Polycystic Liver Disease

A Critical Appraisal of Hepatic Resection, Cyst Fenestration, and Liver Transplantation

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Objective: To identify operative morbidity, mortality, and long-term outcome after operative treatment for symptomatic polycystic liver disease (PLD) and develop a treatment algorithm for patients with PLD.

Background: PLD represents a challenging clinical problem that can result in massive hepatomegaly and various complications, leading to significant decline in health status and quality of life. The optimal surgical treatment for this disease is still evolving.

Methods: All patients who underwent hepatic resection, cyst fenestration, or liver transplantation for PLD from 1985 to 2006 were identified retrospectively. Long-term outcomes were evaluated by patient survey. Mean follow-up was 8 ± 0.5 years.

Results: Of 141 patients (122 women; age: 51 ± 1 years) with PLD, 117 had concomitant polycystic kidney disease. All patients suffered from symptomatic hepatomegaly with 85% being functionally impaired (Eastern Cooperative Oncology Group Performance Status: 1–3). Despite significant inferior vena cava or hepatic venous compression in 65%, hepatic function was commonly preserved. A total of 124 patients underwent partial hepatectomy with cyst fenestration, 10 underwent cyst fenestration alone, and 7 underwent liver transplantation for primary treatment of PLD. Overall operative morbidity and mortality was 58% and 4%, respectively, with major complications (Clavien grade: III–V) in 30%. Five- and 10-year survival was 90% and 78%, respectively. Eastern Cooperative Oncology Group Performance Status performance status normalized or improved in 75% of patients and 73% returned to work full-time. At follow-up, health survey scores were similar to the general population despite subsequent recurrence of symptoms in 73% of patients.

Conclusion: Selective patients with massive hepatomegaly from PLD benefit from operative intervention. The type of operation performed is mainly dependent on the distribution of the cysts, coincident sectoral vascular patency and parenchymal preservation, and hepatic reserve. Hepatic resection can be performed with acceptable morbidity and mortality, prompt and durable relief of symptoms, and maintenance of liver function. Cyst fenestration and liver transplantation, though effective in selected patients, are less broadly applicable.

(*Ann Surg* 2009;250: 112–118)

Polycystic liver disease (PLD) is a unique clinical problem frequently associated with autosomal dominant polycystic kidney disease (ADPKD).[1,2] Most patients with PLD do not require intervention for their liver cysts. However, in some patients with PLD, the development of massive hepatomegaly frequently causes pain or compression of the adjacent gastrointestinal tract, vasculature, and diaphragm, affecting the patients' performance status and quality of life.[1,2] Importantly, hepatic function remains remarkably preserved regardless of massive hepatomegaly. Medical treatment of symptoms has had limited effectiveness, because neither prevention of cyst volume expansion, nor reduction of extant cyst volume by medication has been established. Consequently, operative treatment aimed at hepatic volume reduction has been undertaken as a treatment option. Operative approaches have varied depending upon the size, number, and extent of hepatic cysts. Regardless of operative approach, the long-term outcome after operative treatment for PLD is poorly understood. Moreover, no standardized criteria for selection of patients for operation exist.

Previously, we have reported short-term outcomes for hepatic resection and cyst fenestration in symptomatic patients with hepatomegaly from PLD.[3,4] Since, we have continued evaluating our operative approach as well as alternatives with a broader clinical spectrum of patients with symptomatic hepatomegaly from PLD. This study reports our single-center experience with patients who underwent partial hepatectomy with remnant cyst fenestration, cyst fenestration alone, or liver transplantation for treatment of clinically significant hepatomegaly from PLD. Disease-specific factors relevant for operative management and long-term outcome were identified to help formulate a rational treatment algorithm for patients with this unique disease.

METHODS

All patients with PLD who underwent partial hepatectomy with cyst fenestration of the liver remnant, cyst fenestration alone, or liver transplantation at Mayo Clinic Rochester from 1985 to 2006 were identified. PLD was defined as at least 20 simple cysts greater than 1 cm in diameter within the liver in the absence of infectious, parasitic, or traumatic causes. Clinical records were reviewed retrospectively. Patients with PLD who underwent operations of the liver for reasons other than control of symptoms or complications from liver cysts were specifically excluded. Patients with PLD and ADPKD who underwent cyst fenestration of renal cysts only were also excluded. Standard terminology was used for the type of hepatic resection performed; though, exact classification of hepatic resection was limited due to distortion of hepatic anatomy in most patients. Perioperative morbidity and mortality included complications or death within the hospital stay or within 30 days of operation. Perioperative morbidity was categorized according to Clavien and coworkers classification.[5] Patients' vital status was obtained through outpatient and hospital records, documents of communication with health care providers, and retrieval of death certificates. Age-based life expectancy was calculated utilizing National Center for Health Statistics data.[6] Long-term outcomes were evaluated by patient survey. The survey audited patients' symptom status, Eastern Cooperative Oncology Group Performance Status (ECOG-PS),[7] and

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ISSN: 0003-4932/09/25001-0112

DOI: 10.1097/SLA.0b013e3181ad83dc

health status utilizing the norm based SF-36 (version 2) questionnaire (QualityMetric Inc, Lincoln, RI). The study was approved by the Mayo Clinic Rochester Institutional Review Board and research authorization was provided by all patients.

