Reprint of Recovery programme for ICU survivors has no effect on relatives' quality of life

Secondary analysis of the RAPIT-study

Bohart, Søs; Egerod, Ingrid; Bestle, Morten H.; Overgaard, Dorthe; Christensen, Doris F.; Jensen, Janet F.

Published in:
Intensive and Critical Care Nursing

DOI:
10.1016/j.iccn.2018.11.009

Publication date:
2019

Document version
Publisher's PDF, also known as Version of record

Intensive & Critical Care Nursing 50 (2019) 111–117

Contents lists available at ScienceDirect

Intensive & Critical Care Nursing

journal homepage: www.elsevier.com/iccn

Research article

Reprint of Recovery programme for ICU survivors has no effect on relatives' quality of life: Secondary analysis of the RAPIT-study ☆

Søs Bohart [a,*], Ingrid Egerod [b], Morten H. Bestle [c], Dorthe Overgaard [d], Doris F. Christensen [c], Janet F. Jensen [e]

[a] Department of Anesthesiology, Herlev Hospital, University of Copenhagen, Herlev Ringvej 75, 2730 Herlev, Denmark
[b] Health & Medical Sciences, University of Copenhagen, and Intensive Care Unit 4131, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen, Denmark
[c] Nordsjællands Hospital, Dyrehavevej 29, 3400 Hillerød, Denmark
[d] Institution of Nursing, Metropolitan University College, Tagensvej 86, 2200 Copenhagen, Denmark
[e] Department of Anesthesiology, Holbæk Hospital, Smedelundsgade 60, 4300 Holbæk and Nordsjællands Hospital, University of Copenhagen, Dyrehavevej 29, 3400 Hilleroed, Denmark

ARTICLE INFO

Article history:
Accepted 4 March 2018

Keywords:
Aftercare
Family
Follow-up
ICU clinic
Intensive care
Mental health
Multicentre
Quality of life
Randomised controlled trial
Relatives

ABSTRACT

Background: Relatives of intensive care patients are at risk of developing symptoms of anxiety, depression and posttraumatic stress resulting in reduced health-related quality of life. Recovery programmes for patients have been implemented, but their effect on relatives is uncertain.
Aim: To determine whether relatives benefit from a recovery programme intended for intensive care survivors.
Research design: A randomised controlled trial of 181 adult relatives: intervention group (n = 87), control group (n = 94).
Setting: Ten intensive care units in Denmark.
Main outcome measures: Primary outcome: health-related quality of life (HRQOL). Secondary outcomes: Sense of coherence (SOC), and symptoms of anxiety, depression and posttraumatic stress, compared to standard care at 12 months after intensive care discharge.
Results: No difference in HRQOL between groups was observed at 12 months (mean difference in mental component summary score, 1.35 [CI 95%: −3.13; 5.82], p = 0.55; and physical component summery score, 1.86 [CI 95%: −1.88; 5.59], p = 0.33). No differences were found in secondary outcomes.
Conclusion: The recovery programme intended for intensive care survivors did not have an effect on the relatives. Future recovery programmes should be targeted to help both patient and family, and future research should be conducted on a larger scale to make conclusions with higher probability.

Implications for Clinical Practice

- This study highlights the potential to improve health related quality of life sense of coherence, symptoms of anxiety, depression and posttraumatic stress disorder on relatives of intensive care unit survivors.
- The recovery programme intended for survivors indicated no effectiveness on relatives' health-related quality of life, sense of coherence and psychological health.
- Results generated from this study show that health-related quality of life, sense of coherence, and psychological health of relatives are better than found in previous studies.
- Future research should be conducted on a larger scale with intervention targeting patient and relatives based on their individual need during recovery of critical illness.

DOI of original article: https://doi.org/10.1016/j.iccn.2018.03.002

☆ A production error resulted in this article inadvertently being printed in a regular issue. The article is reprinted here for reader convenience and for the continuity of the special issue. For citation purposes, please use the original publication details: Intensive & Critical Care Nursing, Volume 47C, August 2018, Pages 39–45, DOI of the original article: http://doi.org/10.1016/j.iccn.2018.03.002.

* Corresponding author.
E-mail addresses: soes.bohart@regionh.dk (S. Bohart), Ingrid.egerod@regionh.dk (I. Egerod), morten.bestle@regionh.dk (M.H. Bestle), doov@phmetropol.dk (D. Overgaard), jfje@regionsjaelland.dk (J.F. Jensen).

https://doi.org/10.1016/j.iccn.2018.11.009
0964-3397/

Introduction

Relatives of intensive care patients are exposed to stress due to the critical and life-threatening condition of a loved one (Van Beusekom et al., 2016). In the intensive care unit (ICU) the relatives are faced with stressors such as feelings of helplessness, uncertainty regarding treatment and prognosis, lack of sleep and insufficient information (Frivold et al., 2016; Matt et al., 2017). Stressors may affect the relatives negatively and persist up to 12 months after ICU discharge (Ashby and Stoffell, 1995; Azoulay et al., 2005; Jones et al., 2004; Matt et al., 2017; van Beusekom et al., 2016).

