Received: 27 September 2022 | Revised: 4 January 2023 | Accepted: 4 January 2023

DOI: 10.1111/hepr.13880

ORIGINAL ARTICLE

Hepatology Research JSH

Quality of life in Dutch patients with primary biliary cholangitis: Discrepancies between patients' perspectives and objective disease parameters

Rozanne C. de Veer[1] | Maria C. van Hooff[1] | Geraldine da Silva[1] | Maren H. Harms[1] | Herold J. Metselaar[1] | José Willemse[2] | Elaine Utomo[3] | Adriaan J. van der Meer[1]

[1]Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, The Netherlands

[2]Dutch Liver Patients Association, Hoogland, The Netherlands

[3]Independent Researcher, Berkel en Rodenrijs, The Netherlands

Correspondence
Adriaan J. van der Meer, Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Doctor Molewaterplein 40, NA building, Floor 6, Rotterdam 3015 GD, The Netherlands.
Email: a.vandermeer@erasmusmc.nl

Abstract

Aim: This study aims to assess the health-related quality of life (HRQoL) in a Dutch population of patients with primary biliary cholangitis (PBC) in relation to the prognosis and need for second line-therapy, based on both objective disease parameters and patients' perspectives.

Methods: In this cross-sectional multicenter study, HRQoL was assessed by using the Dutch PBC-40 according to objective clinical parameters and patients' perspectives on treatment and prognosis.

Results: In total, 178/269 (66%) patients responded; mean age 61.2 (SD 9.9) years and 165 (92.7%) women. The PBC-40 domain scores did not differ according to the GLOBE score response ($p > 0.05$ for all) or according to the POISE criteria ($p > 0.05$), except for the domain itch ($p = 0.031$). Patients who considered their survival to be impaired scored higher on all domains as compared to those expecting a normal prognosis ($p < 0.05$). Similarly, PBC-40 domain scores were higher among patients who considered that they were in need of additional therapy compared to those who did not ($p < 0.05$ for all, except for domain itch [$p = 0.056$]). However, 45/62 (72.6%) patients with a self-expected impaired prognosis had a GLOBE score indicative of a normal prognosis. Twenty-five of the 40 (62.5%) patients who believed they needed additional therapy were below POISE criteria.

Conclusion: The HRQoL of patients with PBC was impaired in terms of non-favorable disease status according to the expectations of patients, but not according to objective disease parameters. Substantial discrepancies between patients' perspectives and objective parameters were observed, which highlights the need for better patient guidance among patient with PBC.

Abbreviations: ALP, alkaline phosphatase; DLPA, Dutch Liver Patients Association; HRQoL, health-related quality of life; IQR, interquartile range; PBC, primary biliary cholangitis; POISE, Perioperative Ischemic Evaluation Study; UDCA, ursodeoxycholic acid; ULN, upper limit of normal.

KEYWORDS
health-related quality of life, primary biliary cholangitis

INTRODUCTION

Primary biliary cholangitis is a rare chronic cholestatic liver disease with autoimmune features that predominantly affects middle-aged women and may progress to end-stage liver disease.[1] Although patients with PBC may be asymptomatic at time of diagnosis, they can experience various serious complaints such as fatigue, pruritus, abdominal discomfort, and cognitive impairment during the course of their disease.[2] These symptoms can negatively impact their HRQoL.[3–6] Over the past decades, recognizing and understanding factors related to the HRQoL in chronic liver diseases has gained ground in clinical practice.[7] In 2005, Jacoby and colleagues developed and validated the PBC-40, the first and only PBC-specific quality of life measure.[8] Since then, the PBC-40 has been adopted and translated into different languages and is now broadly used as a tool to assess the HRQoL of PBC patients in clinical practice as well as in the setting of research.[9–12]

In addition to assessing the quality of life of patients with PBC, it may be important to consider the patient's perspective on their chronic liver disease. Better understanding of patients' expectations regarding their prognosis and treatment could improve patient counseling, which may benefit their management and compliance in order to improve the HRQoL and clinical outcome. In this study, we aimed to assess the HRQoL in a Dutch cohort of PBC patients, both in relation to objective disease parameters and the patients' perspectives on treatment and prognosis.

METHODS

Study population and design

All members of the DLPA who were registered with a diagnosis of PBC and patients with PBC who were in follow-up at the outpatient clinic of the department of Gastroenterology and Hepatology of the Erasmus University Medical Center Rotterdam received an invitation between August and October 2020 to participate in this study. Patients who had an established PBC diagnosis according to the guideline published by the European Association for the Study of the Liver were eligible for inclusion.[2] Patients received the Dutch PBC-40, a self-reported questionnaire, through postal mail. In addition, patients were asked about their demographic characteristics and their views on treatment and prognosis.

