Liver Transplantation for Sclerosing Cholangitis

SHUNJI NARUMI, JOHN P. ROBERTS, JEAN C. EMOND, JOHN LAKE, AND NANCY L. ASCHER

The clinical course of 37 patients who underwent 46 liver transplantations for primary (n = 33) and secondary (n = 4) sclerosing cholangitis was reviewed. The median follow-up was 37 months. The patient and graft survivals for patients with primary sclerosing cholangitis at 1, 2, and 5 years were 96.9%, 91.6%, 87.9%, and 83.1%, 74.2%, 65.2%, respectively. In the patients with primary sclerosing cholangitis (PSC), prior surgery except for simple cholecystectomy was associated with significantly greater operative time and blood loss. No cholangiocarcinoma was identified at the time of transplantation. Human leukocyte antigen typing for PSC patients was heavily weighed toward B8 (58.8%) compared with control (11.8%). Sixty-two percent of patients with PSC also had inflammatory bowel disease. Moderate or severe rejection requiring OKT3, "rescue therapy" with FK506, or retransplantation was relatively higher in patients with inflammatory bowel disease (70%) versus patients without inflammatory bowel disease (36.4%) and a matched control group (37.5%). Progressive inflammatory bowel disease was seen in 6 of 19 patients, with 3 developing cancer and a dysplasia. Two patients in the entire group died of sepsis and 3 of colon cancer (2 recurrent and 1 primary). These data demonstrate that excellent survival results can be achieved in this group of patients. Rejection is frequent and often severe and steroid refractory. Colon cancer represents the most frequent cause of death in PSC patients after liver transplantation and demands constant attention. (HEPATOLOGY 1995;22:451-457.)

Primary sclerosing cholangitis (PSC) is a form of chronic liver disease of unknown cause characterized by chronic cholestasis caused by diffuse inflammation and fibrosis of both the intrahepatic and extrahepatic biliary tree.[1] For patients who develop end-stage PSC, orthotopic liver transplantation (OLT) is the only effective therapeutic currently available.[2,3] Because PSC is an autoimmune disease, an important issue after transplantation is the potential for ongoing immunologic injury to the liver or biliary tree after transplantation manifested either by an increased incidence or severity of allograft rejection or recurrent disease.

In addition, patients with PSC often have concomitant inflammatory bowel disease (IBD), most commonly ulcerative colitis. This chronic inflammatory condition may flare after transplantation and, more importantly, predispose patients to an increased risk of colon cancer. This raises the issue of how chronic immunosuppression after transplantation may impact on the status of IBD or the development of malignancy. In this report, we have reviewed the clinical experience for 33 PSC and 4 secondary sclerosing cholangitis patients after liver transplantation. The aim of this study was (1) to determine the patient and graft survival rates and the reasons for graft loss, (2) to determine the incidence and severity of allograft rejection in recipients with PSC, (3) to assess the influence of prior abdominal surgery in the patients with primary and secondary sclerosing cholangitis on the operative course and outcome after OLT, and (4) to characterize the clinical course and severity of IBD posttransplantation.

PATIENTS AND METHODS

Over a $5\frac{1}{2}$-year period (from February 1988 to November 1993), 480 liver transplantations (including 36 retransplantations) were performed in adults at the University of California, San Francisco Medical Center. Patients with primary and secondary sclerosing cholangitis who received liver transplantation during this period were studied retrospectively through hospital and clinic charts. The diagnosis of sclerosing cholangitis was made by endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography showing typical radiographic findings of sclerosing ducts pretransplantation and histologic examination of the explant. The operative procedure was performed using standard techniques without the use of venovenous bypass. Care was taken to resect as much host common bile duct as possible with surrounding nodal tissue. Choledochojejunostomy with a Roux-en-Y biliary anastomosis was performed for biliary reconstruction. Frozen sections of suspicious lymph nodes were examined histologically before dissection of the liver.

The primary immunosuppression regimen included polyclonal antilymphocyte preparation for 3 to 5 days, azathioprine (2 mg/kg), prednisone, and delayed oral cyclosporine, administered once adequate renal function was established. HLA typing was routinely performed just before transplantation using standard serological techniques. The recurrence of PSC post-OLT was diagnosed based on the presence of cholestatic biochemistries and a radiographic appearance of

Abbreviations: PSC, primary sclerosing cholangitis; OLT, orthotopic liver transplantation; IBD, inflammatory bowel disease; SSC, secondary sclerosing cholangitis; UC, ulcerative colitis.

From the Department of Surgery, Liver Transplant Division, University of California, San Francisco, CA.