It has been documented that relatives of ICU patients are at high risk of developing symptoms of anxiety, depression and post-traumatic stress (PTSD) during and after the ICU stay (Davidson et al., 2012; Frivold et al., 2016; McAdam et al., 2012; Pochard et al., 2005). This cluster of complications is known as "post-intensive care syndrome-family" (PICS-F) (Davidson et al., 2012). PICS-F is associated with reduced health-related quality of life (HRQOL) and the mental health component in particular is decreased compared to an age- and gender-matched population (Angus and Carlet, 2003; Matt et al., 2017; Rueckriegel et al., 2015; van Beusekom et al., 2016). A survey (n = 143) showed that nearly half of the relatives are affected by PICS-F at three months after ICU with outcomes reporting the prevalence of symptoms of anxiety (39%), depression (29%), and PTSD (47%), (Matt et al., 2017). Similar results were found at 6–12 months after ICU showing symptoms of anxiety (15–24%), depression (23–44%), and PTSD (32–80%), respectively (van Beusekom et al., 2016).

The quality of life of the relatives might be affected by the quality of life of the patients. A four-year cohort study (n = 57) showed that HRQOL of relatives was affected by patients' physical and mental problems (Rodriguez et al., 2005). Moreover, Matt et al. (2017) found a positive association between patients' HRQOL and the mental health of relatives after ICU (Matt et al., 2017).

Different types of family-centred interventions have been tested in ICU and found to improve the level of satisfaction in patients and relatives (Goldfarb et al., 2017). It has been recommended to involve relatives as an integrated part of patients' admission (Goldfarb et al., 2017).

Qualitative studies have indicated that post-ICU follow-up interventions might strengthen relatives' sense of coherence (SOC) related to the management of ongoing challenges (Frivold et al., 2016; Long et al., 2016). Post-ICU follow-up is valued and beneficial for patients and relatives alike (Frivold et al., 2016). Interventions specifically targeting the relatives of ICU survivors are lacking (Jones et al., 2004; Svenningsen et al., 2017). To address this gap, we developed a nurse-led individualised recovery programme aimed at ICU survivors to improve HRQOL, SOC, and psychological health in patient and relatives after intensive care (Jensen et al., 2016). The Recovery and Aftercare in Post-Intensive Care Therapy patients (RAPIT) study investigated the effect of the recovery programme on patients and their relatives (Jensen et al., 2016).

Study aim and objectives

The aim of the study was to determine whether relatives benefit from a recovery programme intended for intensive care survivors.

The objectives of the study were to evaluate:

1. Primary objective: The mental component score from The Medical Health Survey Short-Form 36 (SF-36) after a recovery programme compared to standard care (SC) at 12 months after ICU discharge.
2. Secondary objectives: The level of SOC and symptoms of anxiety, depression and PTSD after a recovery programme compared to SC at 3 and 12 months after ICU discharge.

Methods

The present study is a secondary analysis of the RAPIT-study treating data from relatives (Jensen et al., 2016). Analyses of patient data are detailed in previous publication (Jensen et al., 2016). The CONsolidated Standards of Reporting Trials (CONSORT) guideline was followed when reporting the study (Boutron, 2008).

Study design

The study was a multicentre, non-blinded, two-armed, pragmatic randomised controlled trial (RCT). Enrolment of relatives was made on the basis of patients from the RAPIT-study who were randomly assigned in a 1:1 ratio to receive the recovery programme or SC. Treatment allocation was concealed by random selection of opaque sealed envelopes in permuted blocks. The data analysis was blinded, but the recovery programme could not be blinded.

Setting and participants

The study was conducted in 2012–2015 in 10 ICUs (level II-III) in four out of five regions in Denmark. Participants were relatives of intensive care patients recruited through the RAPIT-study (Fig. 1). Relatives were invited to participate up to one month after ICU, by patient consent. Self-reported postal questionnaires were sent at three and 12 months after ICU. Participants were Danish-speaking adults (>18 years) that were relatives of ICU patients who participated in the RAPIT-study. Relatives of patients who died during the study were registered as non-responders.

Intervention and standard care

The intervention was a recovery programme consisting of three consultations conducted by specially trained study nurses. The first consultation was conducted at the hospital with the patient and relatives at one to three months post-ICU. The dialogue focused on supporting the patient in constructing an illness narrative aided by photographs of the patient during the ICU-stay and revisiting ICU. The second and third consultations were conducted by telephone with patients at five and 10 months post-ICU. The dialogue focused on issues of importance to the patients. Standard care included informational needs of patients and relatives and patient care including light sedation, early mobilisation, physical rehabilitation and ICU discharge without follow-up.

Outcome measures

The primary outcome was HRQOL at 12 months post-ICU. Secondary outcomes were HRQOL at three months, and SOC, anxiety, depression, PTSD at three and 12 months post-ICU.

HRQOL was assessed by SF-36, a validated and reliable questionnaire that summarises self-evaluated health in 36 items (Bjørner et al., 1997). The questionnaire is designed to represent the most important health profile from eight multi-items scales or two aggregated summary scores: Physical Component Score (PCS) and Mental Component Score (MCS) (Bjørner et al., 1997). The scores range from 0 to 100 with higher scores reflecting better health. MCS was the primary outcome in this study.

