Post-traumatic stress disorder in living donors after pediatric liver transplantation

A cross-sectional investigation study

Yimao Zhang, MD^a, Junxiang Wang, MD^a, Shuguang Jin, MD^{a,*}, Bo Xiang, MD^a, Jiaying Yang, MD^b, Kewei Li, MD^a, Bing Huang, MD^c, Wei Lai, MD^d, Lunan Yan, MD^b, Jichun Zhao, MD^c

Abstract

Liver transplantation can lead to post-traumatic stress disorder (PTSD) in recipients, but the risk factors associated with PTSD in living donors are unknown. To investigate this progression in pediatric living donors, a cross-sectional investigation was carried out.

All participants completed 2 questionnaires: a PTSD self-rating scale (PTSD-SS) and a validated Chinese version of the Medical Outcomes Study Short Form-36 (SF-36). Clinical and demographic data were collected from medical records and self-report questionnaires. Univariate analysis was conducted to identify statistical differences.

The prevalence of full PTSD (all symptom clusters) and partial PTSD (2 out of 3 symptom clusters) was 12.1% and 31.1%, respectively. Those with an educational status of elementary school (P = .001), who were donors to their children (P = .008), who were in the first 6 months after transplant (P < .001), or were involved in transplants where the recipients had severe complications (P = .02) were more likely to have higher PTSD-SS scores than other groups. The non-PTSD group had a higher health-related quality-of-life score compared with the full and partial PTSD groups in the domains of physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. In addition, the occurrence of PTSD was related to a poorer quality of life.

The occurrence of PTSD was common in living donors after pediatric liver transplantation. Those with a lower educational status, who were donors to their children, were in the first 6 months after transplant, or were involved in transplants where the recipients had severe complications were most likely to experience PTSD. Post-traumatic stress symptom severity was significantly associated with a poorer quality of life after transplant.

Abbreviations: HRQoL = health-related quality of life, PTSD = post-traumatic stress disorder, PTSD-SS = post-traumatic stress disorder self-rating scale, SF-36 = Study Short Form-36.

Keywords: living donor, pediatric liver transplant, post-traumatic stress disorder, quality of life, SF-36

1. Introduction

Post-traumatic stress disorder (PTSD) is a debilitating mental disorder related to directly experiencing or witnessing a traumatic, tragic, or terrifying event.^[1,2] People with PTSD usually have persistent frightening thoughts and memories of the ordeal and feel emotionally numb.^[3,4] While many of those who experience traumatic events can recover well without treatment, if the biological and adaptive coping responses are inadequate or

Editor: Ediriweera Desapriya.

Funding: This study was supported by Natural Science Foundation of China (81571473).

^a Department of Pediatric Surgery, ^b Department of Liver Surgery, ^c Department of Vascular Surgery, ^d Department of Intensive Care Unit, West China Hospital of Sichuan University, Chengdu City, Sichuan Province, China.

* Correspondence: Shuguang Jin, Department of Pediatric Surgery, West China Hospital of Sichuan University, Chengdu City, Sichuan Province, China (e-mail: shgjin2003@aliyun.com).

Copyright © 2019 the Author(s). Published by Wolters Kluwer Health, Inc. This is an open access article distributed under the Creative Commons Attribution License 4.0 (CCBY), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Medicine (2019) 98:20(e15565)

Received: 20 December 2018 / Received in final form: 10 April 2019 / Accepted: 11 April 2019

http://dx.doi.org/10.1097/MD.000000000015565

the stress becomes overwhelming, psychological distress can intensify over time and eventually lead to PTSD. Surgical innovations and improvements in immunosuppressants have radically changed the prognosis for solid organ transplant recipients in recent years. This is also true of pediatric liver transplantation, for which outcomes and prognoses have improved.^[5] Despite these advances, however, liver transplantation still has a huge physical and psychological impact on recipients and living donors. We have previously reported on PTSD in adult liver transplant recipients.^[6] In this study, we aim to report on PTSD, including prevalence, potential risk factors, and self-reported health-related quality of life (HRQoL), in living donors after pediatric liver transplantation.

