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A recovery program to improve quality of life, sense of coherence and psychological health in ICU survivors: a multicenter randomized controlled trial, the RAPIT study

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Abstract

Purpose: The aim of this randomized controlled trial (RCT) was to test the effectiveness of a post-ICU recovery program compared to standard care during the first year after ICU discharge.

Methods: A pragmatic, non-blinded, multicenter, parallel-group RCT was conducted between December 2012 and December 2015, at ten intensive care units (ICUs) in Denmark. We randomly assigned 386 adult patients (≥18 years) after receiving mechanical ventilation (≥48 h) to standard care (SC) plus a nurse-led intensive care recovery program or standard care alone after ICU discharge (190 intervention, 196 SC). Primary outcome was health-related quality of life (HRQOL) at 12 months. Secondary outcomes were sense of coherence (SOC), anxiety, depression, and post-traumatic stress disorder (PTSD) assessed at 3 and 12 months after ICU discharge including utilization of healthcare services at 12 months.

Results: At 12 months, we found no differences in HRQOL between groups (mean difference in the Physical Component Summary score, 1.41 [95 % CI, −1.53 to 4.35; $p = 0.35$] ($n = 235$); and in the Mental Component Summary score, 1.92 [95 % CI, −1.06 to 4.90; $p = 0.11$] ($n = 235$). No differences were found on self-reported SOC ($p = 0.63$), anxiety ($p = 0.68$), depression ($p = 0.67$), PTSD ($p = 0.27$), or the utilization of healthcare services including rehabilitation. We found a difference on anxiety, when a cut-off point ≥11 was applied, in per protocol analysis of complete cases at 3 months favoring the intervention (8.8 % vs. 16.2 %, $p = 0.04$).

Conclusions: The tested recovery program was not superior to standard care during the first 12 months post-ICU.

Trial registration: The trial is registered at Clinicaltrials.gov, identification no. NCT01721239.

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This work was performed at 10 ICUs in Denmark: Nordsjællands Hospital; Herlev Hospital; Hospitalsenheden Horsens; Nykøbing Falster Sygehus; Næstved Sygehus; Rigshospitalet, Heart Center 2143; Sygehus Sønderjylland, Department at Aabenraa and Sønderborg; Sydvestjysk Sygehus, Esbjerg Sygehus; Odense Universitetshospital, Svendborg.

Take-home message: Our nurse-led ICU recovery program failed to effectively improve patients' health-related quality of life during the first year after ICU discharge.

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Keywords: Intensive care, Aftercare, ICU clinic, Follow-up, Rehabilitation, Multicenter randomized clinical controlled trial

Introduction

Critical illness and admission to the intensive care unit (ICU) often lead to impairments in physical, cognitive, or mental health status, thereby reducing health-related quality of life (HRQOL) and prolonging short- and long-term recovery [1]. As more patients survive critical illness with impairements, post-ICU programs are emerging to promote psychological recovery [2, 3]. In the UK, the National Institute for Health and Care Excellence (NICE) provided recommendations for post-ICU rehabilitation including review of anxiety, depression, and post-traumatic stress disorder (PTSD) [4]. A randomized clinical trial (RCT) showed that ICU diaries could reduce newly onset PTSD, but evidence of the effectiveness of post-ICU recovery programs is sparse [5]. Qualitative studies have shown the potential benefits of follow-up programs that help patients create a coherent illness trajectory [6]. Most programs have been nurse-led with some multidisciplinary team involvement [3, 7, 8].

In the Scandinavian countries many follow-up programs have emerged, but none have been comprehensive or systematic [7]. In Denmark, ICU follow-up has been an adjunct to conventional rehabilitation. The Danish welfare system is based on equal access and all patients have a right to publicly financed rehabilitation after hospitalization, if ordered by a physician [9]. A discharge rehabilitation plan usually includes physical training, but rarely psychological recovery [9]. To address this gap, we developed a nurse-led individualized recovery program to improve psychological health after intensive care [10]. We hypothesized that a program using person-centered communication to facilitate the construction of a coherent illness narrative would benefit the patient after ICU discharge. The aim of this RCT was to test the effectiveness of a post-ICU recovery program on physical and psychological HRQOL, sense of coherence (SOC), anxiety, depression, and PTSD, and healthcare service utilization compared to standard care (SC) 12 months after ICU discharge.

Materials and methods

Study design

The RAPIT trial (Recovery and Aftercare in Post-Intensive care Therapy patients) was a multicenter, non-blinded, two-armed, parallel-group, pragmatic RCT conducted at 10 ICUs in Denmark to assess the effectiveness of the recovery program. The study design was pragmatic in terms of administrating flexible treatment regimens to adjust time and dose according to clinical needs. Patients were randomly assigned in a 1:1 ratio to receive SC plus the recovery program or SC alone. Treatment allocation was concealed by random selection of opaque sealed envelopes in permuted blocks of six. The site received a new block when two envelopes remained.

