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ORIGINAL ARTICLE

Outcome and Quality of Life in Patients With Polycystic Liver Disease After Liver or Combined Liver-Kidney Transplantation

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In advanced stages of polycystic liver disease, often associated with polycystic kidney disease, a curative therapy is liver or combined liver-kidney transplantation. However, little is known about long-term outcome and quality of life. Between 1990 and 2003, 36 patients (32 female, 4 male) with polycystic liver or combined liver-kidney disease underwent liver (n = 21) or liver-kidney (n = 15) transplantation at our center. Main indications for liver transplantation were cachexia, muscle atrophy, loss of weight, recurrent cyst infections, portal hypertension, and ascites. Apart from clinical parameters, 2 anonymous questionnaires (standard short form 36 and self-designed) addressing quality of life and social status were evaluated. Five patients (14 %) died due to sepsis or myocardial infarction with pneumonia, all within 61 days after transplantation. The follow-up time of the remaining 31 patients ranged from 5 to 156 months, with a mean of 62 months. Of the 23 (74%) answered the questionnaires, 91% of patients felt "much better" or "better," only 9% felt "worse" than before, and 52% of patients participated in sports regularly. Fatigue, physical fitness, loss of appetite, and vomiting improved significantly after transplantation. Physical attractiveness and interest in sex increased as well. Professional occupation did not change for 71% of patients. Family situation before and after transplantation changed in 1 case only. Finally, 78% of patients said they would opt for transplantation again, while 17% were undecided; 1 patient would not repeat transplantation. In conclusion, patients with advanced polycystic liver or polycystic liver-kidney disease have an excellent survival rate and an improved quality of life after liver or combined liver-kidney transplantation. ***Liver Transpl 12:1268-1277, 2006.*** © **2006 AASLD.**

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Autosomal dominant polycystic kidney disease is often associated with polycystic liver disease. It is a dominantly inherited condition with 2 known polycystic kidney disease loci on chromosome 4q21-q23 (polycystic kidney disease 2) or 16p13.3-p13.12 (polycystic kidney disease 1).[1-3] In the last decade it has been recognized that there is another genetic entity for a much less frequent form of autosomal dominant polycystic liver disease without any associated renal involvement.[4] Recently it has been found to be linked to mutations on chromosome 19p13.2-13.1,[2,5] although linkage studies support the existence of other gene loci.[6] Mutations in the protein kinase C substrate 80K-H gene and the SEC63 gene have also been found in association with autosomal dominant polycystic liver disease.[6-8]

Patients with advanced polycystic liver disease may suffer from abdominal pain, hepatomegaly, caval compression, anorexia, cyst infections, dyspnea, portal hypertension (rare), and severely reduced quality of life.[1,9] To reduce the discomfort and physical impairment related to the enormous liver size, several therapeutic procedures, which include cyst fenestration alone, liver

Abbreviation: SF-36, short form 36.

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resection alone or in combination with cyst fenestration, and percutaneous drainage with sclerosing treatment, have been administered. Open laparotomy for cyst fenestration[10] is no longer recommended, because laparoscopic cyst fenestration leads to less morbidity and mortality compared to open surgical laparotomy.[11] The method with the lowest complication rate is percutaneous aspiration combined with sclerotherapy.[1,12,13] Highly symptomatic patients with polycystic liver disease almost exhaust conservative therapeutic options, and surgery is considered the best possible procedure. Gigot et al.[10,14] reported on an extensive fenestration technique that is effective in relieving symptoms in patients with polycystic liver disease. There was no mortality, but postoperative morbidity occurred in 50% of patients, mainly from biliary complications. The mean liver reduction rate was 43%. In the long-term observation, some patients had a significant disease progression after extensive cyst fenestration operation. Que et al.[15] reported on a large series with 31 patients who underwent combined liver resection and fenestration due to massive, highly symptomatic polycystic liver disease. The mean liver volume was reduced from 9,357 mL to 3,567 mL. Fifty-eight percent of the patients experienced complications, usually transient pleural effusions or transient ascites. Of 29 surviving patients with adequate follow-up, 28 have experienced immediate and sustained relief of symptoms and improvement in quality of life. Sequential computed tomography scans before and after surgery suggested that hepatic enlargement mainly resulted from the expansion of existing cysts rather than from the development of new cysts.[15] Yang et al.[16] reported on combined hepatic resection with cystic fenestration in 7 patients with advanced polycystic liver disease. There was no hospital death. All patients had ascites after surgery and were treated by diuretics and drainage for about 11 days. No significant development of cysts in the previously spared liver segments during a mean follow-up period of 20.4 months has been reported.[16] Tan et al.[17] described good results after combined treatment of resection and fenestration in patients with symptomatic polycystic liver disease. Until now, orthotopic liver transplantation has been the only approach to cure the disease. It usually leads to excellent symptomatic relief, but it is a costly and an invasive procedure. Since some patients with combined polycystic kidney and liver disease also have renal insufficiency, combined liver-kidney transplantation is the preferred treatment option.

Usually, patients with advanced stages of liver cirrhosis feel their deteriorating health condition with no improvement of liver function without transplantation. Under these circumstances, patients easily agree to liver transplantation, knowing about the perioperative risks and long-term complications. In contrast, patients with advanced polycystic liver disease often have normal liver function and do not suffer from a life-threatening condition. Even if their quality of life is dramatically reduced, they often wait for prolonged periods of time before deciding to consent to liver transplantation. Under these premises, improvement of quality of life should be a major goal of any transplantation indication. There are few data on long-term outcome of patients with polycystic liver disease after liver transplantation, and there is no study addressing the quality of life of these patients in detail.

Therefore, the aim of the present study was to review the outcome of 36 patients with polycystic liver disease who underwent orthotopic liver transplantation or combined liver-kidney transplantation at Hannover Medical School between 1990 and 2003. In particular, the quality of life after transplantation was investigated by evaluation of 2 questionnaires addressing items of general physical and mental health and changes in private life.