Radiographic volumetric measurements of the liver were performed on axial computed tomography or magnetic resonance imaging studies with up to 7 mm slice thickness utilizing QReads version 4.1.8 clinical image software (Mayo Clinic, Rochester, MN). For hepatic volumetric measurements, the combined volume of hepatic parenchyma and intrahepatic cysts, excluding gallbladder, inferior vena cava, and extrahepatic portal structures, was evaluated on preoperative, immediate postoperative (within 3 months of operation), and follow-up imaging studies when performed at Mayo Clinic Rochester and available in electronic format. Similar volumetric measurements were obtained from both kidneys including the renal pelvis, but excluding extrarenal hilar structures. An axial cross-section area of the inferior vena cava (IVC) was measured at the point of maximal compression within the retro-hepatic segment (*a*) and within the supra-hepatic segment above the diaphragm (*b*) using QReads software. A degree of IVC compression was calculated according to the following formula: $= [1 - (a/b)] \times 100$. Body surface area was calculated according to Mosteller formula.[8]

Descriptive statistics were reported as percentage or mean ± SEM unless specified otherwise. Two-sample *t* test, χ^2 test (or Fisher exact test), one-way ANOVA, and log-rank test were used for univariate analyses. Survival was calculated using Kaplan-Meier estimates. $P < 0.05$ were considered to be statistically significant. All statistical analyses were performed utilizing SAS version 9.0 computer software (SAS Institute Inc, Cary, NC).

RESULTS

Patient Characteristics and Preoperative Findings

During the study period, 141 patients with PLD underwent partial hepatic resection with remnant cyst fenestration, cyst fenestration alone, or orthotopic liver transplantation for symptoms or complications related to PLD at Mayo Clinic Rochester. The study group included 122 women and 19 men with a mean age of 51 ± 1 years (range: 34–80 years). All patients were clinically symptomatic. The most common symptoms at presentation were gastrointestinal symptoms of early satiety, nausea, dyspepsia, or heartburn (73%), abdominal or back pain (65%), abdominal fullness or discomfort (60%), fatigue (45%), orthopnea or shortness of breath (41%), malnutrition or muscle wasting (22%), and leg edema (17%); whereas biliary symptoms of jaundice (3%) or cholangitis (1%) were rare. Ascites was recognized clinically in 13% of patients. The mean duration of symptoms was 7 ± 1 years. Performance status was affected significantly by the disease in 85% of patients (ECOG-PS: 1–3; Table 1).

Of 141 patients with PLD, 117 (83%) had concomitant ADPKD. Nonhepatorenal cysts were found in the ovaries in 7 patients and pancreas in 6 patients. A history of intracranial aneurysms and valvular heart disease was found in 21 and 14 patients, respectively. ADPKD resulted in chronic renal insufficiency (defined as need for renal transplantation, need for hemodialysis, or serum creatinine ≥1.3 mg/dL for females/≥1.5 mg/dL for males) in 74 patients prior to liver operation. Of the 74 patients with chronic renal insufficiency, 47 were treated medically, 14 required hemodialysis, and 13 had undergone renal transplantation prior to liver operation.

TABLE 1. ECOG Performance Status Before and After Operative Treatment for PLD ($P < 0.0001$)

	Immediate Preoperative (n = 141)	At Follow-Up (n = 78)
ECOG-PS 0	15%	68%
ECOG-PS 1	57%	22%
ECOG-PS 2	24%	10%
ECOG-PS 3	4%	0%
ECOG-PS 4	0%	0%

Hepatic function commonly was preserved (mean: total bilirubin, 0.9 ± 0.2 mg/dL; albumin, 3.9 ± 0.1 g/dL; prothrombin time, 11.2 ± 0.1 seconds; aspartate aminotransferase, 31 ± 3 U/L; alanine aminotransferase, 27 ± 3 U/L; alkaline phosphatase, 237 ± 15 U/L; and platelet count, 228 ± 6 × 10^9/L). Three patients had hepatic venous compression associated with an increase in bilirubin >2 mg/dL and aspartate aminotransferase >60 U/L presumably due to incomplete chronic hepatic venous outflow obstruction, 2 patients had chronic hepatitis B infection, and 1 patient had chronic hepatitis B and C infection. None of the 141 patients had evidence of liver cirrhosis. Prior to admission to our institution, 13 patients (9%) had undergone hepatic operations without symptom relief including hepatic cyst fenestration in 11, left lateral sectorectomy in 1, and cystjejunostomy in 1. Additionally, 22 patients (16%) had prior percutaneous hepatic cyst aspiration including 8 patients with concomitant cyst ethanol ablation. Twelve patients (9%) had had a prior nephrectomy.

