Journal of Critical Care 53 (2019) 149–154

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.journals.elsevier.com/journal-of-critical-care

Comparative validation of three screening instruments for posttraumatic stress disorder after intensive care

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ARTICLE INFO

Keywords:
Posttraumatic stress disorder
Intensive care
Sepsis
Screening
Sensitivity
Specificity

ABSTRACT

Purpose: Aim of the present study was to compare the validity of three screening instruments to assess symptoms of posttraumatic stress disorder (PTSD) after intensive care of sepsis.
Material and methods: Participants were recruited within a large multicenter patient cohort study on long-term sequelae of sepsis. Adult patients (n = 83) on average four months after intensive care of (severe) sepsis or septic shock were included (median age 64 years, 60% male). PTSD symptom severity was assessed by three different self-report measures: two versions of the Posttraumatic Stress Scale (PTSS-10; PTSS-14), and the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5). A clinical PTSD diagnosis was derived by using the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).
Results: Ten patients (12%) were diagnosed with PTSD. PTSS-10, PTSS-14, and PCL-5 revealed good reliability and concurrent validity. PTSS-14 showed the best accuracy in screening patients at risk for PTSD after intensive care with 80% sensitivity and 92% specificity at the recommended cutoff of 40.
Conclusions: Compared to PTSS-10 and PCL-5, PTSS-14 appeared more appropriate for post-ICU PTSD screening when validated against a DSM-5 diagnostic interview.

1. Introduction

Posttraumatic Stress Disorder (PTSD) is a common trauma and stress-related disorder that occurs following direct or indirect exposure to real or threatened death, actual or threatened serious injury or actual or threatened sexual violence [1]. PTSD is a common long-term outcome after intensive care of critical illness [2] and is considered as part of the Post-intensive care syndrome (PICS) [3]. The disorder is typically characterized by symptoms of flashbacks, nightmares, avoidance of trauma-related stimuli, difficulty concentration and sleeping, irritability and memory problems. Within the first year after ICU discharge median point prevalence of clinically relevant PTSD symptoms is about 20% [2,4,5].

Data from epidemiologic surveys indicate that a large majority of PTSD patients suffer from comorbid psychiatric disorders, most commonly depressive disorders, substance use disorders, and other anxiety disorders [6,7]. PTSD causes significant impairment in long-term daily functioning and quality of life [2] and might have negative effects on physical health [8]. Since PTSD might often persist for years if untreated [6], early screening of PTSD is inevitable to identify all patients at risk for developing PTSD in need of diagnostic follow-up. This requires sensitive instruments that can be applied efficiently in clinical practice.

Criteria for deriving a PTSD diagnosis are defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM). Since its inclusion in DSM-III, PTSD has undergone a number of changes in its diagnostic criteria [9]. Current PTSD symptom clusters are intrusion, avoidance, alterations in arousal and reactivity, and negative alterations in cognition and mood [1].

Meanwhile, several self-report instruments exist for screening patients at risk for PTSD. These measures have been developed according to defined symptoms of different versions of DSM current at the time of the instrument's development. Aim of the current study is to compare the validity and further psychometric properties of three screening instruments of PTSD in patients after intensive care: the Post-traumatic

Abbreviations: AUC, Area under the curve; BSI, Brief Symptom Inventory; CAPS-5, Clinician-Administered PTSD Scale for DSM-5; CI, Confidence Interval; DSM, Diagnostic and Statistical Manual of Mental Disorders; EQ-5D-5L, health questionnaire of the EuroQol group; GSI, Global Severity Index; ICU, Intensive care unit; IES-R, Impact of Event Scale-Revised; IQR, Interquartile range; LEC-5, Life Events Checklist for DSM-5; Mdn, Median; MSC, Mid-German Sepsis Cohort; NPV, negative predictive value; PCL-5, PTSD Checklist for DSM-5; PICS, Post-intensive care syndrome; PPV, positive predictive value; PSS-SR, PTSD Symptom Scale - Self Report; PTSS, Posttraumatic Stress Scale; PTSD, Posttraumatic Stress Disorder; ROC, Receiver operating characteristic.