Received August 25, 1994; accepted March 9, 1995.

Address reprint requests to: Shunji Narumi, MD, PhD, University of California, San Francisco, Department of Surgery, Liver Transplant Division, 505 Parnassus Ave, Room M-896, Box 0780, San Francisco, CA 94143-0780.

0270-9139/95/2202-0012$3.00/0

multiple biliary strictures with histologic changes consistent with recurrent PSC in the absence of other histologic evidence for rejection and in the setting of normal hepatic artery blood flow.

For HLA B8 and DR52 analysis of white PSC patients, an age- and sex-matched control group was obtained. Subjects were randomly selected from the data sheet, which included age, sex, original disease, date of transplantation, and race. They were transplant recipients without PSC, peripheral blood cells, or autoimmune liver disease who underwent transplantation within 6 months of the study subjects.

Statistical Analysis. The values of variables examined are expressed as the mean ± SD. Univariate analysis was performed by nonparametric Mann-Whitney U test for unpaired study and χ^2 test for categorical variables. A P value of $< .05$ was considered significant. Actuarial survival probabilities were calculated by Kaplan-Meier curves.

RESULTS

Patient Demographics. Between February 1988 and November 1993, 37 patients with sclerosing cholangitis (33 primary, 4 secondary) underwent OLT with 46 grafts. The mean duration of follow-up was 37.5 ± 18.9 months (median, 35.8; range, 6 to 73.0 months). In patients with PSC, 19 were men or boys and 14 were women or girls; and all 4 patients with secondary sclerosing cholangitis (SSC) were female.

PSC was diagnosed a median of 60 months before OLT (range, 2 to 262 months).

One patient with PSC had an adenocarcinoma of the colon removed by left colectomy 3 years before liver transplantation and 1 SSC patient had an adenocarcinoma of the colon with left lobe liver metastasis treated by colectomy, left lobectomy of the liver followed by intraarterial chemotherapy with floxuridine 3 years before liver transplantation. Toxicity from the chemotherapy resulted in diffuse sclerosis of the patient's bile ducts. No cholangiocarcinomas were identified in any hepatectomy specimens after careful inspection.

In the 33 patients with PSC, 22 patients (67%) had a history of IBD; 16 of 22 patients (73%) had ulcerative colitis (UC), and 6 patients had a diagnosis of Crohn's disease. All patients with PSC underwent colonoscopy with mucosal biopsies before OLT (Table 1).

Survival. The actuarial patient survivals of the entire group at 1 year, 2 year, and 5 years were 94.4%, 91.6%, and 83.6%, and the actuarial graft survivals were 84.4%, 76.6%, and 65.0% (Fig. 1). For the patients with PSC alone, clinical survivals were 96.9%, 91.6%, and 87.9%, and graft survivals were 83.1%, 74.2%, and 65.2%, respectively. The indications for retransplantation were refractory rejection (3), hepatic artery thrombosis (2), primary nonfunction (2), recurrent PSC (1), and acquired hepatitis of unknown cause (1). Four patients developed recurrence of the PSC (12.5%); 2 of them had UC. The timing of the diagnosis of recurrent PSC was 7, 8, 12, and 45 months after transplantation, respectively (Table 2). Recurrence was diagnosed mainly based on histological features, which showed periportal fibrosis, pericholangitis without severe mixed cell infiltration in the portal triad, and also radiographic evidence of intrahepatic bile duct narrowing or multiple strictures that were compatible with PSC.

Five patients died after transplantation. The cause of death was infection in two, recurrent colon cancer in two, and *de novo* colon cancer in one.

TABLE 1. Patient Demographics of Sclerosing Cholangitis

Variable	Finding
Patients/grafts	33/42 (PSC) 4/4 (SCC)
Age	43 (28-69)
Sex (male:female)	19:14 (PSC) 0:4 (SCC)
Duration of illness (months)	60 (2-262)
Follow-up (months)	36 (6-73)
Inflammatory bowel disease	22/33 (PSC)
Ulcerative colitis	16/22 (IBD)
Crohn's disease	6/22 (IBD)

NOTE. Values are median (range).

