Postoperative Psychiatric Complications in Living Liver Donors

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ABSTRACT

Background. To understand the impact of psychologic variables on donor quality of life, we studied long-term data on postoperative psychiatric complications in living liver donors. This study is a focused psychological investigation of diagnoses, treatments, and long-term clinical courses of living liver donors with psychiatric complications.

Methods. Of the 142 donors who underwent live-donor liver transplantation at Nagoya University Hospital between April 2004 and July 2014, we investigated those without a history of mental illness who had developed such illness after transplantation and required psychiatric treatment.

Results. A total of 6 (4.2%) donors developed the following psychiatric complications after transplantation: major depressive disorder (n = 2), panic disorder (n = 2), conversion disorder (n = 1), and substance use disorder (n = 1). Concerning psychiatric treatment, all donors received antianxiety drugs, 3 took antidepressants, and supportive psychiatric therapy was concomitantly provided to all subjects. The average treatment period was 53.3 months. Regarding subject outcomes, 3 donors achieved remission, and the other 3 continued treatment. All subjects showed improvement in Global Assessment of Functioning Scale.

Conclusion. It is important to accurately diagnose postoperative psychiatric complications and provide long-term treatment in close coordination with transplant surgeons.

LIVE-DONOR liver transplantation has been performed since 1988, partially because of a lack of donated livers [1]. Of all the types of medical services, surgery for organ donors is the only one without medical indications, so close attention needs to be paid to donors' health and safety. In 2000, the Live Donor Consensus Group issued a statement regarding donor protection [2] that reconfirmed that donors should voluntarily provide organs with a full understanding of the associated benefits and risks. Since the statement was issued, physicians have held discussions with donors regarding postoperative complications [3–10]. These discussions had previously focused on physical complications, but researchers also began to pay attention to psychiatric complications. In 2001, Fukunishi et al [11] reported depression in 3.4% of the subjects (4/116) after live-donor liver transplantation. In 2003, a retrospective study was conducted to investigate complications among all donors in Japan, which found that 0.16% of them had developed depression [10]. In 2007, Trotter et al [12] conducted a multicenter study of psychiatric complications, in which 4.1% of the subjects developed mental illnesses. In 2011, a study to monitor the long-term clinical courses of donors after live-donor liver transplantation found that 8% developed mental illness [13]. In 2013, a study involving 21 countries reported that complications were noted in 24% of the subjects (n = 11,553) after live-donor liver transplantation [14]. This study did not investigate mental illness, but, among the 23 deceased donors (0.04%), 5 had committed suicide, presumably due to mental illness.

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0041-1345/15
http://dx.doi.org/10.1016/j.transproceed.2015.06.021

However, in many of these existing studies, the definition of a psychiatric complication was ambiguous, psychiatrists did not provide diagnoses or treatments, and it was unknown whether donors had their mental illnesses before or after their transplantation took place [15]. This present study is a focused psychological investigation of diagnoses, treatments, and long-term (average treatment period: 53.3 months) clinical courses of living liver donors with psychiatric complications. We defined a psychiatric complication as a post-transplantation diagnosis of mental illness given by psychiatrists to a donor without a history of mental illness, who required regular psychiatric treatment both before and after discharge.

SUBJECTS AND METHODS

Background

At Nagoya University Hospital, approximately 20 cases of liver transplantation are performed annually. In 2004, a transplantation medical team consisting of transplant surgeons, gastroenterologists, psychiatrists, transplant coordinators, and psychologists was created, and they regularly hold interprofessional conferences.

Procedure for Assessing Donors From a Psychiatric Aspect

In line with the ethical guidelines of the Japan Society for Transplantation, all potential donors were evaluated from both physical and psychiatric aspects after obtaining their written informed consent in the Department of Transplantation Surgery. For donor protection, psychiatric assessment was performed by independent psychiatrists and psychologists with expertise in transplantation. They investigated whether donors intended to provide their liver, and whether they fully understood the risks and benefits associated with transplantation. Their mental illnesses were evaluated through thorough history-taking and screening conducted based on the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) [16] (SCID) [17].

Diagnoses of Psychiatric Complications

If psychiatric problems were suspected in a patient after transplantation, transplant surgeons or coordinators consulted physicians in the Department of Psychiatry. Psychiatrists with expertise in transplantation reviewed the necessity for psychiatric diagnosis and intervention. Diagnoses of mental illnesses were made based on SCID [17].

Subjects

Of the 142 patients who underwent live-donor liver transplantation at Nagoya University Hospital between April 2004 and July 2014, our study investigated those without a history of mental illness who had developed such an illness after transplantation and required psychiatric treatment.

