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Effect of a primary care management intervention on mental-health-related quality of life among survivors of sepsis: a randomized clinical trial

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Abstract

Importance—Sepsis survivors face long-term sequelae which diminish health-related quality of life (HRQoL) and result in increased care needs in the primary care setting as medication, physiotherapy or mental health care.

Objective—To examine if a primary care-based intervention improves mental HRQoL

Design, Setting and Participants—A randomized clinical trial was conducted between February 2011 and December 2014. 291 patients ≥18 years who survived sepsis (including septic shock) were recruited from nine intensive care units (ICU) across Germany.

Intervention—Participants were randomized to usual care (n=143) or to a 12-month intervention (n=148). Usual care was provided by their primary care physician (PCP) and included periodic contacts, referrals to specialists and prescription of medication and/or other treatment. The intervention additionally included PCP and patient training, case management provided by trained nurses and clinical decision support for PCPs by consulting physicians.

Main outcome—The primary outcome was change in mental HRQoL between ICU discharge and six months post-ICU using the Mental Component Summary (MCS) of the Short-Form Health Survey 36 (SF-36; range 0-100; higher ratings indicating lower impairment, minimal clinically important difference five score points).

Results—The mean age of the 291 patients was 61.6 years (SD 14.4), 66.2% (n=192) were male, and 84.4% (n=244) required mechanical ventilation during their ICU stay (median 12 days, range 0-134). At six and 12 months post-ICU, 75.3% (n=219, 112 intervention, 107 control) and 69.4% (n=202, 107 intervention, 95 control) completed follow-up, respectively. Overall mortality was 13.7% at six months (40 deaths, 21 intervention, 19 control) and 18.2% at 12 months (53 deaths, 27 intervention, 26 control). Among intervention group patients, 104 (70.3%) received the intervention at high levels of integrity. There was neither a significant difference in change of MCS scores (intervention group baseline, mean=49.1, six months=52.9, change=3.79 score points (95%CI 1.05; 6.54) vs. control group baseline, mean =49.3, six months=51.0, change=1.64 score points (95%CI -1.22; 4.51) mean treatment effect=2.15 (95%CI -1.79; 6.09); p=0.28), nor in PCP care delivered between both groups.

Conclusions and relevance—Among sepsis survivors, a primary-care-focused team-based intervention did not improve mental HRQoL or impact PCP care compared with usual care.

Trial Registration—ISRCTN registry; http://www.isrctn.com/ISRCTN61744782

Introduction

Sepsis is a major health problem worldwide.[1] In 2008, it has been estimated to occur in 2% of hospitalized patients in the United States and is expected to rise further in the future, with an even higher incidence in developing countries.[2] The risk of dying from sepsis has decreased in recent decades due to earlier detection and more effective treatment.[3] Although more patients survive sepsis and are increasingly discharged from hospital[4], they often experience functional disability, cognitive impairment and psychiatric morbidity[5,6], resulting in diminished health-related quality of life (HRQoL)[7], increased healthcare costs[8,9] and burden on patients and their families.[7,10]

Many sepsis survivors have multiple medical comorbidities that are typically managed in primary care. Yet, interventions for managing sepsis sequelae in primary care have not been developed.[5,11] A systematic review of outpatient interventions for patients surviving critical illnesses showed heterogeneous and small effects on clinical outcomes such as depression and posttraumatic stress disorder (PTSD) symptoms.[12] Studies with post-ICU follow-ups of six months or more are rare.[7]

The purpose of this randomized clinical trial was to assess whether a primary care-based intervention[13] would improve mental-health-related quality of life among survivors of sepsis compared with usual care.

Methods

Study design and population

A multicenter, non-blinded, two-arm randomized clinical trial was performed. The institutional review board of the Jena University Hospital approved the study protocol (file 3001/111). All patients and primary care physicians (PCPs) in the study provided written informed consent. Serious adverse events were reported to a data and safety monitoring board. Patients were recruited in nine ICU study centers across Germany between February 2011 and December 2013. Follow-up assessments were completed in December 2014. Patients were eligible for inclusion if they were adult (≥18 years old) survivors of severe sepsis, (now defined as ‘sepsis’[14]) or septic shock, and fluent in the German language. Clinical diagnoses on sepsis were made by intensivists according to International Classification of Diseases-10 (ICD-10) codes (R65.1/R57.2) and ACCP/SCCM consensus criteria.[15] Baseline interviews of patients were conducted by the study team within one month of ICU discharge. Key exclusion criteria was cognitive impairment, as determined by the Telephone Interview of Cognitive Status (TICS-M, score≤27).[16] After determining patient eligibility, the study team invited each patient's PCP to participate in the trial.

