What's on your mind?
Annema-de Jong, Coby

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CHAPTER 7

A PROSPECTIVE COHORT STUDY ON POSTTRAUMATIC STRESS DISORDER IN LIVER TRANSPLANTATION RECIPIENTS BEFORE AND AFTER TRANSPLANTATION: PREVALENCE, SYMPTOM OCCURRENCE, AND INTRUSIVE MEMORIES

Coby Annema, Gerda Drent, Petrie F. Roodbol, Herold J. Metselaar, Bart van Hoek, Robert J. Porte, Maya J. Schroeters, Adelita V. Ranchor

Submitted
ABSTRACT

Objective
This study aimed at increasing the understanding of posttraumatic stress disorder (PTSD) in liver transplant patients by describing the course of PTSD, symptom occurrence, psychological co-morbidity, and the nature of re-experiencing symptoms.

Methods
A prospective cohort study was performed among 95 liver transplant recipients from the waiting-list period, up until one year post-transplantation. Respondents filled out a questionnaire regarding psychological functioning (PTSD, anxiety, and depression) before, and at 3, 6, and 12 months post-transplantation. Both quantitative and qualitative methods were used to analyze the data.

Results
Before transplantation, full PTSD was present in 10.5% and partial PTSD in 6.3% of the respondents. In all cases, co-morbid conditions of anxiety and/or depression were present. After transplantation, no new onset of full PTSD was found. New onset of partial PTSD was found in six respondents. Arousal symptoms were the most frequently reported symptoms, but were found not to be distinctive for PTSD in transplant patients because of the overlap with disease- and treatment-related symptoms. Re-experiencing symptoms before transplantation were mostly related to waiting for a donor organ and the upcoming surgery; after transplantation this was related to aspects of the hospital stay.

Conclusions
In liver transplant patients, PTSD is more often present before transplantation than after transplantation. Being diagnosed with a life-threatening disease seems to be the main stressor. If a diagnosis of PTSD is suspected, assessment by a clinician is warranted because of the overlap with symptoms of anxiety and depression, and disease- and treatment-related symptoms.
INTRODUCTION

Since the introduction of the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) in 1994, being diagnosed with a life-threatening illness has been introduced as a potential stressor event for posttraumatic stress disorder (PTSD). Since then, PTSD has been described in a variety of somatic diseases and treatments, including organ transplantation. However, contrary to other stressful events that may lead to PTSD, such as rape or car accidents, being diagnosed with a life-threatening illness is not a single event but a process, comprising a number of stressors that may lead to a traumatic experience.

In patients diagnosed with end-stage liver disease, liver transplantation is the only treatment option. In the liver transplant process several stressors that may be traumatic are present. First, transplant candidates find themselves diagnosed with a potentially life-ending disease, for which a donor organ is needed to survive, but where it is uncertain if this donor organ will arrive in time. Each year approximately 15% of transplant candidates die while on the organ transplant waiting list. Second, if a donor organ becomes available, patients have to undergo major surgery, often followed by known risk factors for PTSD: a stay on the intensive care unit (ICU) and delirium. Third, after a successful transplantation, patients have to adjust to a life with a life-long regimen of immunosuppressive drugs and life-style rules but they may as well have to deal with serious, potentially life-ending, complications, such as rejection of the graft, or the development of cardiovascular diseases or cancer. All these factors make PTSD a reasonable concern for the transplant population.

So far, the focus of the studies on PTSD after organ transplantation has mainly been on assessing prevalence rates, identifying risk factors for the development of PTSD, and the impact of PTSD on outcomes after transplantation. A recent systematic review showed that, after organ transplantation, clinically relevant symptom levels of PTSD were present in 0-46% of transplant recipients, while clinician-ascertained PTSD was present in 1-16% of the cases. Studies on transplant candidates are limited and mainly retrospective in nature, showing that clinically relevant symptom levels of PTSD are present in 7-25% while 2-6% of transplant candidates satisfy the criteria for PTSD. Little attention has been paid to which aspects of the transplant process are traumatic in nature, to the occurrence of specific symptoms of PTSD, and to the overlap of PTSD symptoms with other psychological disorders. Furthermore, prospective studies examining the course of PTSD in the same patient group, before and after transplantation, are lacking. Examining these aspects may help to gain a better understanding of the concept of PTSD in the transplant population.

