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# Psychosocial outcome and resilience after paediatric liver transplantation in young adults

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## KEYWORDS

Liver transplantation;  
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Quality of life;  
Transition;  
Adherence

## Summary

**Background and objective:** The long-term psychosocial outcome of young adults after paediatric liver transplantation (LT) was investigated with the focus on day-to-day living. We aimed to capture patients' subjective perceptions of well-being and autonomy based on key physical outcome parameters.

**Methods:** All patients following paediatric LT at Hannover Medical School born before 2002 with a post-transplant follow-up of at least four years were included in this study. This retrospective observational study compared psychosocial parameters obtained from a self-designed 77-item questionnaire with standard clinical outcome variables.

**Results:** Eighty-two patients (male: 57%) aged 13–41 years were included in the survey within a three-month period (response rate: 41%). With an adherence rate of 33%, all but two patients were immunosuppressed. In total, 53 patients had transitioned to adult care largely without problems. Eighty-three percent ( $n=68$ ) evaluated their current health status as "(very) good". Sixty-seven patients (82%) did not experience health-related anxiety in daily life.

**Abbreviations:** LT, liver transplantation; HRQL, health-related quality of life; ESPGHAN, European Society for Paediatric Gastroenterology Hepatology and Nutrition; EASL, European Association for the Study of the Liver; KT, kidney transplantation; ADHD, attention deficit hyperactivity disorder; BMI, body mass index.

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*Conclusions:* Our results demonstrate psychological stability and high self-esteem of young patients, as well as good integration into society and a high degree of normality during daily life after LT. Adherence rates are lower than anticipated and do not correlate with patients' understanding of their medical condition.

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## Introduction

Young adults, liver transplanted in childhood, face various and specific challenges compared to their peers undergoing transplantation in later life or without transplantation at all. The young age at disease onset in chronic physical illness may lead to a specific psychosocial experience of normality and perception of quality of life. Iatrogenic, external, factors, such as lifelong immunosuppression may provoke different response patterns in patients transplanted in childhood compared with patients transplanted later and following normal development and settlement in adult life [1,2]. Previous studies demonstrated that following solid organ transplantation in childhood patients show a higher risk of cognitive and academic limitations [3]. The physical function and the health-related quality of life (HRQL) have also been reported to be impaired compared to the general population [4,5].

For a long time, psychological research has made a distinction between physical and psychological health [6]. Psychological indicators are typically related to health and well-being (e.g., satisfaction), whereas physical indicators comprise physical functioning (e.g., biological markers). Although both types of indicators are strongly inter-related, they can also diverge from each other. For instance, reduced physical functioning does not necessarily correlate with reduced life satisfaction or vice versa [7]. Thus, it is important to focus on patients' evaluations of their subjective well-being beyond medical assessment parameters.

To gather additional information beyond standardised assessment tools, such as Paediatric Quality of Life Inventory (PedsQL), this retrospective single-centre study focused on day-to-day routine and emotional quality of life by using a self-designed questionnaire. The following topics were investigated: transition to adult care, physical development and limitations, risk behaviour, emotional quality of life, family status and the desire to have children, as well as education and profession, satisfaction with medical care, medication, adherence, transition to adult care and patients' autonomy. Especially as the time of transition is indicated to be associated with higher non-adherence rates and graft loss [8,9]. By contrast, better knowledge of their immunosuppressive regime has shown to be associated with greater adherence rates [10]. The recent transition guidelines of the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) and the European Association for the Study of the Liver (EASL) also underline the increased significance and complexity of transition [11].

## Subjects and methods

All patients following paediatric LT at Hannover Medical School born before 2002 with a post-transplant follow-up of at least four years were included in this study. Documented clinical outcome parameters included graft rejections, retransplantations and physical development. Only biopsy-proven graft rejections were taken into account. The body mass index (BMI) was adjusted to aged-based percentiles [12]. For all patients < 18 years, linear growth impairment was defined as a height < 10th height for age percentile [12]. For adults, linear growth impairment was analysed using the genetic target height according to Tanner [13].

All patients were contacted by mail at least twice, and non-responders were contacted by phone or mail. Completed questionnaires were included in the study within a three-month deadline. The only exclusion criterion was the inability to complete the questionnaire without external support ( $n = 1$ ). The Research Ethics Committee of Hannover Medical School approved this study (No. 2658-2015).