Medicine

2. Methods

2.1. Participants

From January, 2008 to August, 2018, 154 consecutive living donors for pediatric liver transplantation at West China Hospital of Sichuan University were approached for participation. The investigation extended from July, 2017 to August, 2018. Inclusion criteria were: aged over 18 years and with a postsurgery period over 12 months. The exclusion criterion was severe medical complications that prevented the donors from completing the questionnaires or limited their expression. Donors who were lost to follow-up were also excluded from this study. All participants were required to complete a PTSD self-rating scale

The authors have no conflicts of interest.

(PTSD-SS) and a validated Chinese version^[7] of the Medical Outcomes Study Short Form-36 (SF-36).^[8,9] Questionnaires were completed by interview or mail. Clinical and demographic data were collected from medical records and self-report questionnaires.

2.2. Instruments

Post-traumatic stress disorder is an anxiety disorder characterized by 3 general symptom clusters: re-experiencing traumatic events; avoidance of people, places, or things that serve as reminders of the trauma; and chronic hyperarousal symptoms. The PTSD-SS is a 24-item self-reported inventory in which each item is rated on a 5-point scale of distress (1-5) ranging from "not at all" to "extremely" distressing. Moreover, PTSD can be categorized into "full PTSD" or "partial PTSD." PTSD in participants who scored a minimum of 1 on re-experiencing symptoms, 3 on avoidance symptoms, and 2 on hyperarousal symptoms at a severity level of at least 3 (midrange) per item were defined as having full PTSD. PTSD in participants who experienced 2 of the 3 symptom clusters was defined as partial. Total symptom severity of post-traumatic stress was measured by summing the severity ratings of individual items. The internal consistency (Cronbach α), and split-half and test-retest reliability coefficients were 0.9207, 0.9539, and 0.8677, respectively. The validity of the PTSD-SS was confirmed.^[10]

Health-related quality of life was assessed by the Chinese version of the SF-36^[7,8,9]—a valid and self-administered questionnaire used internationally to measure 8 major health concepts: physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health over 12 months. Role-physical condition included limit in time of tasks, accomplishment with tasks, limit types of tasks, and difficulty with tasks. The raw scores of each subscale were transformed into scores that ranged from 0 to 100. Higher scores indicated higher levels of function or well-being.

2.3. Ethical considerations

The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Ethics Committee of West China Hospital of Sichuan University. All participants provided written informed consent.

2.4. Statistical analysis

Statistical analysis was performed by SPSS 25 statistical software. Between-group differences were tested by the independent-samples Student *t* test, analysis of variance, or nonparametric test, as appropriate. Multiple comparisons of observed means were performed by the Student–Newman–Keuls test when equal variances could be assumed and by the Games–Howell procedure when they could not. A probability value of P < .05 represented a statistically significant difference.

3. Results

3.1. Donor characteristics

Among the total pediatric liver transplant donors, 14 were lost to follow-up, and 8 were unable to read Chinese. Finally, 132 donors (85.7%) were included in this study. The results of the PTSD-SS and SF-36 questionnaires completed by interview or

Table			
Demons	 ~~~	-+-	

Table 4

U	onors	characteristics.	