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https://doi.org/10.1016/j.jcrc.2019.06.016
0883-9441/

stress scale-10 (PTSS-10) developed according the diagnostic criteria of DSM-III-R, the Post-traumatic stress scale-14 (PTSS-14) reflecting the PTSD criteria defined in DSM-IV, and the PTSD Checklist for DSM-5 (PCL-5). A clinical interview known as the gold standard of PTSD assessment according to DSM-5 was used as reference.

2. Material and methods

2.1. Study design

The current study is an observational, add-on study to a large cohort study conducted in five intensive care units in Germany.

2.2. Setting and procedure

Participants were recruited within a multicenter cohort study on long-term sequelae of sepsis, the Mid-German Sepsis Cohort (MSC) [10]. The study was registered at the German Clinical Trials Register (No. DRKS00010050). Both, the MSC and the current add-on study were approved by the Local Ethics Committee of the Friedrich-Schiller University, Jena, Germany (No 4669-01/16 and No 5063-02/17). All patients provided written informed consent for the MSC study and gave informed consent to the add-on study orally on the telephone.

Follow-up assessments of the MSC study were scheduled after three, six, 12 months and then annually after ICU discharge, conducted by trained study nurses, physicians or experienced medical students by phone calls. During follow-up interviews of the MSC study, patients were invited to also participate in this add-on study. In case of consent, a researcher (HK) contacted the patient and scheduled an appointment for a telephone interview. A timeline including all assessments is shown in Fig. 1.

2.3. Participants and sample size

Since this is an add-on study, we included patients fulfilling the inclusion criteria of the MSC study. Patients aged ≥18 years were consecutively enrolled into MSC after receiving intensive care for (severe) sepsis or septic shock [10]. In addition, exclusion criteria for this add-on study were inability to speak or hear, index trauma (most severe traumatic event in life) other than ICU experience, refusal to participate in the add-on study. We consecutively enrolled patients in our study until 10 participants were identified as PTSD cases by the clinical interview. Using a sample size of n ≈ 80, one can estimate a two-sided 95% confidence interval for an expected proportion, e.g. sensitivity or specificity, of 95% with a precision of ±5% (width of the confidence interval) or an expected proportion of 90% with a precision of ±7%.

2.4. Measures

2.4.1. Self-report instruments

To ensure that participants´ index trauma was related to ICU experiences patients responded to the revised Life Events Checklist for DSM-5 (LEC-5), a self-report measure designed to screen for potentially traumatic events in a respondent's lifetime [11]. The Posttraumatic Stress Scale (PTSS) was originally developed according to DSM-III-R criteria of PTSD and validated for patients after intensive care (PTSS-10) [12]. Patients were asked to assess the frequency of ten common PTSD symptoms, on a seven-point Likert scale from 1 (never) to 7 (always). Item scores were summed up to a total score (range 10–70). A total score above 35 was suggested to indicate clinically relevant PTSD symptoms.. To reflect the changes in DSM-IV, a refined 14-item version of PTSS was developed [13] that was also translated into German (PTSS-14) [14]. A cutoff value of 45 indicated presumable PTSD.

To assess PTSD symptom severity according to DSM-5, the German version of the Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5), a 20-item self-report measure was used [15,16]. A total symptom severity score (range 0–80) was obtained by summing the scores for each of the 20 items with higher scores indicating more severe symptoms. A cutoff score of 33 was used for a provisional PTSD diagnosis [17]. The PCL-5 was previously reported to have good internal consistency, test-retest reliability, and high diagnostic accuracy [18].