In order to achieve the above objectives, a 77-item questionnaire was developed by a multi-disciplinary group and active patient feedback. It was given priority over standardised assessment tools, such as Paediatric Quality of Life Inventory (PedsQL), to encapsulate additional topics, such as family status, education level and the wish for special pregnancy or career consultation. Furthermore, paediatric questionnaires would not have covered cohorts of various ages up to adulthood, which were combined in this study. The general topics and detailed questions for the questionnaire were gathered during a multi-disciplinary conference with transplant surgeons, paediatric hepatologists and gastroenterologists, nurses, nutritionists and psychologists. The questionnaire was pilot tested with five test participants of various ages from 16 to 50 years on the basis of personal interviews. The group of participants included two patients following paediatric liver transplantation, one patient suffering from a chronic inflammatory bowel disease and two healthy controls. The questionnaire was adjusted, mainly regarding the use of medical terms, using the experiences of these trial runs. The patients were asked to respond without external support.

Non-adherence was defined as every deviation from "never" to "always" on a five-step scale, regarding the occurrence of irregularity in the use of medication. Only one question was open-ended, allowing patients to describe their transition to adult care. The transition age is defined as 18 years of age. Assessments concerning the emotional quality of life and the satisfaction with the medical information

provided were performed on a five-step scale. Medical history was verified through comparison with electronic patient records. Additionally, the exact diagnosis and type of split grafts were researched.

Data analysis was executed using IBM SPSS Statistics for Windows, Version 23.0. Armonk, New York. Quantitative data were expressed as median and range or mean and standard deviation ( $\pm$ SD), frequencies and/or percentages. Percent values refer to valid percentages that do not include missing data, but absolute values are always indicated. Correlations between variables were analysed using the pair-sample *t*-test. Results with a *P*-value  $> 0.05$  were defined as non-significant. The reference date for the time elapsed since LT was the 1st of September 2015.

## Results

Overall, 366 patients transplanted between 1972 and 2011 met the inclusion criteria, 94 of whom had died since LT (25.7%). Due to unknown addresses, 67 patients were lost to follow-up. Except for one subsequently excluded patient, 82 completed questionnaires were included in the study (response rate: 41% of 205 contacted patents). Demographic characteristics of the 82 patients included are displayed

in Table 1a. At the time of the study, ages ranged from 13 to 41 years (median: 21.5). Patients underwent LT at a median age of 6 years. The median time elapsed since LT was 14.5 years (range: 4–32). Eighteen patients (22%) were underweight, and 11 patients were obese (14%). Two patients  $< 18$  years and eleven adult patients suffered from linear growth impairment (15.9%). The main indication for LT was biliary atresia ( $n = 33$ ). Eleven patients underwent a living transplantation. Regarding the types of transplants, 64.6% ( $n = 53$ ) underwent a split LT. The overall incidence rate of graft rejections was 53.7% ( $n = 44$ ). Eleven patients underwent a liver retransplantation.

All but two patients received immunosuppressive therapy ( $n = 80$ ). Seventy patients received calcineurin inhibitor agents and 21% ( $n = 17$ ) received an oral steroid therapy within the last 6 months. Regarding the use of medication, 66.7% ( $n = 52$ ) confessed irregularities (“rarely” = 35; “occasionally” = 17). Therefore, only 33% could be considered as strictly adherent ( $n = 26$ ). At the time of the study, 46 patients had transitioned to adult care. Eight patients (17.4%) reported problems, including poor preparation for the transition, rarely performed medical examinations and an impersonal interaction. Most patients were well aware of their medical history. Fifty-five patients were able to name the exact date of their LT (70.5%). The majority was satisfied (87.2%) with their current health status by evaluating it as “good” ( $n = 43$ ) or “very good” ( $n = 25$ ). Any physical limitations noted within 4 weeks before the survey were reported in 14 cases. Twelve patients reported smoking cigarettes (14.8%). Sixty patients (75%) did not consume alcohol four weeks prior to the survey.

The results concerning the emotional quality of life are summarised in Fig. 1. Overall, most patients did not face health-related fears during their daily routine. Eight patients had problems accepting their transplant as a part of their body initially, and one patient still had these issues at the time of the study. Five patients, three females and two men (25–33 years) had at least one child of their own. Establishing a family was important to 27.6% ( $n = 22$ ) and very important to 36.3% ( $n = 29$ ). 13 women sought special expert advice on pregnancy. Three women, separately, reported a pregnancy without the delivery of a child born alive. Most patients were still in school ( $n = 30$ ), did an apprenticeship ( $n = 9$ ) or were studying ( $n = 6$ ) at the time of the study. Thirty-four patients repeated at least one school year (one = 24, two = 8, three = 2) without correlation to their age at LT. Twenty-one patients were working full-time (48.8%). Six patients were working part-time or were unemployed. Overall, 37 patients felt limited concerning their choice of career, and 26 wished for special career counselling.