PATIENTS AND METHODS

Patients

Thirty-six patients (32 women/4 men) with a mean age of 48 ± 9 years (range, 23 to 65 years) underwent liver transplantation between April 1990 and March 2003. Patients' characteristics are shown in Tables 1 and 2. Thirty-three patients received a cadaveric full-size liver, 2 patients received a cadaveric split liver (liver segments V-VIII), and 1 patient received a living donor-related split liver from her husband (right liver lobe). All patients complained of abdominal distension and severe discomfort. Other symptoms included cachexia or severe malnutrition (n = 25), recurrent cyst infections (n = 7), dyspnea (n = 8), and portal hypertension with esophageal varices bleeding (n = 2) or ascites (n = 10). All patients had a negative hepatitis serology before transplantation. Ultrasound scan to differentiate between isolated polycystic liver or combined polycystic liver and kidney disease was performed in every patient. Kidney function (creatinine clearance, serum creatinine, or glomerular filtration rate) was determined before transplantation and at the end of follow-up. Of 36 patients, 15 underwent combined liver-kidney transplantation because of progressive renal impairment (with a glomerular filtration rate below 30 mL/min) (n = 4) or complete renal insufficiency (n = 11) with a need for hemodialysis, caused by polycystic kidney disease. In 1 patient both polycystic kidneys had been removed several years before transplantation. Seven patients had an isolated polycystic liver disease, and 29 patients had combined polycystic kidney and liver disease. Of these 29 patients, 14 underwent only liver transplantation. The majority of patients (28 of 36) had undergone palliative procedures prior to liver transplantation; 6 of them had had previous surgery (cyst fenestration or partial liver resection) and 22 of them had undergone percutaneous cyst drainage with sclerotherapy.

Liver transplantation was performed in a standardized procedure. Following cross-clamping of the inferior vena cava, hepatectomy was performed and the donor liver implanted with end-to-end anastomosis of the suprahepatic and infrahepatic inferior vena cava, portal vein, and an arterial reconstruction using the Carrell patch technique. The bile duct anastomosis was done side-to-side or end-to-end depending on the lumen of the bile duct. In case of combined liver and kidney

TABLE 1. Characteristics of Patients With Polycystic Liver Disease Undergoing Liver Transplantation

Patient No.	Age at Tx (y)	Gender	Main Symptoms	Tx	Weight of Liver (kg)	Complications Requiring Surgery	Stay in Hospital (d)	Follow-up (mo), alive	Current Immunosuppressive Regimen	Deaths	GFR, End of Follow-up (mL//min)
1	23	M	Portal hypertension, recurrent massive upper gastrointestinal bleeding	Full-size liver	6.2	None	32	151	TRL	No	76
2	41	F	Ascites, cachexia, cyst infections, dyspnea	Full-size liver	9.4	None	40	10	TRL + Pred + MMF	No	61
3	42	M	Cachexia, compression of duodenum, vomiting	Full-size liver	4.7	None	31	6	CsA + Pred	No	118
4	39	F	Cachexia, impairment of food intake	Full-size liver	17.0	None	24	110	Pred + MMF	No	27
5	53	F	Recurrent cyst infections	Full-size liver	2.8	None	32	5	CsA + Pred + MMF	No	28
6	37	F	Ascites, cachexia	Full-size liver	13.0	None	76	119	TRL	No	47
7	53	F	Cachexia, impairment of food intake	Full-size liver	6.5	Bleeding	19	28	CsA + Pred + MMF	No	36
8	45	F	Cachexia, no appetite, severe pain at costal arch	Split liver	5.1	None	60	34	TRL	No	51
9	46	F	Cachexia, impairment of food intake	Full-size liver	7.9	None	47			47 days, sepsis	
10	59	M	Loss of muscles, cachexia, impairment of food intake	Full-size liver	10.9	None	29	33	CsA + Pred	No	109
11	54	F	Cachexia, impairment of food intake	Living Related	3.0	Thrombectomy of Right hepatic artery	17	32	TRL + Pred	No	18
12	58	F	Cachexia, impairment of food intake	Full-size liver	9.0	None	42	67	CsA	No	29
13	57	F	Portal hypertension	Full-size liver	8.2	None	24	5	Pred + MMF	No	46
14	42	F	Dyspnea, impairment of food intake, partial thrombosis of the infrahepatic vena cava	Full-size liver	6.9	None	18	57	TRL + Pred	No	86
15	36	F	Cachexia, dyspnea	Full-size liver	2.9	None	13	29	CsA + Pred	No	99
16	41	F	Cachexia, impairment of food intake	Full-size liver	5.1	None	25	139	CsA + Aza	No	Hemodialysis
17	41	F	Cachexia, sitting was impossible, impairment of food intake	Full-size liver	10.6	None	16	36	CsA + Pred	No	82
18	48	F	Cachexia, impairment of food intake, vomiting	Full-size liver	8.5	Stomach ulcer perforation	55	103	TRL	No	21
19	65	M	No appetite, abdominal pain, cachexia	Full-size liver	10.0	None	20	28	CsA + Pred + MMF	No	28
20	47	F	Recurrent cyst infections	Full-size liver	4.0	Initial graft nonfunction, re-LTx	61			61 days, re-LTx, pneumonia, myocardial infarction	
21	41	F	Cachexia, only small portion of food intake possible, vomiting	Full-size liver	8.7	None	45			45 days, sepsis	

Abbreviations: Tx, transplantation; GFR, glomerular filtration rate; F, female; TRL, tacrolimus; Pred, prednisolone; MMF, mycophenolate mofetil; M, male; CsA, cyclosporine; Aza, azathioprine.

transplantation, the kidney was transplanted subsequent to the liver transplantation. The donor kidney was placed in standard into the right or left iliac groove using an abdominal approach. In patients with very large polycystic kidneys, along with clinical problems such as bleeding into the cysts or cyst infections, 1 or both kidneys were removed before implantation.