Patients consented to medical chart review to collect objective disease parameters from their treating physician. The collected clinical data included information on the date of diagnosis, liver biochemistry, cirrhosis status, and treatment. The study protocol was approved by the Ethical Committee of the Erasmus Medical Center in Rotterdam and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Questionnaires

The Dutch PBC-40 is a validated Dutch translation of the original PBC-40,[8] which is a disease-specific measure to determine the HRQoL in patients with PBC.[11] It covers six domains (symptoms, itch, fatigue, cognition, emotional, and social) through 40 quality of life statements, with higher scores denoting a worse HRQoL (1–5-point Likert scale for each statement). The domain symptoms consists of 7 items (possible range, 7–35 points), itch 3 items (3–15 points), fatigue 11 items (11–55 points), cognition 6 items (6–30 points), emotional 3 items (3–15 points), and social 10 items (10–50 points).

Through four simple multiple-choice questions patients reported on their treatment status, need for additional therapy, and expected prognosis in comparison to their peers. No objective scores were obtained from this questionnaire. The questions were:

1. Do you think you need to use ursodeoxycholic acid for the rest of your life?
   a. No/b. Yes/c. I don't know
2. Do you ever forget to take ursodeoxycholic acid?
   a. Never or seldom/b. Sometimes (monthly)/c. Regularly (weekly)
3. Do you think you need additional medication for your PBC at this time?
   a. No/b. Yes (to reduce complaints, to improve prognosis, or for other reasons)
4. How do you consider your life expectancy in comparison to an average person of your age and gender?
   a. Reduced/b. Equal/c. Better

Statistical analyses

Data are presented as mean with SD in case of normal distribution, and otherwise as median with IQR. Categorical variables are described as frequencies (*n*, [%]). For comparisons of continuous or categorical variables the χ^2-test, Mann–Whitney *U*-test, and Kruskal–Wallis test were used, where appropriate.

In case items of the PBC-40 domains were missing (defined as missed, duplicated, or does not apply answers), the whole domain was discarded if fewer than 50% of items were completed. If more than 50% of the items were completed, the median value of the completed items in the domain was allocated to the missing items.[8] The distribution of the severity within each PBC-40 domain was categorized into four groups: none, mild, moderate, and severe. "None" was defined as the minimum score, "mild" was defined as a score between the minimum score and one-third of the full score, "moderate" was defined as a score between one-third and two-thirds of the full score, and "severe" was defined as a score between two-thirds of the full score and the full score.[6]

The objective need for additional therapy was determined by the POISE criteria.[13] Patients with an ALP >1.67 × ULN and/or a bilirubin >1.0 × ULN were considered to be in need of add-on therapy. The GLOBE score was used to determine the predicted long-term survival free of liver transplantation. The GLOBE score was calculated with the formula: 0.044378 × age + 0.93982 × LN (bilirubin) + 0.335648 × LN (ALP) + 2.266708 × albumin + 0.002581 × platelets (per 10^9/L) + 1.216865 (bilirubin and ALP in ULN and albumin in "times lower limit of normal"). The previously reported age-specific thresholds were used to categorize patients in having a normal prognosis compared to the matched general population, or an impaired prognosis compared to their peers.[14]

All statistical tests were two-sided, and a *p*-value of <0.05 was considered to be statistically significant. Statistical analyses were carried out in SPSS Statistics version 28.0 (IBM Corp.).

RESULTS

Cohort characteristics

In total, 178 of the 269 patients with PBC returned completed questionnaires and were eligible for inclusion, resulting in an overall response rate of 66%. The mean age was 61.2 years at time of participation and the vast majority of the patients were women (92.7%) (Table 1). More than half of the participants (52.5%) were diagnosed with PBC more than 10 years ago. Patients were treated in 52 different hospitals; 93 (52.3%) patients were followed in university hospitals and 85 (47.7%) were followed in general hospitals. Treatment with UDCA and bezafibrate was reported in 170 (96.0%) and 37 (20.8%) patients, respectively. Mean UDCA dose was 13.8 (3.6) mg/kg, with 61 (35.9%) patients reporting a daily dose <13 mg/kg. A lifelong need for UDCA was expected by the vast majority (n = 163, 95.9%). Only 4 patients (2.4%) reported to forget UDCA regularly (i.e., on a weekly basis).

