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## Strategies to improve the outcome of biliary atresia

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Quality of life in adult survivors of  
biliary atresia with or without  
liver transplantation:  
results from a national cohort

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## **ABSTRACT**

### **Introduction**

Biliary atresia (BA) is a rare cholestatic disease of infancy. Kasai portoenterostomy and liver transplantation (OLT) are the two sequential treatment options. An increasing number of patients survive into adulthood. Little is known about their health-related quality of life (HRQOL). We examined HRQOL in young adult BA survivors.

### **Patients and methods**

RAND-36 and Liver Disease Index Score (LDSI) questionnaires were sent to all eligible adult BA patients. Clinical characteristics were obtained from the NeSBAR (Netherlands Study group on Biliary Atresia Registry) and the national pediatric OLT databases. RAND-36 domain and summary scores were compared to those of an age-matched Dutch comparison group (ANOVA). Pearson correlations and t-tests were performed to examine effects of several variables on HRQOL.

### **Results**

Mean RAND-36 domain and summary scores of transplanted (n=25) and non-transplanted (n=15) BA patients (response 74%) were similar to those of the comparison group, with the single exception of a decreased general health perception ( $p=0.0004$ ) in non-transplanted females ( $63\pm 21$  vs.  $75\pm 17$ ). RAND-36 domain and summary scores were not significantly correlated to age at OLT, time since OLT, serum bilirubin, ASAT or albumin levels, but were moderately to strongly correlated to LDSI total scores (r-values between 0.35-0.77).

### **Conclusion**

Overall, young adult BA patients have a HRQOL similar to an age-matched comparison group. However, general health perception of non-transplanted females was decreased. HRQOL is correlated to liver disease symptoms but not to liver biochemistry parameters. Non-transplanted females and patients suffering from liver disease associated symptoms may be a target for tailored supportive interventions.

## INTRODUCTION

Biliary atresia (BA) is a rare cholestatic disease in infants, with an unknown origin. The prognosis is fatal when untreated. With the development of the portoenterostomy according to Kasai since 1959, the survival has improved markedly.<sup>82</sup> However, in most cases the liver is already severely fibrosed at the time of Kasai surgery. Even when restoration of bile flow is achieved, problems may arise because of ongoing liver fibrosis. The second treatment option is orthotopic liver transplantation (OLT), which was introduced in the early 1970's in adults and gradually also in infants. Currently, ten-year survival rates of 75-80% are achieved after OLT.<sup>42,47</sup> Approximately a fifth of BA patients reach adulthood without OLT.<sup>103</sup> As a result of these two treatment modalities, BA is currently a disease with an increasing number of patients reaching adulthood.<sup>103,154</sup>

Most patients with a transplanted liver need to take life-long immunosuppressive drugs and may experience drug side effects and recurrent infections. Chronic rejection of the liver may also ensue.<sup>42,150</sup> About 20% of adult non-transplanted BA patients exhibit normal liver biochemistry tests, while in the majority liver damage is (slowly) progressive.<sup>34,103,154</sup> Most studies on the outcome of BA have focussed on mortality and morbidity, but with increasing survival health-related quality of life (HRQOL) becomes an important outcome measure as well.<sup>32,147,151</sup>

The HRQOL of patients with chronic liver disease or with a transplanted liver has been studied rather extensively.<sup>42,55,75,106,211,212</sup> However, most patient groups were heterogeneous with respect to etiology and most studies were performed in either children or middle-aged adults.<sup>3,180</sup> BA patients are usually underrepresented in these studies. To our knowledge, only one study measured the HRQOL of non-transplanted adolescent BA patients.<sup>70</sup> In that study, HRQOL was found to be marginally lowered in BA patients from Japan and normal in those from the United Kingdom when compared to the respective reference groups. Knowledge of the HRQOL of specific subpopulations of patients allows fine-tuning of patient care and may influence treatment choices in individual patients.

The first aim of the current study was to examine the HRQOL in young adults surviving BA in a national cohort, by comparing their HRQOL to that of an age-matched comparison group derived from a previous Dutch study.<sup>164</sup> Our expectation is that BA patients have a decreased HRQOL as compared to young adults who are not confronted with a serious condition such as BA. Secondly, we hypothesize that transplanted patients' HRQOL is increased as compared to that of non-transplanted BA patients. Finally, we examined the effect of several sociodemographic and clinical factors on HRQOL such as gender, age at OLT, serum liver biochemistry parameters and liver disease symptoms to investigate which patients are more at risk for HRQOL problems.