PTSD is characterized by symptoms of re-experiencing, avoidance, and arousal. Symptoms of re-experiencing include recurrent dreams, intrusive memories, or flashbacks related to the event. Since symptoms of intrusive re-experiencing are seen as the core symptom of PTSD, examining the nature of these symptoms in transplant patients can provide valuable insight into stressors associated with PTSD in this population. The symptom clusters of avoidance and arousal are more general in nature, and show an overlap with mood and anxiety disorders. Avoidance symptoms refer to the avoid-
ance of distressing memories, thoughts, feelings, or reminders of the event, but also detachment from others, and hopelessness about the future. Arousal symptoms are characterized by aggressive behavior, sleep disorders, and hyper-vigilance. Because of the overlap with mood and anxiety disorders, it might be hard to disentangle the differences between them. Therefore, examining comorbidity between PTSD, anxiety, and depression, and the overlap of symptoms of anxiety and depression with the symptom clusters of PTSD may help to differentiate between these problems.

Another important aspect to consider is that PTSD symptoms should not be the result of another medical condition, medication, drugs, or alcohol. In liver transplant patients, arousal symptoms like sleeping disorders and concentration problems may also be disease-related. Sleeping disorders are common in liver transplant patients. Before transplantation, 35-73% of the transplant candidates reported poor sleep quality, mainly due to hepatic encephalopathy or to the underlying liver disease. Among transplant recipients, 41-73% reported poor sleep quality mostly due to physical problems. Concentration problems and irritability may also interfere with symptoms of encephalopathy before transplantation. Therefore, examining the occurrence of PTSD symptoms, and the contribution of specific symptom clusters to the diagnosis of PTSD in transplant patients can add to the understanding of PTSD in the transplant population.

The aim of this study was to increase the understanding of PTSD in liver transplant candidates and recipients by describing the course of PTSD from the waiting-list period up until the first year after transplantation, which symptoms of PTSD contribute the most to a diagnosis of PTSD in liver transplant patients, the overlap of PTSD with anxiety and depression, and to examine the nature of re-experiencing symptoms in liver transplant patients.

METHODS

A prospective cohort study on psychological aspects of liver transplantation was performed among transplant patients in all three liver transplant centers in the Netherlands. Transplant candidates who were on the waiting list between October 2009 and April 2013 were asked to participate. Inclusion criteria were: ≥18 years, and receiving medical treatment in one of the three transplant centers. Exclusion criteria were: unable to fill out a questionnaire due to physical, mental, or cognitive functioning, or due to a language barrier.

Eligible transplant candidates (n = 350) received a letter explaining the purpose and procedure of the study, together with an informed consent form and a pre-addressed, stamped return envelope. After written informed consent, respondents received a baseline questionnaire (T0). Measurements of psychological functioning were repeated every six months after inclusion in the study until transplantation. In this study, data from the last measurement-point before the transplant were used to describe PTSD symptoms of liver transplant candidates (T0). After transplantation respondents filled
out a questionnaire at three (T1), six (T2), and twelve (T3) months after the transplant surgery. The institutional review board of the transplant center that initiated the study approved the study, and a positive recommendation of local feasibility was obtained from the other transplant centers (METc2009.190).

Research instruments
To measure symptoms of PTS, the Self-Rating Inventory for Posttraumatic Stress Disorder (SRIP) was used, a Dutch screening instrument that registers symptoms of PTSD. The 22 items, corresponding to the DSM-IV criteria for PTSD, are rated on a 4-point self-report scale (1 = not at all, to 4 = extremely). The SRIP has satisfying psychometric properties: validity (.90), reliability (.92), sensitivity (83%), and specificity (72%). In this study Cronbach’s alphas of the SRIP were, respectively, 0.89 (T0), 0.88 (T1), 0.87 (T2), and 0.87 (T3).

The items of the SRIP are stated in general terms, by referring to a stressful experience that happened in the past. In order to be able to examine symptoms of PTSD related to the end-stage organ disease (T0) or to the transplantation (T1-T3), the items were adjusted by replacing “stressful event” with either “my disease” or “my transplantation.” Respondents who reported having re-experiencing symptoms, such as intrusive thoughts or recurrent dreams, were asked to briefly describe the nature of these re-experiencing symptoms.