Postoperative maintenance immunosuppression consisted of various combinations of an induction agent (anti-thymocyte globulin Fresenius until 1994, basiliximab since 1999), calcineurin inhibitor (cyclosporine or tacrolimus) and proliferation inhibitor (azathioprine or mycophenolate mofetil).

Assessment of Quality of Life

All patients were followed up by regular visits in the outpatient clinic of our transplant center. To assess the quality of life after liver transplantation, 2 different questionnaires were mailed to all patients. Questionnaires were

TABLE 2. Characteristics of Patients With Polycystic Liver and Kidney Disease Undergoing Combined Liver-Kidney Transplantation

No.	Age at Tx (y)	Gender	Main Symptoms	Kidney Function pre-Tx: GFR (mL/min)	Tx	Weight of Liver (kg)	Complications Requiring Surgery	Stay in Hospital (d)	Follow-up (mo), Alive	Current Immunosuppressive Regimen	Deaths	GFR; end of follow-up (mL/min)
22	37	F	Bleeding of esophageal varices, cachexia	HD	Full-size liver	6.1	Bleeding	60	34	TRL + Pred	No	27
23	46	F	Massive ascites, cachexia	HD	Full-size liver	5.3	None	35	143	CsA + Pred	No	54
24	43	F	Cachexia, recurrent pleural effusion, ascites	HD	Full-size liver	6.4	Lung failure caused by interstitial fibrosis requiring single lung Tx	133	134	CsA + Pred + Aza	No	51
25	51	F	Ascites, dyspnea, cachexia	HD	Full-size liver	17.2	Biliary leakage	77	101	TRL	No	102
26	52	F	Recurrent cyst infections and cyst bleedings	HD	Full-size liver	8.3	None	28	47	CsA + Pred	No	68
27	58	F	Ascites, cachexia, impairment of food intake	HD	Full-size liver	4.5	Leakage of the ureter-bladder anastomosis	81	129	CsA + Pred	No	56
28	53	F	Recurrent cyst infections, portal hypertension	26	Re-LTx + NTx after 3 years	5.2	Revision of the anastomosis of hepatic artery	49	66	TRL + Pred	No	76
29	47	F	Cachexia, dyspnea, impairment of food intake	28	Split liver	10.0	Biliary leakage	44	32	TRL + Pred	No	50
30	60	F	Ascites, cachexia, dyspnea, cyst infections	HD	Full-size liver	6.7	Biliary leakage	121	23	CsA + Pred	No	45
31	49	F	Vomiting, impairment of food intake, loss of muscle	30	Full-size liver	4.7	Bleeding	59	33	CsA + Pred	No	61
32	56	F	Ascites, recurrent cyst infections	HD	Full-size liver	12.0	None	30	44	CsA + Pred	No	26
33	54	F	Ascites, cachexia, compression of the vena cava	HD	Full-size liver	20.0	None	108	103	CsA	No	57
34	47	F	Vomiting, impairment of food intake	24	Full-size liver	6.0	Initial graft nonfunction, re-LTx at day 1	32	32	TRL + Pred	No	HD
35	60	F	Cachexia, vomiting, impairment of food intake	HD	Full-size liver	8.7	Perforation of the sigmoid colon with peritonitis	45			45 days, peritonitis with MOF	
36	61	F	Loss of muscle, impairment of food intake, ascites, recurrent pleural effusion	HD	Full-size liver	10.2	None	29			29 days, pneumonia with MOF	

Abbreviations: Tx, transplantation; GFR, glomerular filtration rate; F, female; HD, hemodialysis; TRL, tacrolimus; Pred, Prednisolone; CsA, cyclosporine; Aza, azathioprine; LTx, liver transplantation; NTx, kidney transplantation; MOF, multiorgan failure.

returned anonymously. One questionnaire was the Medical Outcomes Study short form 36 (SF-36),[18-20] a widely used and validated generic health-related quality-of-life questionnaire.

The SF-36 consists of 36 items divided into 8 scales that can be aggregated into 2 summary scores: a mental component summary and a physical component summary. The eight scales are (1) physical functional ability, (2) role (behavior) due to physical impairment, (3) bodily pain, (4) general health, (5) vitality, (6) social functioning, (7) role (behavior) due to emotional impairment, and (8) mental health. Scores for these 8 SF-36 scales range between 0 and 100, whereas the summary scores for the physical component range between 8 and 73, and those for the mental component range between 10 and 74.[18,21] SF-36 scores are available for the German general population and for patients with a variety of chronic conditions.[18,20] We compared the SF-36 scores of transplant recipients with polycystic liver and/or kidney disease with those of the age-matched German general population.

The second questionnaire was self-designed and contained questions about quality of life before and after transplantation, marital status, and employment. The anonymously answered questions included range of age (30-39 years, 40-49 years, 50-59 years, 60-69 years, older than 70 years), gender, liver or combined liver-kidney transplantation, the actual state of health, and different symptoms, as well as well-being in comparison before and after transplantation, the family state, and employment pretransplantation and posttransplantation. We also asked the patients if they would opt again for transplantation and if they or their family members would donate organs in case of brain death. Finally, the habit of participating in sports activities or the interest in details of the donor was included.

Statistical Analyses

Data were expressed as mean ± SD or median and range. The statistical significance between groups was assessed by Mann-Whitney rank sum test (2-tailed) (SPSS for Windows 6.1.3; SPSS Inc., Chicago, IL). I values of <0.05 were considered statistically significant. The overall survival was estimated using the Kaplan-Meier method.