Randomization was stratified by ICU study centers and performed using computer-generated random permutated blocks (block size range 2-6), provided by an independent center for clinical trials at the University of Leipzig.

Intervention

The intervention was based on the Chronic Care Model[17]. Its core components included case management focusing on pro-active patient symptom monitoring, clinical decision support for the PCP and training for both patients and their PCPs in evidence-based care. Three nurses with ICU experience were trained as outpatient case managers of sepsis survivors in an eight hour workshop. The training included information on sepsis sequelae, communication skills, telephone monitoring and behavioral activation of patients that included goal-setting (‘sepsis case manager manual’, Supplement). Each case manager worked with 38-65 patients, starting with a 60-minute face-to-face training on sepsis sequelae (‘sepsis help book’, Supplement) that took place a median of eight days after ICU discharge [Q1=2; Q3=20]. This was followed by monthly telephone contact for six months, then once every three months for the final six months. Case managers monitored patients' symptoms using validated screening tools (‘sepsis-monitoring-checklist’, Supplement) on critical illness polyneuropathy/myopathy, wasting, neurocognitive deficits, PTSD, depressive and pain symptoms, as well as patient self-management behaviors focusing on physical activity and individual self-management goals. Each case manager reported results to one of three assigned consulting physicians (medical doctors with background in primary and critical care), who supervised the case managers and provided clinical decision support to the PCPs using a structured written report which included the ‘sepsis-monitoring checklist’ (Supplement, eFigure 3). The reports were stratified by urgency using a traffic light scheme: red signified “immediate intervention recommended”, yellow “intervention should be considered” and green “acceptable clinical status.” An evidence-based sepsis aftercare training for the patients' PCPs was provided individual, in-person by the consulting physicians (‘sepsis PCP manual’, Supplement). Intervention delivery was considered to have high integrity if the training was delivered to both patients and PCPs and the patient was monitored five or more times.

Control group patients received care as usual from their PCPs without additional information or monitoring. Usual sepsis aftercare included periodic contacts, referrals to specialists and prescription of medication and therapeutic aids, at quantities comparable to those for other populations with multiple chronic conditions[18]. In Germany most primary care practices are privately operated by one or two PCPs with limited access to specialist care.[19] There are no outpatient post-sepsis/ICU follow-up clinics or national treatment guidelines for sepsis aftercare in Germany.

Baseline data and outcomes

Baseline data were collected at in-person interviews with patients while they were still hospitalized. Further clinical data were obtained from their ICU records. Since the majority of patients remained hospitalized and incapacitated, baseline data collection of Activities of Daily Living (ADL), physical function and insomnia was not feasible.

The primary outcome was change in mental HRQoL between ICU discharge and six months post-ICU, as assessed by the Mental Component Summary score (MCS) of the Short Form-36 Health Survey (SF-36, range 0-100 with higher ratings indicating low

impairment[20](+). The SF-36 consists of eight sub-scores and is valid and reliable in both post-ICU[21] and German primary care populations.[22]

Secondary outcomes at six months were derived from (1) the other SF-36 scales (range 0-100(+); (2) overall survival; (3) mental health outcomes including the Major Depression Inventory (MDI, range 0-50, high scores indicate high impairment(-)[23]), the Post-Traumatic Symptom Scale (PTSS-10, range 10-70(-)[24]), the TICS-M (range 0-50(-)[16]; (4) functional outcomes including ADL (range 0-11(+)[25], the Extra Short Musculoskeletal Function Assessment regarding physical function and disability (XSMFA-F/B, range both 0-100(-)[26], the Graded Chronic Pain Scale including a Disability Score and Pain Intensity (GCPS-DS/PI, range 0-100(-)[27], the Neuropathy Symptom Score (NSS, range 0-10(-)[28], the Malnutrition Universal Screening Tool (MUST, range 0,-2(-)[60]) including the Body Mass Index (BMI)[61] and the Regensburg Insomnia Scale (RIS, range 0-40(-).[29]