In the SRIP, five of the PTSD symptoms mentioned in the DSM-IV are split into two separate items. For example, “having difficulty falling or staying asleep” is split into two items: “having difficulty falling asleep” and “having difficulty staying asleep.” To correspond to the DSM-IV criteria, SRIP items that belong to the same PTSD symptom were merged into one item.

A cutoff score of ≥39 was used to identify respondents with clinically relevant symptom levels of PTS. To be able to identify cases of PTSD, all items were recoded into 0 (no symptom of PTSD, scores 1 or 2) and 1 (symptom of PTSD, scores 3 or 4). For each symptom cluster, the number of symptoms was calculated by adding up the recoded symptom scores. Based on DSM-IV-criteria, caseness of full PTSD was defined as the presence of one symptom of re-experiencing, three avoidance symptoms, and two arousal symptoms. Regarding partial PTSD, different criteria have been used in the literature, either satisfying symptom clusters at two of the three symptom clusters, or having one symptom in each symptom cluster. Because intrusive re-experiencing is recognized as the core symptom of PTSD, the latter definition of partial PTSD was used in this study.

To measure psychological co-morbidity, symptoms of anxiety and depression were assessed using, respectively, the short form of the State-Trait Anxiety Inventory (STAI-6) and the Center for Epidemiological Studies Depression Scale (CES-D). The STAI-6 consists of 6 items rated on a 4-point intensity scale (1 = not at all, to 4 = very much), resulting in a total sum score between 6 and 24. Higher scores indicate more symptoms of anxiety. Based on a transformation of the original 20 item scale cutoff of ≥40 for the general population, a cutoff score of ≥12 was used to identify clinically relevant cases. The convergent validity of the STAI-6 with the full form of the STAI showed
a correlation of 0.95. Cronbach’s alpha of the STAI-6 in the present study varied from 0.87 to 0.89 at the different measurement-points.

The CES-D consists of 20 items, scored on a 4-point self-report scale (0 = seldom or never, to 4 = most of the time-always). Higher scores indicate more symptoms of depression. A cutoff score of ≥16 was used to identify clinically relevant cases. Cronbach’s alpha of the CES-D in the present study varied from 0.91 to 0.92 at the different measurement-points.

Demographic variables regarding age, sex, marital status, educational level, nationality, and employment status were retrieved by self-report. Clinical data regarding primary liver disease and time on waiting-list were obtained from the medical record.

**Statistical analyses**

Descriptive statistics were used to calculate mean or median scores, and prevalence rates regarding demographic and clinical characteristics, and prevalence and incidence rates of full and partial PTSD. Differences between groups were analyzed using Fisher’s exact test or \( \chi^2 \)-test for nominal variables. Because of non-normal distribution, the Mann-Whitney U-test was used to analyze differences between groups on continuous variables.

Ordinal Logistic Regression (OLR) analysis was used to identify which symptom clusters contributed the most to the diagnosis of full or partial PTSD, using odds ratios. Pearson’s correlation coefficient was used to examine the association between the symptom clusters of PTSD with symptoms of anxiety and depression.

To analyze the qualitative data regarding re-experiencing symptoms, content analysis was performed by two researchers (GD/CA), independent of each other. Data were examined using a direct approach with a priori categories based on the re-experiencing symptoms in the DSM-IV diagnostic criteria for PTSD. Consensus on the coding was reached if the coding corresponded completely or after discussion about the differences in coding. If no consensus was reached, a third researcher (MJS) was asked to examine the specific data. Data were discussed with all researchers involved to reach final consensus.