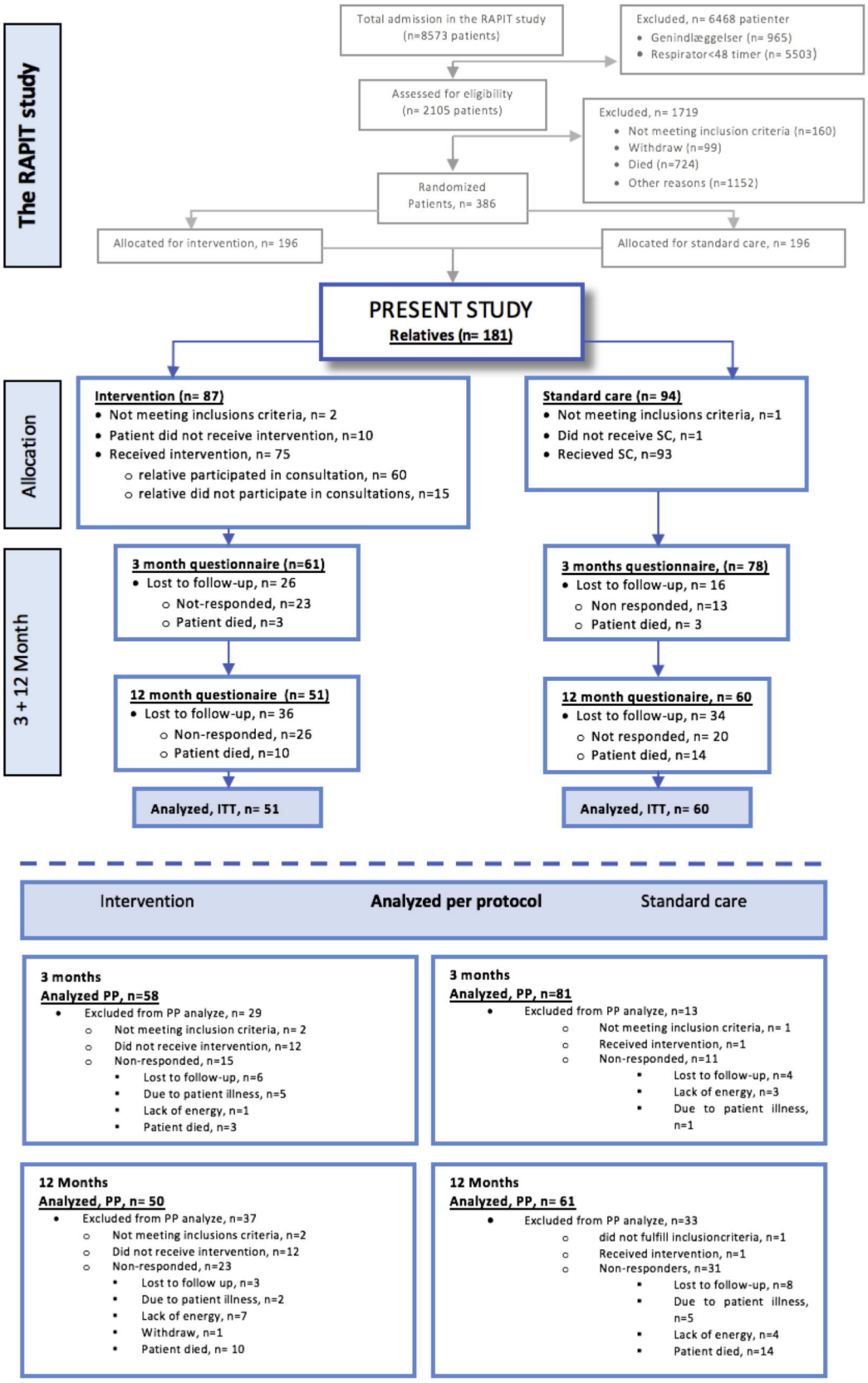

Fig. 1. Flow diagram.

SOC was measured by 13 questions from Sense of Coherence Scale (SOC-13) (Eriksson and Lindstrom, 2005). The scale has acceptability, reliability and validity in various populations, measuring the handling of stressful situations, while maintaining well-being. The scale ranges from 13 to 91; higher scores indicate stronger SOC.

Symptoms of anxiety and depression were assessed by the Hospital Anxiety and Depression Scale (HADS) (Bjelland et al., 2002). It is a validated screening tool with 14 questions that covers both dimensions: anxiety (7 items) and depression (7 items). Subscale scores range from 0 to 21 with higher scores reflecting greater psychological distress (Bjelland et al., 2002).

Symptoms of PTSD were assessed by Harvard Trauma Questionnaire Part IV (HTQ-IV) consisting of 17 + 1 items covering re-experience (5 items), avoidance (7 items), and arousal (5 items). These three core symptoms correspond to DMS-IV criteria for PTSD (Mollica et al., 1992). The scale ranges from 18 to 72; higher scores indicate greater symptoms of PTSD.

Sample size

The study was powered to detect an effect size of a 5-point increase in the SF-36 MCS in the intervention group at 12 months after ICU discharge. Power calculation was based on an expected distribution of MCS from a matched population with a mean of 36.7 (SD 11.7) (Bayen et al., 2013). With a statistical power of 80% and significance level of 0.05, it is estimated that 86 relatives were needed in each group to complete follow-up.

Statistical methods

The statistical analysis plan was conducted in collaboration with a statistician. Primary analysis was based on intention-to-treat (ITT) (Fig. 1). Missing data on surveys were replaced according to the respective manual. Relatives were considered to have received the intervention if the patient attended at least one of the three consultations, which accounted for the per protocol (PP) analysis. Three a priori sensitivity analyses were performed: PP, adjusted analyses for trial centres, and between participating versus non-participating relatives in consultation together with the patient from the intervention group.