Prior to operation, all patients received cross-sectional imaging by abdominal computed tomography and/or magnetic resonance imaging. Radiographic imaging revealed ascites in 24%, intracystic hemorrhage in 16%, and biliary compression in 2%. Ninety-one patients (65%) had evidence of significant peri-hepatic major venous compression: IVC compression in 63%, hepatic venous compression in 18%, and portal venous compression in 2%. Retrievable preoperative cross-sectional imaging studies were available for volumetric analysis in 51 patients. Ninety percent of these had radiographic evidence of IVC compression greater than 60%, including 16% who had an IVC compression greater than 90%. The average hepatic volume was 6695 ± 442 cm^3 (range: 1661–15518 cm^3; n = 51) with a hepatic volume per body surface area of 3670 ± 240 cm^3/body surface area (range: 933–9351 cm^3/body surface area; n = 51). The combined hepato-renal volume was 7902 ± 579 cm^3 (range: 1889–19,827 cm^3; n = 46). There was a correlation between increased combined hepato-renal volume and decreasing ECOG performance status of the patient ($P = 0.037$), but not gastric symptoms, abdominal pain, or abdominal fullness ($P > 0.05$).

PLD-Specific Operative Findings

The primary indication for operation were symptoms affecting quality of life or performance status in 131 patients, severe hepatic venous outflow obstruction with refractory ascites in 6 patients, infected hepatic cysts refractory to medical and percutaneous drainage in 3 patients, and uncontrolled intracystic hemorrhage after percutaneous intervention elsewhere in 1 patient. Anesthetic risk was rated as ASA score I in 1 patient, ASA score II in 41 patients, ASA score III in 86 patients, and ASA score IV in 13 patients. The operative treatment included partial hepatectomy with cyst fenestration of the hepatic remnant in 124 patients, cyst fenestration in 10 patients, and orthotopic liver transplantation in 7 patients.

Partial Hepatectomy With Remnant Cyst Fenestration (n = 124)

Hepatic resection included lobectomy in 67 patients, extended lobectomy in 30 patients, and sectorectomies, or multiple segmentectomies in 27 patients. The average number of liver segments resected per patient was 4 ± 0.1. Additionally, 38% of the 124

patients underwent nonanatomic subsegmentectomies. The average reduction in hepatic volume was 57 ± 3% (range: 17%–87%), based upon 23 patients with available preoperative and immediate postoperative cross-sectional imaging studies. Among these 23 patients, although compression of the IVC improved in 78% postoperatively, 61% had residual IVC compression of greater than 60%. Of the 124 patients, concurrent cholecystectomy was performed in all but 6 patients early in the series. Renal cyst fenestration was performed in 9 patients and nephrectomy in 2 patients. Four patients had evidence of extrahepatic varices. Thirty-three percent of patients required synchronous closure of an umbilical or ventral hernia. Closed suction peritoneal drainage was used in all but 2 patients. The mean wet weight of the resected specimen was 2.3 ± 0.1 kg (range: 0.1–8.7 kg) (though actual weight of the hepatic resection was underestimated because of intraoperative cyst drainage). The mean duration of operation was 324 ± 10 minutes. Average estimated blood loss was 1900 ± 200 mL (median: 1000 mL, range: 200–11300 mL). Inflow vascular occlusion was not used routinely during resection. Packed red blood cell transfusions were given during operation or hospitalization in 80% of patients. The average number of packed red blood cell units used was 6 ± 1 units (median: 3 units) per patient with a significant decrease in requirement throughout the study period (1985–1995: 9 ± 2 units per patient; 1996–2006: 3 ± 1 units per patient; $P = 0.002$).