Process-related outcomes (5) included the Patient Assessment of Care for Chronic Conditions (PACIC, (0-10(+)[30,31] and measures of medication adherence, the modified Morisky questionnaire (range 1-5(-)[32] and the Short Form for Medication Use (KFM, range 0-12(-).[33] In addition, process-related data from PCP documentation (6) were derived, including PCP contacts (no.), referrals to specialists (no.), level of nursing, inability to work (days), remedies and therapeutic aids (no.) and LOS in hospital and rehabilitation clinic (days). All 31 secondary outcomes pre-specified in the statistical analysis plan (SAP) (see Supplement) are reported in the Supplement (eTable 2-8).

In addition, we also included as secondary outcomes all of the above measured at 12 months post-ICU. Outcome assessment was conducted by non-blinded assessors by phone.

Initially, the MCS as well as the Physical Component Summary score (PCS) of the SF-36 were chosen for primary outcome to provide a multicomponent score reflecting HRQoL (as noted in the study protocol[13] and the ISRCTN registration). However, based on review of the literature[12] highlighting the importance of mental health outcomes in post-ICU care, the primary outcome was specified to the MCS.

Statistical analysis

The aim of the study was to detect a difference at six months of five points or more in mean MCS scores since this amount of change is thought to be clinically meaningful.[22] A common standard deviation of 10 was assumed on the basis of a typical German population with acute and chronic diseases.[34] At a two-sided significance levelα = 0.05, a total of 2×86=172 patients were required to detect the above mentioned effect with a power of 90%. Allowing for an additional ~40% for drop-outs and mortality, an initial sample size of 287 was required. The confirmatory test for the primary outcome was Welch's t-test for independent groups which was run in the intention-to-treat population. The confirmatory analyses did not consider intra-practice clustering because n=155 (96.9%) of intervention practices and n=141 (95.1%) of control practices included only one patient. The effect clustering and missing values were explored by e.g. linear mixed models and imputations. Details on methods and results of exploratory sensitivity analyses are provided in the Supplement (eMethods). All secondary outcome analyses were exploratory and not adjusted

for multiple tests. They were done using the t-test, Fisher's exact test and the Wilcoxon-Mann-Whitney test, as appropriate. Overall survival was estimated using the Kaplan-Meier method with study groups compared using the log-rank test. A confirmatory and exploratory two-sided significance level of α=0.05 was applied, and effect size estimates with 95% confidence intervals (95%CI) were reported. All statistical analyses were performed using R (version 3.2.3).[35]

Results

Baseline Characteristics

A total of 361 patients were eligible, of which 291 (80.6%) agreed to participate, with 148 patients randomized to the intervention and 143 patients to the control group (Figure 1). Overall, baseline characteristics were well balanced (Table 1). The mean age of the cohort was 61.6 years (standard deviation (SD) 14.4), 244 patients (84.4%) received mechanical ventilation, the median ICU LOS was 26 days [Q1=13, Q3=46]. Mental HRQoL was close to the normal population (mean MCS 49.0, SD 12.5), physical HRQoL was low (mean SF-36 (PCS) 25.3,SD 8.8). 24.2%. (68 of 281) had substantial depressive symptoms, 14.6% (41 of 281) reported substantial PTSD symptoms and 19.6% (54 of 276) indicated severe pain (Table 1). Among the entire cohort, 59.2% (164 of available 277) reported neuropathic symptoms.

Follow up

All included 291 patients were cared for by 159 intervention PCPs and 148 control PCPs. Due to some patient-initiated PCP changes, the number of PCPs was slightly larger than the number of patients (details see Supplement, eMethods). Among the 307 assigned PCPs, N=294 (95.8%) were willing to participate. Loss to follow-up due to withdrawal or non-response totaled 31 patients (10.7%) at six months and an additional nine patients (3.1%) at 12 months post-ICU, and was evenly distributed across study groups, see Figure 1.

