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BRIEF ARTICLE

Outcome of patients with primary sclerosing cholangitis and ulcerative colitis undergoing colectomy

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Abstract

AIM: To study the outcomes of primary sclerosing cholangitis (PSC) patients with ulcerative colitis (UC) undergoing colectomy.

METHODS: We identified 193 patients with PSC and UC undergoing colectomy at the Mayo Clinic (Rochester, MN, United States), between January 1, 1995 and December 31, 2008 using a computerized record system. Eighty-nine patients were excluded due to unclear diagnosis, liver transplantation prior to colectomy, age less than 18 years, inadequate follow-up data or known cases of cholangiocarcinoma. We retrospectively reviewed data from patient medical records. Clinical information, date of colectomy, preoperative and follow-up liver tests and pathological findings of the colon were reviewed. The Mayo risk score at baseline was calculated to obtain survival estimates for up to 4 years of follow-up. The primary endpoint was defined by the presence of all-cause mortality and/or liver decompensation requiring liver transplantation. All patients who did not have a clinical note on December 31, 2008 were considered as patients with an incomplete follow-up unless they reached a study endpoint (death or underwent liver transplantation) prior to that date. The study was approved by the Institutional Review Boards of the Mayo Clinic.

RESULTS: Of the 2441 patients with PSC observed in this period, 104 patients (4.3%) had UC and underwent colectomy and were included. The median age was 43.2 years, and 67% were male. The leading indications for colectomy were severe colonic inflammation (49%), the presence of colonic dysplasia during routine surveillance (42%) and bowel perforation (3%). Twenty-six patients were lost to follow-up after a median duration of 3.9 years. The remaining 78 patients included 52 patients (66.7%) who were followed for a median duration of 5.5 years and 26 patients (33.3%) who developed primary endpoints including death (n = 13) or underwent liver transplantation (n = 13) with a median follow up of 2.6 years. For the secondary endpoint, the liver complications within 1 mo following the colectomy were found in 9 patients (8.6%) and included worsening liver tests (n = 3), liver failure requiring liver transplantation (n = 2), acute cholangitis (n = 3) and right hepatic vein thrombosis with hepatic infarct (n = 1). A multivariate logistic analysis demonstrated that only lower platelet count and lower albumin level preoperatively were significantly associated with more primary endpoints (OR = 0.99 and 0.05 respectively).

CONCLUSION: One third of patients with PSC and UC

undergoing colectomy died or underwent liver transplantation within 2.6 years. PSC patients with lower platelet counts and lower albumin levels were significantly more likely to have a poorer outcome.

Key words: Prognosis; Colectomy; Primary sclerosing cholangitis; Ulcerative colitis; Outcomes

Core tip: To study the outcomes of primary sclerosing cholangitis (PSC) patients with ulcerative colitis (UC) undergoing colectomy. We identified 193 patients with PSC and UC undergoing colectomy at the Mayo Clinic (Rochester, MN, United States), between January 1, 1995 and December 31, 2008. Eighty-nine patients were excluded. Of the 2441 patients with PSC, 104 patients (4.3%) had UC and underwent colectomy and were included. The median age was 43.2 years. One third of patients with PSC and UC undergoing colectomy died or underwent liver transplantation within 2.6 years. PSC patients with lower platelet counts and lower albumin levels were significantly more likely to have a poorer outcome.

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INTRODUCTION

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease and is associated with inflammatory bowel disease (IBD) in 60%-80% of patients[1-3]. Ulcerative colitis (UC) is more commonly prevalent than Crohn's disease (CD) in patients with PSC[4,5]. The colitis associated with PSC has unique findings and is usually extensive[4,6]. UC in patients with PSC is associated with an increased risk of colorectal neoplasia compared to patients with UC alone (OR = 4.8)[7]. The incidence of colorectal neoplasia at 5 years in PSC patients with IBD is significantly higher than in patients with UC alone (33% *vs* 13%, $P = 0.054$; borderline statistical significance by unmatched log rank test)[4].

A recent study reported that PSC was the third leading cause (15.4%) of abnormal liver tests among 545 patients with underlying IBD undergoing colectomy with ileal pouch-anal anastomosis (IPAA), after a transient elevation of liver tests (49%) and fatty liver (15.4%)[8]. Another study evaluated the progression of liver disease after proctocolectomy in patients with PSC and UC[9]. After proctocolectomy with IPAA, they found that 5 of 30 patients (16.7%) underwent liver transplantation at intervals of 1 to 11 years[9]. Previous studies have shown that patients with liver cirrhosis can experience worsening of their liver disease after surgery and poor outcomes[10,11]. Surgery may lead to severe complications such as decompensated liver disease, worsening of a pre-existing decompensation or even death. Very limited information exists on the prognosis of patients with PSC and UC undergoing colectomy[12]. We aimed to assess the outcomes and predictors of outcomes of PSC patients undergoing colectomy at the Mayo Clinic, Rochester, MN, United States.