The overall perioperative morbidity and mortality after hepatic resection with cyst fenestration was 63% and 3%, respectively. Major complications (Clavien grade: III to V) occurred in 31% (Table 2). Patients with preoperative chronic renal insufficiency had a greater rate of perioperative complications (71%) compared with patients with normal renal function (53%, $P = 0.041$). Ascites and biliary leaks were the most frequent postoperative complications. Persistent postoperative ascites, defined as >500 mL of ascites per day through operatively placed drains after postoperative day 10, was observed in 44 patients (35%), including 19 patients (15%) who had drainage >1000 mL/d after postoperative day (POD) 10. Fifty-nine of the 124 patients (48%) were discharged from the hospital with peritoneal drainage catheters. On average, catheters were removed 21 ± 2 days after operation. Although chronic presence of ascites and malnutrition prior to operation were significant risk factors for the development of complications related to ascites after the operation, preoperative hepatic venous or IVC compression, hypoalbuminemia, and chronic renal failure were not significant (preoperative ascites: 63% vs. 38%, $P = 0.021$; malnutrition: 67% vs. 38%, $P = 0.011$; hepatic vein (HV)/IVC compression: 50% vs. 39%, $P = 0.218$; preoperative albumin <3.5 g/dL: 40% vs. 45%, $P = 0.711$; preoperative creatinine >1.4 mg/dL: 51% vs. 40%, $P = 0.226$). The large fluid shifts occurring during the postoperative recovery period were tolerated well by the majority of patients with ADPKD. Yet, 9 of the 107 patients with ADPKD (8%) had a 50% increase in serum creatinine over baseline after hepatic resection related to hypotension (6 patients) or sepsis (3 patients). This elevation in serum creatinine persisted at hospital discharge in 3% of 107 patients. Reoperation was necessary in 9% of patients during the in-hospital recover period (1985–1995: 12%; 1996–2006: 7%; $P = 0.344$). The reoperative procedures performed during hospitalization included control of hemorrhage in 7 patients, liver transplantation for liver failure in 2 patients, gastrojejunostomy in 1 patient, and abdominal washout in 1 patient. Perioperative mortality occurred in 4 patients due to abdominal sepsis, intraoperative cardiac arrhythmia during liver transplantation, cerebral infarction, or intracranial hemorrhage. Overall, 40% required a postoperative stay in the intensive care unit for an average of 2 ± 0.4 days. The average duration of hospital stay was 13 ± 1 days (median: 10 days).

TABLE 2. Perioperative Complications After Operative Treatment for PLD (n = 141)

	Hepatic Resection (n = 124)	Cyst Fenestration (n = 10)	Liver Transplantation (n = 7)
In-hospital complication rate*	63%	0%	57%
Persistent drainage of ascites	35%	0%	14%
Progression of ascites requiring paracentesis	22%	0%	14%
Bile leak	15%	0%	14%
Pleural effusion requiring thoracocentesis	11%	0%	0%
Intra-abdominal abscess	10%	0%	14%
Postoperative hemorrhage	9%	0%	0%
Main bile duct injury within hepatic remnant	5%	0%	—
Liver failure	3%	0%	0%
Miscellaneous others	21%	0%	29%
Clavien grading			
Grade I	27%	0%	0%
Grade II	6%	0%	0%
Grade III	21%	0%	29%
Grade IV	6%	0%	0%
Grade V, perioperative mortality	3%	0%	29%

*More than one complication per patient possible.

Cyst Fenestration (n = 10)

Cyst fenestration was performed with low operative blood loss (estimated blood loss: 300 ± 100 mL, need for perioperative blood transfusion 10%) and low morbidity (overall complication rate 0%; Table 2). Two of the 10 cyst fenestrations were performed with laparoscopic technique. On average 3 ± 1 cysts were drained during each procedure. The average reduction in liver organ volume after cyst fenestration was 9 ± 4% (range: 5%–13%) in 2 patients who had preoperative as well as immediate postoperative cross-sectional imaging studies available for volumetric analysis. Concurrent cholecystectomy was performed in 6 patients and a peritoneal drain was placed in 6 patients. The average duration of hospital stay was 5 ± 1 days.

Orthotopic Liver Transplantation (n = 7)

Seven patients underwent primary orthotopic diseased donor liver transplantation for primary treatment of symptoms from PLD including 3 patients with simultaneous renal transplantation. None had prior liver operations. All patients were significantly debilitated (ASA III: 2 patients; ASA IV: 5 patients). Three patients were operated with interposition of IVC, while piggy-back technique was used in 4 patients. Veno-venous bypass was necessary in 3 patients with interposition of IVC and 1 patient with piggy-back technique. The recipient hepatectomy was frequently associated with significant blood loss; all patients required perioperative blood transfusion (mean: 13 ± 4 units per patient). The average wet weight of the explanted recipient liver was 8.3 ± 1.2 kg (range: 3.8–11.7 kg). Two patients required in-hospital reoperation for a leak from the bile duct anastomosis or for hepatic artery thrombosis. The perioperative

morbidity was 57% with complications related to ascites in only 1 patient (Table 2). Perioperative mortality was encountered in 2 patients due to myocardial infarction or systemic aspergillosis. All patients required a postoperative stay in the intensive care unit for an average of 14 ± 7 days; with an average hospital stay of 19 ± 5 days.

Long-Term Outcome After Operative Treatment for PLD

All 135 perioperative survivors were followed clinically. Mean duration of follow-up was 8 ± 0.5 years. During follow-up, 13 patients required further interventions on average 6 ± 1 years after initial operation: salvage liver transplantation in 5 [3 patients for control of symptoms 6 ± 3 years after hepatectomy (3-year survival after salvage transplantation 33%), 2 patients for liver failure 9 ± 4 years after hepatectomy (3-year survival after salvage transplantation 100%, $P = 0.199$)], operative cyst fenestration in 3, percutaneous hepatic cyst aspiration and ethanol ablation in 3, and hepatic resection in 2. Eleven patients had refractory ascites after hepatic resection; all due to significant residual IVC/hepatic vein compression. All 11 patients underwent IVC stenting between 0.2 and 15 months after operation. The average prestent IVC pressure gradient was 12 ± 3 mm Hg (n = 10) with a hepatic vein pressure gradient of 10 ± 2 mm Hg (n = 5). Although ascites improved in 7 patients, 4 patients were refractory and required peritoneal-venous shunt placement.