Within the next scheduled MSC follow-up assessments following the interview of this add-on study (T3, Fig. 1), the German version of the Brief Symptom Inventory-18 (BSI-18) [19,20], and the health questionnaire of the EuroQol group (EQ-5D-5L) [21] were applied. The BSI-18 is widely used to assess psychological distress and comorbidities in patients. It contains three subscales with six items each: somatization, depression, and anxiety. Patients evaluate the occurrence of various symptoms on a five-point Likert scale, ranging from 0 (not at all) to 4 (extremely) that can be aggregated to a Global Severity Index (GSI). The three scales each range between 0 and 24 and GSI between 0 and 72, respectively. Internal consistency in the current study was good for the total scale (Cronbach's $\alpha = 0.83$) and acceptable for the subscales ($\alpha = 0.63$ – $\alpha = 0.78$). The EQ-5D-5L was used to measure health-related quality of life on five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) with five levels each ranging from no problems to extreme problems. We used a crude sum score to generate a single one-dimensional index value [22,23]. Additionally, the current subjective health status was assessed via a visual analog scale ranging from 0 (worst health status) to 100 (best health status).

2.4.2. Clinical interview

To derive a PTSD diagnosis, we used the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5) which is a 30-item structured interview

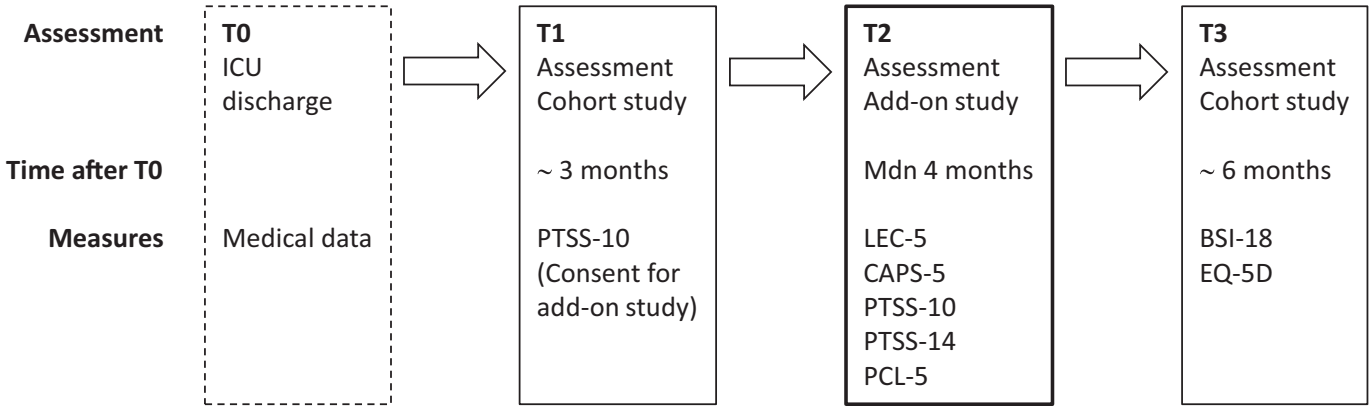

Fig. 1. Timeline of study assessments.

known as the gold standard of PTSD assessment [24]. A PTSD diagnosis requires the presence of least one re-experiencing and avoidance symptom, and two symptoms each of the hyperarousal and negative alterations in cognitions and mood cluster. Besides, the disturbance has to have lasted for at least one month and causes either clinically significant distress or functional impairment [24]. CAPS-5 total symptom severity score was calculated by summing severity scores for the 20 PTSD symptoms of DSM-5 ranging from 0 to 80 with higher scores representing higher symptom severity. To minimize between-interview variability, all measures were assessed via phone calls by a fourth-year medical student (HK) who was trained and supervised by a clinical psychologist (RG).