MATERIALS AND METHODS

This was a retrospective study using a computerized record system of patients who had been diagnosed with PSC and UC and were undergoing colectomy at the Mayo Clinic, Rochester, MN, United States, between January 1, 1995 and December 31, 2008. PSC was defined as present when all the following criteria were met: (1) chronic cholestatic disease of at least six months' duration; (2) elevation of serum alkaline phosphatase (ALP) levels; (3) retrograde, operative, percutaneous or magnetic resonance cholangiography demonstrating intrahepatic and/or extrahepatic biliary duct obstruction, beading or narrowing consistent with PSC; and (4) exclusion of secondary sclerosing cholangitis or other causes of cholestatic liver diseases[3].

A diagnosis of PSC was made using the Hospital International Classification of Disease Adaptation (HICDA) codes of 05760310. A diagnosis of IBD was based on the following HICDA codes: cholangitis, sclerosing (05760310); disease, Crohn's, nos (05630110); enteritis, regional, nos (05630111); ileitis (regional)-see also enteritis (05630112); colitis, Crohn's (05630113); disease, Crohn's, recurrent (05630120); enteritis, regional, recurrent (05630121); colitis, ulcerative, chronic-cuc (05631110); colitis, ulcerative, nos (05631120); colitis, thrombo-ulcerative (05631121); colitis, ulcerative, acute (05631130); colitis, granulomatous (05632110); disease, granulomatous, colon (05632111); disease, inflammatory bowel, nos (05639212). HICDA is an adaptation of the International Classification of Diseases (ICD)-8 for hospital morbidity, which was used at Mayo Clinic to maintain continuity of the Medical Index and the Rochester Epidemiology Project for on-going longitudinal studies[13]. Of the 2441 patients with PSC, we identified 193 PSC patients with IBD (7.9%) who had undergone colectomy and retrospectively reviewed data from their medical records.

We retrospectively reviewed data from the medical records. A detailed history and physical examination was recorded by a health care provider using standardized protocols. Clinical information, date of colectomy, preoperative and follow-up liver tests and pathological findings of the colon were reviewed. The Mayo risk score at baseline was calculated to obtain survival estimates through up to 4 years of follow-up. The Mayo risk score calculations can be accessed from the web site: http://www.mayoclinic.org/gi-rst/mayomodel3.html, and the MELD

model/UNOS modification can be accessed from http://www.mayoclinic.org/ meld/mayomodel6.html.

Inclusion criteria

We included PSC patients who underwent colectomy and had results of preoperative liver tests and at least one post-operatively. Colectomy cases included open or laparoscopic colectomy. All included patients must have had at least one follow-up visit after the colectomy. The liver tests included total bilirubin, direct bilirubin, albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and ALP levels in the serum.

Exclusion criteria

Of the 193 patients with PSC and UC undergoing colectomy, we excluded the patients with the followings: underwent liver transplantation prior to colectomy, inadequate follow-up data, CD, age less than 18 years and known cases of cholangiocarcinoma.

Follow-up data

The primary endpoint was defined as the presence of all-cause mortality and/or liver decompensation requiring liver transplantation and it has been measured at 1 mo and at the end of follow-up. All causes of death listed on the death certificates or pathological findings (underlying, intermediate, immediate and other major conditions) were recorded using the ICD-10 revision.

The secondary end point was defined as the presence of liver complications post-operatively occurred within 1 mo which included ascites, variceal bleeding, clinical hepatic encephalopathy or liver failure and required hospitalization. The worsening liver tests were defined as increases in AST, ALT or total bilirubin to at least 2-fold greater than the baseline values. Other information including the the length of hospital stay and general post-operative complications were recorded.

All patients who did not have a clinical note on December 31, 2008 (the end of follow up in this study) were considered as patients with incomplete follow up unless they developed an endpoint (death or underwent liver transplantation) prior to that date. The study was approved by the Institutional Review Boards of the Mayo Clinic, and all participants provided permission for their medical information to be used for research.