Twenty-seven of the 135 perioperative survivors had died during follow-up. The cause of death in 10 patients was related to PLD and included hepatic cyst or biliary infection in 3, continuous multisystemic demise in 2, complications after late liver transplantation in 2, intestinal ischemia from PLD-related progressive abdominal compartment syndrome observed at other institutions in 2, and hepatic failure in 1. Overall 5-year and 10-year survival rate in the 135 perioperative survivors was 90% and 78%, respectively. Disease-specific 5- and 10-year survival, including only PLD-associated causes of death while censoring other causes of death, was 95% and 90%, respectively. We compared the observed survival to an expected survival in an age-matched US standard population based on data from the National Center for Health Statistics. Each patient's age-based average life expectancy was assessed. The expected age-predicted 10-year survival rate in this study group was 99% and significantly greater than the observed overall survival ($P < 0.0001$) and the disease-specific survival ($P = 0.011$, Fig. 1). The 5-year survival after partial hepatectomy with cyst fenestration, cyst fenestration alone, and liver transplantation was 92%, 90%, and 60%, respectively ($P = 0.310$).

PLD-related health status and overall health status were assessed through a questionnaire and SF-36 survey. Surveys were returned by 78 of the 108 survivors (72%) after a mean follow-up of 9 ± 0.6 years. Of the 78 responders, 73% noted some degree of recurrence or persistence of symptoms. Symptoms reoccurred initially after a mean of 4 ± 1 years. However, compared with the preoperative status, ECOG performance status had normalized or improved in 75% of patients ($P < 0.001$, Table 1); and 73% had returned to work full-time. Of the 78 patients surveyed, 75 (96%) stated that they were glad that they underwent the operation and 71 (91%) stated that they would undergo the operation again if needed. Health status assessed by SF-36 questionnaire showed that the norm-based scores were very close to the US standard population's mean score of 50 and mostly within the range of the standard deviation (1 SD: 40–60, Table 3). At the time of survey, 72% of patients after partial hepatectomy (n = 57) and 75% of patients after cyst fenestration (n = 4) felt that the size of the liver has enlarged since operation, whereas only 13% (n = 61) and 50% (n = 2) thought that the liver was as large as prior to operation, respectively. These findings are consistent with 20 patients who underwent hepatic resection and had immediate postoperative as well as follow-up imaging available; with an average follow-up of 4 ± 1 years. The average liver volume in these 20 patients was 11 ± 10% larger than the initial remnant liver volume after resection; including 10 patients (50%) whose organ volume has stayed the same or decreased.

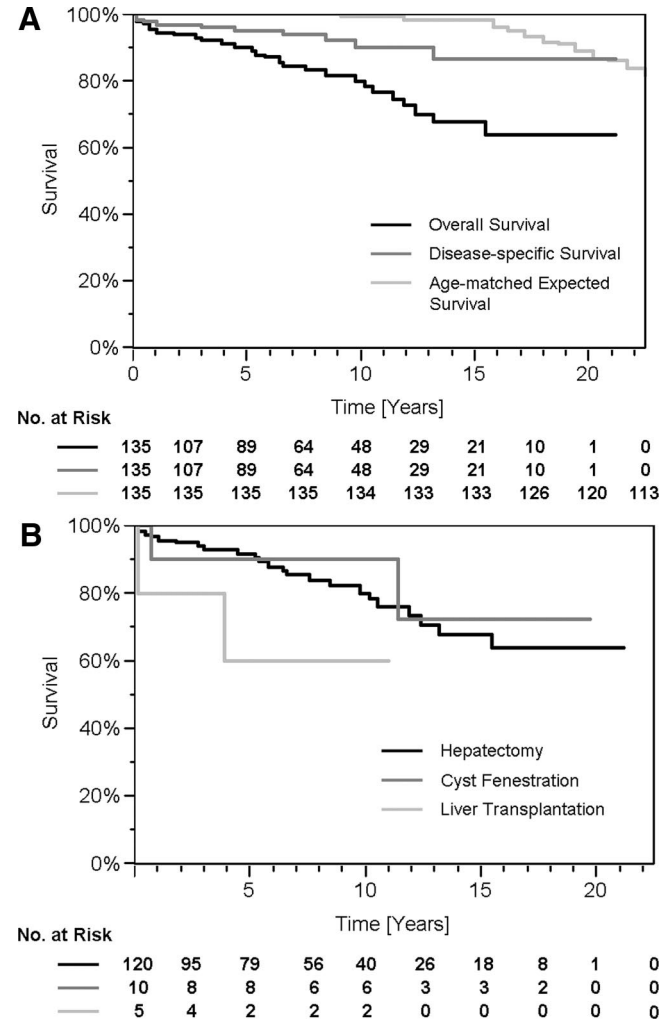

FIGURE 1. Long-term survival in 135 patients after operative treatment for PLD: A, Overall survival compared with disease-specific survival and survival in an age-matched US standard population (log-rank test: $P < 0.0001$); B, Survival dependent on type of operative treatment (log-rank test: $P = 0.310$).