RESULTS

Perioperative Transplantation Characteristics

The mean weight of the excised livers amounted to 8.1 ± 4.0 kg and ranged from 2.9 kg to 20.0 kg (Tables 1 and 2). The mean duration of hospitalization after transplantation of all patients was 46 ± 29 days (13-133 days). After combined liver-kidney transplantation, the mean duration of hospitalization was significantly longer (62 ± 35 [28-133] days; $P = 0.005$) in comparison to liver transplantation alone (35 ± 17 [13-76] days) (Tables 1 and 2).

Two retransplantations were performed within the first days. Two patients had an initial nonfunction of the primary graft within two days. In addition, 11 relaparotomies were required after transplantation for intra-abdominal bleeding (n = 3), biliary leakage (n = 3), thrombectomy of the right hepatic artery (n =1, living-related split transplantation), leakage of the ureterocystoneostomy (n = 1), gastric ulcer perforation (n = 1), and sigmoid colon perforation (n = 1).

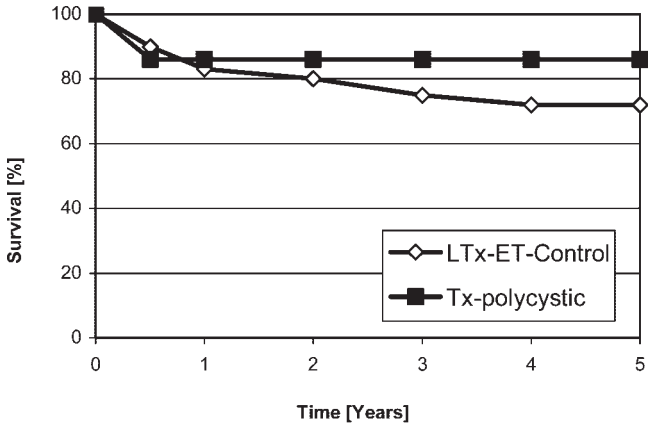

Figure 1. Comparison of survival rates of liver transplant recipients with polycystic liver disease with liver transplant patients who were transplanted due to alcoholic cirrhosis documented by the European Liver Transplant Registry. Survival rates are shown as Kaplan-Meier plots. White triangles represent total survival rates post–liver transplantation (etiology = alcoholic cirrhosis), taken from the European transplant registry. Black squares represent survival rates of patients with polycystic liver or liver-kidney disease post–liver transplantation or combined liver-kidney transplantation.

Complications and Long-term Outcome After Transplantation

The short-term mortality after liver alone or combined liver-kidney transplantation in patients with polycystic liver or liver-kidney disease was 5 out of 36 patients. Four patients died because of sepsis after 29, 45, 45, and 47 days, respectively. Another patient had an initial nonfunction of the liver graft and was retransplanted after 1 day. He died from myocardial infarction and pneumonia 61 days after initial transplantation. So far, there was no additional death after the first 2-month period in this patient group, resulting in a mean follow-up time of 62 ± 48 months (range, 1 to 157 months). The 1- and 5-year patient survival rates amounted to 86%. The survival rates of this study were compared with the survival rates of patients who received liver transplants due to alcoholic cirrhosis as published by the European Liver Transplant Registry (http://www.eltr.org). The 1- and 5-year survival rates of the reported alcoholic cirrhosis were 83% and 72%, respectively (Fig. 1). Acute rejection of the kidney or the liver occurred in 26% and 15%, respectively.

The long-term follow-up in our outpatient clinic confirmed normal liver graft function in all patients and an unimpaired kidney function in 10 of 13 combined transplanted patients. Three weeks after combined

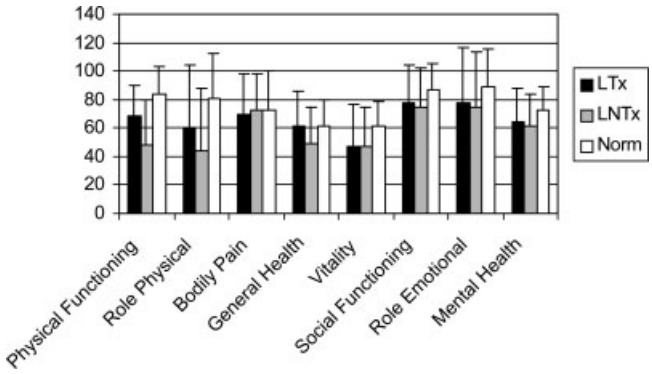

Figure 2. Quality of life (SF-36 questionnaire) for patients with polycystic liver disease who underwent liver (black bars) or combined liver-kidney (gray bars) transplantation in comparison with an age-matched German general population (white bars).

liver-kidney transplantation in 1 patient, pulmonary endangiitis obliterans with interstitial fibrosis was diagnosed by an open lung biopsy. Due to the advanced stage of this disease, the patient underwent a single lung transplantation and is now doing fine more than 11 years after the operation. One patient needed a revision of the anastomosis of the hepatic artery. This patient was successfully retransplanted 3 years after the first transplantation.

Questionnaire SF-36

Of 36 patients, 31 are still alive, of which 23 (74%) answered the questionnaires. In comparison to the age-matched German general population, the transplant recipients had a similar quality of life with regard to items such as "bodily pain," "general health," "social functioning," "role emotional," "vitality, and mental health." The items "physical function" (general population 84 vs. transplant recipients 60, respectively; $P > 0.05$) and the "role physical" (81 vs. 53, respectively; $P > 0.05$) tended to be better in the general population compared to the transplant recipients but did not reach statistical significance (Fig. 2). In subgroup analysis, "physical functioning" and "role physical" of the liver transplant recipients were not found to be significantly better than for combined liver-kidney-transplant recipients (68 vs. 48 and 60 vs. 44, $P > 0.05$ and $P > 0.05$, respectively).