2.5. Statistical methods

We used standard descriptive statistics to summarize the data of patients (e.g. continuous: median with interquartile range (IQR), count: absolute and relative frequencies). We compared participants that were included in the add-on study against MSC patients who were invited but not included using Fisher's exact test for nominal data types or Wilcoxon-Mann-Whitney tests for ordinal or continuous, metric data. Associations between sum scores of the screening instruments with the CAPS-5 total symptom severity score were determined by Spearman's rank correlation coefficients (ρ). We calculated sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV) for cutoff values indicating a PTSD diagnosis as suggested in the previous studies [12,14,17]. Receiver operating characteristic (ROC) curves were derived for the total scores of the PTSS-10, the PTSS-14, and the PCL-5 in relation to the PTSD diagnosis obtained by the CAPS-5 as gold standard. Area under the curve (AUC) statistics including 95% confidence intervals (CIs) were computed to measure the performance of the three instruments. We compared symptom scores of the instruments according to the CAPS-5 diagnostic status (PTSD diagnosis vs. no diagnosis). Differences are presented as effect sizes Cohen's d derived from transformed Wilcoxon-Mann-Whitney statistics [25] to allow for a common interpretation of the data, i.e., 0.2 reflecting small, 0.5 medium, and 0.8 large effects [26].

In terms of convergent/divergent validity, associations of symptom scores of the instruments and symptoms of depression, anxiety, and somatization, and health-related quality of life were determined using Spearman's rank correlation coefficients. We applied a significance level $\alpha = 0.05$ (two-sided) and did not correct for multiple testing. All analyses were performed using SPSS Version 24 (SPSS, Chicago, IL).

3. Results

3.1. Characteristics of the participants

We contacted all 144 patients who had been scheduled for a follow-up assessment within the MSC study during a 9-month period from March to November 2017. Of these, 110 agreed to participate in the current study, and 83 patients were fully included (response rate 57.6%; Fig. 2).

Median (Mdn) age of the patients was 64 years, 60% were male. Patients were interviewed four months (Mdn) after ICU discharge (IQR [3; 6]). Median ICU stay was 10 days (IQR [4; 19]) (Table 1).

Compared to the excluded patients who refused the interview, could not be interviewed, or were excluded due to another index trauma (n = 61; Fig. 2), participants had higher PTSD symptom scores (participants: Mdn 19; IQR [15; 26]; dropouts: Mdn 17; IQR [12; 23], p = 0,035; measured by PTSS-10 within the routine MSC assessments at T1). Participants and excluded patients did not differ significantly in other key variables (Table 1).

Ten participants (12.0%) of the final sample were diagnosed with PTSD. As expected, participants with a PTSD diagnosis in the clinical interview CAPS-5, showed higher PTSD symptom scores in the three

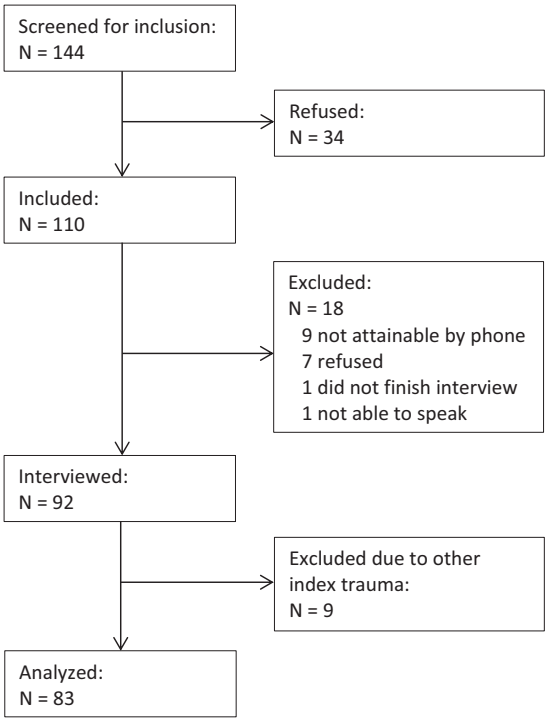

Fig. 2. Flow chart of the study.

screening instruments than participants without PTSD diagnosis. Effect sizes for the difference were large (d = 1.09 to d = 1.28) (Table 2).

