2 weeks, how often have you been bothered by the following problems…?" and the number of patients giving each answer is displayed for each domain.

Frailty

The median score on the CFS was 6. Two patients scored 2 p (well). Two patients scored 4 p (vulnerable) and another two patients scored 6 p (moderately frail). Four patients scored 7 p (severely frail).

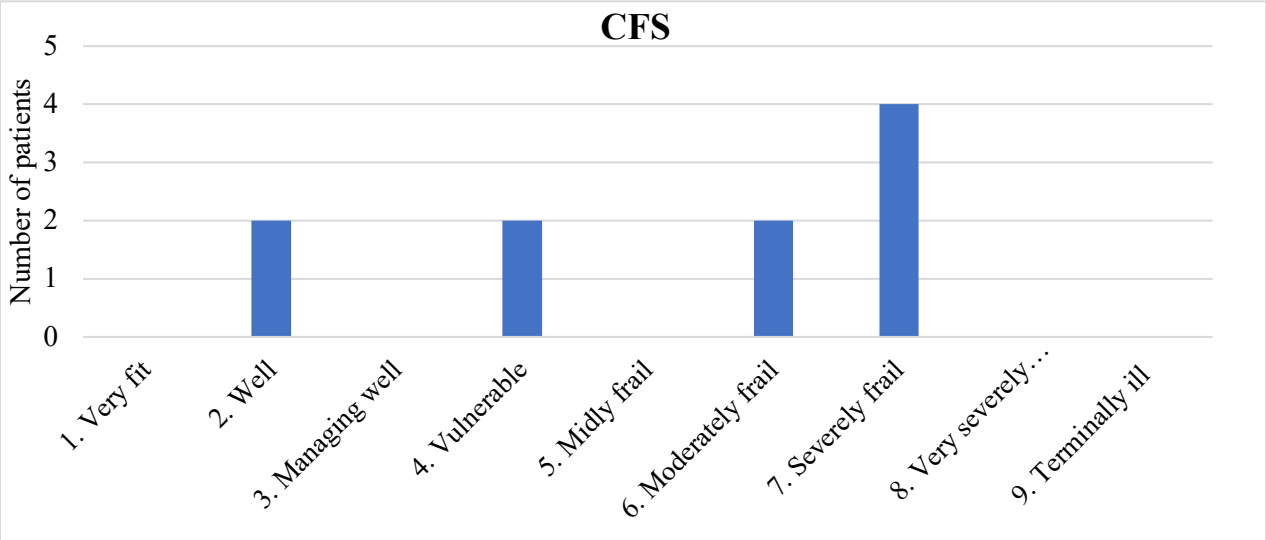

Figure 9 –Frailty was evaluated by the physiotherapist using the Clinical Frailty Scale (CFS). Most patients were deemed moderately or severely frail at the three months follow up visit.

Health Care Consumption and Infectious Complications

Seven patients had been in contact with their general practitioner, family doctor or nurse, or home health care team. Three had visited the emergency department, five had been hospitalized and three had been treated with antibiotics for respiratory tract infection. One patient had not been in contact with the health care since discharge from REMEO.