TABLE 1 Characteristics of a cohort of Dutch patients with primary biliary cholangitis

	N = 178
Age at participation, years[a]	61.2 (9.9)
Female, *n* (%)	165/178 (92.7)
Year of diagnosis[b]	2009 (2002–2015)
Cirrhosis, *n* (%)[c]	28/174 (16.1)
Hospital	
University hospital	93/178 (52.3)
General hospital	84/178 (47.7)
Educational level	
University	21/176 (11.9)
Higher vocational education	49/176 (27.8)
Secondary vocational education	75/176 (42.6)
Primary/secondary education	31/176 (17.6)
UDCA treatment, *n* (%)	170/177 (96.0)
Bezafibrate treatment, *n* (%)	37/175 (21.1)
Pruritus VAS score[b]	1.0 (0.0–4.0)
Serum ALP (U/L)[b]	122 (92–172)
Serum AST (U/L)[b]	30 (25–39)
Serum ALT (U/L)[b]	29 (22–39)
Serum bilirubin (μmol/L)[b]	9 (6–12)
Serum albumin (g/L)[b]	40 (38–44)
Platelet count (×10^3/mm^3)[b]	246 (185–298)

Note: Aspartate aminotransferase (AST) was missing for 7 patients, alanine aminotransferase (ALT) was missing for 4 patients, bilirubin was missing for 5 patients, albumin was missing for 14 patients, platelet count was missing for 7 patients, year of diagnosis was missing for 15 patients, ursodeoxycholic acid (UDCA) treatment was missing for 1 patient, and bezafibrate treatment was missing for 3 patients.

Abbreviations: ALP, alkaline phosphatase; VAS, visual analogue scale.

[a]Data are expressed as mean with SD.

[b]Data is expressed as median with interquartile range.

[c]Data on cirrhosis were missing for 4 patients.

Quality of life in patients with PBC

The HRQoL was assessed by the PBC-40. The medians of the mean score per PBC-40 domain are shown in Figure 1a. The highest median score was observed in the domain fatigue (3.1, IQR 2.3–3.7), followed by the domain symptoms (2.4, IQR 1.8–3.0). The lowest median score was 1.7 (IQR, 1.0–2.5) for the domain itch. The distribution of the severity within each domain is shown in Figure 1b.

In addition, the HRQoL was assessed in different subgroups (Table 2). Among patients treated in university hospitals versus general hospitals, no statistically significantly differences in the domain scores were observed. Among female patients (n = 165), the median domain scores were statistically significantly higher compared to the domain scores in male patients (p < 0.05 for all). Patients with a disease duration >10 years reported statistically significantly lower scores on the domains cognition (13.0, IQR 7.0–17.8), emotional (6.0, IQR 4.0–8.0), and social (21.0, IQR 14.0–29.0) compared to patients with a shorter disease duration (p < 0.05 for all).

Health-related quality of life in relation to need for additional therapy

Among the 172 (97.2%) patients with available laboratory results, 54 (31.4%) had an ALP >1.67 × ULN and/or a bilirubin >1.0 × ULN and were thus considered to need additional therapy according to the POISE criteria. Except for the domain symptoms (18.0 vs. 15.0, p = 0.031), there was no statistically significant difference in the PBC-40 domain scores between patients who were below the POISE criteria and patients who were above the POISE criteria, respectively (Table 3).