Self-created Questionnaire

Our self-created questionnaire addressed state of health or disease-related symptoms and social activity before and after transplantation as well as the patient's general point of view on organ donation and transplantation.

The present subjective health status was considered to be "excellent" in 8.6% of patients, "very well" in 12.9%, "well" in 43.5%, "moderate" in 30.4%, and "poor" in only 4.3%. The subgroup of isolated liver transplanted patients showed a trend toward a better state of health. Asked about well-being before and after transplantation, 91% of patients felt "better" or "much better," and only 9% felt "worse" than before. Again, patients who had undergone only liver transplantation tended to judge their health status as better than combined liver-kidney transplant recipients. None of these patients felt worse than before transplantation. Of the patients who had undergone transplantation for polycystic liver or combined liver-kidney disease, 52% participate in sports regularly. In the subgroups, 67% of the liver transplant recipients participate sports regularly, while only 27% of the combined liver-kidney transplant patients pursue sports.

Figure 3 depicts the mean level of symptom distress for each of the 9 symptom items at baseline before transplantation and after liver or liver-kidney transplantation. The 6 most bothersome symptoms before transplantation were vomiting, sleeplessness, tiredness, efficiency, decreased appetite, and depression. After transplantation, all symptoms had improved significantly ($P = 0.001$ to $P = 0.027$). Physical attractiveness and interest in sex had improved significantly, too ($P = 0.007$ and $P = 0.004$, respectively). Only the power of concentration was unchanged before and after transplantation. Seventy-eight percent of the patients would opt again for transplantation, while 17% were undecided, and 1 patient would refuse transplantation in retrospect.

In addition, the patients were asked about their general attitude toward organ donation. If possible, 75% of the liver transplant recipients would donate an organ, while 25% were undecided. Of the combined liver and renal transplant patients, 91% would donate an organ and only 9% were undecided. We also asked our patients if their family members would be willing to donate organs. Half of the liver transplant recipients said "yes, most family members" would donate organs, 33% said "yes, some of them," and 17% answered "unknown." Of patients who had undergone combined liver-kidney transplantation, 46% said "yes, most family members," and 54% answered "yes, some of them."

Considering their own transplantation, 42% of the liver transplant and 46% of the combined liver-kidney-transplant recipients were interested in obtaining further information about the donor of their organs.

Regarding the social situation, before transplantation 78% (18/23) of the patients lived in a stable partnership, 13% (3/23) were divorced, 4% (1/23) were single, and 4% (1/23) were widowed. The state of family before and after transplantation changed in only 1 case (1 divorce; 4 %). Only 30% (7/23) of the patients were employed full-time, and an additional 13% (3/23) worked part-time before transplantation. Thirteen percent (3/23) worked as housewives and mothers, and 44% (10/23) had retired early. Transplantation did not change the state of profession for 70% (16/23) of the patients. After transplantation, 17% (4/23) worked full-time, 9% (2/23) worked part-time, 9% (2/23) were housewives and mothers, and 65% (15/23) were still in retirement.

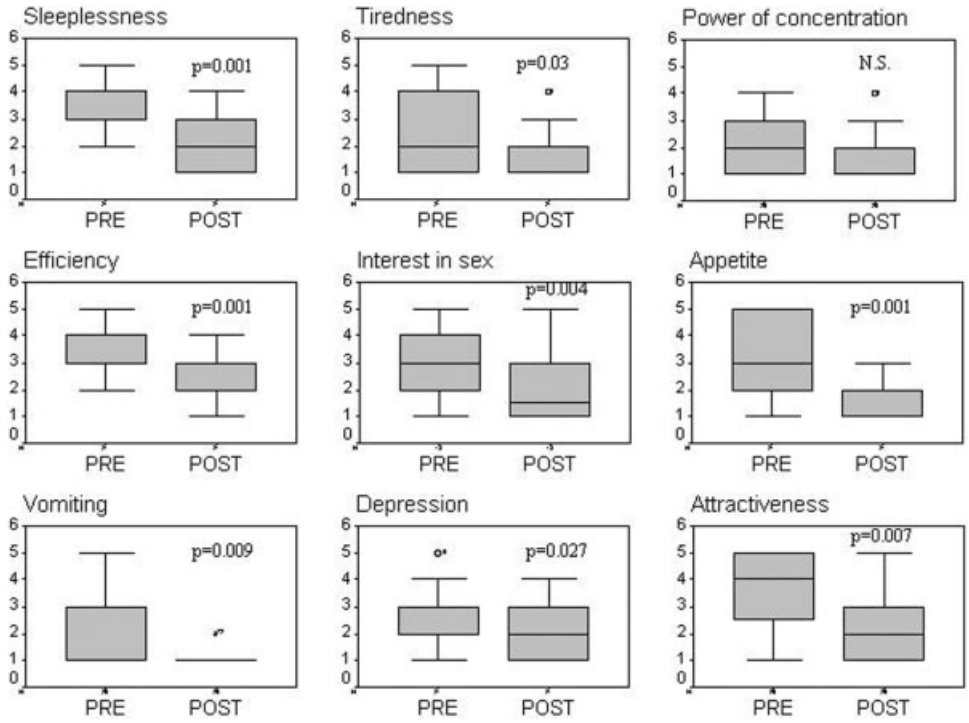

Figure 3. Parameters of quality of life before and after transplantation are shown as box plots. Each parameter is classified in 5 categories of impairment: 1 = no impairment, 2 = little impairment, 3 = moderate impairment, 4 = strong impairment, and 5 = extreme impairment. *P* = level of statistical significance. PRE, pretransplantation; POST, posttransplantation; N.S., not significant.