Only 30 patients were seen by their physicians alone. The majority was satisfied with the information provided about their medication’s effects ( $n = 48$ ) and secondary diseases ( $n = 41$ ). Concerning their indication for LT, 67 patients felt at least “sufficiently” informed. The patients felt the least informed concerning the side effects of their medication (“good”  $n = 22$ , “very good”  $n = 13$ ). Forty-six patients desired further support from the medical staff. Sixteen patients were in contact with other LT patients, whereas the majority ( $n = 69$ ) desired more communication among patients.

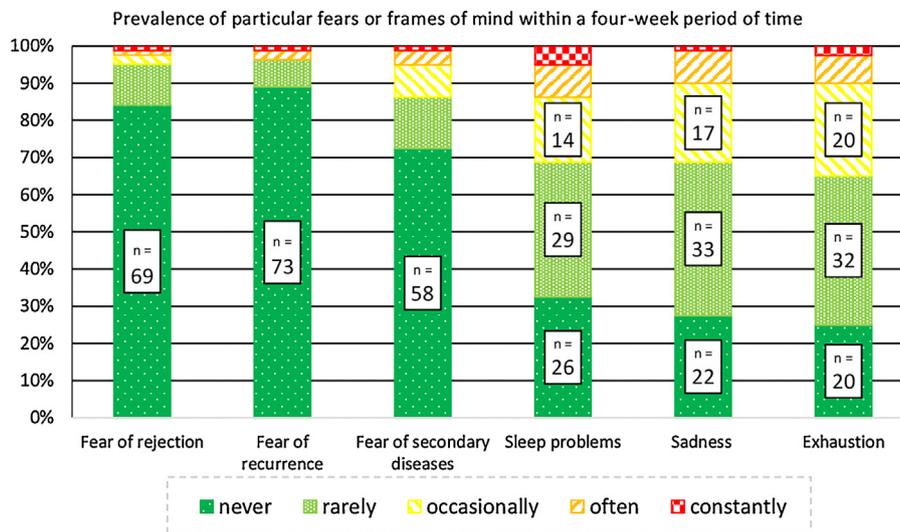
**Table 1a** Demographic information on study population.

Gender: <i>n</i> (%)	Female: 35 (42.7) Male: 47 (57.3)
Age (years) at time of study: median	21.5 (13–41 years)
< 16 years: <i>n</i> (%)	15 (18.3)
16–18 years: <i>n</i> (%)	18 (22)
19–24 years: <i>n</i> (%)	18 (22)
$\geq 25$ years: <i>n</i> (%)	31 (37.8)
Age (years) at LT: median (range)	6 (1 month–17 years)
Time (years) since LT: median (range)	14.5 (4–32 years)
Weight (BMI percentiles)	
Underweight <sup>a</sup> : <i>n</i> (%)	18 (22.2)
Normal weight: <i>n</i> (%)	52 (64.2)
Obesity <sup>b</sup> : <i>n</i> (%)	11 (13.6)
Linear growth impairment: <i>n</i> (%)	13 (15.9)
Indication for LT: <i>n</i> (%)	
Chronic disease	75 (91.5)
Acute liver failure	7 (8.5)
Type of donation: <i>n</i> (%)	
Deceased donation	71 (86.6)
Living transplantation	11 (13.4)
Graft rejections: <i>n</i> (%)	Never: 38 (46.3) Once: 25 (30.5) Multiple: 19 (23.2)
Liver retransplantation total: <i>n</i> (%)	11 (13.4)
One retransplantation	10 (12.2)
Two retransplantations	1 (1.2)
Patients on LT waiting list: <i>n</i> (%)	1 (1.2)
Patients received KT: <i>n</i> (%)	2 (2.4)

LT: (first) liver transplantation; KT: kidney transplantation.

<sup>a</sup> Weight  $< 10$ th percentile for patients  $< 18$  years or a BMI  $< 18.5$  for adults.

<sup>b</sup> Weight  $> 90$ th percentile for patients  $< 18$  years or a BMI  $\geq 25$  for adult patients.



**Figure 1** The figure shows the emotional quality of life by illustrating the prevalence of particular fears or frame of mind within a four-week period of time, entered on the x-axis. The prevalence was divided into five categories as follows: never (dark green), rarely (light green), occasionally (yellow), often (orange) and constantly (red). The percentage distribution of the given answers is entered on the y-axis. The frequencies are specified within the diagram ( $n = x$ ).

Correlations between variables have been analysed but did not show any statistical significance.