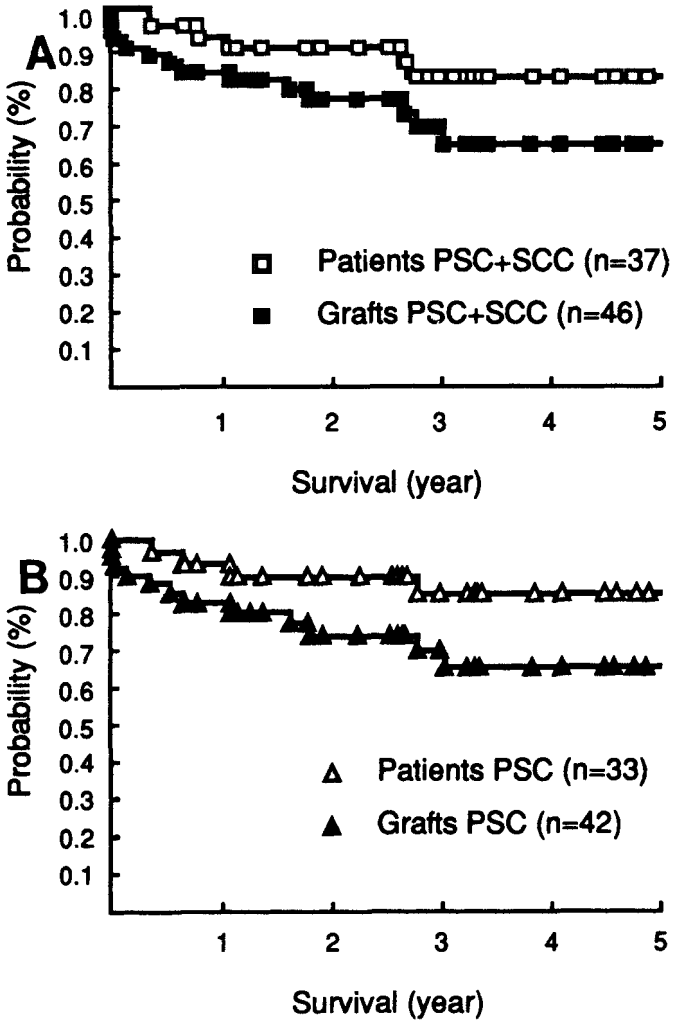

FIG. 1. Patients and graft survival in sclerosing cholangitis analyzed by Kaplan-Meier method. (A) PSC + SCC. (B) PSC only. Mean follow-up time was 32.1 ± 14.6 months.

TABLE 2. Recurrent PSC Patients

No.	Age	Sex	IBD	Rejection	OKT3	Cold Ischemic Time (hour)	Time After Transplantation (months)	Cytomegalovirus Antibody (recipient)	Cytomegalovirus Antibody (donor)
1	56	F	(−)	Moderate	(+)	5.4	45	(+)	(−)
2	47	M	(−)	Moderate	(+)	8.0	7	(−)	(−)
3	43	M	UC	Mild	(−)	5.5	12	(+)	(+)
4	67	M	UC	(−)	(−)	12.3	8	(+)	(−)

Operative Time and Blood Loss. Nine patients (67%) had undergone previous biliary enterostomy. Other surgical histories were cholecystectomy in five patients, bowel surgery for IBD in seven patients, and one patient had both bowel surgery and cholecystectomy (Table 3). The operative time was significantly longer in patients who had undergone biliary enterostomy (8.4 ± 3.1 hours: median, 7.0; range, 5.5 to 15.0 hours) and in those who had undergone bowel surgery (8.8 ± 4.5 hours: median, 6.6; range, 5.5 to 16.5 hours) as compared with those without any abdominal surgical histories (6.0 ± 1.2 hours: median, 6.2; range, 4.3 to 8.5 hours) ($P < .05$). The estimated intraoperative blood loss was relatively greater in the biliary enterostomy group (21.2 ± 38.3 L: median, 4 L; range, 0.5 to 120 L) and in the bowel surgery group (11.9 ± 16.8 L: median, 4.9 L; range, 0.5 to 45.7 L) than in the no surgical history group (3.4 ± 2.3 L: median, 2.8 L; range, 0.6 to 7.3 L) (NS). Simple cholecystectomy did not show any significant influence on either operative time (6.8 ± 1.5 hours: median, 6.1; range, 5.5 to 9.0 hours) or estimated blood loss (4.4 ± 2.7 L: median, 4.0 L; range, 1.8 to 9.0 L) (Fig. 2). The patient who had both cholecystectomy and bowel surgery was included in the bowel surgery group. One patient who required a right atrial thrombectomy secondary to a transjugular intrahepatic portal systemic shunt (TIPS)-associated thrombus was diagnosed just before transplantation and was excluded from this analysis of blood loss and operative time.

Biliary Complications. Biliary complications developed in 11 patients with PSC (33.3%) and in all four patients with SCC ($P < .05$) (Table 4). An anastomotic stricture developed in one PSC patient, whereas it occurred in all four of the SCC patients. Patients who had undergone previous biliary enterostomy had relatively higher incidence of biliary complication (biliary enterostomy 7 of 9, 77.8%; cholecystectomy 2 of 6, 30%; bowel surgery for IBD 4 of 8, 50%; no surgical history 4 of 14, 28.6%) (NS).