Settings and participants

The study was conducted between December 2012 and December 2015 in 10 (level II–III) ICUs; one cardiac and nine general ICUs, in four out of the five regions in Denmark. Patients were consecutively recruited during the first 18 months of the study at four university hospitals, and six university-affiliated hospitals, with a range of 4–14 ICU beds and annual admission rates of 200–830. We included Danish-speaking adults (≥18 years) who had been mechanically ventilated ≥48 h and who did not meet criteria for baseline dementia. Patients were screened for delirium, cognitive impairment, and PTSD within the first month after ICU discharge. Patients, who were not oriented in personal data according to the verbal response in Glasgow Coma Score, with detected delirium using the Confusion Assessment Methods for the ICU (CAM-ICU) at randomization, or enrolled in other follow-up studies were excluded, Fig. 1.

Intervention and standard care

The individualized ICU recovery program was based on literature and theoretical approaches toward psychological recovery including Antonovsky's salutogenic model [11], illness narratives [12], person-centered communication, and elements from guided self-determination [13] and trauma-focused cognitive behavioral therapy [14]. The recovery program consisted of three consultations conducted by trained study nurses. Nurse training included ten workshop days of theory and practice with experts in their field. Included intervention patients received an information pamphlet *Life after ICU* at randomization. First consultation was conducted at the clinic with the patient and close relative at 1–3 months post-ICU. Dialogue focused on past and present as the patient was supported in constructing an illness narrative. A prerequisite for dialogue was the provision of patient photographs taken by ICU nurses during ICU recovery. Second and third consultations at 5 and 10 months post-ICU were conducted by telephone. Patients prepared by completing "Reflection sheets" indicating issues

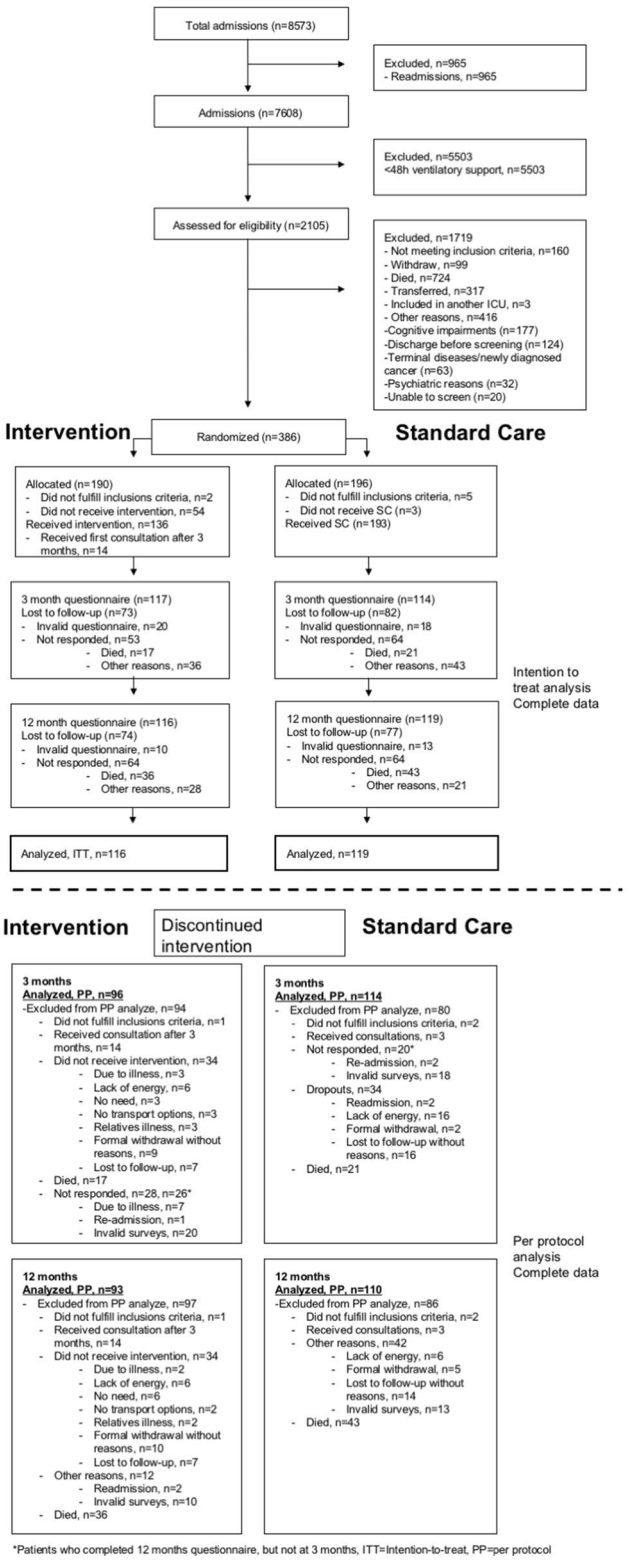

Fig. 1 Flow diagram of the RAPIT study

of importance to the individual. The sheets consisted of 16 unfinished sentences (e.g., "What I want most is…") inspired by guided self-determination [13] (Supplementary Table 1).