Statistical analysis

Statistical analyses were performed with SPSS version 15.0 software. Subjects were categorized by the presence or absence of primary endpoints. Continuous variables were presented as the mean ± SD or median [interquartile range (IQR)] as appropriate. Comparisons between the two groups were performed using independent *t* tests if values were normally distributed or by the Wilcoxon rank sum test if the distribution was not normal. Categorical data were presented as numbers (percentage) and were compared by Fisher's exact test or the χ^2 test where appropriate. All tests were two sided, and the chosen level of significance was $P < 0.05$. A logistic regression analysis was used to identify factors significantly associated with the presence of primary endpoints in PSC patients with UC undergoing colectomy. Only variables with a P value < 0.1 in a univariate analysis were included in the multivariate analysis. We estimated receiver operating characteristic (ROC) curves of related variables for detection of the primary endpoints in patients with PSC to maximize the area under the curve (AUC).

RESULTS

Clinical features at presentation

Of the 2441 patients with PSC, 193 patients with PSC and UC undergoing colectomy were identified. Eighty-nine patients were excluded due to liver transplantation prior to colectomy (n = 30), inadequate follow-up data (n = 35), CD (n = 16), age less than 18 years (n = 6) and known cases of cholangiocarcinoma (n = 2). The remaining of 104 patients (4.3% of 2441 PSC patients) were included in this study. The median age was 43.2 years, and 67% were male. The demographic and biochemical data of the 104 patients are shown in Table 1. The median (IQR) Mayo risk score was -0.05 (-0.7, 1.1) while the median (IQR) MELD score was 9 (6, 12). The leading indications for colectomy were severe colonic inflammation (49%), colonic dysplasia observed during routine surveillance (42%) and bowel perforation (3%). Most of the preoperative total bilirubin, direct bilirubin and albumin levels were within normal range, while the mean ALP value was two fold greater than normal.

Clinical outcomes

Table 1 summarizes the postoperative clinical outcomes of the 104 patients with a median (IQR) hospital stay of 7 d (6, 11). Of 104 patients with PSC and UC, 26 were lost to follow-up after a median duration of 3.9 years. The remaining 78 patients included 52 patients (66.7%) who continued follow up, with a median duration of 5.5 years, and 26 patients developed primary endpoints including death or underwent liver transplantation (33.3%), with a median follow up of 2.6 years (Figure 1). The causes of death of the 13 patients were liver-related complications: hepatocellular carcinoma, hepatic renal syndrome and/or liver failure (n = 4), metastatic cancer to the liver (n = 5), acute cholangitis (n = 1), amyloidosis (n = 1) and unknown causes (n = 2). Two patients died at 10 and 20 d following colectomy. For the secondary endpoint, the liver complications within 1 mo following the colectomy were found in 9 patients (8.6%) and included worsening liver tests (n = 3), liver failure requiring liver transplantation (n = 2), acute cholangitis (n = 3) and right hepatic vein thrombosis with hepatic infarct (n= 1) (Table 2). General postoperative complications were found in 36 patients (34.6%) within 1 mo. The most common complications were anemia or blood loss requiring blood transfusion (n = 11; 10.6%), intra-abdominal abscess requiring drainage (n = 4; 3.8%), acute bowel obstruction

Table 1 Baseline characteristics data, laboratory tests and clinical outcomes of 104 patients with primary sclerosing cholangitis and ulcerative colitis who underwent colectomy