The analyses were assessed by an unpaired *t*-test for the test of the null hypothesis no difference between the interventions and controls including possible group differences between mean changes from three to 12 months post-ICU. In total, 27 missing data from SF-36 and 2 from HADS were identified and replaced.

Results are presented with 95% confidence intervals (95% CI) and P-value was considered statistically significant if it was less than 0.05 ($P < 0.05$). All analyses were conducted using SPSS software version 24.

Ethical considerations

The study was performed in accordance with the Declaration of Helsinki. All patients and relatives gave written informed consent prior to participation (Jensen et al., 2016). The trial was registered at ClinicalTrials.gov (No. NCT03264365) and approved by the National Committee on Health Research ethics (No. 17-000048) and the Danish Data Protection Agency (REG-098-2017).

Results

Participants

Of 386 patients from the RAPIT-study, 181 relatives were allocated to the intervention group (n = 87) and control group (n = 94) (Fig. 1). Baseline characteristics (Table 1) show that the two groups were well balanced according to gender, age and their relationship to the patient. Because the enrolment of relatives was performed on the basis of patients from the RAPIT-study, the patients' baseline characteristics showed no significant difference in age, gender, length of admission, days on mechanical ventilation, admission diagnosis, and clinical variables during the ICU-stay. ITT analyses were performed on relatives in the intervention

Table 1
Baseline characteristics of participants.

Characteristics	Intervention (n = 87)	Control (n = 94)	Δ mean [CI95%]
Relatives			
Age, Median (IQR)	57.4 (50–67)	61.0 (41.75–69.0)	2.08 [−1.91; 6.07]
Sex (male)	22 (25.3%)	30 (31.9%)	−0.07 [−0.20; 0.07]
Relation to ICU-patient (%):			0.03 [−0.17; 0.24]
Spouses/cohabitant	64 (73.6%)	65 (69.1%)	
Children	13 (14.9%)	18 (19.1%)	
Other*	10 (11.5%)	11 (11.7%)	
ICU-patients of the recruited relatives			
Age, Median (IQR)	65 (57–73)	67 (57–74.25)	2.28 [−1.45; 6.02]
Sex (male)	56 (64.4%)	65 (69.1%)	−0.05 [−0.91; 0.09]
Length of ICU stay (days), median (IQR)	11 (5–26)	12 (5–21.25)	−0.12 (−4.56; 4.33)
Mechanically ventilation (hours), median (IQR)	158.18 (96.82–443.6)	188.42 (88.53–399.29)	−28.32 [−23.60; 66.96]
APACHE II score**, median (IQR)	25 (19–32)	26 (20.5–32.5)	0.80 [−1.59; 3.18]
MMSE***, mean (IQR)	27.5 (25–29) (n = 86)	27 (24–29) (n = 93)	−0.83[−1.93; 0.27]
HTQ****, median (IQR)	28 (24–35)#	28 (24–33.25)§	−0.84[−3.04; 1.36]
Pre-existing diseases, median (IQR)	2 (1–3)	2 (1–3)	−0.30 [−0.79; 0.20]
Pre-existing diseases, (>1 disease) (%)	76 (87.4%)	81 (86.2%)	−0.01 [−0.11; 0.09]
Diagnostic groups (n(%)):			0.20 [−0.12; 0.52]
Respiratory	20 (23.0%)	14 (14.9%)	
Cardiovascular	16 (18.4%)	17 (18.1%)	
Sepsis	26 (29.9%)	33 (35.1%)	
Other	25 (28.7%)	30 (31.9%)	

Values are numbers (percentages) of patients unless otherwise indicated. *IQR* interquartile range.
* Siblings, parents, friends, other family members.
** *APACHE-II* Acute Physiology and Chronic Health Evaluation.
*** *MMSE* Mini Mental State Examination.
**** HTQ Harvard Trauma Questionnaire.
\# n = 81, 6 missing.
§ n = 86, 8 missing.

group (n = 51) and control group (n = 60). PP analyses were performed on relatives in the intervention group (n = 50) and control group (n = 61) (Fig. 1).

Among the 181 relatives, 24 were censored because n = 10 patients (11.9%) in the intervention group vs. 14 (14.9%) in the control group had died. The final dropout rate in the questionnaire package was 36 (41%) in the intervention vs. 34 (36%) in the control group. Other reasons for dropout were severe patient illness, lack of energy, and lost to follow-up (Fig. 1).

Outcomes

No statistically significant differences were observed in primary or secondary outcomes measured at three and 12 months (Table 2). ITT analyses showed the intervention group had a mean MCS of 48.83 compared to SC of 50.18 (Δmean 1.35; [95% CI, 3.13–5.82], p = 0.55) at 12 months. PCS had a mean of 47.96 in intervention and 49.82 in SC (Δmean = 1.86; [95% CI, −1.88–5.59]; p = 0.33). Results from the PP analyses showed no differences between groups, the intervention group had a mean MCS of 48.49 vs. 49.95 in the SC group (Δmean = 1.45; [95% CI, −3.12; 6.01]; p = 0.53) and in PCS intervention group had a mean of 48.16 vs. 49.30 (Δmean = 1.5; [95% CI, −2.69–4.99]; p = 0.56) (Table 2). All secondary outcomes, both in the ITT and PP analyses, showed no statistically significant effectiveness on relatives measured by SOC, HADS and HTQ. The prevalence of PTSD was at three and 12 months (ITT-analysis) in the intervention 13.9% vs. 24.2% in the control group, and 15.6% vs. 17.6%, respectively. Difference scores from three to 12 months showed no statistically significant differences between groups (Table 2).