The interview within the add-on study (T2) was conducted 10 days (Mdn; IQR [8; 18]) after the MSC routine assessment (T1). PTSS-10 scores which had been assessed during the interview in our study (Mdn 16; IQR [11; 22]) were lower than PTSS-10 scores that were measured within the MSC assessments shortly before the study interview at T1 (Mdn 19; IQR [15; 26]; p < 0,001) and at the next scheduled MSC follow-up assessments following the interview at T3 (Mdn 20; IQR [13; 26]; p = 0,001).

3.2. Reliability

Internal consistency of all measures was good with Cronbach's α = 0.83 for PTSS-10, 0.88 for PTSS-14, and 0.92 for PCL-5, respectively.

3.3. Concurrent validity

All screening instruments showed concurrent validity when correlated with the CAPS-5 total symptom severity score; PTSS-10: ρ = 0.77, PTSS-14: ρ = 0.82, PCL-5: ρ = 0.90 (p < 0.001 for all instruments). Furthermore, large correlations were found between the three measures, PTSS-10 and PCL-5: ρ = 0.82, PTSS-14 and PCL-5: ρ = 0.85, and PTSS-10 and PTSS-14: ρ = 0.98 (p < 0.001).

3.4. Criterion validity

ROC curve analyses were performed indicating areas under the curve that can be considered as excellent for all three screening instruments (AUC > 0.90; Table 3, Fig. 3). Using cutoff values for a presumable PTSD diagnosis that have been suggested in previous studies, sensitivity of PTSS-10 and PCL-5 was considerable lower (60% and 50%, respectively) than PTSS-14 (80%). Specificity was high for all instruments (> 0.90).

Table 1
Characteristics of the participants (n = 83) and excluded patients (n = 61).

	Included n = 83	Excluded n = 61	p-value
Sex, n (%)			0.60[c]
Female	33 (39.8)	21 (34.4)	
Male	50 (60.2)	40 (65.6)	
Age (yrs), Median (IQR)	64 (56; 71)	65 (57; 76)	0.19[d]
ICU stay (days), Median (IQR)	10 (4; 19)	8 (3; 17)	0.50[d]
Max. SOFA-Score, Median (IQR)[a]	13 (10; 15)	13 (11; 14)	0.82[d]
Time from ICU discharge to interview (months), Median (IQR)	4 (3; 6)		
Source of infection, n (%)[b]			
Community acquired	43 (51.8)		
Hospital acquired	39 (47.0)		
Mechanical ventilation, n (%)[b]			0.29[c]
Yes	56 (67.5)	35 (58.3)	
No	27 (32.5)	25 (41.7)	
Delirium, n (%)[b]			0.14[c]
Yes	30 (36.1)	14 (23.2)	
No	53 (63.9)	46 (76.7)	
Dialysis, n (%)			0.26[c]
Yes	27 (32.5)	14 (23.0)	
No	56 (67.5)	47 (77.0)	
CPR, n (%)			1.00[c]
Yes	2 (2.4)	1 (1.6%)	
No	81 (97.6)	60 (98.4)	
PTSS-10 score, Median (IQR)[b]	19 (15; 26)	17 (12; 23)	0.035[d]
PTSD (clinical diagnosis based on CAPS-5), n (%)			
Yes	10 (12.0)		
No	67 (80.7)		
Partial	6 (7.2)		

Missing values: [a] n = 17, [b] n = 1; [c] p value from Fisher's exact test; [d] p-value from Wilcoxon-Mann-Whitney test; CAPS-5 = Clinician-Administered PTSD Scale for DSM-5; CPR = Cardiopulmonary resuscitation; IQR = Interquartile range provided by the first and the third quartile; SOFA = Sequential Organ Failure Assessment.