SC included light sedation, early mobilization, daily CAM-ICU delirium assessment, written information for visitors, and ICU discharge without follow-up. ICU diaries were not used, but unplanned ICU visits and access to the medical record after discharge were permitted [9]. Physical training was initiated in the ICU and physical rehabilitation was offered to all patients.

Procedures and assessments

Inclusion procedure: patients were invited to participate at ICU discharge or up to a month later. Patients and relatives in both trial arms were informed of the study in ICU to permit patient photographs; retrospective consent was obtained. At inclusion patients were assessed for delirium, cognitive function, and PTSD prior written consent and before randomization. Patients were approached when delirium was assessed as negative. All staff except patients, relatives, and consultation nurses were blinded for group allocation.

Cognition and PTSD were assessed using the Mini Mental State Examination (MMSE) and Harvard Trauma Questionnaire Part IV (HTQ-IV). Self-reported questionnaire packages were sent by post at 3 and 12 months post-ICU. To increase the response rate a few patients were assisted by phone in completing the questionnaires if unable on their own. We assume this did not induce bias [15].

Outcome measures

The primary outcome was HRQOL at 12 months assessed by The Medical Health Survey Short-Form 36 (SF-36). Secondary outcomes were HRQOL at 3 months, and SOC, anxiety, depression, PTSD at 3 and 12 months, including utilization of healthcare services and mortality at 12 months post-ICU.

HRQOL consists of 36 items generating a health profile of eight subscale scores aggregated into two summary scores: Physical Component Summary (PCS) and Mental Component Summary (MCS). SF-36 is commonly used in ICU survivors with acceptability, reliability, and validity in this population [16].

SOC was measured by the 13-item Orientation to Life Questionnaire covering three dimensions: comprehensibility (5 items), manageability (4 items), and meaningfulness (4 items) [11]. The SOC-13 scale has shown acceptability, reliability, and validity in various populations [17]. We used the total score as outcome; higher scores indicate stronger coherence (range 13–91).

Symptoms of anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) covering two dimensions: anxiety (7 items) and depression (7 items); subscale scores were 0–21 with higher scores reflecting greater psychological distress [18]. HADS is widely used in ICU populations as a reliable and valid instrument [19]. We used a total score and cut-off scores $\geq$11 categorized as "cases" [18].

Symptoms of PTSD were assessed by HTQ-IV consisting of 17 items covering three core symptoms corresponding to DSM-IV criteria for PTSD: re-experience (5 items), avoidance (7 items), and arousal (5 items). This was supplemented by four additional items: one functional and three related to stress [19]. HTQ-IV has been validated in various trauma populations, and used in ICU patients [20]. We used a total score, and a cut-off of $\geq$40 is categorized as "positive PTSD" [20].

Utilization of healthcare services and mortality were obtained from hospital charts combined with self-reported data including initiatives that might promote recovery, such as an ICU diary.

Sample size

The study was powered to detect an effect size of a 5-point increase in the SF-36 MCS score in the intervention group at 12 months post-ICU. Power calculation was based on an expected distribution of MCS from a comparable population with a mean of 44.8 (SD 13.2) [21]. With a statistical power of 80 % and significance level of 0.05, we estimated that 110 patients were needed in each arm to complete follow-up. A total of 380 patients would allow for a predicted 40 % dropout, including the pilot test. The first patients ($n = 27$) were included to train study nurses during the first 4 months.

Statistical methods

Primary analysis was based on intention-to-treat (ITT), Fig. 1. Missing data on surveys were replaced, first according to the respective manual, and then by multiple imputations under the assumption that data were missing at random. We made 25 different datasets with imputations based on a regression model using predictive mean matching [22]. Complete data analysis is presented in Figs. 2 and 3, and missing data imputation is illustrated in Supplementary Tables 2 and 3. Patients were considered to have received the intervention if they attended at least one of the three consultations, which accounted for the per protocol (PP) analysis. Two a priori sensitivity analyses were performed: PP and with patients receiving all three consultations. The distribution of background variables and scores of screening tests were given, but the