DISCUSSION

Our findings demonstrate that selective patients with massive, symptomatic hepatomegaly from PLD benefit from operative intervention. Specifically, we have shown that given at least relative sectorial sparing, hepatic resection with cyst fenestration of the hepatic remnant can be performed with acceptable mortality, prompt and durable symptom relief, and maintained liver function. Although morbidity is significant, once resolved, clinical performance status improves or normalizes. Hepatic resection with cyst fenestration can be considered for most PLD patients with massive hepatomegaly and symptoms sufficiently severe to justify a surgical inter-

TABLE 3. Mean (Range) SF-36 Health Survey Norm-Based Scores After Long-Term Follow-Up for Operative Treated PLD in Reference to the General US Population

	Hepatic Resection (n = 69)	Cyst Fenestration (n = 6)	Liver Transplantation (n = 3)
Physical component score	45 (22–65)	49 (39–58)	56 (50–59)
Physical function	46 (23–57)	42 (28–55)	54 (49–57)
Role physical	45 (18–57)	47 (27–57)	55 (52–57)
Bodily pain	48 (25–62)	56 (42–62)	58 (51–62)
General health	45 (19–64)	51 (46–59)	63 (60–64)
Mental component score	50 (20–72)	49 (35–56)	61 (61–62)
Vitality	48 (21–71)	51 (46–55)	66 (61–71)
Social function	48 (13–57)	51 (35–57)	57 (57–57)
Role emotional	47 (9–56)	40 (17–56)	56 (56–56)
Mental health	51 (22–64)	52 (42–58)	62 (58–64)

vention. Cyst aspiration with sclerosis or cyst fenestration alone and liver transplantation, though effective in selected patients, are less broadly applicable.

Most patients with PLD are asymptomatic and do not require operative intervention.[1] Severely (and in some patients moderate) symptomatic hepatomegaly from PLD is an indication for operation with the implicit aim of reducing hepatic volume. Importantly, we believe that symptoms must significantly alter clinical performance status before operative intervention is undertaken. As a result of our clinical experience, we have developed criteria for operative procedure selection. Selection for each procedure is dependent on the degree of symptoms, distribution of hepatic cysts, volume of noncystic or relatively preserved parenchyma, and vascular anatomy of preserved liver. For patient selection, detailed preoperative assessment is critical. Imaging should clearly detail the portal and hepatic venous anatomy of the anticipated sectoral remnant and the IVC. Magnetic resonance angiography can be helpful in this determination. For this purpose, we classified patients with normal liver function according to clinical and radiographic cross-sectional findings into 4 groups (Table 4, Fig. 2). In general, hepatic resection with cyst fenestration is considered feasible if preoperative evaluation confirms at least single sectoral preservation. Liver transplantation is indicated in the absence of such preservation. Cyst fenestration alone is considered only in patients with large dominant cysts mainly in the anterior hepatic segments. Percutaneous cyst aspiration with or without application of sclerosing agents or selective hepatic artery embolization has limited application in patients with PLD.[1,9] For most patients with symptomatic, massive hepatomegaly, partial hepatectomy with cyst fenestration of the hepatic remnant has been more broadly applicable than liver transplantation. Hepatic resection has been successful providing that at least one hepatic sector is relatively spared of cystic replacement with concurrent preservation of the majority of that sectoral parenchyma and that the afferent and efferent sectoral vasculature is patent to assure adequate liver reserve.

The choice between hepatic resection with remnant cyst fenestration and liver transplantation can be difficult. The former operative approach implies residual hepatic cysts with eventual,

TABLE 4. Classification of PLD With Suggested Treatment in Patients With Normal Liver Function*

	Type A	Type B	Type C	Type D
Symptoms	Absent or mild	Moderate or severe	Severe (or moderate)	Severe (or moderate)
Cyst characteristics	Any	Limited No. large cysts	Any	Any
Areas of relative normal liver parenchyma	Any	≥2 sectors	≥1 sector	<1 sector
Isosectoral portal vein or hepatic vein occlusion of preserved sector	Any	Absent	Absent	Present

*Type A, Observation or medical treatment; Type B, Cyst fenestration; Type C, Partial hepatectomy with remnant cyst fenestration; Type D, Liver transplantation; see Figure 2.