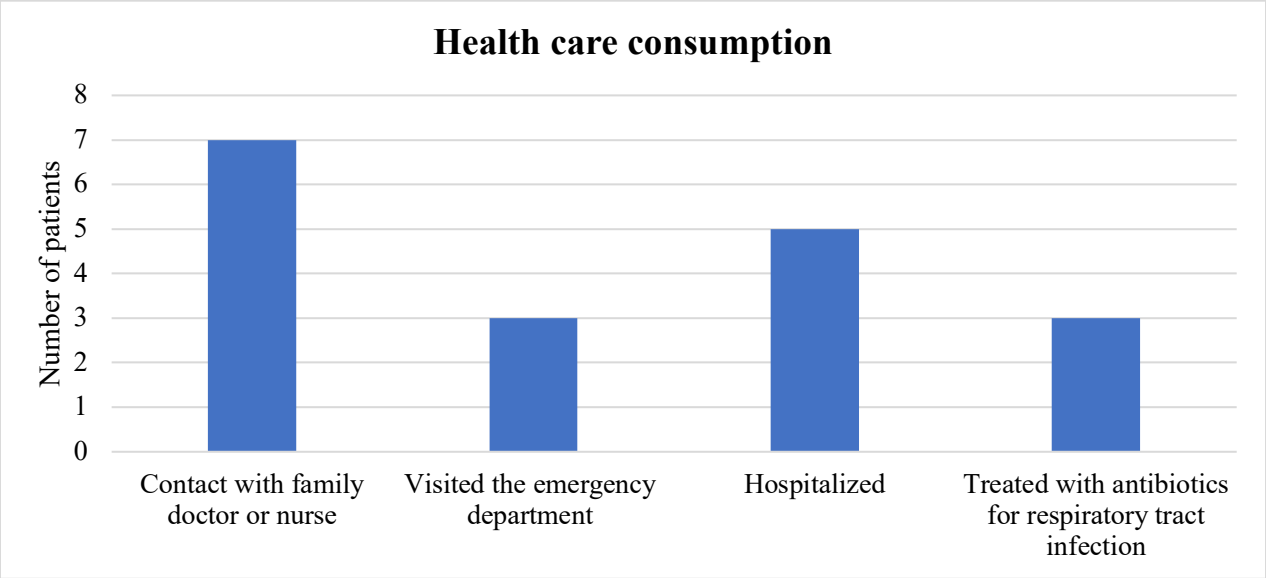

Figure 10 – Patients' contacts with health care after discharge from REMEO.

Discussion

In this pilot study we investigated feasibility of a follow-up program and patient related outcome measures in patients with persistent critical illness treated at a specialized unit in Sweden. We found that the selected questionnaires and evaluation instruments worked well for this patient group, but that there was a large number of patients lost to follow-up, likely because of the timing of the first visit. In patients who came to follow-up, patient related outcome measures showed over all good emotional well-being, despite physical disabilities remaining in many patients.

Content of Follow-up Program

Selecting a battery of tests and questionnaires to evaluate patients after treatment of severe illness is delicate. On the one hand you would like as much information as possible, to adequately describe the patients' characteristics and widely varying functional capacity both physically and mentally. On the other hand, these patients easily fatigue, why the extent of tests and questionnaires need to be limited. Furthermore, many validated instruments are designed for patients with a shorter timeframe of their illness, or with a generally higher level of physical function. The instruments used in this study were chosen after careful consideration and proved both feasible and providing important information. This could be seen by its completion rate which was very high, 100 %. One reason for this may have been that all patients met a physiotherapist during the follow-up visit, offering an opportunity to provide explanations to questions perceived to be unclear.

Timing of Follow-up Visit

The large number of patients lost to follow-up raises some concern regarding feasibility. When exploring the reasons why patients did not attend the three months follow-up visit, it was evident that the timing for many patients was too early. Six patients were still in full time rehabilitation or otherwise hospitalized and another two for other reasons asked to reschedule the visit to six months after discharge. The timing of the follow-up visit has been changed to six months after discharge going forward. Only three patients declined follow-up indicating that patients are willing to participate in the program.

Disease Burden and Mortality

Another concern was that the patients lost to follow-up would have been more severely ill than the patients who were followed up, and that this was the reason for them to be lost to follow-up. However, on the contrary, the study's data shows a tendency to the opposite, though no statistical comparisons

between the groups were made due to the limited number of patients in both groups. Most of the patients included were admitted from an ICU, 60% of the patients followed up and 52% of the patients lost to follow-up. The median number of days in ICU was 26 for followed up patients and 34 for patients lost to follow-up while the median number of days spent in hospital before admittance to REMEO for patients followed up was 40 days and for patients lost to follow-up was 50 days. The median number of days hospitalized at REMEO was 70 days for the follow-up group and 50 days for the lost to follow-up group. The median number of total days in hospital was 130 days for the followed-up group and 100 days for the patients lost to follow-up. One hundred percent of patients that were followed up had a tracheostomy when admitted, while 71% of patients lost to follow-up had a tracheostomy. A majority of patients were decannulated before discharge, 60% in the follow-up group and 71% in the lost to follow-up group. The median number of days from admittance to decannulation was 41 days for the follow-up group and 22 days for the lost to follow-up group. Thus, patients in the lost to follow-up group did not seem more severely ill and it is unlikely that disease severity prevented them from participating in the follow-up program. Both patients followed up in this pilot study and those lost to follow-up, tended to have longer length of stay and lower weaning success rate from mechanical ventilation and decannulation rates than previously documented in patients treated at REMEO[24]. In patients treated between January 2015 and December 2018, median length of stay was 47 days and weaning from mechanical ventilation and decannulation was successful in 89% and 90% of patients respectively. This difference may be due random variation because of the low number of patients included in the present study, but a change in outcome over time cannot be excluded as patients included in the present study were discharged between December 2018 and July 2019.