Patient characteristics[1]	Total (n = 104)	Patients who continued follow-up or developed primary endpoints (n = 78)
Baseline characteristics data		
Age at colectomy (yr)	43 (30-53)	42 (28-52)
Gender, male	70 (67)	56 (72)
Race, Caucasian	98 (94)	76 (97)
Presence of advanced liver fibrosis at baseline	27 (32)	24 (39)
Mayo risk score at baseline	-0.05 (-0.7, 1.1)	-0.001 (-0.8, 1.4)
BMI (kg/m^2)	25 (22.6, 28.6)	24.7 (22, 27.4)
Previous use of immunosuppressive drugs	38 (36.5)	29 (37)
History of receiving ursodeoxycholic acid	33 (31.7)	26 (33.3)
Diabetes mellitus or impaired glucose tolerance	7 (7)	6 (7.6)
History of current smoking	2 (2)	2 (2.6)
Indication for colectomy		
Severe colonic inflammation	51 (49)	37 (47)
Colonic dysplasia	44 (42)	36 (46)
Bowel perforation	3 (2.8)	3 (3.8)
Other indications	6 (5.7)	2 (2.6)
Laboratory tests at baseline		
ALT (< 40 U/L)	70 (43, 113)	73 (43, 135)
AST (< 40 U/L)	50 (30, 96)	55 (32, 100)
Albumin (g/dL)	3.9 (3.5, 4.2)	3.9 (3.5, 4.2)
Total bilirubin (mg/dL)	0.7 (0.5, 1.5)	0.8 (0.5, 1.9)
Direct bilirubin (mg/dL)	0.2 (0.1, 0.7)	0.3 (0.1, 0.9)
ALP (U/L)	359 (194, 657)	385 (197, 839)
Glucose (mg/dL)	93 (86, 106)	93.5 (86, 107)
Creatinine (mg/dL)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)
CA 19-9 (normal < 55 U/mL)	17.2 (8.8, 51)	16.8 (8.5, 51)
Platelet (× 10^9/L)	289 (201, 350)	289 (205, 351)
INR	1 (0.9, 1.1)	1 (0.9, 1.1)
Clinical outcomes at the end of follow-up		
Undergoing Ileal pouch-anal anastomosis	78 (75)	58 (74)
Length of hospital stay (d)	7 (6, 11)	8 (5, 12)
New diagnosis of malignancy after colectomy	32 (30.8)	26 (33.4)
Colorectal cancer	19 (18.3)	13 (16.7)
Other malignancy	13 (12.5)	13 (16.7)
Pathological findings		
Colonic inflammation	62 (60)	45 (57.7)
Presence of colonic dysplasia	24 (23)	21 (27)
Colon cancer	19 (18.3)	12 (15.4)
Post-operative general complications within 1 mo	36 (34.6)	34 (43.6)
Post-operative liver complications within 1 mo	9 (8.7)[2]	9 (11.5)
Results of follow-up		
All-cause mortality	13 (12.5)	13 (16.7)
Liver transplantation	13 (12.5)	13 (16.7)
Continued follow-up	52 (50)	52 (66.6)
Lost to follow-up	13 (25.0)	-

[1]Median (interquartile range; IQR) or n (%); [2]Including worsening liver tests (n = 3), liver failure requiring liver transplantation (n = 2), acute cholangitis (n = 3) and right hepatic vein thrombosis with hepatic infarct (n = 1). BMI: Body mass index; ALT: Alanine transaminase; AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; CA 19-9: Cancer antigen 19-9.

requiring re-exploration (n = 4; 3.8%), bowel ileus (n = 4; 3.8%), high ileostomy output (n = 3; 2.8%), wound infection or delayed wound healing (n = 3; 2.8%) and other complications (n = 8; 7.7%) including urinary retention (n = 3), fever with unknown causes (n = 2), acute pancreatitis (n = 1), abdominal pain with unknown causes (n = 1) and portal vein thrombosis (n = 1).

By the end of the follow-up of patients with PSC and UC who underwent colectomy, 13 patients developed colorectal cancer (15%) and 13 patients (16.7%) were diagnosed with other malignancies. The primary location of the malignancies were cholangiocarcinoma (n = 6), hematologic malignancy (n = 4), gallbladder cancer (n = 1), hepatocellular carcinoma (n = 1) and intradural extramedullary spinal cord tumor (n = 1). Colonic dysplasia was found in 21 patients (21.2%) including low-grade dysplasia in 16 and high grade dysplasia in 5.

Predictors for primary endpoints (death or undergoing liver transplantation)

Table 3 shows the comparison of clinical characteristics of the 78 PSC patients with UC who underwent colectomy based on the presence of primary endpoints. Table 4 shows the results of 3 models from the multivariate analysis to identify the best-fit model for predictors of primary endpoints. Model 1 was the best-fit model, which found that only a higher platelet count and higher albumin level preoperatively were significantly associated with fewer primary endpoints (OR = 0.99 and 0.05, respectively; P < 0.05). Using the ROC curves for the detection of primary endpoints, we found that a preoperative platelet count of 194 × 10^9/L was the best cutoff value based on a sensitivity of 46%, a specificity of 88.5%, a positive predictive value (PPV) of 66.7%, and an negative predictive value (NPV) of 76.7% with an AUC of 0.67. The best cutoff value of the preoperative albumin level for the presence of primary endpoints was 3.7 g/dL with a sensitivity of 73%, a specificity of 82%, a PPV of 70%, an NPV of 84%, and an AUC of 0.80.

Figure 2 shows the survival curve of the 104 patients with PSC and UC who underwent colectomy. The smooth line represents median survival estimates calculated from the Mayo risk scores at baseline, and the stepped line corresponds to survival per the Kaplan-Meier method. The two survival curves were found to significantly differ over this time period (P = 0.01) which indicated that PSC patients with UC who underwent colectomy died or required liver transplantation more often than those PSC patients with UC who had no colectomy regarding to the same baseline calculated Mayo risk scores.