Rejection. The incidence of rejection episodes that required treatment with OKT3, a change in the immunosuppressive regimen (i.e., switch from cyclosporine to FK506), or retransplantation was relatively higher in PSC patients with IBD (70%) as compared with PSC patients without a history of IBD (36.4%), matched control group (37.5%), and SCC (50%) (NS). Two patients were excluded from this portion of analysis because of primary administration of FK506, in a randomized primary trial.

TABLE 3. Previous Surgery in Patients With PSC and SSC

Cholecystectomy	6
Biliary enterostomy	9
Choledochojejunostomy	5
Hepaticojejunostomy	2
Choledochoduodenostomy	1
Cholecystojejunostomy	1
Colectomy with ileostomy	4
Colectomy	2
Colectomy, rectal pullthrough	1
Colectomy, left lobectomy of the liver	1

NOTE. One patient had both cholecystectomy and colectomy.

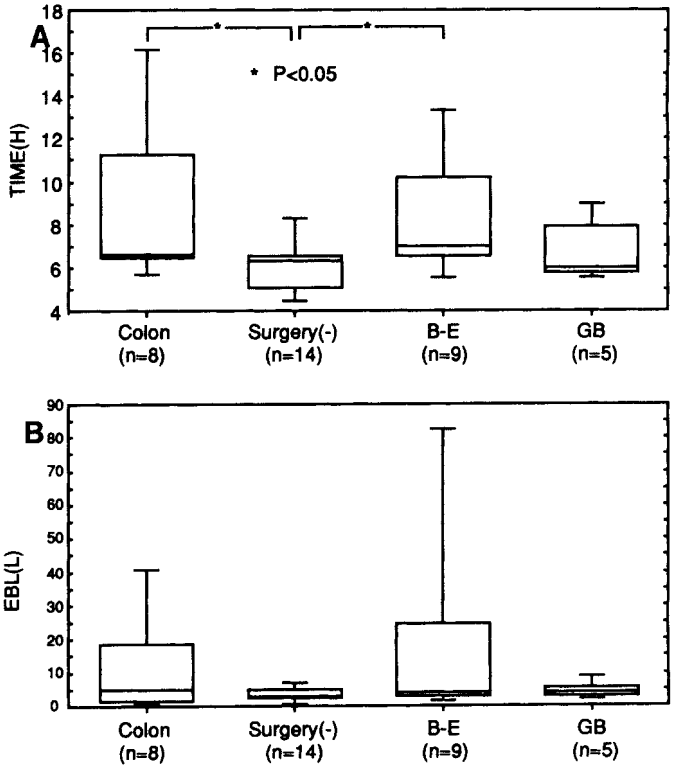

FIG. 2. Influence of previous surgery on the operation of liver transplantation. (A) Operation time ($P < .05$). (B) Estimated blood loss (NS). Colon, bowel surgery for IBD; Surgery(−), no surgical history; B-E, biliary enterostomy; GB, simple cholecystectomy.

TABLE 4. Biliary Complications and Treatment

Complications	Treatment
PSC patients (11 of 33)	
Biliary leak	Surgical revision
Biliary leak	Surgical revision
Biliary leak, stricture	Catheter drainage and dilatation
Anastomotic stricture, stone	Catheter drainage and dilatation
Biliary leak, VBDS, portal vein thrombosis	Retransplantation
VBDS (chronic rejection)	Retransplantation
Intrahepatic stricture (2° to rejection)	OKT3 and dilatation
Intrahepatic stricture (recurrence)	Dilatation
Intrahepatic narrowing (recurrence)	Observation
Intrahepatic bile duct stricture (recurrence)	Retransplantation
Biliary stricture, intrahepatic stone (recurrence)	Surgical revision and dilatation
SCC patients (4 of 4)	
Anastomotic stenosis	Dilatation
Anastomotic stricture, biliary leak	Dilatation and catheter drainage
Biliary leak, anastomotic stricture, liver abscess	Surgical revision
Biliary leak, anastomotic obstruction	Surgical revision and dilatation

Abbreviation: VBDS, vanishing bile duct syndrome.

Sepsis. Three patients developed sepsis after transplant, of which two died within 1 year of transplant. All three patients had histories of bowel resection. Two patients who had undergone previous colectomy died within a year after the transplantation. The third patient who had undergone biliary enterostomy survived.