Complete cases

	SC vs. I [95% CI]	P-value	n_{sc}	n_i
Primary outcomes, 12 months after ICU discharge, ITT				
HRQOL, SF-36 Physical component score	1.41 [-1.53;4.35]	0.35	119	116
HRQOL, SF-36 Mental component score	1.92 [-1.06;4.90]	0.21	119	116
Secondary outcomes, 3 months after ICU discharge, ITT				
HRQOL, SF-36, Physical component score	1.87 [-0.93;4.67]	0.19	114	117
HRQOL, SF-36, Mental component score	-0.41 [-3.20;2.39]	0.78	114	117
SOC, Orientation to Life scale	2.02 [-1.35;5.38]	0.24	137	136
HADS, Anxiety	-0.16 [-1.15;0.82]	0.75	136	136
HADS, Depression	0.10 [-0.84;1.03]	0.84	136	136
HTQ-IV score (PTSD severity)	0.24[-2.07;2.55]	0.84	120	116
Secondary outcomes, 12 months after ICU discharge, ITT				
SOC, Orientation to Life scale	-0.93 [-4.72;2.85]	0.63	133	130
HADS, Anxiety	-0.21 [-1.22;0.80]	0.68	130	131
HADS, Depression	-0.20 [-1.12;0.72]	0.67	130	130
HTQ-IV score (PTSD severity)	-1.42 [-3.94;1.11]	0.27	109	116
Changes between 3-12 months, ITT				
HRQOL, SF-36, Physical component score	0.24 [-2.15;2.62]	0.85	90	93
HRQOL, SF-36, Mental component score	1.63 [-1.38;4.63]	0.29	90	93
SOC, Orientation to Life scale	-2.44 [-6.07;1.19]	0.19	115	116
HADS, Anxiety	-0.05 [-0.99;0.89]	0.92	114	118
HADS, Depression	-0.31 [-1.19;0.57]	0.48	114	117
HTQ-IV score (PTSD severity)	-0.89 [-3.13;1.35]	0.43	87	93
Sensitivity analysis, per protocol analysis				
Primary outcomes, 12 months after ICU discharge, PP				
HRQOL, SF-36 Physical component score	0.67 [-2.60;3.94]	0.69	110	93
HRQOL, SF-36 Mental component score	1.32 [-1.87:4.51]	0.42	110	93
Secondary outcomes, 3 months after ICU discharge, PP				
HRQOL, SF-36, Physical component score	0.60 [-2.38;3.57]	0.69	114	96
HRQOL, SF-36, Mental component score	-0.17 [-3.19;2.84]	0.91	114	96
SOC, Orientation to Life scale	2.90 [-0.60;6.40]	0.11	133	114
HADS, Anxiety	-0.26 [-1.29;0.77]	0.62	133	113
HADS, Depression	0.24 [-0.77;1.25]	0.64	133	113
HTQ-IV score (PTSD severity)	0.06 [-2.40;2.51]	0.96	117	99
Secondary outcomes, 12 months after ICU discharge, PP				
SOC, Orientation to Life scale	-0.34 [-4.38;3.71]	0.87	127	107
HADS, Anxiety	-0.37 [-1.46;0.71]	0.51	124	101
HADS, Depression	-0.07 [-1.08;0.93]	0.89	124	101
HTQ-IV score (PTSD severity)	-1.58 [-4.27;1.10]	0.25	103	90
Changes between 3-12 months, PP				
HRQOL, SF-36, Physical component score	0.72 [-1.74;3.17]	0.56	86	77
HRQOL, SF-36, Mental component score	1.84 [-1.39;5.07]	0.26	86	77
SOC, Orientation to Life scale	-1.64 [-5.46;2.19]	0.40	111	98
HADS, Anxiety	-0.22 [-1.23;0.76]	0.66	110	98
HADS, Depression	-0.59 [-1.50;0.31]	0.20	110	97
HTQ-IV score (PTSD severity)	-1.23 [-3.62;1.17]	0.31	83	80

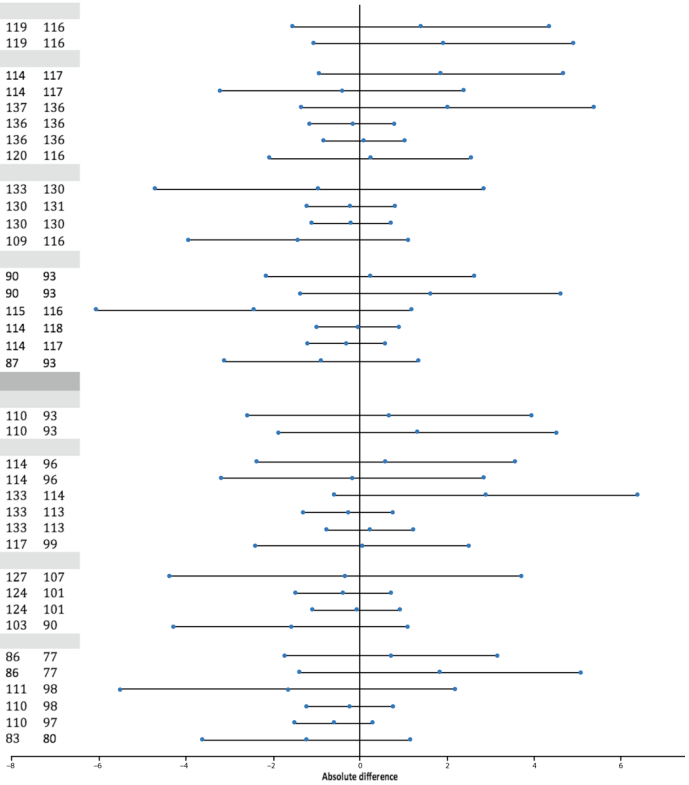

Fig. 2 Results from statistical analysis separated into intention to treat (*ITT*) and per protocol (*PP*) populations with complete cases. The *right column* shows the absolute difference in scores (absolute risk reduction) between standard care and the intervention group, the 95 %, and the *p* value. n_{sc} is the number of observation in the intervention group, n_i is the number of observations in the control group. Note that the confidence intervals are unadjusted