DISCUSSION

Polycystic liver disease with or without associated kidney disease can be an indication for liver or combined liver-kidney transplantation when cachexia, recurrent cyst infections, or other severe complications are present. The first report on liver transplantation in a patient with polycystic liver-kidney disease was by Kwok and Lewin in 1988.[22] Due to massive organomegaly, combined liver-kidney transplantation was performed, but the patient died intraoperatively because of intractable bleeding. Two years later Starzl et al. reported 4 cases of liver or combined liver-kidney transplantation in patients with polycystic disease. One patient died 5 months after transplantation, but the others survived.[23] Until now, 12 transplant centers have presented data on their series of patients transplanted with polycystic liver or combined polycystic liver-kidney disease (Table 3). The number of patients ranged between 1 and 17 and the survival rates varied between 0% and 100% with an overall survival rate of 81%. Most (81%) of the patients who died did not survive the first 2 months after transplantation, demonstrating a considerable risk of early complications but an excellent long-term outcome. Infections were the main cause of death (63%), while 18.5% of the patients died because of intraoperative bleeding complications and 18.5 % died from other causes. In our present analysis we confirmed the excellent survival rate (86%). Five patients died within the first 2 months due to infections (4 patients) and myocardial infarction with pneumonia (1 patient). Among these patients, 1 had been retransplanted due to initial graft nonfunction. Three of these 5 patients were younger than 50 years old and suffered from combined polycystic liver and kidney disease but underwent only liver transplantation. These 3 patients died on sepsis. The increased risk of sepsis in these patients might have been due to bacterial reservoirs in the remaining polycystic kidneys. Another reason for fatal sepsis might have been the very poor nutritional state of these patients.

All of our patients were on the Eurotransplant waiting list. In patients with combined polycystic liver and kidney disease with a glomerular filtration rate below 30 mL/minute, combined liver-kidney transplantation was performed, considering that after transplantation patients often get nephrotoxic immunosuppressive agents like calcineurin inhibitors, which often worsen kidney function. Depending on the blood group, patients waited between 1 and 2 years before they underwent organ transplantation. One woman who in very poor condition received a living-donor-related split liver from her husband (right liver lobe). Patients with polycystic liver disease have low model for end-stage liver disease scores. But in the Eurotransplant area the level of priority can be upgraded after a waiting time of 12 months.

Five patients died within the first 2 months due to infections (4 patients) and myocardial infarction and pneumonia (1 patient). One of these patients had been retransplanted due to initial graft nonfunction. The

TABLE 3. Review of Published Liver Transplantations in Patients With Polycystic Liver Disease in Addition to Our Data

Authors	No. of Patients	Gender Ratio (F/M)	LTx Only (%)	Combined LTx + NTx (%)	Cause of Death	Survival (%)
Kwok and Lewin, 1988[22]	1	1/0	0	100	Intraoperative (bleeding)	0
Starzl et al., 1990[23]	4	4/0	50	50	Fulminant hepatitis B 5 mo post-Tx	75
McPeake and Portmann, 1995[24]	8	8/0	62.5	37.5	Intraoperative; sepsis 1 mo post-Tx; renal failure 2 mo post-Tx	62.5
Washburn et al., 1996[25]	5	4/1	80	20	Intraoperative bleeding	80
Klupp et al., 1996[26]	10	8/2	50	50	Perioperative multiorgan failure	90
Jeyarajah et al., 1998[27]	6	5/1	50	50	Infection 48 mo post-Tx; infection 52 mo post-Tx	66
Swenson et al., 1998[28]	9	8/1	67	33*	Infection 2 mo post-Tx	88
Pirenne et al., 2001[29]	16	16/0	94	6	Intraoperative bleeding; lung cancer	87.5
Takegoshi et al., 2003[30]	1	1/0	100	0	No death	100
Becker et al., 2003[31]	17	17/0	0	100	Infections 29 d, 45 d, and 48 d	82
Gustafsson et al., 2003[32]	7	2/5	57	43	No death	100
Cavallari et al., 2004[33]	2	Unknown	0	100	ARDS within 1 mo; MOF within 1 mo	0
Kirchner et al., 2006	36	32/4	58	42	Sepsis 29 d, 45, and 47 d; myocardial infarction and pneumonia 61 d	86

Abbreviations: F, female; M, male; LTx, liver transplantation; NTx, kidney transplantation; Tx, transplantation; ARDS, acute respiratory distress syndrome; MOF, multiorgan failure.
*One patient received a combined liver-kidney-pancreas transplant.

long-term survival rate in this series of transplanted patients with polycystic liver disease is clearly better than the rate for indication of alcoholic cirrhosis in the European Liver Transplant Registry (Fig. 1), which may be caused by the recurrence of alcohol drinking after transplantation by some of these patients. The United States Scientific Registry of Transplant Recipients (http://www.us-transplant.org) reports the outcome of patients with polycystic disease after liver transplantation between 1987 and 2003. The survival rates for 1, 3, and 5 years were 78.1%, 71.7%, and 68.7%, respectively, in patients undergoing isolated liver transplantation, and 79.5%, 75.5%, and 75.5%, respectively, in patients undergoing combined liver-kidney transplantation.[1] The conclusions of the aforementioned reports often suggest an earlier selection of the affected patients in order to reduce perioperative mortality due to severe cachexia or septic complications after recurrent cyst infections. This is in contrast to the fact that patients often have an unimpaired metabolic liver function and usually do not feel affected by life-threatening disease. In the early stages of polycystic disease, symptoms such as abdominal pain, malnutrition, or reduced physical fitness may not be convincing enough for the patient to accept the risk and complications of organ transplantation. Therefore, besides long-term survival, the changes in quality of life after organ transplantation need to be addressed in more detail. Here, we present the outcome and quality of life in a large series of 36 patients with polycystic liver disease who received a liver or combined liver-kidney transplantation.