Sensitivity analyses

A subset of participating relatives in consultations from the intervention group (n = 60) vs. non-participating relatives (n = 15) showed no difference (mean 1.46; [95% CI, −7.83–10.75]; p = 0.75) in MCS at 12 months post-ICU. The sensitivity analysis with adjustment for trial centres did not alter the results (not presented).

Table 2
Results from statistical analysis separated into intention to treat (ITT) and per protocol (PP) populations with complete cases.

Outcome	Mean Control	Mean Intervention	MeanΔ (CI95%)	p-value	n Control	n Intervention
Primary outcomes, 12 months after ICU, ITT.						
HRQOL, SF-36, MCS	50.18	48.83	1.35(−3.13–5.82)	0.55	60	51
HRQOL, SF-36, PCS	49.82	47.96	1.86 (−1.88–5.59)	0.33	60	51
Secondary outcomes, 3 months after ICU, ITT						
HRQOL, SF-36, MCS	47.34	47.19	−0.13 (−4.23–3.99)	0.95	78	61
HRQOL, SF-36, PCS	51.41	48.26	2.85 (−0.63–6.32)	0.11	78	61
SOC-13	70.57	68.85	1.52 (−3.22–6.26)	0.53	75	55
HADS- A	5.74	6.14	−0.40 (−1.89–1.1)	0.43	81	65
HADS- D	3.11	3.86	−0.75 (−1.95–0.45)	0.97	81	65
HTQ-IV score	29.46	32.29	−2.72 (−5.94–0.50)	0.10	79	63
Secondary outcomes, 12 months after ICU, ITT						
SOC-13	70.03	67.53	2.21 (−3.37–7.80)	0.43	61	50
HADS- A	4.86	5.59	−0.73 (−2.18–0.72)	0.99	66	54
HADS-D	2.71	3.39	−0.68 (−1.89–0.54)	0.16	66	54
HTQ-IV score	29.44	30.51	−1.07 (−4.73–1.85)	0.56	64	51
Difference scores, 3–12 months after ICU, ITT.						
HRQOL, SF-36, MCS	2.51	3.24	−0.73 (−5.16–3.70)	0.75	54	39
HRQOL, SF-36, PCS	−0.32	−0.56	0.24 (−2.40–2.88)	0.86	54	39
SOC-13	1.04	−0.41	1.44 (−3.22–6.10)	0.54	54	42
HADS- A	−1.27	−0.35	−0.93 (−2.13–0.28)	0.89	62	49
HADS- D	−0.74	−0.41	−0.33 (−1.25–0.59)	0.89	62	49
HTQ-IV score	−1.17	−1.38	0.25 (−2.05–2.55)	0.83	60	46
Primary outcomes, 12 months after ICU, PP.						
HRQOL, SF-36, MCS	49.94	48.49	1.45 (−3.12–6.01)	0.53	61	50
HRQOL, SF-36, PCS	49.30	48.16	1.15 (−2.69–4.99)	0.56	61	50
Secondary outcomes, 3 months after ICU, PP						
HRQOL, SF-36, MCS	47.23	46.88	0.34 (−4.23–4.91)	0.88	81	58
HRQOL, SF-36, PCS	50.87	48.46	2.41 (−1.41–6.22)	0.22	81	58
SOC-13	69.91	68.57	1.34 (−3.93–6.62)	0.62	78	52
HADS- A	6.03	6.23	−0.2(−1.83–1.44)	0.40	70	57
HADS- D	3.29	3.88	−0.59 (−1.89–0.71)	0.72	70	57
HTQ-IV score	29.81	32.94	−3.13 (−6.59–0.92)	0.08	82	60
Secondary outcomes, 12 months after ICU, PP						
SOC-13	69.56	67.22	2.34 (−3.39–8.07)	0.42	62	49
HADS- A	4.98	5.65	−0.66 (−2.14–0.82)	0.84	66	51
HADS- D	2.79	3.45	−0.66 (−1.91–0.58)	0.14	66	51
HTQ-IV score	29.51	30.82	−1.31 (−5.05–2.43)	0.49	64	52
Difference scores 3–12 months after ICU, PP.						
HRQOL, SF-36, MCS	2.36	3.57	−1.20 (−5.80–3.39)	0.60	55	38
HRQOL, SF-36, PCS	−0.60	−0.20	−0.40 (−3.10–2.31)	0.77	55	38
SOC-13	0.98	−0.32	1.30 (−3.60–6.19)	0.60	54	41
HADS-A	−2.83	−2.55	−0.27 (−5.52–4.98)	0.89	63	47
HADS-D	−0.71	−0.50	−0.21 (−1.16–0.74)	0.83	62	46
HTQ-IV score	−1.24	−1.49	0.25 (−2.14–2.64)	0.84	60	46

Discussion

The main finding of the present study was that the relatives did not benefit from the recovery programme intended for intensive care survivors. We had expected a statistically significant increase in the MCS scores for participants randomised to intervention compared to controls 12 months post-ICU discharge. Also the secondary objectives (MCS at 3 months, PCS, SOC, anxiety, depression, and PTSD at three and 12 months post-ICU) showed no effectiveness in either primary or secondary outcomes.