## PATIENTS AND METHODS

### *Patients and procedure*

All BA patients born between January 1977 and January 1992, treated in the Netherlands, currently alive at an age of at least 18 years and were eligible. BA patients with psychiatric illness or mental retardation were excluded. In each patient, the diagnosis of BA was confirmed by intraoperative cholangiography and pathology of the resection specimen.<sup>33</sup> Portoenterostomy was performed in one of the six participating Dutch university medical centers specialized in pediatric surgery, and OLT was performed in the national pediatric OLT center in Groningen.

Clinical patient data were retrieved from the NeSBAR (Netherlands Study group on Biliary Atresia and Registry) database and the national pediatric OLT database. Data included gender, birth

date, age at portoenterostomy, age at OLT, comorbidities, and recent serum bilirubin, aspartate amino transferase (ASAT) and albumin measurements.

The study was performed according to the guidelines of the Medical Ethical Committee of the University Medical Center Groningen. A letter explaining the goal of the study, the questionnaires, an informed consent form and a prepaid return envelope were sent by post to all eligible patients.

### *Instruments*

All patients completed the Dutch version of the RAND-36 and the Liver Disease Symptom Index 2.0 (LDSI). Both questionnaires have been validated in the Dutch population.<sup>185,190</sup> The RAND-36 is a generic 36-item questionnaire, of which the reliability and validity have been supported in a wide number of studies.<sup>190</sup> It covers eight domains: physical functioning (Cronbach  $\alpha$  in this study: 0.89), social functioning ( $\alpha$ :0.73), role limitations due to physical health problems ( $\alpha$ :0.92), role limitations due to emotional problems ( $\alpha$ :0.86), mental health ( $\alpha$ :0.78), vitality ( $\alpha$ :0.86), bodily pain ( $\alpha$ :0.79) and general health perception ( $\alpha$ :0.79). The raw scores were converted to a 1-100 scale, with higher scores indicating higher levels of functioning or well-being. Summary scores report physical functioning and mental functioning and were standardized to a mean of 50 and a standard deviation of 10. Results were compared to those of an age-matched comparison group.<sup>164</sup>

The LDSI 2.0 consists of 18 original items and six items developed by the board of the NLV (Dutch Liver Patient Association).<sup>185</sup> Nine items measure the severity of 'itch', 'joint pain', 'pain in the right upper abdomen', 'sleepiness during the day', 'worry about family situation', 'decreased appetite', 'depression', 'fear of complications', and 'jaundice'. Nine additional items measure the hindrance of these symptoms to daily activities. 'Fear of complications' has no accompanying hindrance item, whereas 'itch' has two hindrance items, namely hindrance of itch during the day and during sleep. The NLV items included 'memory problems', 'change of personality', 'hindrance in financial affairs', 'involuntary change in use of time', 'decreased sexual interest' and 'decreased sexual activity'. All LDSI and NLV items were scored on a 5-point Likert scale ranging from 'not at all' (1) to 'to a high extent' (5). The LDSI and NLV item scores were summed to obtain total LDSI scores.

### *Statistical analysis*

Demographic and clinical characteristics of responders and non-responders were compared using Mann-Whitney U-test and Student's t-test to detect possible confounders. Differences in the RAND-36 domain and summary scores between the non-transplanted patients, transplanted patients, and the comparison group were tested using ANOVA's.

Effect sizes according to Cohen were calculated by dividing the difference in mean score between BA patients and the comparison group by the pooled standard deviation of both groups.<sup>24</sup> Effect sizes between 0.20-0.49 were considered small, between 0.50-0.79 medium and  $\geq 0.80$  large. Gender differences were tested using Mann-Whitney U-test. Associations between serum liver biochemistry, age at OLT, current age and LDSI scores with RAND-36 summary and domain scores was examined using Pearson's correlational analysis. Correlations with a coefficient  $< 0.30$  were considered weak, between 0.30-0.50 moderately strong, and  $> 0.50$ , strong.<sup>24</sup> Scores of the LDSI of transplanted and non-transplanted patients were compared using Mann-Whitney U-test. All tests were two-tailed, and p-values  $< 0.05$  were considered significant.