Quality of life emerges as an increasingly important factor in public health, since people realize that general health is not defined just by absence of disease. According to the World Health Organization's definition, emotional and social components need to be considered alongside physical factors. So far, no formal analyses of quality of life using questionnaires have been reported for patients with polycystic liver disease who have undergone liver or combined liver-kidney transplantation. The most common instrument for the assessment of the quality of life is the SF-36 questionnaire,[19] addressing 8 dimensions of health, including physical, emotional, and social components.

Because of the particular situation after organ transplantation for polycystic liver disease, we added a sec-

ond self-designed questionnaire to address physical, emotional, and social changes before and after transplantation as well as the patient attitude on organ transplantation. In the present study 74% of our patients returned the questionnaires for assessment of quality of life, which is in the same range (73-81%)[24,25] as that of transplant patients with other disorders.

The overall quality of life of our transplant recipients was compared to that of an age-matched general population in Germany by analyzing the SF-36 questionnaire addressing impairments by various dimensions of patient health. There were no major differences in the categories of social functioning, role due to emotional abilities, or mental health, demonstrating a successful integration into family and society structures. More interestingly, there was no difference in impairments by general health and bodily pain that would be expected in immunosuppressed transplanted recipients. The SF-36 dimensions "physical functioning," "role due to physical abilities," and "vitality" tended to be reduced in the transplant recipients in comparison to the age-matched population, but it did not reach statistical significance. Considering the severe impairments such as malnutrition up to cachexia and the long-term course of the disease before transplantation, the slightly reduced physical functioning, physical abilities, and vitality can be easily explained and a more severe reduction should be expected. In the subgroup of isolated liver transplanted patients these changes were less severe, corresponding with patients' increased physical activities.

Our self-created questionnaire analyzed physical, emotional, and social changes before and after transplantation in more detail. According to the high score in the SF-36 questionnaire, the vast majority of patients felt excellent, very well, or well after transplantation (Fig. 2). In particular, when asked for the actual state of health, none of the isolated liver transplanted patients felt poor or worse than before transplantation. In other words, all liver transplant patients and 91% of combined liver-kidney transplant patients felt better or even much better than before transplantation. A detailed analysis of major symptoms clearly demonstrated the improvement of all that individual qualities (Fig. 3). This is a striking argument for early transplantation of patients with polycystic liver (and kidney) disease who can be suspected to develop major complications increasing the perioperative risks. The slightly worse quality of life of combined liver-kidney transplanted patients may be explained by the fact that 2 organs systems are affected. In addition, changes in patients' habits due to the need for hemodialysis for many years are likely to account for reduced physical fitness and physical activity. Interestingly, only 27% of the combined liver-kidney transplant recipients but 67% of the liver transplant recipients regularly engage in sports. This could be due to an altered habit of hemodialysis patients that has not changed since transplantation.

We were also interested in the rate of employment of our patients before and after liver or combined liver-kidney transplantation. In our group, most patients were women, so we compared our patients with female series of other studies. Before transplantation, 30% of our patients worked full-time, 13% worked part-time, 13% were housewives and mothers, and 44% had retired early. The rate of employment before transplantation is in line with that of another study, which reported a full-time employment of 43% before transplantation.[26] After transplantation, the employment rate in our group markedly decreased to 17% full-time and 9% part-time working patients, and the rate of early retirements increased to 65%. In comparison to other studies with a full-time employment rate of 33%,[27] the rate of employment in our patients is much lower. The reason might be a well-developed social welfare system with easy access to early retirements.

In conclusion, orthotopic liver transplantation or combined liver-kidney transplantation is a suitable therapeutic approach for polycystic diseases. Since quality of life is improved dramatically after transplantation in advanced-diseased patients, emotional and social components of general health also need to be considered. The increased perioperative risks in patients with severe cachexia or cyst infections suggest the need for earlier transplantation, which is underscored by excellent long-term outcome and increased quality of life.

REFERENCES

1. Everson GT, Taylor MR, Doctor RB. Polycystic disease of the liver. Hepatology 2004;40:774-782.
2. Tahvanainen P, Tahvanainen E, Reijonen H, Halme L, Kääriäinen H, Höckerstedt K. Polycystic liver disease is genetically heterogeneous: clinical and linkage studies in eight Finnish families. J Hepatol 2003;38:39-43.
3. Arnold HL, Harrison SA. New advances in evaluation and management of patients with polycystic liver disease. Am J Gastroenterol 2005;100:2569-2582.
4. Qian Q, Li A, King BF, Kamath PS, Lager DJ, Huston J 3rd, et al. Clinical profile of autosomal dominant polycystic liver disease. Hepatology 2003;37:164-171.
5. Reynolds DM, Falk CT, Li A, King BF, Kamath PS, Huston J 3rd, et al. Identification of a locus for autosomal dominant polycystic liver disease, on chromosome 19p13.2-13.1. Am J Hum Genet 2000;67:1598-1604.
6. Drenth JP, te Morsche RHM, Smink R, Bonifacino JS, Jansen JBMJ. Germline mutations in PRKCSH are associated with autosomal dominant polycystic liver disease. Nat Genet 2003;33:345-347.
7. Li A, Davila S, Furu L, Qian Q, Tian X, Kamath PS, et al. Mutations in PRKCSH cause isolated autosomal dominant polycystic liver disease. Am J Hum Genet 2003;72:691-703.
8. Davila S, Furu L, Gharavi AG, Tian X, Onoe T, Qian Q, Li A, et al. Mutations in SEC63 cause autosomal dominant polycystic liver disease. Nat Genet 2004;36:575-577.
9. Telenti A, Torres VE, Gross JB, Van Scoy RE, Brown ML, Hattery RR. Hepatic cyst infection in autosomal dominant polycystic kidney disease. Mayo Clin Proc 1990;65:933-942.
10. Gigot JF, Jadoul P, Que F, Van Beers BE, Etienne J, Horsmans Y, et al. Adult polycystic liver disease: is fenestration the most adequate operation for long-term management? Ann Surg 1997;225:286-294.