Results

Table 1 shows the demographic characteristics of living liver donors. One donor has comorbid psychiatric disorder. The patient was a 19-year-old woman. She complained of depression, insomnia and hypomania. She was diagnosed with bipolar II disorder (DSM-IV-TR) [16] by the attending psychiatrist. She received appropriate psychiatric treatment and was in remission. Five years later, She was a candidate to donate her liver to her mother who had liver cirrhosis caused by hepatitis C virus (HCV). After the physical and psychiatric assessment for the transplantation, she donated her right lobe to her mother, and 596 days after the donation, she maintained good physical and psychiatric health.

Table 1. Sociodemographic and Clinical Characteristics of Living Liver Donors

Mean duration from donation to the survey (range)	1,986.0 ± 1,160.8 days (8–3,769)
Mean age (range)	36.6 ± 11.4 years (19–62)
Sex	
Male	66
Female	76
Mean operative time	463.7 ± 108.9 min
Mean amount of bleeding	477.3 ± 408.9 mL
Mean weight of the graft	477.3 ± 205.5 g
Graft type	1. Lateral segment 33.1% (n = 47) 2. Left lobe 14.1% (n = 20) 3. Right lobe 52.8 (n = 75)
Mean duration of hospitalization days from donation to leaving the hospital	16.4 ± 6.3 days
Comorbid psychiatric disorder	Bipolar II Disorder (n = 1)
Relationship of donor to recipient	Parent to Child 40.1% (n = 57) (Father to Child n = 23, Mother to Child n = 34) Child to Parent 26.1% (Child to Father n = 18, Child to Mother n = 19) Spouse 22.5% (n = 32) (Husband to Wife n = 13, Wife to Husband n = 19) Sibling 4.9% (n = 7) Grandparent to Grandchild 2.1% (n = 3) Uncle to Nephew 1.4% (n = 2) Aunt to Nephew 1.4% (n = 2) Sister-in-law to Sister-in-law 0.7% (n = 1) Foster daughter to Foster mother 0.7% (n = 1)
Residential status of donor and recipient	Cohabitation 70.4% (n = 100) Separation 25.4% (n = 36) Unknown 4.2% (n = 6)
Marital status	Marriage 69.0% (n = 98) Single 23.2% (n = 33) Divorce after transplantation 4.2% (n = 6) Marriage after transplantation 3.5% (n = 5)

Table 2 shows the diagnosis and mortality of liver transplant recipients. The primary diagnoses of recipients were as follows: biliary atresia (n = 48), cirrhosis caused by HCV (n = 30), primary biliary cirrhosis (PBC) (n = 19), cirrhosis caused by hepatitis B virus (HBV) (n = 15), fulminant hepatitis (n = 7), autoimmune disorders (n = 4), Alagille syndrome (n = 3), hepatoblastoma (n = 3), primary sclerosing cholangitis (PSC) (n = 2), Wilson's disease (n = 2), and others (n = 9). There were 7 recipient deaths (4.9%).

Table 2. Diagnosis and Mortality of Liver Transplant Recipients

Primary diagnosis of recipient	Biliary atresia 33.8% (n = 48)
	Cirrhosis caused by HCV 21.1% (n = 30)
	Primary biliary cirrhosis (PBC) 13.4% (n = 19)
	Cirrhosis caused by HBV 10.6% (n = 15)
	Fulminant hepatitis 5.0% (n = 7)
	Autoimmune disease 2.8% (n = 4)
	Alagille syndrome 2.1% (n = 3)
	Hepatoblastoma 2.1% (n = 3)
	Primary sclerosing cholangitis (PSC) 1.4% (n = 2)
	Wilson's disease 1.4% (n = 2)
	Autosomal recessive polycystic kidney disease (ARPKD) 0.7% (n = 1)
	Ornithine transcarbamylase deficiency 0.7% (n = 1)
	Hypercitrullinemia 0.7% (n = 1)
	Polycystic liver disease (PCLD) 0.7% (n = 1)
	Non-B, non-C hepatitis 0.7% (n = 1)
	Idiopathic biliary ductopenia 0.7% (n = 1)
	Alcoholic cirrhosis 0.7% (n = 1)
	Cirrhosis of unknown cause 0.7% (n = 1)
	Liver metastasis of solid pseudopapillary tumor (SPT) 0.7% (n = 1)
Recipient death	4.9% (n = 7)

Table 3 shows the incidence of postoperative physical complications among living liver donors, which included fluid collection in 19.7% (n = 28), pleural effusion in 11.3% (n = 16), wound infection in 4.2% (n = 6), numbness in 2.8% (n = 4), pneumonia in 2.8% (n = 4), atelectasis in 2.1% (n = 3), gastric outlet obstruction in 1.4% (n = 2), delayed wound healing in 1.4% (n = 2), bile leakage in 1.4% (n = 2), and other complications in 5.6% (n = 8).