The MCS scores were higher (mean 37 and 41) and PCS similar compared to previous studies (mean 48 and 49) at 12 months post-ICU (Bayen et al., 2013; Rueckriegel et al., 2015), but scores were below the Danish age-matched population (Bjørner et al., 1997). Previous studies have included relatives of ICU-patients with severe brain injuries (Bayen et al., 2013; Rueckriegel et al., 2015). This population might differ from the population in our study and this can perhaps explain why MCS was observed as higher in present study while the PCS was similar (Bayen et al., 2013; Rueckriegel et al., 2015). MCS scores were also lower among relatives of general ICU patients at three months (44.05) than found in our study (Azoulay et al., 2005). As such, the results are inconclusive.

The SOC of relatives in our study was higher than those found in other studies, including studies in breast cancer patients (6 months, mean 59) and patients with schizophrenia (mean 64) (Khanjari et al., 2012; Mizuno et al., 2012). However, the SOC in our study was similar to two population studies in Denmark (mean 65) and Sweden (mean 70), respectively (Due and Holstein, 1998; Nilsson et al., 2010).

Symptoms of anxiety, depression and PTSD in our study was lower than seen in similar studies including cross-sectional studies (anxiety 6.5–7, depression 4–5) (McAdam et al., 2012; Matt et al., 2017) and multicentre trials with relatives of ICU patients (Jones et al., 2004; Carson et al., 2016). A RCT including relatives of patients with chronic critical illness evaluated family palliative care-led meetings and found no effect on anxiety (7.2 and 6.4; Δmean 0.8; $p = 0.12$), depression (4.9 and 5.0; Δmean 0.8; $p = 0.97$), and PTSD (Δmean 4.1, $p = 0.05$) at 3 months post-ICU (Carson et al., 2016). Another RCT testing ICU diaries used by relatives demonstrated higher levels of anxiety (6.8 and 7.3), depression (3.7 and 4.6), and PTSD (prevalence: 49% PTSD) than our study (Jones et al., 2004). These two trials found conflicting evidence of the effectiveness of the intervention on relatives' PTSD, which might be explained by the different content of the interventions (Carson et al., 2016; Jones et al., 2004). Two systematic reviews evaluated the effectiveness of post-ICU follow-up interventions and concluded that there was limited effectiveness on relatives' psychological health with the exception of an ICU-diary intervention aiming at reducing relatives' PTSD (Ullman et al., 2015; Lasiter et al., 2016). Our study observed no beneficial or detrimental effectiveness at 3 and 12 months post-ICU, but observed lower symptoms of PTSD by the HTQ-IV, when compared to a Danish population of elderly bereaved (mean-age 75, mean 51) (Elklit and O'connor, 2005).

Relatives in the present study had a high MCS, maintained strong SOC and had few symptoms of anxiety, depression and PTSD at three and 12 months post-ICU. Overall, enrolment of relatives was made on the basis of patients' consent to the RAPIT-study, and they had surprisingly fewer negative consequences than anticipated when we initiated the trial and compared the findings to other studies. Potential explanations for this variation and lack of benefit of the programme's effectiveness might be attributed to the patients' HRQOL. The RAPIT-study found that post-ICU survivors had a relatively satisfactory life with higher HRQOL, strong SOC, and less psychological complications in comparison to the literature in general (Jensen et al., 2016). Only 47% of relatives from the patients in the RAPIT-study participated in the present study, and 39% of relatives dropped out during the one-year follow-up.

The drop-out rate might be a matter of concern. In a prospective multicentre study both patients (n = 289) and relatives (n = 471) were interviewed about anxiety, depression and PTSD symptoms to compare the incidence of these symptoms in couples (Fumis et al., 2015). Fumis et al. (2015) showed that relatives' symptoms persisted at 3 months, while they decreased in patients (Fumis et al., 2015). Fumis et al. (2015) indicated that non-responding participants could be suffering and therefore avoided contact with the memories and might have been at risk for PTSD (Fumis et al., 2015). It is unknown if this is the case in the present study, but it could also be attributed to the relevance of the intervention for relatives that might need other interventions to aid psychological recovery (Aitken et al., 2017). The intervention may have been inappropriate for relative's psychological health as only few symptoms were recorded, or that a single consultation had insufficient impact. Our intervention could, perhaps, be improved by reengineering the RAPIT-study to target the relatives as well as the patients to accommodate their needs in an interprofessional team and increasing the frequency of consultations, or by including an ICU diary (Jones et al., 2004). Research in interventions that focus on relatives are missing and should be a priority in future research. These results highlight the need for further research into intervention for both patient and relatives based on their individual need during recovery of critical illness. Relatives of ICU survivors may have existential issues as patients, and these are not captured in the questionnaires used in this study. We recommend that new instruments are developed and validated to assess specific problems of relatives, as some issues are lost in generic instruments.

Limitations

This present study was strengthened by the multi-centre RCT design increasing generalisability. Imputations of data were made to avoid bias (Sterne et al., 2009). All questionnaires used have been validated, however none of them have been validated specifically for relatives of post-ICU patients. Our greatest limitation was sample size; we did not achieve the target sample size because participants were limited to relatives of patients in the RAPIT-study. The RAPIT-study suffered big expected losses to follow-up partly because of high mortality rate. Moreover, the RAPIT-study did not show superiority regarding the patients' HRQOL (Jensen et al., 2016), and given the evidence showing that QOL of patients affects their relatives, the limited effectiveness was unsurprising.