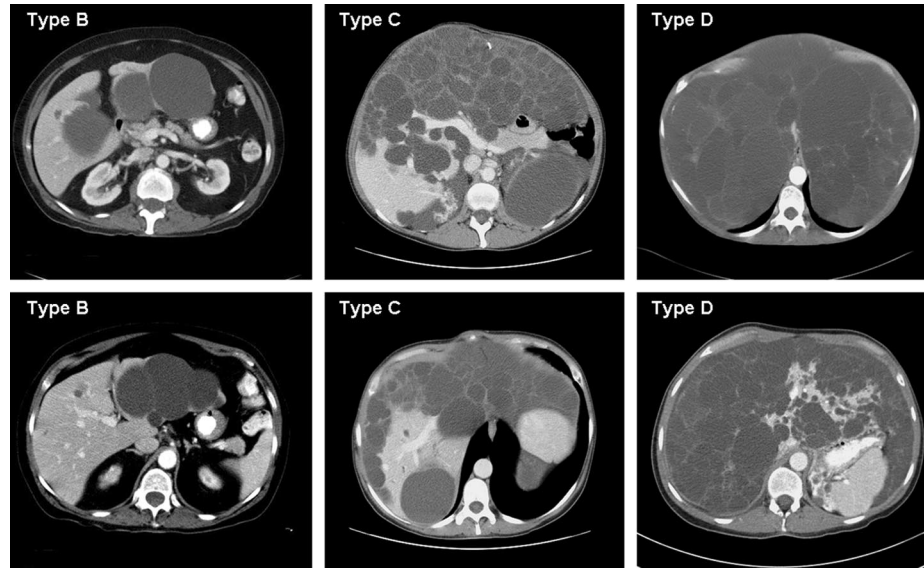

FIGURE 2. Classification of PLD on preoperative computed tomography scan: Left, Typical findings for type B PLD; Middle, Type C PLD with patent iso-sectoral portal and hepatic vein and relatively preserved parenchymal sector; Right, Type D PLD with absence of preserved parenchymal sector.

though indolent, progression, whereas the latter approach obviates any residual cysts but requires lifelong immunosuppression. Liver graft allocation is difficult for patients with PLD because symptoms rather than liver failure are the usual indications for transplantation. Both operations may be confounded by the need for renal transplantation which is unrelated to the presentation of the hepatic disease. Extending hepatectomy, to avoid a predominantly cystic remnant, risks liver failure and dictates consideration of liver transplantation. It is important to emphasize surgical experience with major hepatic resections and transplantation and multidisciplinary institutional support in offering the full extent of a tailored treatment. Both resection and transplantation are technically demanding and perioperative care is complex. We believe referral to a tertiary center with an experienced team of surgeons, hepatologists, and nephrologists is preferable for optimal patient management. Specifically, minimal operative treatment in a highly symptomatic patient who needs extensive intervention will inevitably result in treatment failure, will potentially compromise further treatment, and should be avoided.

The technique for hepatic resection in patients with PLD differs from that in patients without PLD. Several key points warrant comment. The polycystic liver is not only large, but rigid. Consequently, mobility is decreased and access to vascular supply more difficult. In our study, the average preoperative liver volume was 6695 $\pm$ 442 cm^3, nearly 6-times greater than the average liver volume of 1100 $\pm$ 190 cm^3 in healthy patients with noncystic, noncirrhotic livers[10,11]; emphasizing the massive degree of hepatomegaly seen in patients with PLD who require operative intervention. Both, exposure and mobilization are facilitated by fenestration of selected cysts. Cysts should be fenestrated centrally to avoid vessels within the intervening septa. Lymphatic vessels near the hilum and within the hepatic ligaments are frequently dilated and should be ligated. Once the hilum is exposed, the lobar hepatic artery, portal vein, and bile duct are isolated and divided before parenchymal transection. Hepatic venous exposure before transection is rarely possible and division is undertaken only after completion of the parenchymal dissection. Fenestration of cysts along the transection plane is essential for division of the liver. We have found the ultrasonic surgical aspirator useful because it facilitates transection of islands of normal liver and rapidly aspirates cyst fluid after division of the cyst wall thus permitting concurrent use of electrocautery for hemostasis. The ultrasonic surgical aspirator, however, does disrupt small bile ducts adjacent to vessels and suture ligatures should be used frequently to reduce postoperative bile leaks. Hepatic division is challenged by displaced hepatic vessels and bile ducts, as well as large intrahepatic collateral veins often traversing the parenchyma. Hemorrhage can occur from small veins or regional venous collaterals, which tend to retract into cysts and necessitate suture ligation. Although clinically attractive, the use of staplers to divide the parenchyma has been disappointing due to thickness of the convergent cysts or interface. Simple suture ligatures have proved most reliable. Partial hepatectomy demands preservation of both the portal and hepatic venous systems of the remnant, which can be challenging due to cyst displacement of normal anatomy. All cysts near the major hepatic veins and the IVC should be fenestrated widely to optimize postoperative patency. Specifically, at least half the circumference of the IVC should be exposed and freed of cysts during major hepatectomies. After resection, fenestration and unroofing of cysts in the remnant liver further reduces liver volume. We recommend perihepatic drain placement to address intra-abdominal fluid accumulation and control potential biliary leakage. Although postoperative percutaneous drainage can be performed, it can be challenging due to the irregular liver contour with multiple pockets created by unroofed cysts.