Table 4 shows the postoperative psychiatric complications in living liver donors. Of the 142 subjects, psychiatric complications occurred in 6 cases (4.2%) (Clavien classification of surgical complications [18]:IIIa = 2,II= 4). The mean age of the 1 male and 5 female donors was 35.3 ± 12.2 years (range 27–52 years). Marital status was 4 marriages, 1 remarriage after transplantation, and 1 single. The social functions were 2 workers and 4 housewives. The relationship of donor to recipient was as follows: mother (n = 2), wife (n = 2), sibling (n = 1), and adopted child approved by the Ethics Review Committee (n = 1). Among the recipients, 3 were cured, 1 died, 1 developed mental retardation, and 1 developed liver dysfunctions of unknown cause. Donor postsurgical length of stay was 29 ± 13.8 days. Postoperative physical complications included inferior vena cava thrombosis, wound infection, severe anemia with homologous blood transfusion in case 1, and bile leakage in case 4. The mean duration from donation to the diagnosis of psychiatric disorder was 252.0 ± 196.3 days. Psychiatric diagnoses were major depressive disorders (n = 2), panic disorders (n = 2), conversion disorders (n = 1), and substance use disorders (n = 1).

Table 3. Postoperative Physical Complications in Living Liver Donors % (N)

Fluid collection	19.7 (n = 28)
Pleural effusion	11.3 (n = 16)
Wound infection	4.2 (n = 6)
Numbness	2.8 (n = 4)
Pneumonia	2.8 (n = 4)
Atelectasis	2.1 (n = 3)
Gastric outlet obstruction	1.4 (n = 2)
Delayed wound healing	1.4 (n = 2)
Bile leakage	1.4 (n = 2)
Lung infarction	0.7 (n = 1)
Ileus	0.7 (n = 1)
Severe anemia with homologous blood transfusion	0.7 (n = 1)
Brachial plexus palsy	0.7 (n = 1)
Intra-abdominal abscess	0.7 (n = 1)
Inferior vena cava thrombosis	0.7 (n = 1)
Prostatitis	0.7 (n = 1)
Median neuropathy	0.7 (n = 1)

Psychosocial and environmental stressors at the onset of psychiatric disorders were 1 recipient death (n = 1), recipient in sequelae (n = 1), deterioration of a relationship with the recipient (n = 2), and deterioration of a relationship with the family (n = 4). The mean duration of psychiatric treatment was 1581.2 ± 1619.9 SD days. Psychiatric treatment included both psychotherapy and psychopharmacology for all donors. With regard to psychopharmacology, minor tranquilizers were administered to all donors and antidepressants were administered to 3 donors. Psychotherapy was provided for all donors. The clinical courses of the psychiatric disorders were assessed with The Global Assessment of Functioning Scale (GAF Scale) for each year (Fig 1).

DISCUSSION

In the present study, we investigated the clinical characteristics and courses of 6 living liver donors who had developed psychiatric complications after transplantation. In the study, 4.2% of the subjects developed psychiatric complications. This rate was similar to that (3.4% [4/116]) reported by Fukunishi et al [11]; however, that study also involved those who had developed mental illnesses before transplantation. Umeshita et al [10] investigated all donors in Japan and found that, among the potential psychiatric complications, depression was noted in 0.16% of subjects (3 of 1841). Six years later, they conducted another investigation, in which psychological problems were observed in 0.14% of subjects (5 of 3565). These rates were much lower than those reported in other previous studies, possibly due to the retrospective nature of these 2 studies and the absence of psychiatric diagnoses. In the present study, screening was performed based on the SCID, and accurate psychiatric diagnoses were provided. In a study conducted by Trotter et al [12], psychiatric complications were observed in 4.1% of subjects (16/392), a percentage similar to that reported in our study. They identified marked psychiatric complications in 3 subjects, including 2 patients who had committed suicide. In contrast, such complications were not observed in the present study. Sotiropoulos et al [13] monitored the long-term clinical courses of organ donors, 7.2% (6/83) of whom developed depression. All patients received pharmacotherapy with antidepressants. In addition, 2 patients