## RESULTS

### Patient characteristics

Fifty-four BA patients were eligible and asked to participate. Of those, 40 patients agreed (response rate 74%). One patient had to be excluded because of a major depression. Characteristics of responders and non-responders are shown in Table 1. One included non-transplanted patient had cystic fibrosis. Two of the patients (both responders) underwent an explorative laparotomy without portoenterostomy, and subsequently an OLT at the ages of 0.8 and 2.6 years, respectively. Recent laboratory measurements from one transplanted patient (responder) who received follow-up care in another adult OLT center were unavailable.

**Table 1:** Demographic and clinical characteristics of the study group.

	BA non-transplanted			BA transplanted		
	Responders	Non-responders	p-value	Responders	Non-responders	p-value
<b>Number</b>	25	5		15	9	0.08*
<b>Gender (% male)</b>	52%	40%	1.0	67%	22%	0.09
<b>Age at survey (years)</b>	23.2 (18.9-30.4)	23.6 (20.1-32.2)	0.49	22.4 (18.9-30.8)	22.3 (18.9-32.2)	0.82
<b>Age at surgery (days)</b>	58 (35-117)	64 (48-68)	0.83	60 (43-126)	46 (32-175)	0.17
<b>Age OLT (years)</b>	NA	NA		5.2 (0.7-17.1)	11.7 (0.8-15.0)	0.61
<b>Comorbidities</b>	1#	-		-	-	
<b>Current bilirubin (µmol/L)</b>	17 (5-71)	14 (6-46)	0.72	17 (5-36)	16 (5-23)	0.31
<b>Current ASAT (U/L)</b>	27 (6-160)	77 (20-101)	0.06	30 (16-96)	40 (23-77)	0.17
<b>Current albumin (g/L)</b>	41 (36-54)	40 (39-40)	0.19	47 (42-49)	43 (30-47)	0.02

Data expressed as median (range); \* $\chi^2$  test of the distribution of responders and non-responders over the two study groups; #Cystic fibrosis; NA, not applicable.

### Health-related quality of life

The mean scores on seven of the eight dimensions of the RAND-36 and the physical and mental summary scores were not significantly different between the three groups (Table 2). A significant effect of group was found in general health perception ( $p=0.004$ ). Consequent analysis revealed that non-transplanted patients had significantly lower scores on general health perception than transplanted BA patients and to the comparison group (Table 2). The effect of group on physical role functioning just failed to reach significance ( $p=0.05$ ), and comparison between the non-transplanted patients and the comparison group revealed a medium effect size (0.32). Univariate analyses showed no significant relationships between age and the RAND domain or summary scores ( $r$  varied between 0.002 and 0.31). Moderately strong correlations were found with pain (-0.30) in non-transplanted patients, and with emotional role-functioning (0.31) and pain (0.31) in transplanted patients. An effect of gender was only detected in general health perception of non-transplanted patients: women scored significantly lower than men ( $52\pm 15$  for females vs.  $74\pm 21$  for males;  $p=0.0004$ ).

**Table 2:** Descriptives of the RAND-36 of non-transplanted and transplanted BA patients and an age-matched comparison group.

	BA non-OLT n=25	BA OLT n=15	Comparison group <sup>164</sup> n=500	p-value*	Effect size		
					Non-OLT vs. comparison	OLT vs. comparison	Non-OLT vs. OLT
<b>Age</b>	23.5±3.3	23.2±4.0	24.2±3.8	0.41			
<b>Physical Functioning</b>	91±17	96±6	93±14	0.60	0.14	0.19	0.37
<b>Social functioning</b>	88±19	88±16	87±18	0.97	0.03	0.05	0.02
<b>Physical role-functioning</b>	73±40	85±35	87±27	0.05	0.50	0.07	0.32
<b>Emotional role-functioning</b>	81±35	91±27	87±29	0.51	0.21	0.13	0.31
<b>Mental health</b>	76±17	81±11	76±15	0.48	0.03	0.32	0.35
<b>Vitality</b>	64±23	72±19	65±17	0.34	0.05	0.39	0.34
<b>Bodily pain</b>	84±19	91±18	87±19	0.52	0.17	0.20	0.38
<b>General health</b>	63±21	75±15	75±17	0.004	0.69	0.01	0.63
<b>Mental summary score</b>	51±10	53±6	50±10	0.57	0.04	0.28	0.28
<b>Physical summary score</b>	50±9	54±6	50±10	0.39	0.02	0.36	0.42

Data expressed as mean±SD; \*ANOVA. Effect size was calculated as the difference in mean score divided by the pooled standard deviation.

