**Supplementary Table 1.** Baseline characteristics in patients with PSC stratified by ALP (normal vs abnormal)

|  |  |  |  |
| --- | --- | --- | --- |
| Parameter | Abnormal ALP n=67 | Normal ALP n=32 | p-value |
| Males, no. (%) | 37 (55) | 13 (41) | 0.17 |
| Age at survey, mean±SD (years) | 45.7 ± 15.4 | 47.0 ± 14.8 | 0.69 |
| Caucasian, no. (%) | 52 (78) | 29 (91) | 0.12 |
| BMI, mean±SD (kg/m2) | 24.9 ± 4.0 | 26.2 ± 4.9 | 0.18 |
| Years of liver disease, mean±SD | 7.3 ± 5.9 | 6.9 ± 6.1 | 0.76 |
| Years of IBD, mean±SD  | 11.8 ± 10.8 | 19.1 ± 11.5 | **0.01** |
| Presence of IBD, no. (%) | 52 (78) | 22 (70) | 0.34 |
| Colectomy, no (%) | 5 (8) | 6 (19) | 0.10 |
| UDCA ever, no. (%) | 54 (81) | 24 (75) | 0.52 |
| UDCA at survey, no. (%) | 35 (52) | 15 (47) | 0.62 |
| Cirrhosis, no. (%) | 34 (51) | 13 (41) | 0.35 |
| Decompensation, no. (%) | 14 (21) | 2 (6) | **0.06** |
| Social History |   |   |   |
| History of smoking, no. (%) | 2 (3) | 2 (6) | 0.44 |
| Alcohol excess, no. (%) | 1 (2) | 0 | 0.49 |
| Married, no. (%) | 42 (63) | 19 (59) | 0.75 |
| Employed/Studying, no. (%) | 53 (79) | 18 (56) | **0.02** |
| Laboratory parameters, mean±SD |   |   |   |
| ALP (IU/L) | 311.2 ± 199 | 100.3 ± 25.0 | **<0.001** |
| ALT (IU/L) | 85.9 ± 103 | 29.1 ± 18.0 | **0.003** |
| AST (IU/L) | 66.8 ± 64.0 | 26.4 ± 9.8 | **0.001** |
| INR | 1.03 ± 0.17 | 1.03 ± 0.10 | 0.83 |
| Bilirubin (mg/dL) | 24.0 ± 29.9 | 11.8 ± 8.5 | **0.03** |
| Creatinine (µmol/L) | 68.1 ± 14.0 | 70.3 ± 12.3 | 0.47 |
| Hemoglobin (g/dL) | 132.6 ± 17.8 | 140.2 ± 13.9 | **0.04** |
| Platelets (x109/L) | 246.0 ± 157.5 | 309.7 ± 119.0 | **0.05** |

PSC, primary sclerosing cholangitis; ALP, alkaline phosphatase; IBD, inflammatory bowel disease; SD, standard deviation; BMI, body mass index; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio.