Conclusion

This study did not demonstrate statistically significant effect of the recovery programme on relatives' HRQOL, SOC, symptoms of anxiety, depression and PTSD at three or 12 months post-ICU. The study indicates that HRQOL in relatives may be higher than found in previous studies and this may contribute to power calculations in future studies. Future studies should be conducted on a larger scale and aimed specifically at relatives to make conclusions with a higher probability.

Funding source

The study was supported by The Novo Nordisk Foundation [NNF13OC0006107], the Danish Nursing Organization, and Nordsjællands Hospital, University of Copenhagen, Denmark.

Conflicts of interest

No conflict of interest has been declared by the authors.

Ethical statement and clinical trial information

The trial protocol was registered at ClinicalTrials.gov (NCT03264365). Ethical approval given by the National Committee on Health Research ethics (No. 17-000048) and the Danish Data Protection Agency (REG-098-2017). PARTICIPANTS CONSENTED (CONSENT FORM GIVEN) for the data collection to be carried.

Author declaration

The authors meet the criteria for authorship, have approved the final article and all those entitled to authorship are listed as author.

Acknowledgements

We wish to thank all the patients and relatives for their participation and the nurses in the RAPIT group for their engagement and collaboration during the study. The RAPIT Steering Committee: Jensen, Overgaard, Christensen, Bestle, and Egerod. RAPIT Group (in addition to the authors): Department of Anesthesiology: Hansen R.L., Kjerrumgård H., Nordsjælland Hospital, Copenhagen University Hospital; Figgé CFN, Østergaard K, Nykøbing Falster Hospital; Jeppesen MJ, Klausholm AD, Joergensen JV, Bødker K, Lehmkuhl L, Svendborg Hospital, Odense University Hospital; Pedersen ASB, Brix LD, Grode LB, Hospitalsenheden Horsens; Christoffersen S, Milling RW, Næstved Hospital, Copenhagen University Hospital; Wiborg E, Bundgaard BS, Aabenraa Hospital, South Jutland Hospital; Mortensen CB, Larsen CF, Knudsen H, Herlev Hospital, Copenhagen University Hospital; Markussen HB, Eriksen C, Jensen U, Sønderborg Hospital, South Jutland Hospital; Nielsen S, Larsen MC, Heart Centre, Rigshospitalet, Copenhagen University Hospital; Skjølstrup KK, Knudsen B, Fischer S, Esbjerg, Sydvestjysk Hospital. We wish to thank statistician KB Christensen, Section of Biostatistics, University of Copenhagen for assistance in conducting the analysis plan and JY Moberg and S Bohart for their valuable support in first draft of the manuscript.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.iccn.2018.03.002.

References

Aitken, L.M., Rattray, J., Kenardy, J., Hull, A.M., Ullman, A.J., Le Brocque, R., Mitchell, M., Davis, C., Castillo, M.I., Macfarlane, B., 2017. Perspectives of patients and family members regarding psychological support using intensive care diaries: an exploratory mixed methods study. J Crit Care 38, 263–268.

Angus, D.C., Carlet, J., 2003. Surviving intensive care: a report from the 2002 Brussels Roundtable. Intensive Care Med. 29 (3), 368–377.

Ashby, M., Stoffell, B., 1995. Artificial hydration and alimentation at the end of life: a reply to Craig. J. Med. Ethics 21 (3), 135–143.

Azoulay, E., Pochard, F., Kentish-Barnes, N., Chevret, S., Aboab, J., Adrie, C., Schlemmer, B., 2005. Risk of post-traumatic stress symptoms in family members of intensive care unit patients. Am. J. Respir. Crit. Care Med. 171 (9), 987–994.

Bayen, E., Pradat-Diehl, P., Jourdan, C., Ghout, I., Bosserelle, V., Azerad, S., Azouvi, P., 2013. Predictors of informal care burden 1 year after a severe traumatic brain injury: results from the PariS-TBI study. J. Head Trauma Rehabil. 28 (6), 408–418.

Bjelland, I., Dahl, A.A., Haug, T.T., Neckelmann, D., 2002. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. J. Psychosom. Res. 52 (2), 69–77.

Bjørner, J.B., Damsgaard, M.T., Watt, T., Bech, P., Rasmussen, N.K., 1997. Dansk manual til SF-36: Et spørgeskema om helbredsstatus. Lægemiddel industri foreningen.

Boutron, I.E.A., 2008. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. Am. Coll. Phys. 148, 295–309.

Carson, S.S., Cox, C.E., Wallenstein, S., Hanson, L.C., Danis, M., Tulsky, J.A., Nelson, J.E., 2016. Effect of palliative care-led meetings for families of patients with chronic critical illness: a rando mized clinical trial. JAMA 316 (1), 51–62.

Davidson, J.E., Jones, C., Bienvenu, O.J., 2012. Family response to critical illness: postintensive care syndrome-family. Crit. Care Med. 40 (2), 618–624.

Due, E.P., Holstein, B.E., 1998. Sense of coherence, social class and health in a Danish population study. Ugeskr. Laeger 160 (51), 7424–7429.