Complete cases

	OR [95% CI]	P-value	$n_{sc\ cases}$	$n_{i\ cases}$
Secondary outcomes, 3 months, cut-off defined as ' Cases', ITT				
Anxiety at 3 months, cut-off ≥11	0.50 [0.24;1.06]	0.07	22 (16.2 %)	12 (8.8 %)
Depression at 3 months, cut-off ≥11	0.66 [0.29;1.48]	0.31	16 (11.8 %)	11 (8.1 %)
PTSD at 3 months, cut-off ≥40	1.23 [0.74;2.06]	0.43	39 (32.5 %)	45 (38.8 %)
Secondary outcomes, 12 months, cut-off defined as ' Cases', ITT				
Anxiety at 12 months, cut-off ≥11	0.91 [0.40;2.07]	0.82	13 (10.0 %)	12 (9.2 %)
Depression at 12 months, cut-off ≥11	1.10 [0.47;2.59]	0.83	11 (8.5 %)	12 (9.2 %)
PTSD at 12 months, cut-off ≥40	1.00 [0.58;1.73]	1.00	35 (32.1 %)	35 (30.2 %)
Sensitivity analysis, per protocol analysis				
Secondary outcomes, 3 months, cut-off defined as ' Cases', PP				
Anxiety at 3 months, cut-off ≥11	0.42 [0.18;0.96]	0.04	20 (16.9 %)	9 (7.8 %)
Depression at 3 months, cut-off ≥11	0.51 [0.21;1.26]	0.15	15 (12.7 %)	8 (7.0 %)
PTSD at 3 months, cut-off ≥40	1.08 [0.62;1.90]	0.79	34 (28.8 %)	35 (30.4 %)
Secondary outcomes, 12 months, cut-off defined as ' Cases', PP				
Anxiety at 12 months, cut-off ≥11	0.74 [0.27;2.07]	0.57	12 (9.6 %)	6 (7.3 %)
Depression at 12 months, cut-off ≥11	0.97 [0.36;2.61]	0.95	11 (8.8 %)	7 (8.5 %)
PTSD at 12 months, cut-off ≥40	0.88 [0.46;1.67]	0.69	33 (26.8 %)	20 (24.4 %)

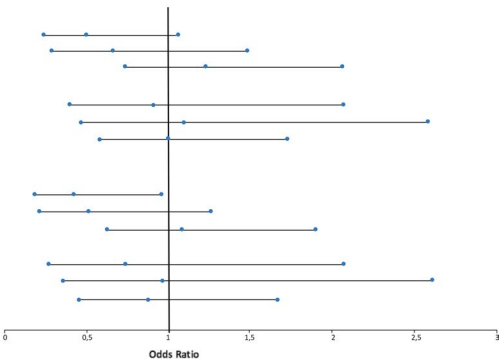

Fig. 3 Results from statistical analysis separated into intention to treat (*ITT*) and per protocol (*PP*) populations with cut-off categorized as "cases" with complete cases. The *right column* shows the absolute difference in scores (absolute risk reduction) between standard care and the intervention group, the 95 %, and the *p* value. n_{sc} is the number of observations in the intervention group, n_i is the number of observations in the control group. Note that the confidence intervals are unadjusted

potential difference between groups was not significance tested to avoid unnecessary testing [23]. Independent-sample *t* tests were used to compare means between two groups for continuous variables, and linear models were used to adjust for trial centers. Dichotomous data were analyzed using logistic models to adjust for trial centers. Results are presented according to the type of variable with confidence intervals (95 % CI) using a two-tailed $P < 0.05$. SPSS software version 23 was used.

Ethical considerations

The trial was performed in accordance with the Declaration of Helsinki. All patients and relatives gave written informed consent prior to participation. Photographs were taken and kept at ICU until patient handover, requiring consent. The trial was registered at www.clinicaltrials.gov (no. NCT01721239) and approved by the National Committee on Health Research ethics (no. H-1-2012-FSP-60) and the Danish Data Protection Agency (Umbrella notification no. 2007-58-0015 and project no. 01863 HIH-2012-011).

Results

Participants

During the study period, 2105 patients were assessed for eligibility and 1719 were excluded (Fig. 1). The remaining 386 were randomized. Baseline characteristics showed that the groups were well balanced (Table 1). Among randomized patients 36 (19 %) vs. 43 (22 %) in intervention vs. SC group died within the first year post-ICU. The dropout rate in the questionnaire package was 17.6 % (34 in each arm) at 3 months, and 6 % at 12 months (13 vs 19). Non-responders were 11.9 % at 3 months (26 vs. 20) and none at 12 months. Dropouts were more likely to be single men with longer duration of mechanical ventilation, readmitted to ICU, or higher MMSE score at randomization. Patients who died were older with pre-existing diseases, persisting co-morbidities, readmissions, higher APACHE II score, longer sedation time, and a higher PTSD score at randomization. Of the remaining 154 surviving patients in the intervention group, 88 % received at least one consultation and 71 % received all three consultations (Table 2).