**Supplementary Table 2.** Mean SF-36, PHQ-9 and SIBDQ scores between patients with PSC and other diseases

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Quality of Life Scores (mean±SE) | PSC n=99 | PBC n=26 | Other Cholestatic n=16 | IBD n = 21 | p-value | PSC-IBD n=74 | PSC-NIBD n=25 | p-value |
| SF-36 subscores (mean±SE) |  |  |  |  |  |  |  |  |
| Physical functioninga | 81.7 ± 2.7 | 74.4 ± 4.9 | 83.4 ± 6.4 | 80.5 ± 4.6 | 0.80 | 84.9 ± 2.9 | 72.2 ± 6.0 | **0.03** |
| Role physicalb | 72.0 ± 3.9 | 59.4 ± 8.4 | 65.6 ± 10.2 | 48.8 ± 11.0 | 0.10 | 77.7± 2.9 | 81.1 ± 4.3 | 0.50 |
| Bodily pain | 78.1 ± 2.2 | 71.4 ± 5.0 | 70.7 ± 7.9 | 67.4 ± 5.8 | 0.23 | 73.7 ± 4.3 | 67 ± 8.7 | 0.50 |
| General Healthc | 50.6 ± 2.2 | 52.1 ± 4.0 | 54.1 ± 5.6 | 50.5 ± 4.7 | 0.06 | 79.3 ± 3.8 | 74.8 ± 7.3 | 0.58 |
| Vitalityd | 51.8 ± 2.3 | 47.8 ± 4.2 | 49.4 ± 5.0 | 45.7 ± 4.4 | 0.39 | 72.3 ± 2.2 | 70.4 ± 4.2 | 0.68 |
| Social functioninge | 78.6 ± 2.4 | 72.2 ± 4.8 | 81.3 ± 5.2 | 67.8 ± 6.0 | 0.53 | 52.8 ± 2.7 | 48.8 ± 4.5 | 0.45 |
| Role emotionalf | 78.1 ± 3.4 | 59.0 ± 8.3 | 79.2 ± 9.1 | 61.9 ± 9.3 | 0.36 | 79.2 ± 2.5 | 74.9 ± 4.3 | 0.39 |
| Mental healthg | 71.8 ± 2.0 | 73.7 ± 3.6 | 74.8 ± 4.9 | 68.8 ± 4.1 | 0.33 | 50.9 ± 2.5 | 49.8 ± 4.4 | 0.83 |
| Physical component score | 45.7 ± 1.0 | 42.9 ± 2.2 | 44.3 ± 3.2 | 42.8 ± 2.9 | 0.72 | 46.6 ± 1.1 | 42.9 ± 2.3 | 0.10 |
| Mental component score | 45.5 ± 1.2 | 43.7 ± 2.3 | 46.9 ± 3.7 | 41.5 ± 2.7 | 0.20 | 45.3 ± 1.4 | 46.0 ± 2.4 | 0.13 |
|  |  |  |  |  |  |  |  |  |
| PHQ-9h | 5.6 ± 0.6 | 6.6 ± 1.3 | 4.3 ± 1.3 | 6.2 ± 1.2 | 0.64 | 5.7 ± 0.7 | 5.2 ± 1.3 | 0.76 |
| SIBDQi | 53.7 ± 1.0 | 52.1 ± 2.4 | 56.6 ± 2.4 | 50.7 ± 2.2 | 0.29 | 53.9 ± 1.1 | 53.0 ± 2.1 | 0.69 |
| a 8 PSC patients missing <50% of answers |   |   |   |   |   |   |
| b 3 patients missing <50% of answers (PSC 1, IBD 2) and 1 Other cholestatic patient with all answers left blank |   |   |
| c 3 patients with PSC missing <50% of answers |   |   |   |   |   |   |
| d 7 patients missing <50% of answers (PSC 6, Other cholestatic 1) |   |   |   |   |   |
| e 7 patients missing <50% of answers (PSC 4, PBC 2, Other cholestatic 1) |   |   |   |   |   |
| f 1 Other cholestatic patient with with all answers left blank |   |   |   |   |   |
| g 3 patients missing <50% of answers (PSC 1, PBC 1, IBD 1) |   |   |   |   |   |
|  h 1 PSC patient missing response |
|  i 22 patients missing <50% of answers (PSC: 9, PBC: 12, Other cholestatic: 1) |

SF-36, Short Form-36; PHQ-9, Patient Health Questionnaire; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; PSC, primary sclerosing cholangitis; SE, standard error; PBC, primary biliary cholangitis; IBD, inflammatory bowel disease; NIBD, no IBD.