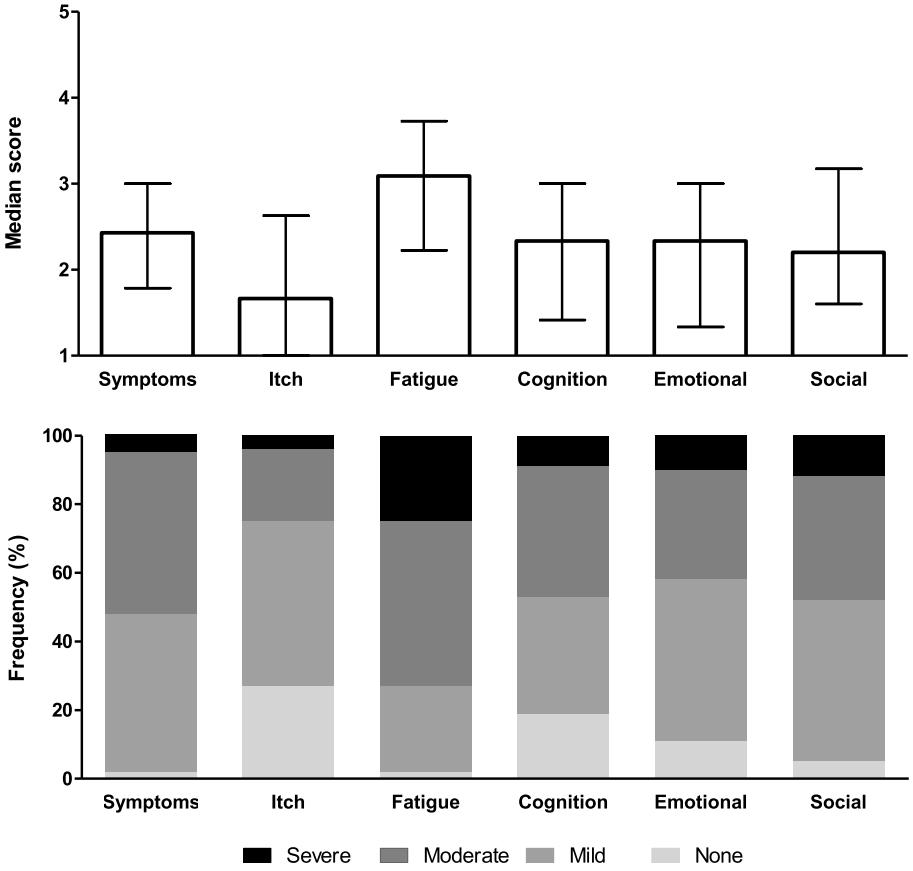

FIGURE 1 Median domain scores and distribution of severity of the PBC-40 domains in Dutch patients with primary biliary cholangitis ($n = 178$). (a) Medians of the mean scores of PBC-40 domains: symptoms 2.4 (1.8–3.0), itch 1.7 (1.0–2.5), fatigue 3.1 (2.3–3.7), cognition 2.3 (1.5–3.0), emotional 2.3 (1.3–3.0), and social 2.2 (1.6–3.2). Error bars represent interquartile ranges. (b) Distribution of severity of each PBC-40 domain (severe; moderate; mild; none): symptoms (6%; 47%; 45%; 2%), itch (4%; 21%; 48%; 27%), fatigue (25%; 48%; 25%; 2%), cognition (9%; 38%; 34%; 19%); emotional (10%; 32%; 47%; 11%), and social (12%; 36%; 47%; 5%)

A total of 171 patients completed the question whether they considered they were in need of additional therapy for their PBC, of whom 40 (23.4%) patients answered "yes". Among these 40 patients, all PBC-40 domain scores were statistically significantly higher as compared to patients who did not consider they were in need of additional therapy ($p < 0.05$ for all), except for the domain itch (7.0 vs. 5.0, respectively, $p = 0.056$) which showed a trend (Table 3).

Of the 40 patients who considered they were in need of add-on therapy, 25 (62.5%) had ALP and bilirubin levels below the POISE criteria. Among those who did not consider they were in need of add-on therapy ($n = 131$), 37 (28.2%) patients had an unfavorable POISE status.

Health-related quality of life in relation to prognosis

The GLOBE score could be calculated in 164 patients; among them, 134 (81.2%) patients had a predicted prognosis comparable to that of their peers based on the age-specific cut-offs (i.e., normal prognosis). There were no statistically significant differences in the six domains' scores between patients with a predicted impaired prognosis and patients with a predicted normal prognosis (Table 3).

Sixty-seven (38.7%) of the 173 patients who reported on their self-expected prognosis considered their prognosis to be reduced compared to their peers. Among these 67 patients, the median total domain scores were 19.0 (13.0–22.5) for the domain symptoms, 37.0 (31.0–43.0) for the domain fatigue, 17.0 (12.0–21.0) for the domain cognition, 8.0 (7.0–11.0) for the domain emotional, and 28.5 (20.0–34.0) for the domain social. These median total domain scores were all statistically significantly higher compared to the median domain scores of patients who expected their prognosis to be normal ($p < 0.001$ for all, Table 3).

The GLOBE score was available for 62 of the 67 patients who expected a reduced prognosis. Contrary to their expectations, 45 (67.2%) patients actually had a normal prognosis based on the GLOBE score. Among 106 patients with a self-expected normal prognosis, 12 (11.3%) patients had an impaired prognosis based on the GLOBE score.

DISCUSSION

This was the first study to assess the HRQoL in a Dutch population of PBC patients in relation to objective disease parameters and

TABLE 2 PBC-40 domain scores according to different subgroups of Dutch patients with primary biliary cholangitis