Elklit, A., O'Connor, M., 2005. Post-traumatic stress disorder in a Danish population of elderly bereaved. Scand. J. Psychol. 46 (5), 439–445.

Eriksson, M., Lindstrom, B., 2005. Validity of Antonovsky's sense of coherence scale: a systematic review. J. Epidemiol. Commun. Health 59 (6), 460–466.

Frivold, G., Slettebo, A., Dale, B., 2016. Family members' lived experiences of everyday life after intensive care treatment of a loved one: a phenomenological hermeneutical study. J. Clin. Nurs. 25 (3–4), 392–402.

Fumis, R.R., Ranzani, O.T., Martins, P.S., Schettino, G., 2015. Emotional disorders in pairs of patients and their family members during and after ICU stay. PLoS One 10 (1).

Goldfarb, M.J., Bibas, L., Bartlett, V., Jones, H., Khan, N., 2017. Outcomes of patient- and family-centered care interventions in the ICU: a systematic review and meta-analysis. Crit. Care Med.

Jensen, J.F., Egerod, I., Bestle, M.H., Christensen, D.F., Elklit, A., Hansen, R.L., Overgaard, D., 2016. 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. Intensive Care Med. 42 (11), 1733–1743.

Jones, C., Skirrow, P., Griffiths, R.D., Humphris, G., Ingleby, S., Eddleston, J., Gager, M., 2004. Post-traumatic stress disorder-related symptoms in relatives of patients following intensive care. Intensive Care Med. 30 (3), 456–460.

Khanjari, S., Oskouie, F., Langius-Eklof, A., 2012. Lower sense of coherence, negative religious coping, and disease severity as indicators of a decrease in quality of life in Iranian family caregivers of relatives with breast cancer during the first 6 months after diagnosis. Cancer Nurs. 35 (2), 148–156.

Lasiter, S., Oles, S.K., Mundell, J., London, S., Khan, B., siter et al.. Critical care follow-up clinics: a scoping review of interventions and outcomes. Clin. Nurse Spec. 30 (4), 227–237.

Long, A.C., Kross, E.K., Curtis, J.R., 2016. Family-centered outcomes during and after critical illness: current outcomes and opportunities for future investigation. Curr. Opin. Crit. Care 22 (6), 613–620.

Matt, B., Schwarzkopf, D., Reinhart, K., Konig, C., Hartog, C.S., 2017. Relatives' perception of stressors and psychological outcomes – results from a survey study. J. Crit. Care 39, 172–177.

McAdam, J.L., Fontaine, D.K., White, D.B., Dracup, K.A., Puntillo, K.A., 2012. Psychological symptoms of family members of high-risk intensive care unit patients. Am. J. Crit. Care 21 (6), 386–393. quiz 394.

Mizuno, E., Iwasaki, M., Sakai, I., Kamizawa, N., 2012. Sence of coherence and quality of life in family caregivers of persons with schizophrenia living in the community. Arch. Psychiatr. Nurs. 26 (4), 295–306.

Mollica, R.F., Caspi-Yavin, Y., Bollini, P., Truong, T., Tor, S., Lavelle, J., 1992. The Harvard Trauma Questionnaire. Validating a cross-cultural instrument for measuring torture, trauma, and posttraumatic stress disorder in Indochinese refugees. J. Nerv. Ment. Dis. 180 (2), 111–116.

Nilsson, K.W., Leppert, J., Simonsson, B., Starrin, B., 2010. Sense of coherence and psychological well-being: improvement with age. J. Epidemiol. Community Health 64 (4), 347–352.

Pochard, F., Darmon, M., Fassier, T., Bollaert, P.E., Cheval, C., Coloigner, M., Azoulay, E., 2005. Symptoms of anxiety and depression in family members of intensive care unit patients before discharge or death. A prospective multicenter study. J. Crit. Care 20 (1), 90–96.

Rodriguez, A.M., Gregorio, M.A., Rodriguez, A.G., 2005. Psychological repercussions in family members of hospitalised critical condition patients. J. Psychosom. Res. 58 (5), 447–451.

Rueckriegel, S.M., Baron, M., Domschke, K., Neuderth, S., Kunze, E., Kessler, A.F., Ernestus, R.I., 2015. Trauma- and distress-associated mental illness symptoms in close relatives of patients with severe traumatic brain injury and high-grade subarachnoid hemorrhage. Acta Neurochir. (Wien) 157 (8), 1329–1336. discussion 1336.

Sterne, J.A., White, I.R., Carlin, J.B., Spratt, M., Royston, P., Kenward, M.G., Carpenter, J.R., 2009. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. BMJ 338, b2393.

Svenningsen, H., Langhorn, L., Agard, A.S., Dreyer, P., 2017. Post-ICU symptoms, consequences, and follow-up: an integrative review. Nurs. Crit. Care 22 (4), 212–220.

Ullman, A.J., Aitken, L.M., Rattray, J., Kenardy, J., Le Brocque, R., MacGillivray, S., Hull, A.M., 2015. Intensive care diaries to promote recovery for patients and families after critical illness: a Cochrane systematic review. Int. J. Nurs. Stud. 52 (7), 1243–1253.

van Beusekom, I., Bakhshi-Raiez, F., de Keizer, N.F., Dongelmans, D.A., van der Schaaf, M., 2016. Reported burden on informal caregivers of ICU survivors: a literature review. Crit. Care 20, 16.