**Supplementary Table 3.** Mean LDQOL and PBC-40 scores stratified by liver disease subtype

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Quality of Life Scores (mean±SE) | PSC n=99 | PBC n=26 | Other cholestatic n=16 | p-value | PSC-IBD n=74 | PSC-NIBD n=25 | p-value |
| LDQOLa  |   |   |   |   |   |   |   |
| Symptoms of Liver Disease  | 80.5 ± 1.5 | 76.0 ± 3.9 | 81.3 ± 2.7 | 0.41 | 80.6 ± 1.7 | 79.9 ± 3.5 | 0.84 |
| Effects of Liver Disease  | 83.3 ± 1.9 | 81.5 ± 4.0 | 86.8 ± 4.4 | 0.68 | 83.6 ± 2.2 | 82.4 ± 4.1 | 0.85 |
| Concentration | 84.4 ± 1.8 | 84.7 ± 4.9 | 89.3 ± 3.6 | 0.63 | 85.3 ± 2.1 | 81.9 ± 3.7 | 0.42 |
| Memory | 78.3 ± 2.0 | 77.2 ± 5.3 | 91.1 ± 2.7 | 0.06 | 78.0 ± 2.5 | 79.1 ± 3.3 | 0.82 |
| Quality of Social Interaction | 74.5 ± 1.6 | 75.8 ±2.8 | 74.9 ± 3.3 | 0.94 | 74.3 ± 1.8 | 75.1 ± 3.3 | 0.83 |
| Health Distress  | 75.4 ± 2.6 | 76.4 ± 5.4 | 76.3 ± 5.6 | 0.98 | 74.4 ± 3.1 | 78.4 ± 4.8 | 0.50 |
| Sleep | 59.7 ± 2.2 | 54.8 ± 5.1 | 59.7 ± 5.6 | 0.62 | 59.6 ± 2.4 | 60.0 ± 5.0 | 0.94 |
| Loneliness | 84.1 ± 1.8 | 85.0 ±4.1 | 82.5 ± 5.4 | 0.92 | 84.5 ± 2.1 | 82.8 ± 4.0 | 0.66 |
| Hopelessness | 69.1 ± 2.7 | 77.3 ± 4.2 | 67.3 ± 6.1 | 0.31 | 69.3 ± 3.3 | 68.4 ± 4.5 | 0.88 |
| Stigma of Liver Disease  | 89.7 ± 1.7 | 89.8 ± 3.9 | 93.3 ± 2.9 | 0.74 | 89.9 ± 1.9 | 89.2 ± 4.0 | 0.86 |
| Sexual Functioning  | 71.5 ± 3.4 | 60.7 ± 6.8 | 80.6 ± 6.5 | 0.14 | 72.9 ± 3.7 | 67.5 ± 7.9 | 0.50 |
| Sexual Problems  | 76.2 ± 3.5 | 55.4 ± 8.0 | 78.7 ± 6.6 | **0.02** | 74.5 ± 3.9 | 81.2 ± 7.0 | 0.40 |
| PBC-40b |   |   |   |   |   |   |   |
| Symptoms | 13.4 ± 0.5 | 15.5 ± 0.9 | 12.4 ± 1.1 | 0.09 | 13.6 ± 0.6 | 12.7 ± 1.1 | 0.44 |
| Itch | 5.0 ± 0.3 | 4.7 ± 0.6 | 4.3 ± 0.4 | 0.60 | 5.0 ± 0.3 | 5.0 ± 0.6 | 1.00 |
| Fatigue | 25.7 ± 1.1 | 28.6 ± 2.1 | 24.9 ± 2.4 | 0.45 | 25.2 ± 1.2 | 27.2 ± 2.7 | 0.44 |
| Cognitive | 11.7 ± 0.5 | 12.3 ± 1.2 | 10.3 ± 1.2 | 0.49 | 11.5 ± 0.6 | 12.3 ± 1.0 | 0.52 |
| Social | 21.1 ± 0.9 | 19.9 ± 1.6 | 21.0 ± 1.3 | 0.59 | 21.7 ± 0.9 | 19.8 ± 0.9 | 0.19 |
| Emotional | 7.6 ± 0.3 | 7.0 ± 0.7 | 7.1 ± 0.3 | 0.59 | 7.7 ± 0.3  | 7.2 ± 0.4 | 0.38 |
| a LDQOL missing completely for 1 patient with PBC; Insufficient data available for all but the Loneliness, Hopelessness and Stigma of Liver Disease subscores for 1 patient with PSC; Insufficient data available for calculation of Sexual Function in 14 patients (PSC: 10, PBC: 4) and of Sexual Problems in 60 patients (PSC: 42, PBC: 10, Other cholestatic: 8).  |
| b Insufficient data for the calculation of the following PBC-40 subscores: Symptoms (PBC: 1), Itch (PSC: 2, PBC: 1), Fatigue (PSC: 2, PBC: 1), Cognitive (PSC: 3, PBC: 1), Socioemotional (PSC: 4, PBC: 1)  |