Influence on IBD. Progressive IBD was seen in 6 of 19 patients (31.5%) who had not had total colectomy before transplantation, including development of colon cancer in three patients with UC (two patients developed recurrent cancer, one patient developed *de novo* cancer). In addition, one patient developed dysplasia. The patient with *de novo* cancer and the patient with dysplasia are currently alive. Severity and timing of IBD progression after the transplantation are described in Table 5.

HLA Typing. HLA B8 and DR52 from tissue typing studies were examined in the PSC patients and their donors. The incidence of B8 was significantly higher in PSC patients than in matched control group (55.6% vs. 11.1%) ($P < .05$), but not significant for DR52 (77.8% vs. 66.7%) (Table 6).

In four recurrent PSC patients, one had both B8- and DR52-positive graft, and two had DR52-positive graft. Eight grafts were positive for both B8 and DR52, and six grafts had survived.

DISCUSSION

Among several indications for liver transplantation, primary sclerosing cholangitis is a common disease, especially in whites. Transplantation for primary sclerosing cholangitis varies in incidence from 5.4% to 14.6%.[2,4-6] In the current series, 37 patients underwent transplantation for both primary and secondary sclerosing cholangitis. These patients represent 7.7% of the patients undergoing transplantation at our institute consistent with other series. PSC has been reported to be associated with IBD in 65.4% to 70% of the patients.[1,2,5] Our data are consistent with these figures, 66.7% (22 of 33) of PSC patients had IBD (16 patients [48.5%] with UC and 6 patients [18.2%] with Crohn's disease).

The actuarial survival reported in the literature ranged between 71% and 88% for the PSC patients who underwent liver transplantation.[2,5,7,8] Wiesner described the natural course of PSC.[9] In the Mayo survival model for PSC, 1-year, 2-year, and 5-year survival rates were proposed in low-risk group to be 98.1%, 97.0%, and 91.0%; moderate group: 89.1%, 81.0%, and 55.0%; and high-risk group: 73.0%, 53.0%, and 16.0%, respectively.[10] The overall results in our group of sclerosing cholangitis patients were 94.4%, 91.6%, and 83.6% at 1, 2, and 5 years. For patients with PSC alone, they were 96.9%, 93.4%, and 87.9%. The risk score was calculated by the formula composed of bilirubin, histological stage, age, and a history of splenomegaly.[10] According to that formula, 19 of our patients had moderate risk (with two deaths), and 18 of our patients were at high risk (with three deaths). The 1-year, 2-year, and 5-year survival rates of those groups were calculated to be 94.7%, 94.7%, and 86.8% in the moderate-risk group and 93.8%, 87.5%, and 78.8% in the high-risk group, respectively. Our results surpassed the presumptive natural course of PSC, and the group as a whole fared better than expected for patients with moderate risk.

Some surgeons have argued against palliative operations like biliary enterostomy or portosystemic shunt and recommended early referral for liver transplantation because of a concern for increased complications (including increased blood loss) and poor prognosis after subsequent transplantation.[5,7,9,11-13] The current investigation shows a significant association between a surgical history of biliary enterostomy or bowel resection and longer operative time. These factors also show a relative correlation with greater blood loss. The median blood loss and operative time in the group without previous surgery were almost the same as those in the subgroup of patients with the other diseases such as alcohol-induced cirrhosis (data not shown). In spite of longer and more difficult surgery these patients enjoyed survival that compared favorably with the rest of our series; they were not compromised by previous surgery. In addition, a history of previous biliary surgery (except for simple cholecystectomy) was associated with an increased incidence of biliary complications after transplantation in PSC patients. All four SCC patients had previous biliary tract surgery and developed biliary complications associated with anastomotic strictures. This finding could be explained by local adhesions of the bowel associated with previous biliary

TABLE 5. Severity and Timing of IBD Progression After Transplantation

No.	Age	Sex	IBD	IBD (yrs)	IBD Severity After Transplantation	Time After Transplantation (mos)	Treatment	Status
1	46	M	UC	20	Frequent diarrhea, bloody stool	19	Medication	Alive
2	47	M	Crohn	5	Multiple pseudopolyps, a submucosal lipoma	18	Total colectomy prophylactic APR	Alive
3	51	M	UC	51	Dysplasia	15	Total colectomy	Alive
4	33	M	UC	20	Recurrent colon cancer, multiple lung metastases	20	Chemotherapy, irradiation	Alive
5	57	F	UC	7	Recurrent colon cancer, (Duke's C), liver mets	9	Total colectomy	Dead
6	69	F	UC	30	Rectal cancer (*de novo*) (Duke's B)	27	Proctocolectomy, irradiation	Dead