3.5. Convergent validity

Scores of all three screening instruments (at T2) were associated with psychological comorbidities and health-related quality of life at the next scheduled MSC follow-up assessments following the interview (T3, Table 4). In terms of convergent validity, associations with symptoms of psychological morbidity (depression, anxiety, and somatization) were larger than with quality of life representing a more global measure of health.

4. Discussion

In our study, PTSD diagnosis was derived from a clinical interview considered as the gold standard of assessment. Ten of 83 participants (12%) in our study were diagnosed with PTSD. Other studies reported very heterogeneous PTSD prevalence rates in ICU survivors ranging from 4% to 62%, while most of the studies only used screening instruments to derive a PTSD diagnosis [2]. Studies using clinical interviews for PTSD diagnosis are much rarer and reported PTSD prevalence rates between 7% and 25% [12,27-30].

Altogether, our results suggest that PTSS-10, PTSS-14, and PCL-5 are clinically useful screening tools for PTSD in patients after intensive care. When using the recommended cutoff values for provisional PTSD diagnosis all measures showed high specificity. However, only PTSS-14 revealed an acceptable sensitivity. Compared to other validation studies using the same German versions of the instruments and identical cutoff values [12,14,16], sensitivity in our study was lower for PTSS-10 and considerably lower for PCL-5. Setting the cutoff lower could increase sensitivity and might help to avoid missing patients at risk in clinical practice.

All three screening instruments showed good levels of concurrent validity when correlated with the symptom severity score obtained by the clinical interview CAPS-5. Moreover, convergent validity was good as all three instruments showed strong associations with measures of psychological distress (anxiety, depression, somatization). Relations to health-related quality of life were smaller. Due to the paper-pencil format and simple scoring all three measures are suitable for administration as part of routine care, although PTSS-14 might be clearly preferred because of its short length and better sensitivity. In terms of feasibility, particularly for large cohort studies aiming at a repetitive assessment of various health indices short instruments are usually needed to reduce the strain of survey participants. It has been shown that the use of shorter instruments is associated with a higher response rate and has been proposed to also result in increased completion, and higher data quality [31-33].

Table 2
Comparison of participants with and without PTSD diagnosis according to the CAPS-5 gold standard.

	PTSD diagnosis n = 10 Median (IQR)	No PTSD diagnosis n = 73 Median (IQR)	Wilcoxon-Mann-Whitney (p-Value)	Cohen's d[a]
PTSS-10 score	37 (39, 43)	15 (10, 19)	54 (<0.001)	1.09
PTSS-14 score	49 (42, 57)	20 (15, 26)	46 (<0.001)	1.12
PCL-5 score	30 (22, 44)	2 (0, 11)	47.5 (<0.001)	1.12
CAPS severity score	26 (24; 38)	0 (0, 5)	13.5 (<0.001)	1.28

IQR = interquartile range provided by the first and the third quartile.
[a] Test statistics of Wilcoxon-Mann-Whitney test transformed in effect size Cohen's d [26].

Table 3
ROC curve analyses for all three screening instruments.

	PTSS-10	PTSS-14	PCL-5
Area under the curve	0.93	0.94	0.94
95% confidence interval	0.84–1.00	0.86–1.00	0.87–1.00
p-value	<0.001	<0.001	<0.001
Suggested cutoff	35[a]	40[b]	33[c]
Sensitivity	60%	80%	50%
Specificity	95.9%	91.8%	95.9%
PPV	66.7%	57.1%	62.5%
NPV	94.6%	97.1%	93.3%

PPV = Positive predictive value, NPV = Negative predictive value.
[a] [12].
[b] [13].
[c] [17].

Table 4
Associations of the three screening instruments (T2) by Spearman's rank correlations with various health indices assessed at the next scheduled MSC follow-up assessment (T3) following the interview (n = 76).