	PBC-40 domains					
	Symptoms	**Itch**	**Fatigue**	**Cognition**	**Emotional**	**Social**
Type of hospital						
University	15.0 (11.5–20.0)	5.0 (4.0–8.0)	32.0 (22.0–40.0)	13.0 (7.0–18.5)	6.5 (4.0–9.8)	21.0 (12.0–31.8)
General	18.0 (13.5–21.0)	5.0 (3.0–21.0)	35.0 (27.0–41.0)	15.0 (10.0–18.0)	7.5 (5.0–9.0)	26.0 (18.0–31.5)
p value	0.056	0.473	0.265	0.366	0.107	0.090
Disease duration						
0–5 years	17.0 (12.5–20.0)	5.0 (3.0–7.0)	37.0 (27.0–42.0)	17.0 (9.8–21.3)	7.0 (6.0–21.3)	27.0 (17.0–33.0)
5–10 years	16.0 (12.0–20.5)	5.0 (3.0–8.0)	35.0 (28.0–43.0)	14.0 (9.0–20.0)	8.0 (5.0–11.0)	27.0 (18.0–34.0)
>10 years	17.3 (13.0–21.0)	5.0 (4.0–8.0)	33.5 (22.0–38.0)	13.0 (7.0–17.8)	6.0 (4.8–8.0)	21.0 (14.0–29.0)
p value	0.746	0.660	0.088	**0.043**	**0.001**	**0.030**
BMI (kg/m^2)						
<25	15.0 (11.0–20.0)	5.0 (3.0–8.0)	30.0 (21.0–38.0)	12.0 (7.0–17.0)	7.0 (4.0–9.0)	21.0 (14.0–29.0)
≥25	18.0 (13.0–22.0)	5.0 (3.0–7.0)	35.0 (28.0–41.0)	15.0 (10.0–20.0)	7.0 (5.0–10.0)	24.5 (16.8–33.0)
p value	**0.025**	0.784	**0.025**	**0.012**	0.134	0.073
Sex						
Male	11.0 (8.0–16.0)	3.5 (3.0–5.8)	24.0 (18.5–36.5)	11.0 (7.0–14.0)	4.0 (3.0–6.0)	15.0 (11.5–27.0)
Female	17.0 (13.0–21.0)	5.0 (3.3–8.0)	34.0 (26.0–41.0)	14.0 (9.0–19.0)	7.0 (5.0–10.0)	23.0 (16.3–32.8)
p value	**0.007**	0.085	**0.028**	**0.046**	**<0.001**	**0.022**
Age at participation (years)						
<60	17.0 (12.5–20.0)	4.5 (3.0–8.5)	35.0 (27.0–41.0)	16.0 (9.0–20.0)	7.0 (6.0–10.0)	27.0 (17.0–33.0)
≥60	16.5 (12.5–21.0)	5.0 (4.0–7.0)	33.0 (22.0–40.0)	13.0 (7.0–18.0)	6.0 (4.0–9.0)	22.0 (15.0–30.0)
p value	0.348	0.759	0.165	0.098	**0.007**	0.071
Educational level						
Secondary (or lower)[a]	18.0 (12.5–20.0)	6.0 (4.0–8.0)	34.0 (25.0–41.0)	14.0 (8.0–18.5)	7.0 (4.4–10.0)	23.0 (16.0–31.3)
Tertiary[b]	15.0 (12.0–20.0)	4.0 (3.0–7.0)	34.0 (23.5–41.0)	13.0 (9.0–18.0)	7.0 (4.5–9.0)	22.0 (16.0–33.0)
p value	0.090	**0.007**	0.761	0.626	0.490	0.786
Cirrhosis						
No	17.0 (12.9–21.0)	5.0 (3.0–7.0)	35.0 (26.0–41.0)	14.0 (8.5–18.0)	7.0 (4.0–10.0)	24.0 (16.0–33.0)
Yes	16.5 (12.1–20.5)	6.5 (3.0–8.0)	29.0 (20.0–36.8)	14.0 (10.0–17.8)	7.0 (4.0–8.0)	19.0 (13.0–28.0)
p value	0.705	0.688	0.050	0.864	0.614	0.081

Note: Significant *p*-values ($p < 0.005$) are in bold.

Abbreviation: BMI, body mass index.

[a]Primary education/secondary education/secondary vocational education.

[b]University/higher vocational education.

patients' perspectives on treatment and prognosis. We showed that the HRQoL was mainly affected by fatigue. No differences in the HRQoL were observed when patients were stratified for severity of disease and prognosis based on objective clinical parameters. The HRQoL was significantly lower in patients who expected their disease to be more severe and patients who considered they were in need of additional therapy. However, there was a substantial discrepancy between the patients' perspectives and their objective disease parameters. Almost 70% of patients with a self-expected impaired prognosis had a GLOBE score indicative of a normal prognosis, and over 60% of patients who believed to need additional therapy were below the POISE criteria. These results emphasize the need for adequate patient counseling, education, and guidance, which could help to improve their self-perceived quality of life.