Abbreviation: APR, abdominoperineal resection.

enterostomy. Creation of a Roux-en-Y jejunostomy for biliary drainage might have compromised blood supply or scarring at the biliary enterostomy. The incidence of biliary complications is high in this series, but it is consistent with the evidence of biliary complications in our series of transplants and comparable to other reports in the literature.[6,8,14] All patients who developed sepsis had undergone previous bowel surgery. These findings convince us of obligatory referral for liver transplantation before multiple palliative surgery for biliary tree, though a single attempt at biliary reconstruction is supported by our study. Biliary complications can be treated with interventional radiologic procedure successfully,[15] as seen in some of our cases shown in Table 4. Although the causes of primary and secondary sclerosing cholangitis are different, the patient groups share clinical features such as biliary cirrhosis, bile duct irregularity, and previous surgical histories. For this reason, we combined these two diseases for the analysis of survival and influence of surgical history on blood loss and operation complications. In terms of survival and the association of previous surgery and blood loss, these two groups are quite similar.

In four PSC patients, their course after transplantation led to the diagnosis of PSC recurrence. Although the definite criteria of the PSC recurrence have not been established, the recurrence was based on specific pathological findings, including significant periportal fibrosis and pericholangitis without severe mixed cell infiltration in the portal triad. These patients also demonstrated radiographic findings compatible with PSC: multiple nonanastomotic strictures. This finding of ductular strictures has also been reported to have an association with long cold ischemic time,[16] ABO-incompatible transplant, cytomegalovirus infection, and chronic rejection.[17] There were a total of seven patients who developed multiple nonanastomotic biliary strictures, including three patients who were diagnosed with vanishing bile duct syndrome after chronic rejection. Cold ischemic time in the entire series was 11.2 ± 4.5 hours. Although these three patients who had developed chronic rejection showed typical pathological features, all of them also had received grafts with longer cold ischemic time than 11.5 hours: 11.7 hours, 14.9 hours, and 26.5 hours, respectively. This evidence is consistent with the possibility that nonanastomotic multiple biliary irregularity could be associated with long cold ischemic time leading to the damage of small arterioles and bile duct ischemia. However, only one of four patients who were diagnosed as recurrent PSC had a long ischemic time (12.3 hours). The ischemic time of the remaining three was short: 5.4 hours, 5.5 hours, and 8 hours (Table 3). Two of these patients had developed moderate rejection necessitating OKT3 treatment, another had mild rejection treated with pulse steroid, and the fourth did not develop significant rejection. All of four patients received ABO-identical grafts. Anti-cytomegalovirus antibody was positive in three recipients but in only one donor. Thus only one of these four patients had a long cold ischemic time, none received ABO incompatible grafts, and the cytomegalovirus rate in this group was the same as the entire group. All four patients developed pathological features consistent with recurrent PSC.

There are a number of reports showing a correlation between PSC and HLA antigens.[18-22] Chapman re-

TABLE 6. HLA B8 and DR52 Antigen Distribution in PSC Patients and Matched Controls

	Sex	Age	B8	DR52	B8/DR52	IBD
PSC	M 11	46.6 ± 11.0	10/18	14/18	9/18	UC:10
	F 7	Range: 23-67	55.6%	77.8%	50.0%	Crohn:4
Control	M 11	46.1 ± 9.9	2/18	12/18	2/18	—
	F 7	Range: 25-64	11.1%	66.7%	11.1%	
P	NS	NS	$P < .05$	NS	$P < .05$	—

ported B8 was positive in all PSC patients.[18] DR52 has also been reported to be associated with PSC.[20,21] We found an association with HLA B8 but not DR52 in our PSC patients compared with matched controls. However, there seemed to be no correlation between B8 positivity and the incidence of recurrence. Interestingly, seven grafts displayed both B8 and DR52 positivity with no recurrence. We feel patients receiving B8- and DR52-positive grafts should be monitored for disease recurrence because of the reported association of B8 and DR52 and PSC,[18,20,21] but the data from our patients only support the observation of B8 and PSC.