Outcomes

No statistically significant difference was observed in primary or secondary outcome measurements at 3 and 12 months (Figs. 2 and 3). The intervention group had a mean PCS score of 39.06 compared to SC with a mean of 37.65 (mean difference 1.41 (95 % CI, −1.53 to 4.35), $p = 0.35$) at 12 months. The intervention group had a mean MCS score of 51.87 vs. 49.95 in SC after 12 months (mean difference 1.92 (CI 95 %, −1.06 to 4.90), $p = 0.21$). The results from PP analysis showed no difference between groups: the PCS mean score was 38.17 vs. 38.79 in intervention vs. SC group (mean difference 0.67 (95 % CI, −2.60 to 3.94), $p = 0.69$), and the MCS mean score was 50.08 vs. 51.80 in the intervention vs. SC group (mean difference 1.32 (95 % CI, −1.87 to 4.51), $p = 0.42$). Figure 2 shows non-significant results from the sensitivity analysis in 110 patients receiving at least one consultation.

In Fig. 2 secondary outcomes show no effectiveness of the ICU recovery program on SOC, anxiety, depression, or PTSD. The sensitivity analysis with patients receiving all three consultations, and adjustment for trial units did not alter the results (not presented). The change scores between 3 and 12 months were insignificant on primary and secondary measurements (Fig. 2).

The PP analysis showed a significantly smaller proportion of intervention vs. SC patients, who were above the cut-off of 11 on the HADS scale for anxiety at 3 months after ICU discharge (20 vs. 9) with an odds ratio of 0.42 (95 % CI, 0.18 to 0.96, $p = 0.04$), Fig. 3, but this was not found in other analyses (Supplementary Material). The rate of pre-existing PTSD was 30.5 vs. 29.4 % in the intervention vs. SC group. After excluding pre-existing PTSD at 12 months, the incidence of new onset PTSD was 15.6 % ($n = 24$) vs. 15 % ($n = 23$) in the intervention vs. SC group (Supplementary Tables 4 and 5). No adverse events were seen.

Utilization of healthcare services during the first year post-ICU

A similar proportion of patients in the two study groups received rehabilitation during hospitalization and the first year after (28.9 % vs. 30.6 in intervention vs. SC group), Table 2. Out-patient healthcare services included airway control, smoking cessation, and nurse/physician consultations. These services were provided for reasons of poor general health and categorized as "non-structured rehabilitation".

Discussion

The present trial of a nurse-led post-ICU recovery program showed no difference in HRQOL or secondary outcomes during the first 12 months after ICU discharge. An exploratory analysis showed a significant difference in anxiety in the complete analysis at 3 months, but this was not sustained. Primary outcome analysis of HRQOL in the two groups showed no difference at 12 months. PCS scores were lower and MCS scores higher compared to previous studies including physical rehabilitation at 3 and 12 months post-ICU [2, 24–26], but generally lower than the Danish aged-matched population [27]. SOC was higher than seen in a Danish population study (mean 65) [28] and a Chinese post-ICU study (mean 51.8) [29], but

Table 1 Baseline characteristics of patients recruited after ICU discharge

	Standard care ($n = 196$)	Intervention ($n = 190$)
Sociodemographic data (median, IQR)		
Age, median (IQR)	67.5 (58–75)	66 (57.75–73.5)
Sex (male)	117 (59.7 %)	112 (58.9 %)
Educational level (years), median (IQR)	10.0 (7–13)	10.0 (7.9–13)
Marital status		
Cohabiting	116 (59.2 %)	102 (53.7 %)
Living alone	82 (41.8 %)	88 (46.3 %)
Occupational status pre-ICU (employment)	45 (23.0 %)	46 (24.2 %)
Pre-existing diseases (1 disease)	57 (29.1 %)	51 (26.8 %)
Pre-existing diseases (>1 diseases)	113 (57.7 %)	118 (62.1)
Pre-existing diseases, median (IQR)	2.0 (1–3)	2.0 (1–3)
Diagnostic groups (*n*, percentages)		
Diagnosis at ICU admission*		
Neurological	6 (3.1 %)	12 (6.3 %)
Respiratory	68 (33.7 %)	70 (36.8 %)
Cardiovascular	33 (16.8 %)	26 (13.8 %)
Gastrointestinal	18 (9.2 %)	21 (11.1 %)
Renal	4 (2.0 %)	1 (0.5 %)
Hematological	0	1 (0.5 %)
Endocrinology or metabolic	3 (1.5 %)	0
Sepsis	56 (28.6 %)	56 (29.4 %)
Trauma and intoxications	8 (4.1 %)	3 (1.6)
Clinical variables during ICU stay		
Medical ICU	122 (62.2 %)	131 (68.9 %)
APACHE II score, median (IQR)	24.5 (20.0–30.0)	25.0 (19.0–30.3)
SAPS II score, median (IQR)	48.5 (39.3–60)	44.5 (35.0–54.3)
Mechanically ventilation (hours), median (IQR)	172.0 (90.0–346.0)	159.1 (83.5–384.7)
Sedative used	163 (83.2 %) median 4.0 (2–8)	161 (82.1 %) median 4.0 (2–10)
Co-morbidities during ICU stay		
No. co-morbidities, median (IQR)	2.0 (1–3)	2.0 (1–3)
Delirium (days), median (IQR)**	0 (0–1)	0 (1–2)
Days measured delirium, median (IQR)	6 (2–11)	6 (3–11)
Not assessed delirium during ICU-stay	19 (9.7 %)	18 (9.5 %)
Delirium unable to assess***	1 (0–3)	1 (0–3)
Renal replacement therapy	26 (13.3 %)	17 (8.9 %)
Specific healthcare services planned or initiated during ICU		
Physiotherapist (ICU)	138/196 (70.4 %)	126/190 (66.3 %)
Physiotherapist (continuing at the general ward)	151/196 (77.0 %)	141/190 (74.2 %)
Occupational therapist	72/196 (36.7 %)	74/190 (38.9 %)
Dietitian	79/196 (40.3 %)	75/190 (39.5 %)
At ICU discharge		
Length of ICU stay (days), median (IQR)	9 (6–18)	10 (5–20)