The domain scores observed in this cohort were largely comparable to that of previous European studies. These studies showed

TABLE 3 PBC-40 domain scores according to objective laboratory parameters and primary biliary cholangitis patients' perspectives

	PBC-40 domains					
	Symptoms	**Itch**	**Fatigue**	**Cognition**	**Emotional**	**Social**
POISE criteria						
Below POISE	18.0 (12.5–21.0)	5.0 (3.0–7.0)	35.0 (26.0–41.3)	15.0 (8.5–18.5)	7.0 (5.0–10.0)	24.0 (17.0–33.0)
Above POISE	5.0 (11.9–18.6)	6.0 (3.5–9.0)	31.0 (22.0–38.0)	12.5 (8.0–18.3)	6.0 (4.0–9.5)	22.0 (14.0–28.5)
p value	**0.031**	0.234	0.078	0.416	0.203	0.116
Need for therapy according to the patient						
No	16.0 (12.0–20.5)	5.0 (3.0–7.0)	32.0 (23.0–39.0)	13.0 (8.0–18.0)	7.0 (4.0–8.0)	22.0 (15.0–31.0)
Yes	18.5 (14.5–22.8)	7.0 (4.0–8.5)	40.0 (30.3–44.8)	17.5 (10.0–21.5)	10.0 (7.0–11.0)	28.0 (21.0–34.0)
p value	**0.021**	0.056	**0.001**	**0.017**	**<0.001**	**<0.001**
Prognosis according to the GLOBE score						
Normal prognosis	17.0 (13.0–21.0)	5.0 (3.8–7.0)	34.0 (25.8–41.0)	13.0 (7.5–18.0)	7.0 (4.0–9.0)	23.0 (16.0–32.3)
Impaired prognosis	16.3 (11.9–20.6)	7.0 (3.0–11.0)	31.0 (22.8–38.0)	15.5 (10.0–20.3)	7.0 (4.5–10.5)	20.0 (14.5–32.5)
p value	0.705	0.092	0.436	0.158	0.212	0.429
Patients' perspective on prognosis						
Normal prognosis	15.0 (11.5–20.0)	5.0 (4.0–6.3)	30.0 (20.0–38.0)	12.0 (6.0–17.0)	5.5 (4.0–8.0)	20.0 (14.0–28.0)
Impaired prognosis	19.0 (13.0–22.5)	7.0 (3.0–8.0)	37.0 (31.0–43.0)	17.0 (12.0–21.0)	8.0 (7.0–11.0)	28.5 (20.0–34.0)
p value	**0.003**	0.202	**<0.001**	**<0.001**	**<0.001**	**<0.001**

Note: Significant *p*-values ($p < 0.005$) are in bold.

that fatigue represented the major burden on the HRQoL for patients with PBC.[8,15,16] Indeed, in our cohort the highest score was observed in the domain fatigue. In addition, the proportion of patients who scored "moderate" or "severe" in the domain fatigue was 73%, which was by far the highest percentage compared to the other domains (ranging from 25% to 53%). Adequate attention to fatigue is important; Jones et al. have related fatigue to unfavorable liver transplant-free survival in a prospective, albeit small ($n = 136$), study.[17] In our study, the scores in the domain fatigue of the PBC-40 did not differ according to the prognosis of patients, but the cross-sectional design limited us to assessment of the predicted prognosis based on the GLOBE score.[14] However, the GLOBE score has been validated as a highly accurate objective prognostic index for survival free of liver transplantation among patients with PBC.[18] The difference between our finding and that of the previous study could be related to differences in the studied populations and by the fact that we have not included matched patients without fatigue as a comparator.

Interestingly, disease duration was associated with several PBC-40 domain scores. The longer the disease duration, the lower the scores on the domains cognition, emotional, and social. This association remained stable after adjusting for age and gender (data not shown). Therefore, the burden on emotional, social, and cognitive levels seems to decrease with increasing disease duration, which could reflect the coping of patients over time. Previously, the UK-PBC group showed that the burden of HRQoL decreased with increasing age.[19] In line with previous reports, no differences in the HRQoL were observed when patients were stratified according to long-term prognosis and disease activity based on objective disease parameters such as the GLOBE score and POISE criteria.[3,5,9,20]

A relevant finding of this study was that patients who expected their prognosis to be reduced as compared to their peers, had a significantly impaired HRQoL compared to patients who expected their prognosis to be similar to their peers. While this appears logical, it is relevant to point out that the vast majority of patients did not adequately estimate their prognosis. More than two-thirds of patients who reported their self-expected prognosis to be reduced actually had a normal prognosis according to the GLOBE score. The patients' perspective on their prognosis can be the result of their unfavorable HRQoL, mainly due to fatigue, which has both a central component (sleep disturbance, cognitive impairment) and a peripheral component (muscle dysfunction, inability to sustain exercise).[21] Unfortunately, medical therapy to reduce symptoms and, thereby, improve the HRQoL remains an unmet clinical need in PBC today. Irrespective of symptoms, however, a negative prognostic perspective may reduce the patients' HRQoL by itself as well. It would be interesting to study whether adequate patient guidance and counseling can overcome the frequent misperceptions and would benefit the HRQoL. Nevertheless, the current results highlight the relevance of the worldwide PBC patient associations, who hold key positions in the education of patients and should thus be supported.