DISCUSSION

Our study indicates that one third of PSC patients with UC who underwent colectomy died or required liver transplantation within an average interval of 2.6 years. This result was similar to a previous study from the Cleveland Clinic showing that 38% of cirrhotic patients with PSC who underwent colectomy experienced early

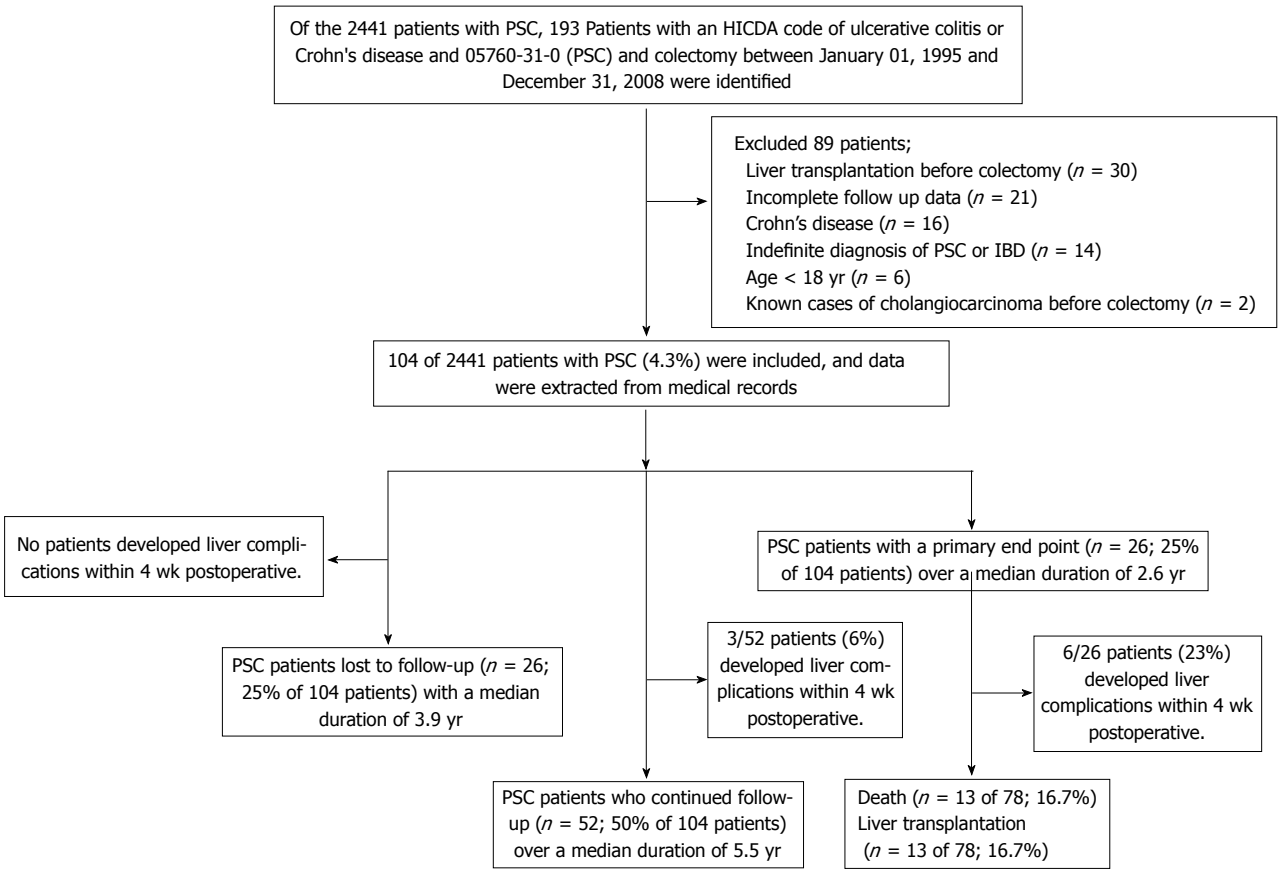

Figure 1 Outcomes of 104 patients with primary sclerosing cholangitis and ulcerative colitis who underwent colectomy. IBD: Inflammatory bowel disease; PSC: Primary sclerosing cholangitis; HICDA: Hospital international classification of disease adaptation.