### *Liver disease symptoms*

The mean scores of the LDSI questionnaire and NLV items did not exceed 2.4. However, individual patients scored maximum at a number of items (Table 3).

Female non-transplanted BA patients had more 'pain in the right upper abdomen' (2.1±1.3 vs 1.0±0.0, p=0.005) and 'hindrance of pain in the right upper abdomen' (1.6±1.0 vs 1.0±0.0, p=0.03) compared to their male counterparts. Finally, female transplanted BA patients reported significantly more 'hindrance in financial affairs' than transplanted males (3.6±1.7 vs. 1.7±1.3, p=0.03). No further gender differences were detected. Total LDSI scores were not significantly correlated to serum total bilirubin, ASAT, or albumin levels (*r* varied between 0.08 and 0.35 and was moderately strong for serum bilirubin (-0.30) in non-transplanted patients, and for serum albumin (0.35) in transplanted patients).

### *Correlations between clinical factors and HRQOL*

Moderately strong to strong significant associations between LDSI and RAND-36 domain and summary scores were found in the non-transplanted and transplanted patients with one exception: the correlation between emotional role functioning and LDSI scores in transplanted BA patients was not significant (*r*=0.06, *p*=0.8, Table 4). There were no significant correlations between RAND-36 domain or summary scores of non-transplanted or transplanted BA patients with serum ASAT, bilirubin or albumin levels, age at OLT or time elapsed since OLT (*r* varied between 0.000 and 0.43).

**Table 3:** Liver Disease Symptom Index 2.0 scores of young adult transplanted and non-transplanted BA patients.

	BA non-transplanted n=25		BA transplanted n=15		p-value*
	Mean±SD	Median (range)	Mean±SD	Median (range)	
<b>Itch</b>	1.9±1.2	1(1-5)	1.6±0.9	1(1-4)	0.62
<b>Hindrance itch during day</b>	1.3±0.7	1(1-4)	1.1±0.4	1(1-2)	0.54
<b>Hindrance itch during sleep</b>	1.4±1.0	1(1-4)	1.0±0.0	1(1-1)	0.07
<b>Joint pain</b>	1.7±1.2	1(1-5)	1.9±1.2	1(1-4)	0.54
<b>Hindrance joint pain</b>	1.5±1.0	1(1-5)	1.3±1.0	1(1-4)	0.73
<b>Pain right upper abdomen</b>	1.5±1.0	1(1-5)	1.3±1.0	1(1-3)	0.79
<b>Hindrance pain right upper abdomen</b>	1.3±0.7	1(1-4)	1.0±0.0	1(1-1)	0.11
<b>Sleepiness during day</b>	2.4±1.2	2(1-5)	1.9±0.9	2(1-4)	0.21
<b>Hindrance sleepiness during day</b>	1.9±1.2	1(1-5)	1.4±0.7	1(1-3)	0.17
<b>Worry about family situation</b>	1.3±0.7	1(1-4)	1.7±1.2	1(1-4)	0.57
<b>Hindrance worry about family situation</b>	1.2±0.6	1(1-4)	1.2±0.6	1(1-3)	0.61
<b>Decreased appetite</b>	1.3±0.7	1(1-4)	1.5±0.9	1(1-4)	0.27
<b>Hindrance decreased appetite</b>	1.1±0.3	1(1-2)	1.5±0.7	1(1-3)	0.04
<b>Depression</b>	1.4±0.7	1(1-4)	1.1±0.3	1(1-2)	0.10
<b>Hindrance depression</b>	1.1±0.6	1(1-4)	1.0±0.0	1(1-1)	0.44
<b>Fear of complications</b>	1.3±0.7	1(1-4)	1.3±0.6	1(1-3)	0.97
<b>Jaundice</b>	1.1±0.4	1(1-3)	1.0±0.0	1(1-1)	0.27
<b>Hindrance jaundice</b>	1.0±0.0	1(1-1)	1.0±0.0	1(1-1)	0.99
<b>Memory problems</b>	1.5±1.0	1(1-5)	1.1±0.3	1(1-2)	0.96
<b>Change of personality</b>	1.2±0.5	1(1-3)	1.8±1.2	1(1-5)	0.03
<b>Hindrance in financial affairs</b>	1.5±0.9	1(1-4)	2.3±1.7	1(1-5)	0.10
<b>Involuntary change in use of time</b>	1.5±0.9	1(1-4)	1.7±1.3	1(1-5)	0.92
<b>Decreased sexual interest</b>	1.1±0.4	1(1-3)	1.0±0.0	1(1-1)	0.43
<b>Decreased sexual activity</b>	1.1±0.4	1(1-3)	1.0±0.0	1(1-1)	0.43

\*Mann-Whitney U test



**Table 4:** Pearson's correlational analysis of RAND-36 domain scores, and total Liver Disease Symptom Index 2.0 (LDSI) scores.