PSC, primary sclerosing cholangitis; PBC, primary biliary cholangitis; PSC-IBD, PSC with inflammatory bowel disease; PSC-NIBD, PSC without inflammatory bowel disease; SE, standard error; LDQOL, Liver Disease Quality of Life; PBC-40, Primary biliary cholangitis-40.

**Supplementary Table 4.** Mean SF-36, LDQOL, PBC-40, PHQ-9 and SIBDQ scores in patients with PSC stratified by ALP (normal vs abnormal)

|  |  |  |  |
| --- | --- | --- | --- |
| Quality of Life Scores (mean±SE) | Abnormal ALP n=67 | Normal ALP n=32 | p-value |
| SF-36 subscores (mean±SE) |   |   |   |
| Physical functioning | 80.5 ± 3.4 | 84.2 ± 4.3 | 0.53 |
| Role physical | 69.8 ± 4.8 | 76.6 ± 6.5 | 0.41 |
| Bodily pain | 77.6 ± 2.8 | 79.3 ± 3.4 | 0.72 |
| General Health | 48.4 ± 2.7 | 55.3 ± 3.5 | 0.13 |
| Vitality | 52.6 ± 2.7 | 50.0 ± 4.2 | 0.59 |
| Social functioning | 80.3 ± 2.8 | 75.0 ± 4.4 | 0.31 |
| Role emotional | 78.6 ± 4.1 | 77.1 ± 5.9 | 0.83 |
| Mental health | 73.4 ± 2.1 | 68.4 ± 4.2 | 0.22 |
| Physical component score | 44.5 ± 1.3 | 48.0 ± 1.7 | 0.11 |
| Mental component score | 46.7 ± 1.3 | 43.0 ± 2.6 | 0.15 |
| LDQOL |   |   |   |
| Symptoms of Liver Disease  | 80.6 ± 1.9 | 80.1 ± 2.5 | 0.89 |
| Effects of Liver Disease  | 81.7 ± 2.5 | 86.4 ± 2.8 | 0.24 |
| Concentration | 84.4 ± 2.2 | 84.4 ± 3.0 | 0.99 |
| Memory | 77.2 ± 2.6 | 81.0 ± 3.1 | 0.37 |
| Quality of Social Interaction | 75.4 ± 1.8 | 71.8 ± 3.2 | 0.29 |
| Health Distress  | 73.1 ± 3.2 | 80.7 ± 4.2 | 0.16 |
| Sleep | 59.2 ± 2.6 | 60.9 ± 4.1 | 0.70 |
| Loneliness | 85.7 ± 1.8 | 81.1 ± 4.3 | 0.24 |
| Hopelessness | 70.1 ± 3.0  | 66.9 ± 5.6 | 0.57 |
| Stigma of Liver Disease  | 89.8 ± 2.1 | 89.5 ± 3.3 | 0.93 |
| Sexual Functioning  | 70.8 ± 4.2 | 75.2 ± 5.6 | 0.54 |
| Sexual Problems  | 73.1 ± 4.3 | 74.9 ± 6.2 | 0.80 |
| PBC-40 |   |   |   |
| Symptoms | 13.3 ± 0.6 | 13.5 ± 1.0 | 0.88 |
| Itch | 5.5 ± 0.4 | 4.0 ± 0.3 | **0.01** |
| Fatigue | 26.2 ± 1.4 | 24.8 ± 1.9 | 0.56 |
| Cognitive | 11.8 ± 0.7 | 11.3 ± 0.8 | 0.65 |
| Social | 20.4 ± 1.0 | 22.6 ± 1.6 | 0.23 |
| Emotional | 7.3 ± 0.4 | 8.1 ± 0.6 | 0.26 |
| PHQ-9 | 5.1 ± 0.7 | 6.5 ± 1.3 | 0.29 |
| SIBDQ | 54.2 ± 1.2 | 52.8 ± 1.5 | 0.50 |