similar to a Swedish population of patients suffering from myocardial infarction (mean 70.4) [30]. A similar Swedish RCT of psychological distress in primary care (using acupuncture alone) found that SOC increased (mean 55.4 to 68.1) in both intervention groups during an 8-week period, and (53.1 to 56.3) in the SC arm, which was lower than the SOC in the present study [31].

The prevalence of anxiety and depression in the present trial was lower than other similar studies [2, 26, 32]. It is possible that our intervention relieved anxiety

Table 1 continued

	Standard care ($n = 196$)	Intervention ($n = 190$)
MMSE at enrollment, median (IQR)[$]	26.5 (23.0–29.0)	27.0 (24.0–29.0)
HTQ-VI at enrollment, median (IQR)[$$]	28.5 (24.0–33.0)	28.5 (24.0–36.0)

Values are numbers (percentages) of patients unless otherwise indicated

IQR interquartile range, *APACHE-II* Acute Physiology and Chronic Health Evaluation, *SAPS II* Simplified Acute Physiology Score, Co-morbidities defined as illness developed during ICU (e.g., ATIN, sepsis, multiorgan failure)

* All patients diagnosed with "respiratory insufficiency" were recoded into the primary diagnosis causing respiratory insufficiency according to the medical chart (52 % of the patients had this diagnosis)

** Delirium assessed using CAM-ICU

*** Due to RASS −4 and −5

[§] 52 missed drawing, and 23 missed writing due to physical impairments. Total missing: intervention, 27; control group, 29

[$$] 41 missing in intervention, 52 missing in control group

by supporting the patients in constructing their illness narrative. Physical rehabilitation may influence the level of anxiety, but there was no difference between groups. A study testing ICU diaries reduced the prevalence of anxiety and depression, albeit mean HADS scores were higher than the present study [32]. Another study testing ICU diaries reduced the incidence of new onset PTSD (13.1 vs. 5 %) [33]. Our 3-month PTSD was higher, 15 % in both groups, but similar to other studies [26, 34].

Survivors in our study had a high MCS, maintained strong SOC, experienced less anxiety and depression, and had a PTSD similar to other studies [2, 32, 33]. These findings might in part be attributed to the availability of tax-paid rehabilitation services; surveys have shown that Danish patients generally feel well informed and confident about the individualized service offered [35].

Our intervention could, perhaps, be improved by increasing the frequency of consultations, initiating the intervention earlier [36], or by using an ICU diary [33]. Also, we could have investigated the provision of psychological support by the general practitioner, or designed an interprofessional ICU recovery program including psychologists.

Patient characteristics in our study differed from other studies in that patients were older and had a higher APACHE II score, but were similar in terms of ICU length of stay and mechanical ventilation [2, 32, 33]. The mortality rate, however, was high, which might be explained by the high APACHE II scores in the sample. A study similar to ours failed to show difference in HRQOL [2]. Survivors might revert to chronic critical illness with disability forcing them to redefine their quality of life (QOL) [37]. QOL is a dynamic concept with individual interpretation of feelings, such as happiness, as described in the response shift theory [38]. QOL is interchangeable leading to the concept of response shift theory [39]. Values and self-evaluation change according to circumstances and might lead to a redefinition of QOL. This indicates that changes in HRQOL might be a natural response.