	PTSS-10	PTSS-14	PCL-5
BSI depression	0.48 (p < 0.001)	0.53 (p < 0.001)	0.54 (p < 0.001)
BSI anxiety	0.52 (p < 0.001)	0.57 (p < 0.001)	0.56 (p < 0.001)
BSI somatization	0.54 (p < 0.001)	0.54 (p < 0.001)	0.50 (p < 0.001)
BSI Global Severity Index	0.64 (p < 0.001)	0.68 (p < 0.001)	0.66 (p < 0.001)
EQ-5D-5L	0.33 (p = 0.003)	0.33 (p = 0.004)	0.18 (p = 0.11)
EQ-5D health status (VAS)	−0.34 (p = 0.003)	−0.35 (p = 0.002)	−0.29 (p = 0.01)

Note: $N = 76$ due to missings in scheduled assessments within the MSC study.

4.1. Strengths and limitations

A strength of our study is that we tested the accuracy of three screening instruments that are already commonly used in various populations including ICU patients. Patients received simultaneously all three instruments as well as the best available reference standard, i.e., a clinical diagnostic interview for obtaining a PTSD diagnosis. In this regard, our study validated PTSS-14 on the basis of clinical diagnostic interview as gold standard while previous studies [13,14] used commonly applied self-report questionnaires for confirming a PTSD diagnosis. Participants of our study were consecutively enrolled using broad inclusion criteria. Compared to patients excluded from our analysis no significant differences in demographic and clinical characteristics appeared. Our sample could be therefore regarded as representative of the typical patient population with sepsis at the study sites.

However, our study also has some limitations. First, the final sample was relatively small and the number of PTSD cases was limited to 10. This might have hampered the ROC curve analyses by increasing the uncertainty of estimations. Second, the evaluated instruments were applied only at one time point. For that reason, we did not determine test-retest reliability of the measures. However, previous studies have proven that all questionnaires show high test-retest reliability, intraclass correlation coefficient $\alpha = 0.89$ to 0.91 [12,13,16]. Third, participants´ self-reported PTSD symptoms scores seem to be subject to changes: when measured in this add-on study (T2) scores were lower compared to the scores assessed at the routine MSC assessments before (T1) and after the study interview (T3). Fourth, a considerable number of patients invited to our study refused participation or had to be excluded (42%). Those who participated in our study showed significantly lower PTSD symptom scores than excluded patients in the prior MSC routine assessments. Therefore we cannot rule out that our findings could be affected by selection bias. Fifth, although we used broad inclusion criteria, our results are limited to patients with (severe) sepsis in Germany and results might have been different for other groups of ICU patients. Finally, our validation study was restricted to the Posttraumatic Stress Scale (PTSS) with its 10 and 14-item versions and the most recent Posttraumatic Stress Disorder Checklist for DSM-5 (PCL-5). Other measures such as the Impact of Event Scale-Revised (IES-R) or the PTSD Symptom Scale - Self Report (PSS-SR) were not considered in our study. The IES-R has been most commonly used in studies of critical illness survivors [2] and was recently recommended as core outcome measure for clinical research in survivors of acute respiratory failure [34].

Additionally, the PSS-SR was used to measure PTSD in one of the largest ICU studies [35]. However, PTSS-10 and PTSS-14 are instruments that have also been frequently used in ICU survivors [2], and PCL-5 is one of the few screening instruments reflecting current DSM-5 diagnostic criteria.

5. Conclusions

PTSS-10, PTSS-14, and PCL-5 are commonly used measures for screening patients at risk of PTSD with good reliability and concurrent validity. In this small study, the PTSS-14 performed better than the PTSS-10 and PCL-5 for PTSD screening, with higher sensitivity. The PTSS-14 includes numbing and intrusion symptoms, unlike the PTSS-10. The PTSS-14 may also be preferred to the PCL-5 for reasons of homogeneity and comparability of research findings, since it has already been used in various ICU studies [2]. Although PTSS-14 was developed according to DSM-IV diagnostic criteria of PTSD it performed well in making provisional PTSD diagnosis in reference to the most current diagnostic manual of mental disorders DSM-5.