## Discussion

Our findings suggest good clinical and psychosocial outcomes in long-term survivors after paediatric LT, with restrictions regarding the prevalence of sleep problems. Patients managed their daily routine with a good and emotionally stable quality of life. These patients were able to participate in a social life, start a family and work full-time, despite their medical needs. We were able to demonstrate adequate social functioning, including the ability to graduate from school and to find full-time employment, despite some impairment of HRQL. This observation is in line with the results of Fredericks et al. [3]. The percentage of patients who repeated at least one year in school was comparable with other studies [14]. Regarding health-related fears, we relied on the patients' self-reports and their credibility, given that the measurement is subjective. Most patients did not experience health-related fears regarding graft rejection, recrudescence or secondary diseases. Other studies reported larger percentages of anxious patients [3]. Furthermore, the patients perceived their current health status as even better than the general German population [15]. Nevertheless, we have to consider the relatively high rate of sleep problems, sadness and exhaustion as shown in Fig. 1. Unfortunately, there are no comparable data in healthy peers. The high incidence of sleep problems after paediatric liver transplants has been analysed by Fredericks et al. [16]. Although this study focused on a younger patient population, paediatric LT seems to be associated with sleep problems.

The percentage of smokers within the study population was significantly reduced (9.7%) compared with the general population [17]. The high rate of alcohol abstinence dis-

plays the health-conscious behaviour of patients after LT. Nevertheless, our results have also demonstrated an unexpectedly high non-adherence rate similar to former studies [18,19]. Despite the high risk for serious consequences of non-adherence, including chronic rejection, graft loss and general morbidity we could not identify definitive evidence of such complications in our study cohort. However novel strategies to improve adherence need to be developed, especially during the transition to adult care. To avoid problems during this period, the transition should be prepared early. An important factor in this context is the patient's autonomy. Considering the high rate of patients who are still accompanied to medical follow-ups by their parents, patients should be encouraged to be more independent. We advocate that adolescent patients should have the opportunity to be seen by their physicians on their own at least for parts of their medical follow-up consultations. We note that adolescents and their parents may not generally accept this approach as recently shown by Junge et al. [20].

As another strategy to improve patients' autonomy, we introduced dedicated transition workshops aiming to communicate knowledge of liver function and dysfunction, raise awareness of medical needs and increase adherence rates. Our study results indicated topics which were in need of improvement such as medical adherence, preparation for the transition to adult care, career opportunities, sexuality and advice on pregnancy and family planning. The recent position paper from ESPGHAN and EASL underlines the importance of these subjects as well [10]. All liver transplanted patients over the age of 15 years are invited to attend these weekend seminars twice within a year. Seminars are partly segregated according to the patients' gender. The discussions were accompanied by clinicians, nurses, social psychologists and former paediatric patients. Experience has demonstrated that these seminars encourage communication among patients beyond the organized

**Table 1b** Comparison of demographic information.

	Study population (n = 82)	Post-transplant survivors (n = 272)
Gender (male)	57.3% (n = 47)	53% (n = 144)
Acute liver failure	8.5% (n = 7)	11% (n = 30)
Living transplantation	13.4% (n = 11)	7.4% (n = 20)
Liver retransplantation	13.4% (n = 11)	13.5% (n = 37)
Age (years) at time of study (median)	21.5	24.2
Age (years) at transplantation (median)	6	6.5
Time (years) since transplantation (median)	14.5	7.7

meetings. The evaluation and acceptance of these seminars were recently analysed by Junge et al. [20]. Results of their study have shown that the process to improve the transition to adult care is not completed yet and may lead to combined paediatric-adult outpatient clinics.

Our study demonstrated that most patients had at least a basic understanding of their medical background and that they felt sufficiently informed about their medical issues. Still, the high non-adherence rate may reveal either a lack of awareness about the risk of serious consequences incurred by non-adherence or some degree of denial of these. In order to improve patients' knowledge, all patients were given a comprehensive book of information adjusted to their age and their primary disease [21]. The book covers the functions of the liver, the reasons for liver transplantation as well as immunosuppression and its concepts. Furthermore, the results of this study are included.

Due to the moderate response rate to our survey, the possibility of a statistical bias cannot be completely excluded. However, the comparison between the study population and all long-term survivors exhibits good concordance (Table 1b). Furthermore, the demographic characteristics were comparable to other studies [8]. The lack of standardisation of our questionnaire limits comparability and generalisability of our findings, however our self-designed questionnaire focusses on features of daily routines and the relevance of daily clinical problems. Our data illustrates coping strategies and daily life long-term after liver transplantation in childhood.

## Conclusion

Our study demonstrates good psychosocial outcomes after paediatric LT with restrictions regarding the prevalence of sleep problems and exhaustion. Thus, LT reverses medical outcomes for patients with end-stage liver diseases including major components of their HRQL. Patients' knowledge about their own medical condition appears to be sufficient, but this does not reflect on satisfactory adherence rates. Novel approaches to increase adherence rates other than by communicating rational knowledge and understanding may need to be found. Our findings indicate the importance of improving patients' autonomy as an important factor for the long-term success of liver transplantation. Our data identifies the needs of our patients including the necessity of career advice and family planning.

## Disclosure of interest

The authors declare that they have no competing interest.

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