Table 4. Postoperative Psychiatric Complications in Living Liver Donors

No.	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	27	32	50	22	30	51
Sex	Female	Female	Female	Males	Female	Female
Marital status	Married	Married	Married	Single	Divorce after transplantation	Married
Social Function	Worker	Housewife	Housewife	Worker	Housewife	Housewife
Relationship with recipient	Foster mother	Mother	Wife	Younger brother	Mother	Wife
Outcome of recipient	Death	Mental retardation	Recovery	Recovery	Recovery	Liver dysfunction of unknown cause
Mean duration of hospitalization from donation to leaving the hospital (days)	41	17	33	49	18	18
Postoperative physical complications in donors	Inferior vena cava thrombosis, Wound infection, Severe anemia with homologous blood transfusion	–	–	Bile leakage	–	–
Duration from donation to the time diagnosed with psychiatric disorder (days)	18	40	657	143	396	14
Psychiatric diagnosis (DSM-IV-TR)	Conversion disorder	Panic disorder	Major depressive disorder	Substance abuse	Panic disorder	Major depressive disorder
Psychosocial and environmental stressors that may affect the psychiatric disorders	Recipient death	Psychological conflict with mother-in-law	Psychological conflict with family	Psychological conflict with recipient	Psychological conflict with husband	Psychological conflict with recipient
Duration of psychiatric treatment (days)	3703	3366	1697	343	308	76
Psychiatric treatment	Minor tranquilizer (Alprazolam) Supportive Psychotherapy	Minor tranquilizer (clotiazepam) Antidepressant (Escitalopram) Supportive Psychotherapy	Minor tranquilizer (Alprazolam) Antidepressant (sertraline) Supportive Psychotherapy	Minor tranquilizer (Alprazolam) Supportive Psychotherapy	Minor tranquilizer (Alprazolam) Supportive Psychotherapy	Minor tranquilizer (Alprazolam) Antidepressant (Mirtazapine) Supportive Psychotherapy
Outcome of psychiatric disorder	Under treatment	Under treatment	Under treatment at another hospital	Cure	Cure	Cure
GAF Scale before and after psychiatric treatment	25→70	55→65	25→60	45→80	35→85	50→90
Clavien's classification	GIIIa	GII	GII	GIIIa	GII	GII

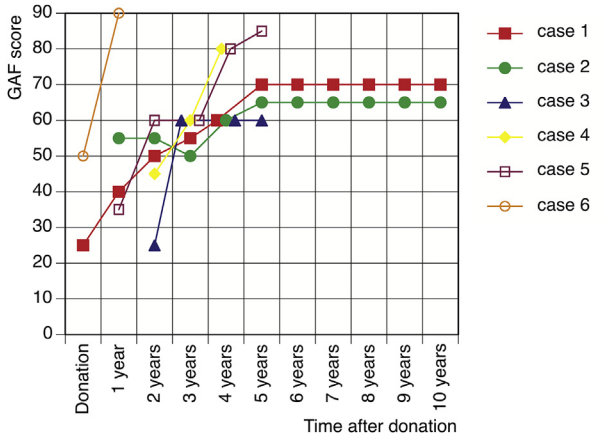

Fig 1. The GAF Scale after donation. The clinical course of the psychiatric disorders were assessed with the GAF Scale for each year.

and 1 patient received out- and inpatient psychotherapy, respectively. Moreover, 3 donors with severe symptoms required regular consultations with clinical psychologists. In the present study, all 6 patients with psychiatric complications received pharmacotherapy with antianxiety drugs combined with outpatient psychotherapy, and 3 also took antidepressants. As a result, all 6 patients showed improvement in their psychiatric symptoms and social functions.

We suggest that organ donors' psychiatric complications are markedly attributable to psychological burdens caused by transplantation. Our study subjects also exhibited transplant-related psychological burdens, such as recipients' deaths, conflicts with recipients, and the worsening of family relationships. These problems could be resolved with supportive psychotherapy. However, we assume that psychological burdens are not the sole cause of psychiatric symptoms. In recent years, researchers have suggested that mental illness occurs through interaction between genetic and environmental factors, and so we should not regard psychological factors as the sole cause of such an illness. In the present study, 4.2% of the subjects developed psychiatric complications. However, in Japan, the prevalence of mental illness among liver donors has been reported to be 8.8% [19]. In other words, the likelihood that mental illness occurs due to causes other than transplantation cannot be denied. It is important to accurately diagnose postoperative psychiatric complications and to continue to provide appropriate treatment, regardless of the causes of these complications.

One of the study limitations was that subjects' mental illnesses might have been underestimated, because postoperative consultations with the Department of Psychiatry were initiated by transplant surgeons and coordinators, and possibly because the incidence rate of mental illness is lower among organ donors than the general population. In addition, it has been suggested that organ donors have a more favorable health status than the general population [20], which might have contributed to the low incidence rate of mental illness among our subjects.

We are planning to conduct a prospective multicenter study involving more subjects to investigate factors responsible for the onset of psychiatric complications and the association of these problems with physical complications.

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