Three patients died before the scheduled follow-up. The one-year mortality for patients discharged from REMEO from January 2015 to December 2018 was 20%, with the majority dead within three months after discharge[24], so this is expected. The overall mortality at REMEO is low, with only 3% in-patient mortality, while most other specialized units report higher rates with 10-17% in-patient mortality and 33-50% one-year mortality[9,25–27].

Data Collected at Follow-up Visits

Health Related Quality of Life

Two different instruments for evaluation of perceived HRQoL was used in this study. RAND-36 is a validated, free and widely used instrument for measurement of HRQoL[15]. It is included in many

Swedish Intensive care follow-up programs and very similar to the Short Form health survey (SF-36). EQ-5D-5L is less complex, and also widely used internationally. Both instruments proved suitable and the results were similar with better scores for emotional than for physical components in line with previous studies[14].

According to RAND-36, the patients in this study had a general health median score of 43 p. Data from the Swedish Intensive care Register (SIR) report 52 p for patients followed up after intensive care in Swedish ICUs[28]. Our study group and patients reported to SIR are difficult to compare for several reasons. All our patients had very long intensive care stays, setting them apart from the general patient population reported to SIR with a low proportion of persistent or chronic critical illness. Moreover, we made our evaluation approximately three months after discharge, while the SIR collects data from two months after discharge. However, our results suggest that despite the severe illness experienced by our patients and their long intensive care treatment, their HRQoL was similar to the general Swedish ICU patient population's. Patients in this study perceived their emotional HRQoL as quite good with a median score of 83 p for *role limitation caused by emotional problems* and a median score of 80 p for *emotional well-being*. The Swedish Intensive care Register report mean scores of 51 p and 70 p respectively, two months after discharge from an ICU[28]. The relatively high scores on emotional and mental health were perceived by our patients despite their, in many cases, severe physical limitations, which were generally more pronounced than in the SIR-reported ICU population. Health related quality of life as measured by the EQ-5D-5L showed similar results as RAND-36, and 60% of the patients suffered no problems with anxiety and depression while 40% had severe problems with mobility. Half of the patients managed, despite limited mobility, independent self-care. This was likely because mobility includes the ability to walk about, while self-care focusses on the patient's ability to wash and dress themselves, which can be performed sitting.

Functional and Physical Status

Physical function is required for many activities, including the activities of daily living. The Katz ADL proved easy to use for a trained physiotherapist and provided useful information on patients' ability to perform the tasks of daily living. Half of the patients were independent in all or in all except one activity of daily living (Katz ADL summary score ≥ 5), while 50% had a severely impaired or limited function (Katz ADL summary score ≤ 3). The CPAx instrument evaluates other components of physical status and also includes important information on breathing and evacuation of secretions, which are both very important for respiratory vulnerable or tracheostomized patients. Three months after discharge from the unit, the CPAx score was 41-50 p for 60% of the patients which indicates a

high physical function, while four patients had lower scores. The Katz ADL score and CPAx score together indicate that there is a wide range in functional and physical status three months after discharge. The relatively high functional and physical status for some of the patients are in line with recent studies by Jubran *et al*. They found that 78% were independent in terms of activities of daily living after six months, and that functional recovery in patients treated in an LTACH were better than in patients requiring PMV managed at an ICU. Jubran *et al* also found that the Katz ADL summary score increased with better handgrip strength[9]. Further longitudinal follow-up will be needed to show if increased handgrip strength gives higher Katz ADL summary scores in our patient cohort as well.

Patients who were decannulated at discharge had a Katz ADL median score of 5.5 p (IQR 3.5-6.0) and a CPAx median score of 45 p (IQR 43-48). Those who were discharged with a tracheostomy had generally lower scores with a Katz ADL median score of 1.5 p (IQR 1.0-3.0) and a CPAx median score of 30 p (IQR 21-39). Patients not possible to decannulate, despite the very active multidisciplinary team rehabilitation approach, are likely to experience an incomplete recovery reflected also in their lower physical and functional scores. The number of patients examined in this study was too small to evaluate the possibility to decannulate in relation to the FOIS. The patients who had a low Katz ADL-score (≤ 2) were all discharged to a rehabilitation ward or to previous home with personal assistance. The patients who were discharged to their previous home with personal assistance also needed mechanical ventilation.