Intervention delivery

Of the 148 patients assigned to the intervention, 130 (87.8%) received patient training from case managers and 125 (84.5%) of their PCPs received training from a consulting physician. There was a mean gap of 62.38 days [Q1=36, Q3=99] between ICU discharge and PCP training, caused by the wide range of patient clinical courses. 104 (70.3%) patients in the intervention group received the planned intervention at high levels of intervention integrity (see Supplement, eFigure2). Incomplete intervention was usually due to death of the patient (n=24 (54%) of those with less than five monitoring calls). Reduction of motoric function (n=204, 27.1%) and pain intensity (n=201, 27.2%) were the post-sepsis symptoms most rated “red” (=“immediate intervention recommended”) in all 756 structured monitoring reports (see Supplement, eTables 10).

No adverse events related to the intervention were reported.

Primary outcome

There was no significant difference between both groups in the primary outcome: The mean change MCS score was 3.79 score points (95%CI, 1.05; 6.54) for the intervention and 1.64 score points (95%CI, 1.22; 4.51) for the control group, leading to a mean treatment effect of 2.15 (95%CI -1.79; 6.09); p=0.28; baseline, mean=49.1 intervention vs. 49.3 control; six months, mean=52.9 intervention vs. 51.0 control (all data related to n=200 patients (n=104 intervention, n=96 control) with both MCS scores available at baseline and six months; due to rounding, change scores presented may not add up precisely). These results were unchanged in several sensitivity analyses (Supplement, eTable 1).

Secondary outcomes

A total of 63 secondary outcomes were analyzed at both six and 12 months (including the 12-month MCS). A respective 28 (six month) and 30 (12 month) outcomes did not show significant differences (at an uncorrected α=0.05) between both groups, including physical HRQoL and mental health outcomes (Supplement, eTables 2-3). Overall mortality at six and 12 months post-ICU was n=40 (13.7%) and n=53 (18.2%), respectively (Supplement, eFigure1). If any, potential intervention effects were observed in measures of functional outcomes only: At the six months, sepsis survivors receiving the intervention had better physical functioning (XSFMA-F, mean (95%CI), 38.0 (32.5; 43.5) vs.46.9 (40.9; 52.9); p=0.04, difference (95%CI) -8.9 (-17.02;-0.78), less physical disability (XSFMA-B,, 42.5 (36.6; 48.4) vs. 52.4 (46.2; 58.7); p=0.03, difference (95%CI) -9.9 (-18,49;-1.31) and fewer ADL impairments, mean (95%CI), 8.6 (8.0; 9.1) vs. 7.6 (7.0; 8.2);p=0.03; difference (95%CI) 1.0 (0.16;1.84) than usual care. After adjusting for pre-specified baseline covariates, these potential effects were persistent. In addition, sepsis survivors receiving the intervention had potentially fewer sleep impairments at 12 months post-ICU than controls (RIS, mean (95%CI), 10.3 (9.2; 11.4) vs. 12.1 (10.8; 13.4); difference (95%CI) -1.8 (-3.5;-0.10).

Finally, the PCP documentation data at six and 12 months provided no evidence for group differences in PCP care (Supplement, eTable 8).

Discussion

Among sepsis survivors, a primary-care-based intervention, compared with usual care, did not improve mental HRQoL.

To our knowledge, this is the first large scale, randomized controlled clinical trial of an intervention to improve outcomes in sepsis survivors in primary care.

This sample of sepsis survivors had similar mean ages and rates of existing comorbidities as compared to other cohorts.[36,37] The prevalence of depressive and PTSD symptoms was slightly below other critical illness survivor populations,[38,39] whereas neuropathic symptoms and severe pain were more frequent.[40,41] Physical function, as measured by the SF-36 PF, was substantially lower than in the German population (mean 85.71 (SD 22.1), n=2886)[34], and also lower than in some comparable cohorts[42,43] and intervention studies.[44,45] Thus,

patients may have been more sensitive to the intervention's focus on increasing motivation to be physically active.

Study patients were exposed to longer durations of mechanical ventilation and ICU LOS than reported in other studies.[4] ICU LOS and duration of mechanical ventilation were shown to generally be longer in Europe than in the US, especially in sepsis survivors.[46,47] In addition, extensive ICU LOS may have facilitated patient identification by the intensivists.