Table 2 Nine patients with primary sclerosing cholangitis and ulcerative colitis who underwent colectomy had worsening liver tests postoperatively

Case, Sex	Age at colectomy (yr)	Presence of advanced liver fibrosis	Pathological findings in the colon	Blood loss requiring transfusion	Liver complications	Other complications	Length of stay (d)	Presence of primary endpoints	Duration of follow up (yr)
1, M	28	Yes	Moderate inflammation	No	Worsening liver tests	Abdominal pain, Dehydration	18	No	8.5
2, M	28	Yes	Transverse colon cancer grade 3/4 T3N2	Yes; 2 units	Worsening liver tests	High ileostomy output	15	Death; colon cancer metastasis to liver	1.2
3, F	52	Yes	Mild inflammation	No	Worsening liver tests	Delayed wound healing, Blood loss	8	Death; liver failure	0.3
4, M	32	No	Moderate inflammation	No	Acute cholangitis	None	9	Liver transplant	1.1
5, M	33	Yes	Moderate inflammation	No	Acute cholangitis	None	6	No	8.3
6, F	54	No	Mild inflammation	Yes; 6 units	Liver failure	Severe blood loss, shock	8	Liver transplant; liver failure	0.3
7, F	21	Yes	Necrotized distal ileum with perforation	Yes; 9 units	Liver failure	DIC, Respiratory failure, GI-bleeding	30	Death; liver failure	0.03 (12 d)
8, F	21	No	Moderate inflammation	Yes; 2 units	SMV and hepatic vein thrombosis	Anemia,	15	Death; liver failure	8
9, M	41	No	Moderate inflammation	No	Acute cholangitis	Wound infection	10	No	3.6

M: Male; F: Female; DIC: Disseminated intravascular coagulation; HCC: Hepatocellular carcinoma; SMV: Superior mesenteric vein.

Table 3 A comparison of the clinical characteristics of 78 patients with primary sclerosing cholangitis and ulcerative colitis who underwent colectomy categorized by the presence or absence of primary endpoints

Clinical characteristics[1]	Without primary endpoints (n = 52)	With primary endpoints (n = 26)	P value[2]
Gender, %female	11 (21)	11 (42)	0.05[2]
Age at colectomy (yr)	38.7 (27.8, 51.6)	45.8 (29.4, 52)	0.40
Presence of advanced liver fibrosis	12 (23)	12 (46)	0.03[2]
Pre-operative Mayo risk score	-0.1 (-0.9, 0.9)	1.3 (-0.2, 2.2)	0.01[2]
Pre-operative MELD score	7 (6, 9)	14 (11, 18)	< 0.001[2]
History of anemia or blood loss requiring a post-operative blood transfusion within 1 mo	4 (7.7)	7 (27)	0.02[2]
Post-operative liver complications within 1 mo	3 (5.8)	6 (23)	0.02[2]
Length of hospital stay (d)	7 (5, 10)	9 (7, 15)	0.07
Hemoglobin (g/dL)	13.1 (11.9, 14.4)	10.8 (9.8, 13.1)	< 0.001[2]
Platelet count (× 10^9/L)	296 (247, 357)	244 (126, 337)	0.02[2]
INR	0.9 (0.9, 1.0)	1.1 (1.1, 1.3)	< 0.001[2]
Total bilirubin (mg/dL)	0.7 (0.5, 1.3)	2.3 (0.6, 5.0)	0.001[2]
Direct bilirubin (mg/dL)	0.2 (0.1, 0.4)	0.9 (0.2, 3.5)	0.002[2]
ALP (U/L)	352 (180, 494)	709 (276, 1232)	0.003[2]
AST (U/L)	44 (31, 90)	80 (36, 129)	0.09
Albumin (g/dL)	4.1 (3.4, 4.3)	3.5 (3.3, 3.9)	< 0.001[2]
Duration of follow up from colectomy to the last follow-up (yr)	5.5 (3.8, 8.8)	2.6 (0.8, 5.6)	0.007[2]

[1]Median [interquartile range (IQR)] or n (%); [2]P value < 0.05 for primary sclerosing cholangitis patients with or without primary endpoints and those variables with a P value < 0.1 in a univariate analysis were included in the multivariate analysis. AST: Aspartate aminotransferase; ALP: Alkaline phosphatase; MELD: Model for End-Stage Liver Disease.