11. Konstadoulakis MM, Gomatos IP, Albanopoulos K, Alexakis N, Leandros E. Laparoscopic fenestration for the treatment of patients with severe adult polycystic liver disease. Am J Surg 2005;189:71-75.
12. van Sonnenberg E, Wroblicka JT, D'Agostino HB, Mathieson JR, Casola G, O'Laoide R, Cooperberg PL. Symptomatic hepatic cysts: percutaneous drainage and sclerosis. Radiology 1994;190:387-392.
13. Tikkakoski T, Makela JT, Leinonen S, Paivansalo M, Merikanto J, Karttunen A, et al. Treatment of symptomatic congenital hepatic cysts with single-session percutaneous drainage and ethanol sclerosis: technique and outcome. J Vasc Interv Radiol 1996;7:235-239.
14. Gigot JF, Metairie S, Etienne J, Horsmans Y, van Beers BE, Sempoux C, et al. The surgical management of congenital liver cysts. Surg Endosc 2001;15:357-363.
15. Que F, Nagorney DM, Gross JB Jr, Torres VE. Liver resection and cyst fenestration in the treatment of severe polycystic liver disease. Gastroenterology 1995;108:487-494.
16. Yang GS, Li QG, Lu JH, Yang N, Zhang HB, Zhou XP. Combined hepatic resection with fenestration for highly symptomatic polycystic liver disease: a report on seven patients. World J Gastroenterol 2004;10:2598-2526.
17. Tan YM, Ooi LL. Highly symptomatic adult polycystic liver disease: options and results of surgical management. ANZ J Surg 2004;74:653-657.
18. Ware J, Sherbourne C. The MOS 36-item short form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30:473-482.
19. Ware J, Snow K, Kosinski M, Gandek B. SF-36 Health Survey Manual and Interpretation Guide. Boston: The Health Institute, New England Medical Center; 1993.
20. Ware J, Kosinski M, Keller S. SF-36 Physical and Mental Health Summary Scales: a User's Manual. Boston: The Health Institute, New England Medical Center; 1994.
21. Younossi ZM, Boparai N, Price LL, Kiwi ML, McCormick M, Guyatt G. Health-related quality of life in chronic liver disease: the impact of type and severity of disease. Am J Gastroenterol 2001;96:2199-2205.
22. Kwok MK, Lewin KJ. Massive hepatomegaly in adult polycystic liver disease. Am J Surg Pathol 1988;12:321-324.
23. Starzl TE, Reyes J, Tzakies A, Mieles L, Todo S, Gordon R. Liver transplantation for polycystic liver disease. Arch Surg 1990;125:575-577.
24. McPeake FR, Portmann B. Hepatic malignancy, Budd-Chiari syndrome and space-occupying conditions. In: Williams R, Portmann B, Tan KC, eds. The Practice of Liver Transplantation. New York, N.Y.: Churchill Livingstone; 1995:57-71.
25. Washburn WK, Johnson LB, Lewis WD, Jenkins RL. Liver transplantation for adult polycystic liver disease. Liver Transpl Surg 1996;2:17-22.
26. Klupp J, Bechstein WO, Lobeck H, Neuhaus P. Orthotope Lebertransplantation zur Therapie der fortgeschrittenen polycystischen Lebererkrankung [German]. Chirurg 1996;67:515-521.
27. Jeyarajah D, Gonwa T, Testa G, Abbasoglu O, Goldstein R, Husberg B, et al. Liver and kidney transplantation for polycystic disease. Transplantation 1998;66:529-544.
28. Swenson K, Seu P, Kinkhabwala M, Maggard M, Martin P, Goss J, Busuttil R. Liver transplantation for adult polycystic liver disease. Hepatology 1998;28:412-415.
29. Pirenne J, Aerts R, Yoong K, Gunson B, Koshiba T, Fourneau I, et al. Liver transplantation for polycystic liver disease. Liver Transpl 2001;7:238-245.
30. Takegoshi K, Tanaka K, Nomura H, Miyagi K, Taira S, Takayanagi N. Successful living donor liver transplantation for polycystic liver in a patient with autosomal-dominant polycystic kidney disease. J Clin Gastroenterol 2001;33:229-231.
31. Becker T, Nyibata M, Lueck R, Bektas H, Demirci G, Lehner F, et al. Results of combined and sequential liver-kidney transplantation. Liver Transpl 2003;9:1067-1078.
32. Gustafsson BI, Friman S, Mjornstedt L, Olausson M, Backman L. Liver transplantation for polycystic liver disease–indications and outcome. Transplant Proc 2003;35: 813-814.
33. Cavallari G, Nardo B, Montalti R, Beltempo P, Bertelli R, Puviani L, et al. Combined liver-kidney transplantation: experience at Bologna's transplant center. Transplant Proc 2004;36:541-542.
34. Saldeen S, Friman S, Olausson M, Olsson R. Follow-up after liver transplantation for primary sclerosing cholangitis: effects on survival, quality of life, and colitis. Scand J Gastroenterol 1999;34:535-540.
35. Gross CR, Malinchoc M, Kim WR, Evans RW, Wiesner RH, Petz JL, et al. Quality of life before and after liver transplantation for cholestatic liver disease. Hepatology 1999; 29:356-364.
36. Walter M, Moyzes D, Rose M, Neuhaus R, Danzer G, Klapp BF. Psychosomatic interrelations following liver transplantation. Clin Transplant 2001;16:301-305.
37. Blanch J, Sureda B, Flaviá M, Marcos V, de Pablo J, De Lazzari E, et al. Psychosocial adjustment to orthotopic liver transplantation in 266 recipients. Liver Transpl 2004;10:228-234.