The incidence of moderate or refractory rejection that required OKT3, "rescue therapy," or retransplantation was relatively higher in PSC with IBD compared with the three other groups, PSC patients without IBD compared with a matched control group, and patients with SCC. McEntee et al described that PSC had a higher incidence of ductopenic rejection or diffuse biliary stricture.[7] There are some reports on presumptive recurrence of PSC after liver transplantation.[3,23,24] Four PSC patients were diagnosed to have PSC recurrence diagnosed by intrahepatic biliary abnormalities. All of them showed histological periportal fibrosis, pericholangitis without severe mixed cell infiltration in the portal triad, and radiographic intrahepatic bile duct narrowing or multiple strictures that were compatible with PSC. Neither definitive criteria for discriminating rejection from recurrence nor evident verification whether those diffuse strictures were caused by chronic rejection or recurrence of PSC could be obtained, but these findings are suggestive and may dictate an increased immunosuppressive regimen for PSC patients, especially those suffering with IBD. Considering the relatively high incidence of biliary tract complication in these patients, it is additionally difficult to differentiate recurrent PSC from a process akin to secondary sclerosing cholangitis with the transplanted liver.

Malignant status has been considered as a relative contraindication for liver transplantation because of the low survival rate.[25,26] PSC has been reported to be a premalignant condition to develop cholangiocarcinoma.[27] We found no incidental cholangiocarcinomas in this series, but we abandoned a single transplantation in a patient with obvious cholangiocarcinoma and metastasis. This patient is not reported here. Ten percent of PSC patients who underwent liver transplantation are reported to have unsuspected cholangiocarcinoma.[11] And also it is well established that the incidence of colon carcinoma is increased in patients with ulcerative colitis.[28] The longer the duration of IBD, the higher the likelihood of development of colon cancer.[25] In our series of PSC patients with UC, two patients developed recurrent colon cancer, one developed primary colon cancer, and one developed dysplasia. In one case, the patient died 3 years after transplantation. In a recent case, the patient underwent liver transplantation 8 years after colectomy but developed recurrent colon cancer 9 months after the transplantation and died 4 months later. One SCC patient underwent colectomy and left lobectomy of the liver because of metastasis 3 years before transplantation. At the time of transplantation, no intraabdominal lymph nodes were positive for tumor by frozen or permanent sections, but she developed recurrence of cancer in multiple sites 1 year later. The patient underwent resection of metastatic lesions in the pleural space and splenectomy; she survived 2 years after detection of the first metastasis. As a consequence of experience in these patients, we believe there is considerable risk for *de novo* and recurrent cancer in the population after transplantation. Careful repeated examination with serum carcinoembryonic antigen, colonoscopy, and ultrasound or computed tomography scan should be included in the posttransplantation follow-up of these patients.

In summary, we report our experience of liver transplantation for sclerosing cholangitis. These data demonstrate that excellent results can be achieved in this group of patients, rejection is frequent, and continued attention to the progression of IBD, including development of malignancy, is essential.

Acknowledgment: We would like to thank Bev Nikolai, RN, for her outstanding contribution to this work relating to extraction of data.

REFERENCES

1. Wiesner RH. Primary sclerosing cholangitis. In: Schiff L, Schiff ER, eds. Diseases of the liver. Vol 2, Ed 7. Philadelphia: Lippincott, 1993:411-426.
2. Marsh JWJ, Iwatsuki S, Makowka L, Esquivel CO, Gordon RD, Todo S, Tzakis A, et al. Orthotopic liver transplantation for primary sclerosing cholangitis. Ann Surg 1988;207:21-25.
3. Harrison J, McMaster P. The role of orthotopic liver transplantation in the management of sclerosing cholangitis. HEPATOLOGY 1994;20:14S-19S.
4. Scharschmidt BF. Human liver transplantation: analysis of data on 540 patients from four centers. HEPATOLOGY 1984;4:95S-101S.
5. Langnas AN, Grazi GL, Stratta RJ, Wood RP, Marujo W, Markin RS, Donovan J, et al. Primary sclerosing cholangitis: the emerging role for liver transplantation. Am J Gastroenterol 1990; 85:1136-1141.
6. Stephans J, Goldstein R, Crippin J, Husberg B, Holman M, Gonwa TA, Klintmalm G. Effects of orthotopic liver transplantation and immunosuppression on inflammatory bowel disease in primary sclerosing cholangitis patients. Transplant Proc 1993;25:1122-1123.
7. McEntee G, Wiesner RH, Rosen C, Cooper J, Wahlstrom E. A comparative study of patients undergoing liver transplantation for primary sclerosing cholangitis. Transplant Proc 1991; 23:1563-1564.
8. Shaked A, Colonna J, Goldstein L, Busuttil RW. The interrelation between sclerosing cholangitis and ulcerative colitis in patients undergoing liver transplantation. Ann Surg 1992;215:598-605.
9. Wiesner RH, Grambsh PM, Dicson ER, Ludwig J, MacCarty RL, Hunter EB, Fleming TR, et al. Primary sclerosing cholangitis: natural history, prognostic factors and survival analysis. HEPATOLOGY 1989;10:430-436.
10. Dickson ER, Murtaugh PA, Wiesner RH, Grambsch PM, Fleming TR, Ludwig J, LaRusso NF, et al. Primary sclerosing cholangitis: Refinement and validation of survival models. Gastroenterology 1992;103:1893-1901.
11. Martin FM, Rossi RL, Nugent FW, Scholz FJ, Jenkins RL, Lewis