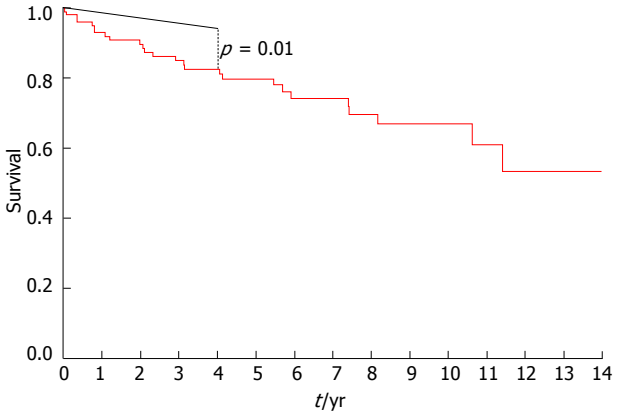

Figure 2 The survival curves of 104 patients with primary sclerosing cholangitis and ulcerative colitis undergoing colectomy. The smooth line represents the median survival estimate calculated from the Mayo risk scores at baseline, and the stepped line corresponds to survival calculated using the Kaplan-Meier method. The two survival curves were found to significantly differ over this time period (P = 0.01) which indicated that primary sclerosing cholangitis (PSC) patients with ulcerative colitis who underwent colectomy died or required liver transplantation more often than those PSC patient with ulcerative colitis who had no colectomy regarding to the same baseline calculated Mayo risk scores.

postoperative death compared to 0% of non-cirrhotic patients[14]. However, the previous study was limited by the small number of included patients with PSC who underwent colectomy (n = 24) and the need for a preoperative diagnosis of cirrhosis. The present study builds on previous reports from our center regarding the risk of colectomy in patients with PSC and UC[15,16].

However, three previous studies reported that proctocolectomy had little effect on the progression of liver disease in patients with PSC and UC and there was no significant difference in the survival of patients undergoing colectomy compared to unoperated patients[17-20]. A study from England showed that PSC patients who underwent colectomy prior to or concurrent with liver transplantation (n = 17) had a mortality rate of 12%, and they concluded that colectomy was a relatively safe procedure and believed that considering colectomy pre-, during, or shortly after liver transplantation in selected patients with risk factors for colorectal cancer would reduce the risk of colorectal cancer[19]. The low colectomy rate of 4% in our study might reflect the usually quiescent colitis in PSC. The majority of our patients were the large duct PSC which might have an impact on the poorer outcome from liver complications[9,21,22]. Recently, the outcomes after elective colectomy in patients with cirrhosis were examined and showed that cirrhotic patients undergoing colectomy had a 3.7-fold increased risk of death (HR of 3.7; 95%CI: 2.6-5.2)[23]. The in-hospital mortality (6%), length of stay (9 d), and total expenses of cirrhotic patients were significantly higher than for those without cirrhosis[23,24].

Our results showed that a lower platelet count and lower albumin level preoperatively were associated with poorer outcomes. Thus, using simple preoperative blood test screening may provide useful information for monitoring patients pre-operatively. The timing of colectomy is an important issue. Recently, a study from Italy[20] showed that eight of 16 patients with PSC and UC post-liver transplantation had active colitis despite immunosuppressive medications with a median interval from liver transplantation to colectomy of 6.5 years. Few studies showed that the colitis condition in PSC patients with UC remained inactive or under controlled of at least 60% of cases after orthotopic liver transplantation[25,26]. Another studied revealed that liver transplantation for PSC independently reduced the need for colectomy (HR = 0.43; 95%CI: 0.25-0.75; P = 0.003)[11] Additionally, the presence of colon carcinoma and high grade dysplasia were more frequent in the non liver transplantation group and this group of patient had increased inflammation of the colonic mucosa at histology (P = 0.011)[10]. Thus, the patients with severe progressive PSC requiring liver transplantation should proceeded for supportive care of colitis and listed for liver transplantation which might reduced the disease activity of UC and the need for colectomy[10,11].

About 17% of our PSC patients with UC developed colorectal cancer, which was similar to a previous report from England showing that the cumulative risks of developing colorectal cancer in patients with an intact colon and IBD were 14% and 17% after 5 and 10 years, respec-

Table 4 Multivariate analysis models showing the association between primary sclerosing cholangitis patients with ulcerative colitis who underwent colectomy and the primary endpoints

Multivariate analysis	*P* value	OR	95%CI
Model 1[1]			
Platelet (× 10^9/L)	0.030	0.991	0.98-0.999
Albumin (g/dL)	0.006	0.05	0.007-0.44
Model 2[2]			
Pre-operative Mayo risk score	0.390	1.2	0.77-1.97
Hemoglobin (g/dL)	0.010	0.6	0.45-0.91
Model 3[3]			
Pre-operative MELD score	0.090	18.6	0.6-567
Hemoglobin (g/dL)	0.090	0.03	0.001-1.9