**RESULTS**

**Study population**

Of the 350 eligible transplant candidates, 241 (69%) agreed to participate. Of these, 116 received a transplant within the study period. However, for 21 respondents, data-sets were incomplete and therefore excluded from analyses. Reasons for missing data were: deceased (n = 12), hospitalization at measurement-point (n = 3), lost to follow-up (n = 3), questionnaire not returned (n = 2), and re-transplantation (n = 1). Demographic and clinical characteristics of the total study population, and included and excluded respondents are shown in Table 1. No significant differences were found between respondents included or excluded from the analyses.
Table 1: Demographic and clinical characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>All respondents n = 116</th>
<th>Respondents included in analyses n = 95</th>
<th>Respondents excluded from analyses n = 21</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex: Male</td>
<td>76 (65.5)</td>
<td>63 (66.3)</td>
<td>13 (61.9)</td>
<td>0.80</td>
</tr>
<tr>
<td>Living situation: With partner</td>
<td>89 (76.7)</td>
<td>71 (74.7)</td>
<td>18 (85.7)</td>
<td>0.40</td>
</tr>
<tr>
<td>Educational level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td>21 (18.3)</td>
<td>15 (16.0)</td>
<td>6 (28.6)</td>
<td>0.18</td>
</tr>
<tr>
<td>Secondary</td>
<td>54 (47.0)</td>
<td>43 (45.7)</td>
<td>11 (52.4)</td>
<td></td>
</tr>
<tr>
<td>University</td>
<td>40 (34.8)</td>
<td>36 (38.3)</td>
<td>4 (19.0)</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Working</td>
<td>32 (27.6)</td>
<td>28 (29.5)</td>
<td>4 (19.0)</td>
<td>0.53</td>
</tr>
<tr>
<td>Sick-leave/disabled</td>
<td>59 (50.9)</td>
<td>48 (50.5)</td>
<td>11 (52.4)</td>
<td></td>
</tr>
<tr>
<td>Retired/homemaker/student</td>
<td>25 (21.6)</td>
<td>19 (20.0)</td>
<td>6 (28.6)</td>
<td></td>
</tr>
<tr>
<td>Nationality: Dutch</td>
<td>109 (94.0)</td>
<td>91 (95.8)</td>
<td>18 (85.7)</td>
<td>0.11</td>
</tr>
<tr>
<td>Primary liver disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biliary cirrhosis</td>
<td>40 (34.5)</td>
<td>36 (37.9)</td>
<td>4 (19.0)</td>
<td>0.10</td>
</tr>
<tr>
<td>Metabolic disorder</td>
<td>14 (12.1)</td>
<td>11 (11.6)</td>
<td>3 (14.3)</td>
<td>0.72</td>
</tr>
<tr>
<td>Cirrhosis unknown etiology</td>
<td>9 (7.8)</td>
<td>6 (6.3)</td>
<td>3 (14.3)</td>
<td>0.21</td>
</tr>
<tr>
<td>Alcoholic cirrhosis</td>
<td>26 (22.4)</td>
<td>22 (23.2)</td>
<td>4 (19.0)</td>
<td>0.78</td>
</tr>
<tr>
<td>Viral hepatitis</td>
<td>17 (14.7)</td>
<td>11 (11.6)</td>
<td>6 (28.6)</td>
<td>0.08</td>
</tr>
<tr>
<td>Other</td>
<td>9 (7.8)</td>
<td>9 (9.5)</td>
<td>0 (0)</td>
<td>0.36</td>
</tr>
<tr>
<td>Mean (SD)/median (range)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (at time of transplantation)</td>
<td>50.8 (11.4)</td>
<td>50.3 (11.3)</td>
<td>53.4 (12.2)</td>
<td>0.20</td>
</tr>
<tr>
<td>Time on waiting-list (in months)</td>
<td>9.4 (0.2-77.5)</td>
<td>9.5 (0.2-77.5)</td>
<td>8.5 (1.0-24.2)</td>
<td>0.49</td>
</tr>
</tbody>
</table>

Table 2. Prevalence rates based on cutoff score (≥39), and prevalence and (cumulative) incidence rates of full, partial, and no PTSD, based on DSM-IV criteria before and during the first year after transplantation

<table>
<thead>
<tr>
<th></th>
<th>Waiting list</th>
<th>3 months after transplantation</th>
<th>6 months after transplantation</th>
<th>12 months after transplantation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Point-prevalence (n/%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cutoff ≥39</td>
<td>30 (31.6)</td>
<td>15 (15.8)</td>
<td>14 (14.7)</td>
<td>14 (14.7)</td>
</tr>
<tr>
<td>Full PTSD</td>
<td>10 (10.5)</td>
<td>1 (1.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Partial PTSD</td>
<td>6 (6.3)</td>
<td>5 (5.3)</td>
<td>6 (6.3)</td>
<td>3 (3.2)</td>
</tr>
<tr>
<td>No PTSD</td>
<td>79 (83.2)</td>
<td>89 (93.6)</td>
<td>89 (93.6)</td>
<td>92 (96.8)</td>
</tr>
<tr>
<td>Incidence (n/%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full PTSD</td>
<td>10 (10.5)</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Partial PTSD</td>
<td>6 (6.3)</td>
<td>1 (1.1)</td>
<td>3 (3.2)</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Total</td>
<td>16 (16.8)</td>
<td>1 (1.1)</td>
<td>3 (3.2)</td>
<td>2 (2.1)</td>
</tr>
<tr>
<td>Cumulative Incidence</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevalence and incidence rates of PTSD
Table 2 shows the prevalence rates of PTSD at the different measurement-points. Clinically relevant symptomatology, based on the cutoff score (≥39), as well as caseness for PTSD, based on criteria for full and partial PTSD, were more present in the waiting-list period, when compared to the period after transplantation. The cumulative incidence, the proportion of individuals newly diagnosed with full or partial PTSD during the waiting-list period and in the first year after transplantation, was 23.2% (Table 2). After transplantation, no new onset of full PTSD was found, whereas new onset of partial PTSD was found in six transplant recipients.