	Total LDSI score			
	BA non-transplanted n=25		BA transplanted n=15	
	r	p-value	r	p-value
<b>Physical Functioning</b>	-0.47	0.02	-0.56	0.03
<b>Social functioning</b>	-0.65	<0.0001	-0.69	0.004
<b>Physical role-functioning</b>	-0.77	<0.0001	-0.49	0.07
<b>Emotional role-functioning</b>	-0.66	<0.0001	0.06	0.83
<b>Mental health</b>	-0.35	0.09	-0.47	0.08
<b>Vitality</b>	-0.57	0.003	-0.69	0.005
<b>Bodily pain</b>	-0.76	<0.0001	-0.47	0.08
<b>General health</b>	-0.40	0.05	-0.37	0.18
<b>Physical summary score</b>	-0.62	0.001	-0.63	0.01
<b>Mental summary score</b>	-0.54	0.006	-0.43	0.11

## 6

**DISCUSSION**

Overall, this study shows that HRQOL of young adult transplanted and non-transplanted BA patients is comparable to that of an age-matched comparison group in seven of the eight domains tested. This is contrary to our expectation. The single exception was in general health perception which is perceived as decreased by young adult non-transplanted female BA patients as compared to the other two groups. The RAND-36 subscale and summary scores were independent of age and liver biochemistry. Strong to moderately strong correlations were found between the RAND-36 summary and subscale scores and the total liver disease symptom scores, with the exception of emotional role functioning and the LDSI in transplanted patients.

Due to the low number of eligible patients, this study has a low statistical power, a reason why we chose not to focus on p-values only, but to focus on the clinical relevance of differences (effect sizes) as well. The non-transplanted patients in the current study showed a tendency towards lower physical role functioning as compared to the comparison and transplanted patient groups which just failed to reach significance, but with an effect size which suggests clinical relevance. Furthermore, the non-transplanted females had a significantly lower health perception. It is rather surprising that patients with a longstanding chronic disease with impact on several body functions, including major surgery, and lifelong follow-up and medication use, report an HRQOL almost similar to that of an age-matched comparison group. The fact that non-transplanted patients in our study did not require an OLT before reaching adult age indicated, by inference, that the disease had a relatively benign course. Individual patients could even be considered 'cured' based on biochemical and clinical parameters, which may explain the relatively high HRQOL compared to other cholestatic patient groups.<sup>34,106,211,212</sup>

Transplanted BA patients showed an HRQOL similar to the comparison group. Upon detailed analysis, the scores of several domains were slightly higher in transplanted compared with non-transplanted patients, but did not reach significance. This has also been observed in other young adult patient groups, such as childhood cancer survivors and oesophageal atresia survivors.<sup>37,164</sup> It might be explained by the phenomenon of response shift, i.e. a change in one's perception of the quality of one's life to accommodate to illness.<sup>149</sup> It has been proposed that this mechanism is particularly relevant for relatively severe diseases and/or treatments.<sup>164</sup> This assumption might contribute to the (non-significantly) higher scores of the transplanted patients, who have experienced a period of severe illness and a challenging treatment, when compared to those of the comparison group. The comparison of non-transplanted and transplanted patients demonstrates small to moderate effect sizes in all domains, with the exception of the domain of social functioning. The effect sizes suggest that the difference in HRQOL in non-transplanted and transplanted patients might be considered of clinical relevance, although it is much less pronounced than could be anticipated.

Based on liver biochemistry data, the non-responding patients could have a slightly worse clinical condition than the responders. It could therefore not be excluded that the RAND-36 scores might have been slightly lower if these patients had participated. However, liver biochemistry did not significantly correlate with RAND-36 or total LDSI scores in the responding patient population. More specifically, the non-significant relationships between RAND-36 scores and liver biochemistry showed a higher HRQOL together with worse liver biochemistry, and were therefore pointing in the opposite direction than we hypothesized. We have chosen not to exclude patients with major comorbidities unrelated to BA to avoid selection bias. Exclusion of the one patient with cystic fibrosis would not have changed the results. We could not detect a correlation between age at OLT and HRQOL, which might be a consequence of the small sample size and the non-homogeneous distribution in the ages at transplantation.