The need for better patient counseling and guidance was further highlighted by the observation that only one-third of patients who expected to have a reduced prognosis considered that they were in need for additional therapy (data not shown). Furthermore, 28% of

patients who reported that they were not in need of additional therapy were above the biochemical cut-offs of the POISE criteria.

Some limitations should be noted. First, the majority of the patients were recruited through the DLPA, which could have led to a selection bias. These patients might be more aware of their symptoms and more educated about their disease. However, it resulted in the opportunity to include patients outside of a tertiary liver transplant center. Second, as might be expected, the majority of patients were women. The study is not sufficiently powered for strong conclusions related to observed differences between genders. Third, the number of patients with severe liver disease was limited, which could have been related to the approach of collecting questionnaires by post. Fourth, we developed and used four questions to assess patients' perspectives regarding treatment and prognosis in this study, which have not been validated. The multiple-choice questions were simple, however, and clearly interpreted by patients who were interviewed on the questions during the preparation phase of this study. In addition, the questions do not allow detailed analyses with respect to the underlying reasons for the patients' answers. The patients' perspectives were thus only crudely assessed in our study. Still, we consider that the need for more awareness on patient counseling and education is valid based on our methodology and results. Finally, as there was no control group, no comparisons with a normal population could be made in terms of the degree of impairment of the HRQoL. Therefore, it is impossible to confirm that the complaints are indeed disease-specific. However, the domain scores were comparable with studies from other countries who did compare their results to a control population.

In conclusion, the HRQoL in a Dutch population of PBC patients is comparable with that in other European populations, and is associated with the patients' perspectives on their prognosis and need for additional therapy. Importantly, however, these patients' perspectives are largely discrepant with their objective disease parameters, indicating the need for additional therapy and prognosis. Our study therefore implies a need for better patient counseling, education, and guidance in PBC care.

ACKNOWLEDGMENTS

Thanks to all the patients who gave their time and effort to participate.

CONFLICT OF INTEREST

Adriaan J. van der Meer reports speakers fees from Zambon Nederland B.V., unrestricted grants from CymaBay Therapeutics, Gilead Sciences, MSD, and Zambon Nederland B.V., and fees for consulting work from Intercept Pharma Benelux and AOP Health. The other authors declare that they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Due to the nature of this research, participants of this study did not agree for their data to be shared publicly, so supporting data is not available.

ETHICS STATEMENT

Approval of the research protocol by an institutional review board: The study protocol was approved by the Ethical Committee of the Erasmus Medical Center in Rotterdam and was conducted in accordance with the Declaration of Helsinki.

Informed consent: Written informed consent was obtained from all patients.

Registry and the Registration No. of the study/trial: N/A.

Animal studies: N/A.

Research involving recombinant DNA: N/A.