There was no evidence for a differential treatment effect on the study's primary outcome, post-sepsis MCS scores. This finding is similar to previous trials of care management interventions following critical illness[12,44,45,48]. The absence of an intervention effect on the primary and most secondary outcomes can be considered along the PICO frameworks:[49]

Population

The studied cohort experienced heterogeneous clinical multiple conditions. This primary-care based intervention may not have been sufficiently focused in order to address all their diverse medical and psychological needs.[50] Future trials may evaluate interventions in different patient subgroups targeting specific post-sepsis sequelae. Larger samples should be included, in order to address smaller but potentially still clinically relevant effects of primary care interventions.

Intervention

The exploratory analyses indicated no intervention effects on mental health symptoms. These results may reflect lack of intervention intensity and specificity, or absence of clinically effective interventions. However, there is growing evidence that following critical illness, mental health outcomes can be improved through effective psychological interventions targeting specific syndromes.[50,51]

Controls

According to process data derived from control PCPs (Supplement, eTable 8), usual sepsis aftercare in Germany seems to be highly intensive. PCP training and consultation may have been insufficient to yield a meaningful improvement in the level of care. Observational research may provide more insights in existing usual sepsis aftercare in diverse health care systems.

Outcome

The wide range of post-sepsis sequelae may not be adequately reflected in a rather global outcome measure change such as the SF-36 MCS. Furthermore, cohort's baseline mental HRQoL was similar to healthy population norms in Germany, reflecting a limited potential for improvement in the MCS. Finally, the exclusion of patients with more severe cognitive dysfunction may have led to a ceiling effect compared to other trials. For future trials, more specific primary outcomes should be considered.

Up to years after the ICU discharge many patients seem to share their needs with a reliable medical professional[52]. Yet the PCP isn't involved systematically in post ICU care.[53,54] This

study may shed light on the PCP relevance, addressing major concerns recently identified as "barriers to practice."[55] These include checks on transition from ICU through to community reintegration, linkage and clinical decision support to primary care, inclusion of a case manager and educational information for patients and PCPs. Compared to the large scale PRaCTICAL trial on follow-up care in ICU-clinics[45] this study defines a clear function for the PCP in sepsis aftercare. Follow-up care combining specialized ICU-clinics and integrated PCP may improve outcomes.

This study's exploratory findings suggest possible improvements of physical function and ADL impairments. Additional research is needed to confirm these results. Possible mechanisms of action for these findings may include increased patient motivation (despite of the presence of pain) to partake in physical activity due to regular case manager phone calls with goal-setting and basic behavioral activation. Increased PCP supportiveness in the intervention group may also have motivated patients to be more pro-active, possibly reflected by the increased rating in number of PACIC items (Supplement, eTable 9).

This study has strengths and limitations. It was possible to enroll a large number of patients in spite of the challenges of recruiting critically ill patients for research.[56] Intervention integrity went as planned[57] (Supplement, eFigure 2), including the acceptance of an external medical consultant by the patient's PCP. These findings are encouraging for further interventions in the primary care setting.

Loss to follow-up was balanced between the groups and low, in contrast to sample size calculations which allowed for 40% drop out. Baseline values were missing for some secondary outcomes due to patient's severely impaired clinical condition. A carry-over effect (from treatment to control) may have occurred for one PCP inducing a bias toward a null effect. Calling control patients to collect follow-up data may have led to an intervention effect possibly leading to underestimation of the intervention effects.[58]. In addition, non-blinded outcome assessments may also have biased the results.[59] The intervention is not generalizable to all sepsis survivors seen in various outpatient settings.

Conclusions

Among survivors of sepsis or septic shock, the use of a primary-care-focused team-based intervention, compared with usual care, did not improve mental HrQoL and did not change PCP care. Further research is needed to determine if other approaches to primary care management may be more effective to improve mental HQoL in sepsis survivors.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Points