Symptom occurrence
Figure 1 provides an overview of the percentage of respondents with clinically relevant symptoms (scores 3 or 4) of all PTSD symptoms at the four measurement-points. Regarding re-experiencing symptoms, “recurring dreams” and “intrusive memories” were the most frequently reported symptoms at all measurement-points. In the avoidance symptom cluster, “sense of foreshornted future” and “disinterest in activities” were the most reported symptoms before transplantation. After transplantation, the symptom “forgot important aspects” became most prevalent. The most reported symptoms in the arousal cluster were “having difficulty falling or staying asleep” and “problems concentrating.”
To identify which symptom cluster contributed the most to the diagnosis of either full or partial PTSD, compared to no diagnosis, an OLR analysis was performed. Because of the few cases of full and partial PTSD in the post-transplant period, we were only able to perform this analysis using data from the waiting-list period. The OLR showed that a unit increase in the number of re-experiencing symptoms increased the odds of caseness for partial or full PTSD the most (OR 5.0), when compared to a unit increase in the number of avoidance symptoms (OR 3.9) or arousal symptoms (OR 2.8) (Table 3).

## Psychological comorbidity
Before transplantation, almost all respondents who met the criteria for either full or partial PTSD, also showed clinically relevant symptoms levels of both depression and anxiety (Figure 2). Again, because of the few cases of full and partial PTSD in the post-transplant period, we only performed these analyses using data from the waiting-list period.

To identify which symptom clusters of PTSD showed an overlap with either anxiety or depression, correlations between the number of symptoms in each cluster with the total score on the STAI and the CES-D were examined. Regarding anxiety, all symptom clusters of PTSD were significantly correlated with the STAI-6 total score. The strength of the correlation was moderate for the re-experiencing cluster ($r = 0.32$), and large for both the avoidance symptom cluster ($r = 0.55$) and the arousal symptom cluster ($r = 0.57$). Regarding depression, all symptom clusters of PTSD were also significantly cor-

### Table 3. Unstandardized estimates, 95% Confidence Intervals, and Odds Ratios of the predictive value of the number of symptoms in each cluster to satisfy criteria for partial of full PTSD compared to no PTSD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>P value</th>
<th>95% Confidence Interval</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower</td>
<td>Upper</td>
</tr>
<tr>
<td>Number of re-experiencing symptoms</td>
<td>1.61</td>
<td>0.002</td>
<td>0.59</td>
<td>2.64</td>
</tr>
<tr>
<td>Number of avoidance symptoms</td>
<td>1.37</td>
<td>0.002</td>
<td>0.51</td>
<td>2.23</td>
</tr>
<tr>
<td>Number of arousal symptoms</td>
<td>1.04</td>
<td>0.015</td>
<td>0.20</td>
<td>1.87</td>
</tr>
</tbody>
</table>

Link function = logit

![Figure 2. Percentage of respondents with full or partial PTSD and comorbidity of anxiety and/or depression before transplantation.](image)

Regarding anxiety, all symptom clusters of PTSD were significantly correlated with the STAI-6 total score. The strength of the correlation was moderate for the re-experiencing cluster ($r = 0.32$), and large for both the avoidance symptom cluster ($r = 0.55$) and the arousal symptom cluster ($r = 0.57$).
related with the CES-D total score. The strength of these correlations was moderate for the re-experiencing cluster ($r = 0.39$), and large for both the avoidance symptom cluster ($r = 0.62$) and the arousal symptom cluster ($r = 0.61$).