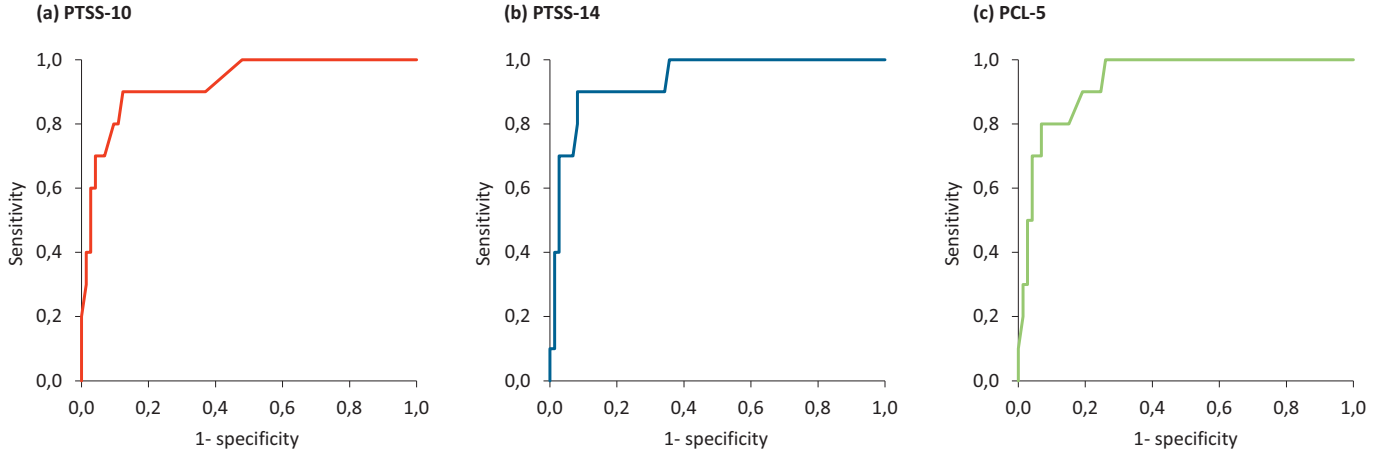

Fig. 3. ROC curves of the three questionnaires for PTSD diagnosis. (a) PTSS-10, (b) PTSS-14, (c) PCL-5.

Ethics approval and consent to participate

Both, the MSC and the current add-on study were approved by the Local Ethics Committee of the Friedrich-Schiller University, Jena, Germany (No 4669-01/16 and No 5063-02/17). All patients provided written informed consent for the MSC and gave informed consent to the add-on study orally on the telephone.

Consent for publication

Not applicable.

Availability of data and material

Data are available from the corresponding author upon request.

Funding

The MSC is funded by the Integrated Research and Treatment Center, Center for Sepsis Control and Care (CSCC), at the Jena University Hospital and the Rudolf Presl GmbH & Co, Kreischa. CSCC is funded by the German Ministry of Education and Research (BMBF no 01EO1502). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Authors' contributions

JR, RG, and AS contributed to the conception and design of the study. HK contacted the participants, conducted all interviews within the add-on study and managed the data. HK and JR analyzed the data. JR wrote the manuscript; all other authors substantially contributed to the interpretation of data and participated in the finalization of the manuscript. All authors read and approved the final manuscript.

Declaration of Competing Interest

The authors declare no competing interests.

Acknowledgements

We kindly thank the MSC team, particularly Heike Romeike, Kirsten Töpfer, and Carolin Fleischmann-Struzek, and the MSC investigators for their support in patient recruitment. We also thank Cornelia Eichhorn and Miriam Kesselmeier for their assistance in extracting MSC study data.

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