Methodological limitations

The present study was strengthened by the multicenter RCT design, rigorous development of the intervention with theory-driven approaches, and implementation by specially trained study nurses. Generalizability was increased by recruitment from 10 ICUs. According to the mortality and dropout rate, we might have recruited some patients that were too ill to participate. We used multiple imputations of data to avoid bias [40]. As multiple imputations should be interpreted with caution we presented the complete data analysis [40]. Our study achieved its target sample size, the intervention was reliably delivered, and nurses showed skillfulness in delivery. Cluster randomization could have improved delivery, but might also have prolonged the study. We did not succeed in providing all first consultations within the first 3 months, risking the development of chronic PTSD. HRQOL, anxiety, and depression were robust and validated in ICU survivors, but SOC and HTQ-IV need to be validated further in studies with ICU survivors. Moreover, ICU survivors have been shown to have existential issues [37] that are not captured in the questionnaires we used. We recommend that new instruments are developed and validated to assess particular problems of post-ICU patients, as some issues are lost in generic instruments.

Delirium assessment was not fully implemented as demonstrated in Table 1. Delirium was assessed on only 6 days whereas the median length of stay was 9–10 days. Another potential limitation is the inability to assess baseline HRQOL. We did not assess HRQOL by proxy because it is a subjective evaluation [38].

Table 2 Delivery of the intervention and healthcare services within the first year after ICU

	Standard care	Intervention
Components delivered in the ICU recovery program		
First consultation (CI) delivered (with flexible time, up to 6 months post-ICU)		136/190 (71.6 %)
Died		27/190 (14.2 %)
Readmission		2/190 (1.1 %)
Did not respond		7/190 (3.7 %)
Lack of energy		6/190 (3.2 %)
No need		3/190 (1.6 %)
Withdraw		9/190 (4.7 %)
Duration, mins (range)		54 (24–108)
Second consultation (CII) delivered		120/190 (63.2 %)
Died		5/190 (2.6 %)
Readmission		1/190 (0.5 %)
Did not respond		4/190 (2.1 %)
No need		6/190 (3.2 %)
Duration, mins (range)		36 (8–107)
Consultation III (CIII) delivered		110/190 (57.9 %)
Died		2/190 (1.1 %)
Expressive aphasia		1/190 (0.5 %)
Withdraw		1/190 (0.5 %)
No need		3/190 (1.6 %)
Did not receive intervention		3/190 (1.6 %)
Duration, mins (range)		37 (14–105)
Other components in the ICU recovery program		
Visit ICU		112/190 (59.0 %)
Received photographs		119/190 (62.6 %)
Information pamphlet *Life after ICU*		190/190 (100 %)
Patient/relative initiatives		
Subject access to medical journal	35/196 (17.9 %)	32/190 (16.8 %)
Physician consultations associated with subject access*	21/196 (10.7 %)	7/190 (3.7 %)
Medical journal online*	30/196 (15.3 %)	33/190 (17.4 %)
Written patient diary from relatives or other non-participating ICUs*	11/196 (5.6 %)	20/190 (10.5 %)
Photographs taken by relatives or patient*	33/196 (16.7 %)	59/190 (31.1 %)
Healthcare services delivered during the first year after ICU discharge		
Specific healthcare services during hospitalization		
Psychologist, social worker or other specialists	21/196 (10.7 %)	26/190 (13.7 %)
Readmissions		
None	65/196 (33.2 %)	52/190 (27.4 %)
One or more	131/196 (66.8 %)	138/190 (72.6 %)
Emergence room (ER contacts)	24/196 (12.2 %)	26/190 (13.7 %)
Out-patient clinics		
No contact	10/196 (5.1 %)	18/190 (9.5 %)
One or more contact	186/196 (94.9 %)	172/190 (90.5 %)
No structured rehabilitation (rehabilitation embedded in ambulatory contacts)	137/196 (69.9 %)	132/190 (69.5 %)
Rehabilitation services		
Rehabilitation at home care facilities (in-hospital or municipalities combined)*	31/196 (15.8 %)	43/190 (22.6 %)
Specialized rehabilitation in total	63/196 (32.1 %)	59/190 (31.1 %)
COPD rehabilitation	16/196 (8.2 %)	14/190 (7.4 %)
Heart rehabilitation	11/196 (5.6 %)	12/190 (6.3 %)
Cancer rehabilitation	15/196 (7.7 %)	12/190 (6.3 %)

Table 2 continued

	Standard care	Intervention
Other rehabilitation (e.g., neuro, pain, psychiatric, social, coordination of care)	18/196 (9.1 %)	17/190 (8.9 %)
Time to initiated rehabilitation (weeks after hospital discharge), mean (SD)	4.49 (8.07)	3.88 (7.08)
Deaths	36 (19 %)	43 (22 %)

Conclusions

This study showed no effectiveness of our ICU recovery program in improving HRQOL, SOC, or reducing symptoms of anxiety, depression, and PTSD in the first 12 months after ICU discharge. Patients had a high MCS, maintained a strong sense of coherence, and low levels of anxiety and depression. PTSD was still high at 12 months post-ICU.

Electronic supplementary material

The online version of this article (doi:10.1007/s00134-016-4522-1) contains supplementary material, which is available to authorized users.

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Compliance with ethical standards

Conflicts of interest

No conflicts of interest have been declared by the authors.

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