**Nature of re-experiencing symptoms**
Because re-experiencing symptoms are seen as the core symptom of PTSD, we were interested in the nature of these symptoms. Of the 95 respondents, 49 (52%) described the content of their re-experiencing symptoms at one or more of the measurement-points. Some respondents mentioned the same symptoms at several measurement-points. Symptoms were therefore merged at the individual level at two measurement-points in time: before and after transplantation.

**Symptoms of re-experiencing before transplantation**
Before transplantation, intrusive thoughts related to the transplant were reported by fourteen (15%) of the respondents. These thoughts were mainly related to the period of waiting for an organ, such as concerns about timely availability of an organ and waiting for “the call.” One respondent experienced a failed attempt to transplant, prior to a successful transplant, because the donor organ was rejected at the final decision, leaving the respondent with concerns about the success of any upcoming organ offer. Other respondents reported that they worried about the transplantation itself. They were concerned about being physically unable to undergo a transplantation because of their deteriorating health status or about the success of the transplant surgery. In addition, concerns about their family were described, mostly in terms of leaving their loved ones behind in case the transplant would not be in time or would be unsuccessful. Two respondents mentioned that they had recurrent dreams about the transplantation or about death. Three respondents mentioned that they felt distress from cues related to medical complications or to the death of a family member with the same liver disease, leaving them with feelings of anxiety for their own future.

**Symptoms of re-experiencing after transplantation**
After transplantation, 32 (34%) of the respondents reported one or more re-experiencing symptoms. Twenty-one respondents reported having intrusive memories or thoughts about the transplant, mostly related to the clinical phase after the transplantation, such as the stay on the ICU or the nursing ward, but also regarding specific aspects of the clinical phase, such as experiencing delirium, interventions that restricted freedom of movement, or the feeling of being totally dependent upon others. Besides this, fears concerning the future, for example about the physical recovery or the possibility of graft loss, were described. Intrusive thoughts related to the death of the donor were also reported.

Recurrent dreams or nightmares about the transplantation were reported by fourteen respondents. These dreams were mostly about aspects of the transplant process, such as the surgery or the ICU stay, but unrealistic dreams were also present (e.g., being hunted by sharks, horror-like dreams). One respondent described a feeling of reliving that consisted of a sensation of choking, which reminded of an experience during the stay
on the ICU. Distress at cues was mentioned by eight respondents. These cues were related to medical complications, such as recurrence of liver disease or signs of rejection, but also sounds or situations that reminded them of the hospital stay. Only one respondent reported physiological reactions to cues. This respondent felt nausea when confronted with reminders of the hospital stay.

DISCUSSION

The results of our study showed that in liver transplant patients clinically relevant PTSD symptomatology is more present than caseness for full and partial PTSD, and that both PTSD symptomatology and caseness is more prevalent in liver transplant candidates than in liver transplant recipients during the first year after transplantation. Remarkably, we found no new onset of full PTSD after transplantation, and only a few cases of new onset of partial PTSD. All respondents with partial or full PTSD before transplantation also showed clinically relevant symptom levels of anxiety and/or depression. Regarding symptom occurrence, arousal symptoms were most present at all measurement-points, especially sleeping disorders and concentration problems. Our qualitative data showed that symptoms of re-experiencing before transplantation were mainly related to the wait for a suitable donor and the upcoming transplant surgery; after transplantation mainly to the clinical phase after the transplant surgery and concerns about the future.

Our findings regarding prevalence rates are in line with other studies that show that PTSD symptomatology is higher than PTSD caseness in patients after medical illness and treatment, and after liver transplantation. However, we found more PTSD caseness before the transplantation than previous studies among transplant candidates. Based on our qualitative data, the most prominent stressor for the development of PTSD in liver transplant candidates seems to be “being diagnosed with a life-threatening disease.” The nature of the re-experiencing symptoms, as described by the respondents, showed that, before transplantation, the unpredictability of the timing of the transplantation, along with deterioration in health status, left transplant candidates not only with concerns about the timely availability of a donor organ but also with concerns about leaving their loved ones behind.