Mental Health

Jubran and coworkers found that patient mental well-being increased within six months after discharge to 92% of scores before illness and that 85% of patients would be willing to undergo PMV again if deemed necessary[9]. We found that patients did not perceive themselves limited by emotional difficulties as evaluated by RAND-36 and had a low rate of anxiety and depression according to EQ-5D-5L. In line with this, PHQ-9 and GAD-7 also showed low scores for depression and anxiety. A vast majority of patients, 80% did not suffer from generalized anxiety, scoring 0-4 p in GAD-7. The mode for all domains in PHQ-9 and GAD-7 were “not at all” and 80% scored 0-9 p in PHQ-9, which is no or mild depression. This is in contrast to earlier studies which indicate that persistently or chronically critically ill patients have considerable problems with depression[11]. However, one patient in the present study scored 20-27 p in PHQ-9 which is classified as severe depression and 15-21 p in GAD-7 which means severe GAD. This was noted by the physiotherapist during the follow-up meeting and the patient was recommended to see the family physician.

Frailty, Health Care Consumption and Infectious Complications

According to the CFS, 60% of the patients were moderately or severely frail, implying need of help with all outside activities, with housekeeping, bathing and walking in stairs, or for the severely frail, complete dependency for personal care. However, again displaying the wide variability, 40% were only vulnerable according to the CFS or even considered well. This is in accordance with the results from Katz ADL and the CPAx scores which also revealed a wide variability among the patients. Frail people are more prone to disease and have a higher need of healthcare than the non-frail. A majority of the followed-up patients, 70%, had been in contact with health care within three months after discharge, 30% had visited the emergency department, and 50% had been hospitalized. However, only 30% had been treated with antibiotics for respiratory tract infection, which is a common complication for patients who have or have had a tracheostomy. This study did not explore the reasons for need of healthcare, and thus we cannot elaborate further on this.

Strengths and Limitations of the Study

This study is the first of its kind in Sweden and provides important information on a patient group that is small in numbers, but consume a vast amount of resources. The study has several strengths, rendering the results useful for future study design, but also weaknesses limiting potential conclusions.

One strength was the completion rate of the questionnaires. One hundred percent of the questionnaires were filled out and all questions in each questionnaire were answered. This was likely contributed to by all patients meeting a physiotherapist during the follow-up visit and the fact that they went through the questionnaires together. Also, there were only two physiotherapists involved and the procedure was thus easy to standardize.

The major limitation of the study was the small number of patients included, which prevented statistical comparisons between groups. The large number of patients lost to follow-up can be perceived as a weakness as the number of patients followed up turned out to be too small for conclusive analysis. However, the reasons why patients were lost to follow-up also provided important information on design of future studies. Thus, though the possibilities of conclusions regarding the patient related outcome measures were restricted, the study still provided important information on feasibility.

Clinical Implications and Future Studies

As the set of questionnaires and test instruments proved both feasible and informative, this set will be used in the future. The timing of the first follow-up visit to the unit will be changed to six months after discharge, rendering visits to be scheduled at six and twelve months, while questionnaires will be sent out and returned by mail three months after discharge. To gain conclusive results about patient related outcome measures, this study needs to be repeated with a larger patient sample. An ethical permit has been obtained for future prospective studies, including patient characteristics before and during care at the unit, treatment performed, and outcome data collected in the complete twelve months follow-up program to contribute to a longitudinal view.

Conclusions

The primary aim of this pilot study was to investigate feasibility of the REMEO follow-up program in preparation for a larger prospective study. The secondary aim was to gain information on patient related outcome measures in patients with persistent critical illness three months after discharge from a specialized unit. The questionnaires, test instruments and set up for the follow-up program proved feasible. The timing for the first follow-up visit will be changed to six months after discharge with the aim to reduce the number of patients lost to follow-up. The patient related outcome measures obtained from the limited number of patients followed up in this study suggest that patients with persistent critical illness treated at a specialized unit have good mental health, half of them are independent in activities of daily living and that the physical function among the patients vary widely.

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