Our study showed that liver volume can be expectedly reduced by more than 50% with sustained improvement in performance and health status. Importantly, however, hepatic resection in patients with PLD is associated with a greater complication rate, longer operative time, and greater blood loss than partial hepatectomy in patients with noncystic, noncirrhotic livers. In our institution, partial hepatectomy for PLD resulted in a 2.3 times greater perioperative morbidity, 1.4 times longer operative time, and 2.3 times greater estimated blood loss when compared with partial hepatectomy for other indications.[12] These findings are consistent with other reports that cite a perioperative morbidity of approximately 52% (from 25 pooled patients in 3 representative studies).[13–15] The main reason for this observation is the technical difficulty of this operation with distortion of normal anatomy resulting in a greater chance of inadvertent injury of blood vessels and bile ducts; resulting in greater blood loss and a higher incidence of bile leaks. Additionally, transient ascites with prolonged drainage is frequently encountered and can be difficult to manage. The cause of the ascites is likely multifactorial and includes persistent cyst secretion, partial hepatic vein or IVC obstruction, lymphatic leakage, renal dysfunction, and malnutrition. Blood transfusion requirement and, to a lesser extent, reoperation rate decreased throughout the study period presumably due to increased experience. Preoperative blood donation is currently recommended routinely to reduce the need for allogenic transfusion. Moreover, given the lack of underlying liver dysfunction, inflow vascular occlusion during liver transection is currently being employed to further reduce transfusion need. Avoidance of blood transfusion when possible is preferred to minimize sensitization of the patient for future need of renal transplantation. However, despite the high risk of this operation, long-term improvement of performance and health status can be achieved in the majority of patients despite of recurrence of frequently minor symptoms.

Cyst fenestration alone should be reserved for patients with less severe disease from a few, superficial, dominant hepatic cysts.[16,17] In some patients, percutaneous cyst aspiration can establish causality between symptoms and a particular cyst. However, independent of improvement in symptoms from aspiration, cyst fluid reaccumulation is inevitable.[1] Regardless of open or laparoscopic approach, cyst fenestration with unroofing of the cyst wall and coagulative ablation of the cyst epithelium optimizes outcome. Symptom relief has been reported in approximately 53% (from 39 pooled patients in 3 representative studies)[18–20] in selected patients compared with 33% (n = 10) in the current study; with an operative morbidity of approximately 44%[18–20] compared with 0% in this study.

Liver transplantation may be indicated in highly symptomatic patients with PLD who are not candidates for partial hepatectomy. In rare patients with hepatic insufficiency mostly due to PLD-unrelated pathology, liver transplantation may also be indicated by the standard criteria used in patients with chronic liver disease. Despite marked hepatomegaly, the volume of the functional liver parenchyma is usually normal and hepatocellular function is preserved.[21] Since PLD patients have essentially normal liver function, calculated MELD scores are low which makes organ allocation more difficult[22]; though, options for appeal through regional review boards are possible. Due to a disadvantage in graft allocation, caval sparing hepatectomy and subsequent living donor liver transplantation might provide a potential alternative for highly selected patients.[22] Prior studies showed that 5-year survival after deceased donor liver or combined liver-kidney transplantation is around 80% with good quality of life.[23,24] These findings are consistent with our experience. Importantly, survival did not significantly differ between patients undergoing resection and liver transplantation. Liver transplantation as a rescue procedure after partial hepatectomy is

uncommon. Our study showed that only 7 of the 124 patients (6%) treated with hepatic resection required salvage liver transplantation due to hepatic failure developed immediately postoperative (n = 2) or during follow-up (n = 2) or due to uncontrollable symptoms during follow-up (n = 3). To date, no clinical trials have been reported comparing outcomes after liver transplantation and hepatic resection with cyst fenestration in patients with PLD and highly symptomatic hepatomegaly. Renal transplantation can be performed synchronous with liver transplantation; however, the decision for renal transplantation should be made independent of the liver disease.

In conclusion, partial hepatectomy with cyst fenestration, cyst fenestration alone, and liver transplantation each play a role in the management of patients with PLD. Cyst fenestration alone can be performed safely, but only provides durable treatment in highly selected patients. Similarly, liver transplantation in light of allocation issues should also be limited to selected patients. Hepatic resection with cyst fenestration currently has the broadest applicability for patients with massive hepatomegaly and highly symptomatic PLD. Although associated with significant morbidity and indolent disease progression, the degree of symptomatic relief and consequential improvement in performance status and overall health warrant its use. Selection of type of treatment should be determined by the patients' individual hepatic anatomy, hepatic reserve, severity of symptoms, and health status in accordance with our suggested PLD classification.

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