In general, females tend to report lower HRQOL than males.<sup>6,53,119,202</sup> This was also observed in the comparison group utilised in the current study.<sup>164</sup> General health perception was the only domain where we detected a gender difference in BA patients. This finding is striking because in the comparison group no gender effect was reported on this domain.<sup>164</sup> The detection of little gender effects might be explained by (again) the relatively low number of adult patients with BA available for study, and the underrepresentation of females in the transplanted responders.

It is tempting to speculate on the origin of the lowered general health perception in non-transplanted females. The clinical condition and the overall LDSI scores of female non-transplanted patients was comparable to that of the males, and they did not have higher total LDSI scores compared to males. Females reported more pain in the right upper abdomen than non-transplanted males. Perhaps the abdominal pain raised concern in the non-transplanted patients, as they might perceive themselves as having a 'diseased' liver in situ. In the current study, the patients' concerns regarding fertility have not been investigated, but these could play a more dominant role in health perception of young adult women. As of yet, the consequences of pregnancy for female BA patients are unclear. There have been reports that liver function in BA patients can deteriorate markedly during pregnancy.<sup>88</sup> In the Netherlands, pregnancy in BA patients is not discouraged unless there are contraindications. However, patients are informed about putative risks and are advised to be under close monitoring when pregnant.

We found a significant correlation between the physical and mental summary scores and most domain scores with the total scores of the LDSI. Therefore, liver disease associated symptoms

seem to be an important determinant of HRQOL, irrespective of disease state. In order to maintain or improve the HRQOL of the individual BA patient, it thus seems important for the physician to focus treatment on the various liver disease-associated problems. Questionnaires such as the LDSI might help to gain insight into the presence of problems in each patient in an outpatient setting. Ongoing disease-associated complaints are difficult to manage and could increase the risk that both patient and physician inappropriately medicalize the complaint. A screening questionnaire may help recognize non-directly medical problems such as hindrance in financial affairs and decreased sexual interest.<sup>181</sup> The expertise of paramedical and psychosocial disciplines such as physiotherapists, dieticians, social workers and psychologists may help patients cope with the sequelae of their disease. In the Netherlands, BA patients awaiting OLT are already managed by a multidisciplinary team. However, many BA patients are transplanted in childhood, and novel problems may arise many years after OLT when the transition into adulthood is to be made. Non-transplanted BA patients are not routinely managed in a multidisciplinary fashion and could be considered an ignored patient group in this respect.

It should be realized that the RAND-36 questionnaire focuses on the functional aspects of HRQOL, and does not measure the patients' satisfaction with functioning.<sup>186</sup> Educational and professional achievements and emotional distress are further important parameters which were beyond the scope of the present study, but which remain to be investigated to gain more insight into disease effects.

A limitation of this study is its cross-sectional design, which precludes analysis of the effects of progression of disease or OLT on HRQOL. Indeed, HRQOL was impaired in some domains in non-transplanted patients in contrast to the transplanted patients. However, we did not aim to evaluate a therapeutic intervention but to assess HRQOL in an understudied patient group. Despite the fact that we had been able to acquire data from a national cohort over many years, the number of adult patients is limited in this study due to the relative low prevalence of BA. We are aware the study consists of a single measurement in young adult life. This feature has the inevitable risk of introducing bias and unknown confounders. The presented results should be validated in other cohorts of young adult BA patients. A longitudinal approach may allow for determination of the magnitude of a possible response shift. It would be interesting to investigate the effects on HRQOL of other factors such as coping style, personality and social support.<sup>42,56,164,216</sup>

To our knowledge, the present study is the first to determine the HRQOL of a national cohort of both transplanted and non-transplanted BA patients. With the current study design we were able to compare BA patients to an age-matched comparison group within our country, thereby avoiding age-induced, social, cultural and economic differences. The results of the present study show that, when BA patients manage to overcome the medical challenges involved with Kasai portoenterostomy and/or OLT, they can achieve a HRQOL similar to age-matched peers. The HRQOL is correlated to liver disease symptoms and not to biochemical markers of clinical condition. Non-transplanted females and patients suffering from liver disease associated symptoms are the groups at risk for HRQOL problems. Management of symptoms by tailored supportive interventions of (para)medical and psychosocial disciplines may be a key factor in maintaining or improving HRQOL in individual BA patients, regardless of disease state.