Variables	Categories	n	%
Sex	Male	60	45.5%
	Female	72	54.5%
Age (y)	≤30	73	55.3%
	>30	59	44.7%
Marital status	Married	126	95.5%
	Unmarried	0	0
	Divorced/widowhood	6	4.5%
Educational status	Elementary school	32	24.2%
	Middle school	48	36.4%
	University	52	39.4%
Occupation	Workers	31	23.5%
	Civil servants	49	37.1%
	Peasants	23	17.4%
	Liberal professionals	29	22.0%
Family income (RMB/mo)	≤5000	36	27.3%
	>5000, ≤10,000	63	47.7%
	>10,000	33	25.0%
Relationship with recipients	Parents	115	87.1%
	Nonparents	17	12.9%
Etiology of recipients' disease	Biliary atresia	84	63.6%
	Hepatic cirrhosis	25	18.9%
	Hepatic tumor	5	3.8%
	Others	18	13.6%
Time since surgery	\leq 6 mos	15	11.4%
	$>$ 6 mos, \leq 1 y	18	13.6%
	>1 y, ≤3 y	78	59.1%
	>3 y	21	15.9%
Condition of recipients	Without severe complications	95	72.0%
	With severe complications	18	13.6%
	Death	19	14.4%

RMB = Renminbi.

* Sum of per cent not equal to 100% due to rounding.

mail were not significantly different. The mean age of the donors was 29.4 ± 8.0 years. The demographic and transplant-related characteristics of the study population are shown in Table 1.

3.2. Prevalence of PTSD

The prevalence of PTSD was as follows: 75 cases (56.8%) did not meet the criteria for partial or full PTSD after liver transplant, 41 (31.1%) met the criteria for partial PTSD, and 16 (12.1%) met the criteria for full PTSD.

The results of analysis of posttraumatic stress are shown in Table 2. There were significant differences in donors in terms of educational status (P=.001), relationship with recipients (P=.008), time since transplant (P<.001), and condition of recipients (P=.02). Those with an educational level of elementary school, who were donors to their own children, were in the first 6 months after transplant, and were involved in transplants where the recipients suffered severe complications were more likely to have a high PTSD score than other groups. According to Fig. 1, the severity of post-traumatic stress in living donors decreased with time after surgery.

The results of the analysis of HRQoL in transplant donors are shown in Table 3. The non-PTSD group had a higher score compared with full and partial PTSD groups in physical function, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health. There were statistically significant differences between the non-PTSD and full

Table 2	
Results of analysis of post-traumatic stress.	

Factors/total symptom severity of post-traumatic stress						
Educational status	University	Middle school	Elementary school		F/T	Р
	31.37±8.65	$37.30 \pm 11.43^{*}$	40.77±13.401 [*]		7.482	.001
Relationship with recipients	Parents	Nonparents				
	39.43±13.01	32.37 ± 8.87			7.186	.008
Time since transplant	\leq 6 mos	>6 mos, ≤ 1 y	>1 y, ≤3 y	>3 y		
	43.96±13.35	40.37 ± 13.92	$31.29 \pm 6.89^{\dagger}$	$31.16 \pm 7.07^{\dagger}$	11.02	<.001
Condition of recipients	Without severe complications	With severe complications	Death			
	35.07 ± 11.97^3	42.58±13.59	34.38 ± 9.67 [‡]		3.773	.02

Only statistically significant data are displayed.

* Compared with group "university" (P < .05).

⁺Compared with group " \leq 6 mos" and ">6 mos, \leq 1 y" (P<.05).

^{\ddagger} Compared with group "without severe complications" (P<.05).

or partial PTSD groups in the role-physical (P < .001), general health (P = .001), vitality (P = .008), social functioning (P = .001), role-emotional (P < .001), and mental health (P = .001) domains. There were also statistically significant differences in the role-emotional domain in the full and partial PTSD groups.

4. Discussion

Post-traumatic stress disorder is prevalent in pediatric transplant recipients.^[11] Previous literature has found the occurrence of PTSD to be associated with poor transplant outcomes, primary disease, educational status, and so on.^[11–14] However, evidence of PTSD in transplant donors has been limited. Therefore, this study conducted a detailed survey, involving the risk factors for PTSD and quality of life, in living donors for pediatric liver transplants, which may contribute to the prevention of PTSD.