REFERENCES

1. Kaplan MM, Gershwin ME. Primary biliary cirrhosis. N Engl J Med. 2005;353(12):1261–73. https://doi.org/10.1056/nejmra043898
2. European Association for the Study of the Liver. Electronic address eee, European Association for the Study of the L. EASL Clinical Practice Guidelines: the diagnosis and management of patients with primary biliary cholangitis. J Hepatol. 2017;67(1):145–72.
3. Mells GF, Pells G, Newton JL, Bathgate AJ, Burroughs AK, Heneghan MA, et al. Impact of primary biliary cirrhosis on perceived quality of life: the UK-PBC national study. Hepatology. 2013;58(1):273–83. https://doi.org/10.1002/hep.26365
4. Carbone M, Mells GF, Pells G, Dawwas MF, Newton JL, Heneghan MA, et al. Sex and age are determinants of the clinical phenotype of primary biliary cirrhosis and response to ursodeoxycholic acid. Gastroenterology. 2013;144(3):560–9. e7; quiz e13-4. https://doi.org/10.1053/j.gastro.2012.12.005
5. Poupon RE, Chretien Y, Chazouilleres O, Poupon R, Chwalow J. Quality of life in patients with primary biliary cirrhosis. Hepatology. 2004;40(2):489–94. https://doi.org/10.1002/hep.20276
6. Yagi M, Tanaka A, Abe M, Namisaki T, Yoshiji H, Takahashi A, et al. Symptoms and health-related quality of life in Japanese patients with primary biliary cholangitis. Sci Rep. 2018;8(1):12542. https://doi.org/10.1038/s41598-018-31063-8
7. Younossi ZM. Chronic liver disease and health-related quality of life. Gastroenterology. 2001;120(1):305–7. https://doi.org/10.1053/gast.2001.22073
8. Jacoby A, Rannard A, Buck D, Bhala N, Newton JL, James OF, et al. Development, validation, and evaluation of the PBC-40, a disease specific health related quality of life measure for primary biliary cirrhosis. Gut. 2005;54(11):1622–9. https://doi.org/10.1136/gut.2005.065862
9. Montali L, Tanaka A, Riva P, Takahashi H, Cocchi C, Ueno Y, et al. A short version of a HRQoL questionnaire for Italian and Japanese patients with Primary Biliary Cirrhosis. Dig Liver Dis. 2010;42(10):718–23. https://doi.org/10.1016/j.dld.2010.01.004
10. Zec S, Popovic D, Matovic V, Nikolic V, Bojovic K, Jovic J, et al. Translation and validation of the Serbian primary biliary cholangitis-40 questionnaire. PLoS One. 2017;12(4):e0175697. https://doi.org/10.1371/journal.pone.0175697
11. de Veer RC, da Silva G, van Hooff MC, Harms MH, Metselaar HJ, Willemse J, et al. Measurement properties of the PBC-40 and PBC-27: a Dutch validation study. BMJ Open Gastroenterol. 2021;8(1):e000758. https://doi.org/10.1136/bmjgast-2021-000758
12. Kim HP, Lieber SR, Rogers ME, Moon AM, Loiselle M, Walker J, et al. A systematic review of patient-reported outcomes in primary biliary cholangitis and primary sclerosing cholangitis. Hepatol Commun. 2020;4(10):1502–15. https://doi.org/10.1002/hep4.1567
13. Nevens F, Andreone P, Mazzella G, Strasser SI, Bowlus C, Invernizzi P, et al. A placebo-controlled trial of obeticholic acid in primary biliary cholangitis. N Engl J Med. 2016;375(7):631–43. https://doi.org/10.1056/nejmoa1509840

14. Lammers WJ, Hirschfield GM, Corpechot C, Nevens F, Lindor KD, Janssen HL, et al. Development and validation of a scoring system to predict outcomes of patients with primary biliary cirrhosis receiving ursodeoxycholic acid therapy. Gastroenterology. 2015;149(7):1804–12. e4. https://doi.org/10.1053/j.gastro.2015.07.061
15. Milovanovic T, Popovic D, Stojkovic Lalosevic M, Dumic I, Dragasevic S, Milosavljevic T. Quality of life in patients with primary biliary cholangitis: a single-center experience in Serbia. Dig Dis. 2020;38(6):515–21. https://doi.org/10.1159/000506980
16. Newton JL, Bhala N, Burt J, Jones DE. Characterisation of the associations and impact of symptoms in primary biliary cirrhosis using a disease specific quality of life measure. J Hepatol. 2006;44(4):776–83. https://doi.org/10.1016/j.jhep.2005.12.012
17. Jones DE, Al-Rifai A, Frith J, Patanwala I, Newton JL. The independent effects of fatigue and UDCA therapy on mortality in primary biliary cirrhosis: results of a 9 year follow-up. J Hepatol. 2010;53(5):911–7. https://doi.org/10.1016/j.jhep.2010.05.026
18. Efe C, Tascilar K, Henriksson I, Lytvyak E, Alalkim F, Trivedi H, et al. Validation of risk scoring systems in ursodeoxycholic acid-treated patients with primary biliary cholangitis. Am J Gastroenterol. 2019;114(7):1101–8. https://doi.org/10.14309/ajg.0000000000000290
19. Dyson JK, Wilkinson N, Jopson L, Mells G, Bathgate A, Heneghan MA, et al. The inter-relationship of symptom severity and quality of life in 2055 patients with primary biliary cholangitis. Aliment Pharmacol Ther. 2016;44(10):1039–50. https://doi.org/10.1111/apt.13794
20. Kaps L, Grambihler A, Yemane B, Nagel M, Labenz C, Ploch P, et al. Symptom burden and treatment response in patients with primary biliary cholangitis (PBC). Dig Dis Sci. 2020;65(10):3006–13. https://doi.org/10.1007/s10620-019-06009-3
21. Jopson L, Jones DE. Fatigue in primary biliary cirrhosis: prevalence, pathogenesis and management. Dig Dis. 2015;33(Suppl 2):109–14. https://doi.org/10.1159/000440757

How to cite this article: de Veer RC, van Hooff MC, da Silva G, Harms MH, Metselaar HJ, Willemse J, et al. Quality of life in Dutch patients with primary biliary cholangitis: discrepancies between patients' perspectives and objective disease parameters. Hepatol Res. 2023;53(5):401–8. https://doi.org/10.1111/hepr.13880