[1]Model 1, to avoid overestimation of the model, we excluded the Mayo risk score and the Model for End-Stage Liver Disease (MELD) score from model 1; [2]Model 2, we included the Mayo risk score in the model and removed the individual variables used for Mayo risk score calculation; [3]Model 3, we included the MELD score in the model and removed the individual variables used for MELD score calculation. $P < 0.05$, all variables with $P < 0.1$ in a univariate analysis were included in the multivariate analysis models.

tively[19]. Recent study showed that the colonic neoplasms that developed in PSC-UC patients were spread throughout the colon on colonoscopy and they were found predominantly on right sided colon[5]. Thus, surveillance colonoscopy and biopsies should be performed in patients with PSC and UC at 1-year to 2-year intervals[3].

The main strengths of our study are the inclusion of a large number of PSC patients with PSC and UC and the available clinical data and pathological findings, which were useful for outcome assessment. However, our study is limited by its retrospective nature in a tertiary center, and it contains data derived from multiple physicians from 1995 to 2008, which may have resulted in a selection bias. Additionally, surgeons excluded the colectomy procedure for all patients with poor liver conditions. Second, we included all PSC patients who underwent colectomy and had results from preoperative liver tests and at least one post-operative test, which may explain the small number of patients with liver complications. Thus, further multicenter prospective studies of post-operative liver complications and poor outcomes in patients with PSC and UC undergoing colectomy should be performed to provide clearer guidance for the selection of patients to be referred for a liver transplantation and colectomy rather than colectomy alone.

Unfortunately, we had to exclude a number of patients (10%) who had incomplete data because they were lost to follow-up. Additionally, the Mayo risk score and MELD score could not be calculated annually from our retrospective data therefore the colectomy might changed the progression of the PSC severity which cannot be concluded. Last, we had only a small number of patients with liver complications, and we can therefore not draw a firm conclusion regarding the association between liver complications and poor outcomes.

In conclusion, one third of PSC patients with UC who underwent colectomy died or underwent liver transplantation within an average interval of 2.6 years. PSC patients with advanced liver fibrosis (lower platelet count and lower albumin level) and UC who underwent colectomy were associated with significantly poorer outcomes.

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COMMENTS

Background

The colitis associated with primary sclerosing cholangitis (PSC) has unique findings and is usually extensive. Ulcerative colitis (UC) in patients with PSC is associated with an increased risk of colorectal neoplasia compared to patients with UC alone. Previous studies have shown that patients with liver cirrhosis can experience worsening of their liver disease after surgery and poor outcomes. Surgery may lead to severe complications such as decompensated liver disease, worsening of a pre-existing decompensation or even death. Very limited information exists on the prognosis of patients with PSC and UC undergoing colectomy.

Research frontiers

Authors aimed to assess the outcomes and predictors of outcomes of PSC patients undergoing colectomy at the Mayo Clinic, Rochester, MN, United States.

Innovations and breakthroughs

One third of patients with PSC and UC undergoing colectomy died or underwent liver transplantation within 2.6 years. PSC patients with lower platelet counts and lower albumin levels were significantly more likely to have a poorer outcome.

Applications

PSC patients with UC who underwent colectomy died or required liver transplantation more often than those PSC patients with UC who had no colectomy regarding to the same baseline calculated Mayo risk scores.

Terminology

The primary endpoint was defined as the presence of all-cause mortality and/or liver decompensation requiring liver transplantation and it has been measured at 1 mo and at the end of follow-up. All causes of death listed on the death certificates or pathological findings (underlying, intermediate, immediate and other major conditions) were recorded using the International Classification of Diseases-10 revision. The secondary end point was defined as the presence of liver complications post-operatively occurred within 1 mo which included ascites, variceal bleeding, clinical hepatic encephalopathy or liver failure and required hospitalization To concisely and accurately describe, define or explain the specific, unique terms that are not familiar to majority of the readers, but are essential for the readers to understand the article.

Peer review

Few studies showed that the colitis condition in PSC patients with UC remained inactive or under controlled of at least 60% of cases after orthotopic liver transplantation. Another studied revealed that liver transplantation for PSC independently reduced the need for colectomy. Additionally, the presence of colon carcinoma and high grade dysplasia were more frequent in the non liver transplantation group and this group of patient had increased inflammation of the colonic mucosa at histology. Thus, the patients with severe progressive PSC requiring liver transplantation should proceeded for supportive care of colitis and listed for liver transplantation which might reduced the disease activity of UC and the need for colectomy.

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