In our survey, the incidences of full and partial PTSD in living donors were 12.1% and 31.1%, respectively, indicating that the development of postoperative full or partial PTSD is common in living donors for pediatric liver transplantation. Currently, most donors are patients or immediate relatives, and the transplantation may be high-risk and unpredictable. Therefore, based on this situation, transplant donors, especially parents, may experience great pressure, both physically and mentally. Young et al^[11] also reported that PTSD seemed to be most common in parents of recipients. Additionally, pediatric recipients are at an important stage of physical and mental development.^[13] Some complications may occur after liver transplant. Long-term use of immunosuppressants may also cause side effects to the body. Apart from this, donors are always anxious about recipients' long-term survival rates and the psychological or social problems that may arise during their development. We also found that the postoperative health status of recipients was closely associated with the occurrence of PTSD in living donors. Thus, it can be seen that because of the particularity of the relationship between donors and recipients in pediatric liver transplantation, severe postoperative stress response or even PTSD are likely in donors.

This study found that higher educational status in donors was a protective factor for the occurrence of PTSD. In addition, the occurrence of PTSD was not only related to pathogenic factors or stress events^[15] but also to emotions, thoughts, behaviors, and physiological reactions due to individual differences.^[16] People with a higher educational status were generally more knowledgeable and found it easier to understand the process and cause



Analysis of health-related quality of life in transplant donors.					
	Full PTSD (mean \pm SD)	Partial PTSD (mean \pm SD)	Non-PTSD (mean \pm SD)	F	Р
Physical function	68.73±39.72	82.04 ± 27.79	82.07 ± 21.54	2.654	.07
Role-physical	51.64 ± 40.99	59.19 ± 36.58	86.19±25.84 [*]	13.96	<.001‡
Bodily pain	64.21 ± 32.75	59.89 ± 20.13	70.46 ± 23.34	1.454	.15
General health	52.81 ± 19.65	51.86 ± 24.16	$68.56 \pm 21.22^*$	8.060	.001 [‡]
Vitality	50.71 ± 30.63	44.88 ± 34.42	62.47 ± 23.45	5.013	.008 [‡]
Social functioning	55.36 ± 32.79	62.96 ± 30.12	$77.96 \pm 21.33^*$	7.625	.001 [‡]
Role-emotional	32.74 ± 36.76	$55.12 \pm 45.24^{\dagger}$	$79.55 \pm 33.27^*$	12.749	<.001‡
Mental health	51.71 ± 30.48	46.74 ± 34.33	$68.13 \pm 24.28^*$	7.536	.001 [‡]

SD = standard deviation; PTSD = post-traumatic stress disorder.

* The statistical difference between non-PTSD and full PTSD & partial PTSD was significant.

[†] The statistical difference between full PTSD and partial PTSD was significant.

[‡] P < 0.05

Table 3

of events. They could, therefore, adapt to sudden stress and manage psychological problems. Moreover, their interpersonal relationships enabled them to receive more support. Additionally, donors with a higher educational status were more likely to have a better job and receive higher compensation, which could have reduced their anxiety about economic burden and the stimulation of stress events.

Postsurgery stage was also associated with the development of PTSD. The severity of post-traumatic stress in donors decreased with time after surgery. Donors generally experienced the most stress and emotional instability in the initial months of the postoperative period. Annema et al^[17] found that in recipients, PTSD was most prevalent in the first year after liver transplantation, which was similar to our results on donors. Generally, stress in donors decreased with improved physical condition and disease resistance in recipients. With time, the occurrence of infection, acute rejection, and frequency of follow-up decreased, which may have contributed to the reduction of adverse stress and the alleviation of scene repetition. Therefore, this survey suggested the necessity of intervention measures to reduce stress stimulation and avoid the development of PTSD during the early post-transplant period.