Question

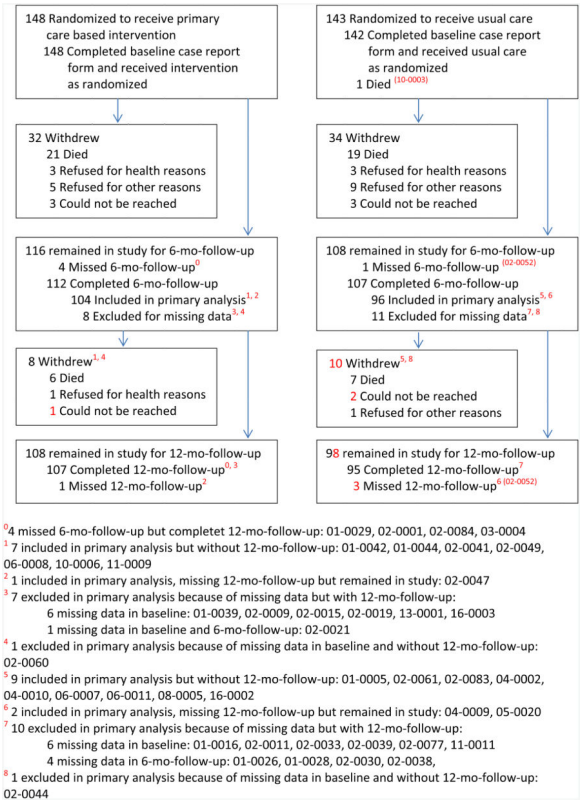
Does a primary care-based management intervention improve mental health-related quality of life (HRQoL) in sepsis survivors?

Findings

A randomized clinical trial was performed with 291 patients for 12 month. The intervention did not improve mental HRQoL.

Meaning

Future research is needed to improve mental HRQL in sepsis survivors.



[0] 4 missed 6-mo-follow-up but completet 12-mo-follow-up: 01-0029, 02-0001, 02-0084, 03-0004

[1] 7 included in primary analysis but without 12-mo-follow-up: 01-0042, 01-0044, 02-0041, 02-0049, 06-0008, 10-0006, 11-0009

[2] 1 included in primary analysis, missing 12-mo-follow-up but remained in study: 02-0047

[3] 7 excluded in primary analysis because of missing data but with 12-mo-follow-up:
6 missing data in baseline: 01-0039, 02-0009, 02-0015, 02-0019, 13-0001, 16-0003
1 missing data in baseline and 6-mo-follow-up: 02-0021

[4] 1 excluded in primary analysis because of missing data in baseline and without 12-mo-follow-up: 02-0060

[5] 9 included in primary analysis but without 12-mo-follow-up: 01-0005, 02-0061, 02-0083, 04-0002, 04-0010, 06-0007, 06-0011, 08-0005, 16-0002

[6] 2 included in primary analysis, missing 12-mo-follow-up but remained in study: 04-0009, 05-0020

[7] 10 excluded in primary analysis because of missing data but with 12-mo-follow-up:
6 missing data in baseline: 01-0016, 02-0011, 02-0033, 02-0039, 02-0077, 11-0011
4 missing data in 6-mo-follow-up: 01-0026, 01-0028, 02-0030, 02-0038,

[8] 1 excluded in primary analysis because of missing data in baseline and without 12-mo-follow-up: 02-0044

Figure 1. CONSORT flow diagram of patient recruitment and retention rates during the study course