Symptoms of re-experiencing after the transplantation were mostly related to the clinical phase after the transplantation (eg, ICU stay, delirium) but also represented current stressors like concerns about the recovery, or conceived future events like fear of graft loss. Although 34% of the respondents reported having intrusive thoughts, dreams, or distress at cues after the transplantation, this did not lead to the onset of full PTSD; furthermore, new onset of partial PTSD was found in 6% of the respondents. This might indicate that, after a successful transplantation, most recipients are capable of successfully processing their transplant experience. Although arousal symptoms were most present at all measurement-points, OLR analyses showed that experiencing more arousal symptoms increased the odds of partial or
full PTSD only to a small extent, whereas experiencing more avoidance symptoms and re-experiencing symptoms increased the likelihood of PTSD to a greater extent. This emphasizes that re-experiencing symptoms are the core symptoms of PTSD and implies that the presence of arousal symptoms is not indicative of PTSD in the liver transplant population. Sleeping disorders and concentration problems are common in both transplant patients, mainly due to physical problems. Therefore, when transplant patients report arousal symptoms, causes other than PTSD should be kept in mind. Moreover, we found that PTSD in liver transplant patients is often accompanied by co-morbid conditions of anxiety and/or depression, and that, especially, avoidance and arousal symptoms show strong correlations with high symptom levels of anxiety and depression. Due to the overlap between symptoms of PTSD with disease and treatment-related symptoms, and with other psychological disorders, the prevalence of PTSD in the transplant population could easily be overestimated. Because it is difficult to disentangle differences between them, it is important to carry out an assessment by a clinician when a diagnosis of PTSD is suspected. In this assessment, anxiety and depression should also be considered. Furthermore, alternative diagnoses, such as an acute stress disorder should be hold in mind, because some of the re-experiencing symptoms described by the respondents were related to current or conceived events (medical complications, fear of graft failure), which could be indicative of an acute stress disorder.

**Strengths and limitations**

The strength of our study is the prospective, longitudinal design, the satisfactory response rate (69%), and adequate sample size (n = 95), which made it possible to follow the course of PTSD in our patient group over time. To our knowledge, no other studies have investigated PTSD in a transplant population during the waiting-list period and after the transplantation. However, because of the prospective design, we could not include transplant recipients who were transplanted soon after placement on the waiting list or patients with acute liver failure. In this specific patient group, the transplantation itself may have a different impact, as shown by Guimaro and colleagues, who found high symptom levels of PTS (46%) in patients transplanted for acute liver failure. Therefore, the course of PTSD in patients with an acute onset of their liver disease or who were on the waiting list for a short period of time, needs to be examined in future research.

A limitation of our study is that, because the start of the study was before the introduction of the DSM-5, we were not able to examine PTSD in our population based on the latest insights. However, a study by O’Donnell and colleagues showed that the prevalence scoring under DSM-5 was not significantly different from DSM-IV. Therefore, the results of our study may also be representative for DSM-5 criteria.

Another limitation was that we only used self-report to assess symptoms of PTSD. A clinician-ascertained diagnosis of PTSD may have added value. Also, the nature of the re-experiencing symptoms was only assessed by self-report. As a consequence of this, not all respondents, who indicated having intrusive memories or dreams, described the content of these thoughts or dreams. In addition, probing questions aimed at gaining more in-depth understanding of the nature of the re-experiencing symptoms was not
possible. For future research, we suggest using interviews to obtain a more in-depth understanding of these symptoms.

In conclusion, in liver transplant patients PTSD symptomatology is more present than PTSD caseness. During the waiting-list period, more patients satisfy the criteria for either full or partial PTSD – often accompanied by co-morbid conditions of anxiety and/or depression – than after the transplant. Having a life-threatening disease was found to be the main stressor for PTSD in transplant patients. Although aspects related to the transplantation itself, such as the stay on the ICU or delirium, were described as stressors after the transplant, this did not lead to development of full PTSD after transplantation. Arousal symptoms, such as sleeping disorders and concentration problems, were most frequently reported by transplant patients. However, these symptoms were not found to be unique to PTSD, whereas symptoms of re-experiencing and avoidance contributed the most to caseness for PTSD. Therefore, when patients report symptoms of re-experiencing transplant, healthcare workers should be aware of the possibility of PTSD. However, because of the overlap with disease and treatment-related factors, and with other psychological disorders, it is difficult to disentangle differences. Therefore, when PTSD is suspected, it seems important to refer to a clinician in order to confirm the diagnosis and subsequently initiate appropriate interventions.
REFERENCES