Many studies have suggested that PTSD may lead to the reduction of quality of life in patients,^[18–24] and this is true in the case of organ transplantation as well. Young et al^[11] reported that PTSD seemed relatively common in parents of pediatric transplant recipients and their quality of life greatly reduced after pediatric bone marrow transplantation. We have previously reported in the case of adult liver transplantation, PTSD always leads to a poor quality of life for the recipients, especially from the mental perspective.^[6] However, this survey showed that donors also experience a lower quality of life, particularly in the domains of mental health, role-emotional, and social functioning. Therefore, PTSD can greatly lower the quality of life of donors. With the improvement of surgical techniques and immunological rejection management, number of cases of living organ transplantation will only increase, and rather rapidly. With the number of transplant donors also continually increasing, it is imperative that the questions of how to decrease stress and improve the quality of postoperative life be answered. Effective interventions must be administered to prevent the development of PTSD and improve HRQoL.

This study may contribute to the prevention of PTSD in pediatric living donors. First, to eliminate anxiety in donors, sufficient communication to enable them to fully understand the operation is essential, especially in donors who are parents of recipients and have lower educational status. Additionally, regular psychological counseling for donors is necessary, especially in the first 6 months after transplant. Different schemes can be decided upon based on donors' educational backgrounds. Moreover, in our study, it was found that donors were more likely to develop PTSD when the recipients suffered severe complications. To avoid this situation, the further improvement of perioperative management, which may reduce the possibilities of severe surgical complications, is required.

Our study also had several limitations. First, as it was a singlecenter study, the generalizability of our results may be limited. Additionally, the sample size was relatively small owing to the low number of pediatric liver transplantations compared with adult transplantation. Apart from this, as compared with longitudinal data, cross-sectional data provide insufficient information to understand the changes in the severity of posttraumatic stress symptoms over time. Therefore, more related studies are needed. Despite these limitations, however, this is the first study to discuss the risk factors for PTSD and quality of life in living donors for pediatric liver transplantation, which may contribute to positive interventions for PTSD.

5. Conclusions

The occurrence of PTSD was common in living donors after pediatric liver transplantation. Those with lower educational status, who were donors to their own children, who were in the first 6 months after transplant, or who were involved in transplants where the recipients suffered severe complications were most likely to experience PTSD. Severity of post-traumatic stress symptoms was significantly associated with a poorer quality of life after transplantation.

Author contributions

Conceptualization: Shuguang Jin. Data curation: Yimao Zhang, Junxiang Wang, Kewei Li. Formal analysis: Shuguang Jin, Bo Xiang. Investigation: Yimao Zhang, Shuguang Jin. Methodology: Jiaying Yang, Bing Huang. Project administration: Yimao Zhang, Junxiang Wang. Resources: Jichun Zhao. Software: Yimao Zhang, Junxiang Wang, Wei Lai, Lunan Yan. Supervision: Shuguang Jin. Validation: Junxiang Wang. Visualization: Shuguang Jin. Writing – original draft: Yimao Zhang.

Writing – review & editing: Shuguang Jin.