Table 1

Baseline characteristics

Characteristics	All (n = 290)	Intervention (n = 148)	Control (n = 142)	NA (i; c)
Sociodemographics				
Age, years, mean (SD)	61.6 (14.4)	62.1 (14.1)	61.2 (14.9)	0; 0
Sex “Male”, No. (%)	192 (66.2)	105 (70.9)	87 (61.3)	0; 0
Family status “Married”, No. (%)	148 (52.1)	84 (57.9)	64 (46.0)	3; 3
Educational status “< High school”, No. (%)	98 (34.0)	54 (36.7)	44 (31.1)	1; 1
Care measures				
Recent surgical history, No. (%)				2; 1
Emergency	106 (36.8)	49 (33.6)	57 (40.1)	
Elective surgery	62 (21.5)	34 (23.3)	28 (19.7)	
No history	73 (25.3)	39 (26.7)	34 (23.9)	
Source of infection, No. (%)				3; 5
Community acquired	102 (36.0)	54 (37.2)	48 (34.8)	
Nosocomial (ICU or IMC)	139 (49.1)	70 (48.3)	69 (50.0)	
Nosocomial (general ward or nursing home)	42 (14.8)	21 (14.5)	21 (15.2)	
ICU length of stay days: median, mean (SD) [Q1;Q3]	26, 34.4 (27.2) [4; 27]	23, 31.5 (27.7) [4; 26]	29, 35.2 (26.7) [5; 28]	16; 11
Mech. ventilation, No. (%)	244 (84.4)	121 (82.3)	123 (86.6)	1; 1
if applicable, days: median, mean (SD) [Q1;Q3]	12, 18.5 (19.2) [4; 27]	10, 17.0 (17.5) [4; 26]	14, 19.9 (20.7) [5; 28]	5; 4
Renal replacement therapy, No. (%)	82 (28.5)	43 (29.3)	39 (27.7)	1; 2
if applicable, days: median, mean (SD)[Q1;Q3]	8, 12.3 (13.2) [4; 15]	7, 11.9 (13.7) [4; 14]	8, 12.8 (12.8) [5; 16]	5; 5
Clinical Measures				
Comorbidity: Charlson Index[a1], mean (SD)	4.0 (2.9)	4.0 (3.0)	4.0 (2.9)	1; 1
ICD-diagnoses, No., median, mean (SD)	9, 10.1 (4.7)	9, 9.6 (4.4)	10, 10.6 (5.1)	6; 7
BMI[b12], mean (SD)	27.3 (6.0)	27.3 (6.0)	27.3 (5.9)	3; 9
Depression				3; 6
MDI[c1], mean (SD)	18.1 (10.0)	18.4 (9.8)	17.8 (10.1)	
Depressive symptoms, No. (%)	68 (24.2)	36 (24.8)	32 (23.5)	
PTSD				3; 6

Characteristics	All (n = 290)	Intervention (n = 148)	Control (n = 142)	NA (i; c)
PTSS-10[d1], mean (SD)	23.6 (10.4)	24.0 (11.0)	23.2 (9.7)	
Score >35, No. (%)	41 (14.6)	22 (15.2)	19 (14.0)	
Cognition: TICS-M[cg2], mean (SD)	33.4 (3.6)	33.7 (3.4)	33.1 (3.9)	1; 0
Neuropathic symptoms				4; 9
NSS[e1] mean (SD)	3.6 (3.2)	3.6 (3.3)	3.7 (3.1)	
Score 3-10, No. (%)	164 (59.2)	83 (57.6)	81 (60.9)	
Pain				
Intensity: GCPS PI[f1] mean (SD)	43.8 (24.4)	43.7 (25.6)	43.9 (23.1)	5; 9
Disability: GCPS DS[f2] mean (SD)	36.2 (34.6)	36.0 (34.5)	36.4 (34.8)	7; 12
Severe pain: GCPS cat. >1, No. (%)	54 (19.6)	26 (18.2)	28 (21.0)	5; 9
Quality-of-Life Measures				
HRQoL				12; 15
SF-36 MCS [f2], mean (SD)	49.0 (12.5)	48.8 (12.5)	49.2 (12.6)	
SF-36 PCS [f2], mean (SD)	25.3 (8.8)	25.9 (9.4)	24.7 (8.0)	

Abbreviations: BMI, Body Mass Index; GCPS DS, Graded Chronic Pain Scale Disability Score; GCPS PI, Graded Chronic Pain Scale Pain Intensity; HRQoL, Health Related Quality Of Life; ICU, intensive care unit; IMC, Intermediate Care; MDI, Major Depression Inventory; NA (i; c), Not Available (intervention; control); NSS, Neuropathic Symptom Score; PTSD, Post Traumatic Stress Disorder; PTSS, Post-Traumatic Symptom Scale; SF-36 MCS, Short Form (36) Health Survey Mental Component Score; SF-36 PCS, Short Form (36) Health Survey Physical Component Score; TICS-M, modified Telephone Interview for Cognitive Status; NA, not available; i, intervention; c, control

Anchors:

[1]high score indicates high impairment,

[2]high score indicates low impairment

Ranges:

[a]The range of possible scores is 0-37,

[b]The range of possible scores is 9-46,

[c]The range of possible scores is 0-50,

[d]The range of possible scores is 10-70,

[e]The range of possible scores is 0-10,

[f]The range of possible scores is 0-100

[g]values only above 27 (inclusion criteria)