WD, Gagner M, et al. Surgical aspects of sclerosing cholangitis. Ann Surg 1990;212:551-558.
12. Ismail T, Angrisani L, Powell JE, Hubscher S, Buckels J, Neuberger J, Elias E, et al. Primary sclerosing cholangitis: surgical options, prognostic variables and outcome. Br J Surg 1991; 78:564-567.
13. Lemmer ER, Bornman PC, Krige JE, Wright JP, Beningfield S, Jaskiewicz K, Kirsch RE, et al. Primary sclerosing cholangitis. Arch Surg 1994;129:723-728.
14. Osorio RW, Freise CE, Stock PG, Lake JR, Ring EJ, Asche NL, Roberts JP, et al. Nonoperative management of biliary leaks after orthotopic liver transplantation. Transplantation 1993; 55:1074-1077.
15. Letourneau JG, Day DL, Hunter DW, Ascher NL, Najarian JS, Thompson WM, Castaneda-Zuniga WR. Biliary complications after liver transplantation in patients with preexisting sclerosing cholangitis. Radiology 1988;167:349-351.
16. Sanchez-Uradazpal L, Gores GJ, Ward EM, Maus TP, Wahlstrom HE, Wiesner RH, Krom RAF, et al. Ischemic-type biliary complications after orthotopic liver transplantation. HEPATOLOGY 1992;16:49-53.
17. Ayres R, Adams D. Acute rejection of human liver allografts. In: Neuberger J, Adams D, eds. Immunology of liver transplantation. London: Edward Arnold, 1993:197-215.
18. Chapman RW, Varghese Z, Gaul R, Patel G, Kokimon N, Sherlock S. Association of primary sclerosing cholangitis with HLA-B8. Gut 1983;24:38-41.
19. Broome U, Glaumann H, Hultcrantz R, Forsum U. Distribution of HLA-DR, HLA-DP, HLA-DQ antigens in liver tissue from patients with primary sclerosing cholangitis. Scand J Gastroenterol 1990;25:54-58.
20. Noguchi K, Kobayashi M, Yagihashi A, Yoshida Y, Terasawa K, Konno A, Ichida F, et al. HLA antigens in primary sclerosing cholangitis. Transplant Proc 1992;24:2775-2776.
21. Prochazka EJ, Terasaki PI, Park MS, Goldstein LI, Busuttil RW. Association of primary sclerosing cholangitis with HLA-DRw52a. N Eng J Med 1990;322:1842-1844.
22. Schrumpf E, Fausa O, Forre O, Dobloug JH, Ritland S, Thorsby E. HLA antigens and immunoregulatory T cells in ulcerative colitis associated with hepatobiliary disease. Scand J Gastroenterol 1982;17:187-191.
23. Hunter EB, Wiesner RH, MacCarty RH, LaRusso NF, Porayko MK, Eid A, Krom RAF. Does primary sclerosing cholangitis recur after liver transplantation? Gastroenterology 1989;96:A610.
24. Lerut J, Demetris AJ, Stieber AC, Marsh JW, Gordon RD, Esquivel CO, Iwatsuki S, et al. Intrahepatic bile duct strictures after human orthotopic liver transplantation: recurrence of primary sclerosing cholangitis or unknown presentation of allograft rejection? Transplant Int 1988;1:127-130.
25. Higashi H, Yamada K, Marsh JW, Tzakis A, Kakizoe S, Starzl TE. Development of colon cancer after liver transplantation for primary sclerosing cholangitis associated with ulcerative colitis. HEPATOLOGY 1990;11:477-480.
26. Delcore R, Eisenach JB, Payne KM, Bhatia P, Forster J. Risk of occult carcinomas in patients undergoing orthotopic liver transplantation for end-stage liver disease secondary to primary sclerosing cholangitis. Transplant Proc 1993;25:1883-1884.
27. Rosen CB, Nagorney DM, Wiesner RH, Coffey RJJ, LaRusso NF. Cholangiocarcinoma complicating primary sclerosing cholangitis. Ann Surg 1991;213:21-25.
28. Mir-Mardjlessi SH, Farmer RG, Easley KA, Beck GJ. Colorectal and extracolonic malignancy in ulcerative colitis. Cancer 1986;58:1569-1574.