References

- Javidi H, Yadollahie M. Post-traumatic stress disorder. Int J Occup Environ Med 2012;3:2–9.
- [2] Pietrzak RH, Goldstein RB, Southwick SM, et al. Psychiatric comorbidity of full and partial posttraumatic stress disorder among older adults in the United States: results from wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. Am J Geriatr Psychiatry 2012; 20:380–90.
- [3] Pietrzak RH, Goldstein RB, Southwick SM, et al. Prevalence and Axis I comorbidity of full and partial posttraumatic stress disorder in the United States: results from Wave 2 of the National Epidemiologic Survey on Alcohol and Related Conditions. J Anxiety Disord 2011;25:456–65.
- [4] Sareen J, Cox BJ, Stein MB, et al. Physical and mental comorbidity, disability, and suicidal behavior associated with posttraumatic stress disorder in a large community sample. Psychosom Med 2007;69:242–8.
- [5] Yazigi NA. Long term outcomes after pediatric liver transplantation. Pediatr Gastroenterol Hepatol Nutr 2013;16:207–18.
- [6] Jin SS, Yan LN, Xiang B, et al. Posttraumatic stress disorder after liver transplant. Hepatobiliary Pancreat Dis Int 2012;11:28–33.
- [7] Li L, Wang HM, Sheng Y. Development and psychometric tests of a Chinese version of the SF-36 Health Survey Scales. Zhonghua Yu Fang Yi Xue Za Zhi 2002;36:109–13.
- [8] Ware JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473–83.
- [9] Ware JE, Snow KK, Kosinski M, et al. SF-36 Health Survey Manual and Interpretation Guide. Boston, MA: The Health Institute, New England Medical Center; 1993.
- [10] Hui WL, Shi WH, Xu DZ, et al. Influencing factors of PTSD in the shipwreck related military rescuer in Yantai. Chin Mental Health J 2001;15:148–9.
- [11] Young GS, Mintzer LL, Seacord D, et al. Symptoms of posttraumatic stress disorder in parents of transplant recipients: incidence, severity, and related factors. Pediatrics 2003;111:725–31.

- [12] Farley LM, DeMaso DR, D'Angelo E, et al. Parenting stress and parental post-traumatic stress disorder in families after pediatric heart transplant. J Heart Lung Transplant 2007;26:120–6.
- [13] Supelana C, Annunziato RA, Kaplan D, et al. PTSD in solid organ transplant recipients: current understanding and future implications. Pediatr Transplant 2016;20:23–33.
- [14] Taskıran G, Sürer Adanır A, Özatalay E. Living with the unknown: posttraumatic stress disorder in pediatric bone marrow transplant survivors and their mothers. Pediatr Hematol Oncol 2016;33:209–18.
- [15] Karam EG1, Friedman MJ, Hill ED, et al. Cumulative traumas and risk thresholds: 12-month PTSD in the World Mental Health (WMH) surveys. Depress Anxiety 2014;31:130–42.
- [16] Kirkpatrick HA, Heller GM. Post-traumatic stress disorder: theory and treatment update. Int J Psychiatry Med 2014;47:337–46.
- [17] Annema C, Drent G, Roodbol PF, et al. A prospective cohort study on posttraumatic stress disorder in liver transplant recipients before and after transplant: prevalence, symptom occurrence, and intrusive memories. J Psychosom Res 2017;95:88–93.
- [18] Baranyi A, Rösler D, Rothenhäusler HB. Stress symptoms and healthrelated quality of life in patients after orthotopic liver transplant. Z Psychosom Med Psychother 2012;58:417–28.
- [19] Guimaro MS, Lacerda SS, Aguilar MR, et al. Post-traumatic stress disorders, mood disorders, and quality of life in transplant recipients with acute liver failure. Transplant Proc 2011;43:187–8.
- [20] Ehlers A, Hackmann A, Grey N, et al. A randomized controlled trial of 7day intensive and standard weekly cognitive therapy for PTSD and emotion-focused supportive therapy. Am J Psychiatry 2014;171:294–304.
- [21] Monson CM, Macdonald A, Vorstenbosch V, et al. Changes in social adjustment with cognitive processing therapy: effects of treatment and association with PTSD symptom change. J Trauma Stress 2012; 25:519–26.
- [22] Schneier FR, Campeas R, Carcamo J, et al. Combined mirtazapine and SSRI treatment of PTSD: a placebo-controlled trial. Depress Anxiety 2015;32:570–9.
- [23] Schnurr PP, Lunney CA. Symptom benchmarks of improved quality of life in PTSD. Depress Anxiety 2016;33:247–55.
- [24] Davidson J1, Rothbaum BO, Tucker P, et al. Venlafaxine extended release in posttraumatic stress disorder: a sertraline- and placebocontrolled study. J Clin Psychopharmacol 2006;26:259–67.