SF-36, Short Form-36; LDQOL, Liver Disease Quality of Life; PBC-40, Primary biliary cholangitis-40; PHQ-9, Patient Health Questionnaire; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; PSC, primary sclerosing cholangitis; ALP, alkaline phosphatase; SE, standard error.

**Supplementary Table 5.** Comparison of linear regression models using each HRQOL instrument

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcome measure | Modela | pooled R2 estimate | pooled SE of estimate  |   |   |
| Physical component score (SF-36) | LDQOL | **0.38** | 8.71 |   |   |
|   | PBC-40 | 0.33 | 9.04 |   |   |
|   | SIBDQ | 0.23 | 9.75 |   |   |
|   | PHQ-9 | 0.15 | 10.23 |   |   |
| Mental component score (SF-36) | LDQOL | **0.55** | 8.17 |   |   |
|   | PBC-40 | 0.42 | 9.33 |   |   |
|   | SIBDQ | 0.39 | 9.54 |   |   |
|   | PHQ-9 | 0.52 | 8.48 |   |   |
| SIBDQ | LDQOL | **0.64** | 5.89 |   |   |
|   | PBC-40 | 0.36 | 7.78 |   |   |
|   | PHQ-9 | 0.41 | 7.51 |   |   |
|   | SF-36\* | 0.51 | 6.80 |   |   |
| PHQ-9 | LDQOL | **0.73** | 3.11 |   |   |
|   | PBC-40 | 0.45 | 4.44 |   |   |
|   | SIBDQ | 0.41 | 4.60 |   |   |
|   | SF-36\* | 0.57 | 3.93 |   |   |
| a All models included presence of PSC, sex, age at time of survey and log ALP at time of survey |
| \* Models containing SF-36 included only the physical and mental component scores |   |

HRQOL, health-related quality of life; SE, standard error; SF-36, Short Form-36; LDQOL, Liver Disease Quality of Life; PBC-40, Primary biliary cholangitis-40; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; PHQ-9, Patient Health Questionnaire.

|  |  |  |
| --- | --- | --- |
| **Supplementary Table 6.** Multivariable analysis of factors affecting PHQ-9 and SIBDQ in patients with PSC |  |  |
| Parameter | B | SE | 95%CI | p-value |
| PHQ-9 |   |   |   |   |
| Primary sclerosing cholangitis | 1.02 | 0.57 | -0.11 - 2.15 | 0.08 |
| Male sex | -0.90 | 0.60 | -2.07 - 0.28 | 0.13 |
| Age (per decade) | 0.22 | 0.48 | -0.07 - 1.18 | 0.65 |
| Currently employed | 0.13 | 0.60 | -1.06 - 1.32 | 0.83 |
| Symptoms (PBC-40) | -0.06 | 0.03 | -0.13 - 0.01 | 0.08 |
| Fatigue (PBC-40) | -0.06 | 0.03 | -0.12 - -0.01 | **0.02** |
| Cognitive (PBC-40) | -0.06 | 0.03 | -0.11 - -0.1 | **0.03** |
| Symptoms (LDQOL) | -0.06 | 0.02 | -0.09 - -0.03 | **<0.001** |
| Concentration (LDQOL) | -0.04 | 0.02 | -0.08 - -0.004 | **0.03** |
| Quality of Social Interaction (LDQOL) | -0.04 | 0.02 | -0.08 - 0.002 | 0.06 |
| Sleep (LDQOL) | 0.04 | 0.08 | -0.12 - 0.19 | 0.65 |
| Loneliness (LDQOL) | -0.03 | 0.05 | -0.12 - 0.07 | 0.55 |
| Stigma (LDQOL) | 0.02 | 0.10 | -0.17 - 0.21 | 0.86 |
| SIBDQ | -0.01 | 0.05 | -0.11 - 0.09 | 0.79 |
| Physical component score (SF-36) | 0.19 | 0.35 | -0.5 - 0.87 | 0.60 |
| Mental component score (SF-36) | -0.96 | 0.38 | -1.71 - -0.22 | **0.01** |
|   |   |   |   |   |
| SIBDQ |   |   |   |   |
| Primary sclerosing cholangitis | -1.03 | 1.21 | -3.43 - 1.37 | 0.40 |
| Male sex | 0.13 | 1.18 | -2.19 - 2.44 | 0.92 |
| Age (per decade) | 0.17 | 0.37 | -0.56 - 0.89 | 0.65 |
| Fatigue (PBC-40) | -0.03 | 0.08 | -0.2 - 0.13 | 0.69 |
| Symptoms (LDQOL) | 0.20 | 0.07 | 0.07 - 0.34 | **0.004** |
| Effects of Liver Disease (LDQOL) | 0.06 | 0.06 | -0.06 - 0.17 | 0.32 |
| Concentration (LDQOL) | 0.07 | 0.06 | -0.06 - 0.2 | 0.27 |
| PHQ-9 | -0.08 | 0.17 | -0.42 - 0.27 | 0.66 |
| Physical component score (SF-36) | 0.72 | 0.73 | -0.72 - 2.15 | 0.33 |
| Mental component score (SF-36) | 2.02 | 0.77 | 0.50 - 3.53 | **0.01** |

PHQ-9, Patient Health Questionnaire; SIBDQ, Short Inflammatory Bowel Disease Questionnaire; SE, standard error; PBC-40, Primary biliary cholangitis-40; LDQOL, Liver Disease Quality of Life; SF-36, Short Form-36.

**Supplementary Table 7.** Qualitative Themes for PSC Patients

|  |  |  |
| --- | --- | --- |
| Question (number of responses) | Themes | n (%) |
| Patient feeling after diagnosis (140) | Existential Denial Depression AcceptanceAnger No response  | 51 (36.4)24 (17.1)23 (16.4)21 (15.0)11 (7.9)10 (10.1)\* |
| Patients’ major worry (102) | Disease Progression SymptomsSocial ImpactNo response | 70 (68.6)18 (17.6)11 (10.8)6 (6.0)\* |
| Impact on Professional Life (95) | No effect ReportedHindrance Impairment | 50 (52.6)30 (31.6)15 (15.8) |
| Affect on Family (94) | No Effect ReportedEmpathy from Family Isolation from Family | 42 (44.6)29 (30.8)23 (24.5) |
| Lifestyle Modifications Since Diagnosis (118) | Physical ActivityDietNo Changes ReportedSocial Activity | 42 (35.6)31 (26.3)25 (21.2)20 (16.9) |
| Diet Modifications Since Diagnosis (103) | Quality of DietNo Changes ReportedEating Behaviours | 70 (68.0)25 (24.3)8 (7.8) |
| Main Need for Newly Diagnosed Patients (107) | SupportInformationHopeNo Response | 46 (43.0)40 (37.4)11 (10.3)10 (10.1)\* |
| Desire for Primary Care Physician to Know (101) | InformationNo Response InnovationSupport/Resources | 48 (47.5)43 (43.4)\*6 (5.9)4 (4.0) |
| Desire for Gastrointestinal Specialist to Know (98) | No Response InformationInnovationSupport/Resources | 52 (52.5)\*28 (28.6)10 (10.2)8 (8.2) |

\* Percentages for no response based on total number of PSC patients rather than total number of responses (ie. n=99).