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Prevalence and Outcomes of Primary Sclerosing Cholangitis in Inflammatory Bowel Disease: A Multinational Study Across Asia

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Abbreviations used in this paper: **ALP, alkaline phosphatase; AOCC, Asian Organization for Crohn's and Colitis; CCA, cholangiocarcinoma; CD, Crohn's disease; CI, confidence interval; ERCP, endoscopic retrograde cholangiopancreatography; HR, hazard ratio; IBD, inflammatory bowel disease; IQR, interquartile range; IRB, Institutional Review Board; KM, Kaplan-Meier; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; MRCP, magnetic resonance cholangiopancreatography; PSC, primary sclerosing cholangitis; SE, standard error; UC, ulcerative colitis; UCAN, ulcerative colitis-associated neoplasia.**

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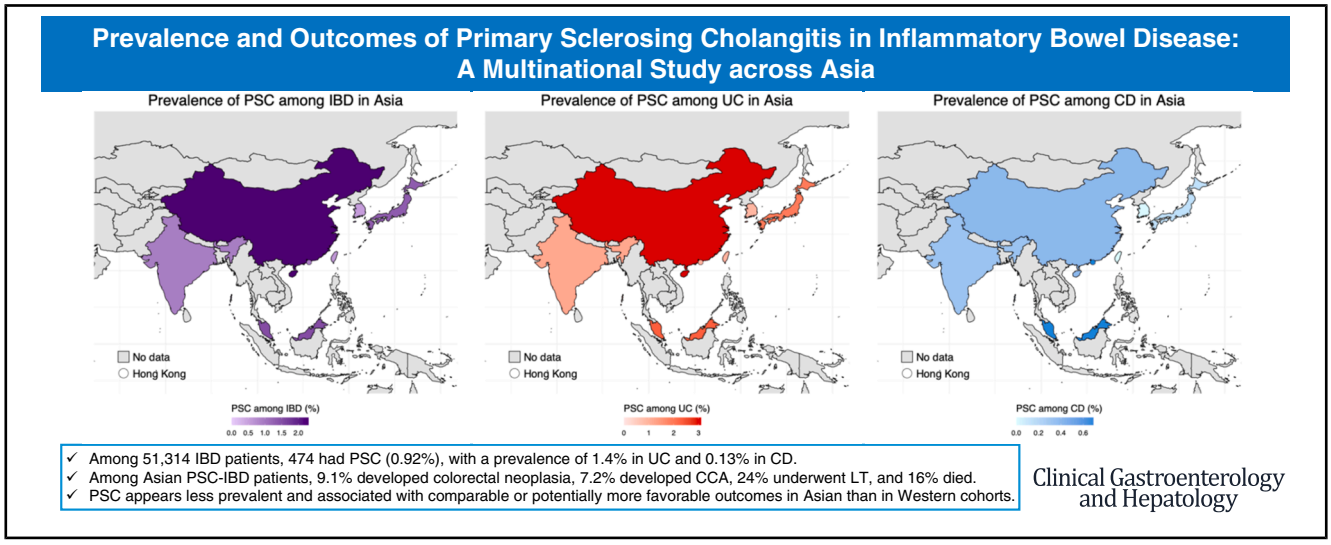

BACKGROUND & AIMS: **Primary sclerosing cholangitis (PSC) frequently coexists with inflammatory bowel disease (IBD). PSC is a progressive disease that may lead to end-stage liver failure requiring liver transplantation (LT). Although PSC-IBD has been extensively studied in Western populations, data from Asia remain limited. We conducted an international multicenter study across Asia to investigate the prevalence of PSC in IBD patients and evaluate its impact on clinical outcomes.**

METHODS: **This retrospective cohort study included patients with IBD from 25 hospitals in 6 Asian countries. The primary endpoint was the prevalence of PSC in patients with IBD. The secondary endpoints included the incidence of colorectal neoplasia and IBD-related surgery following IBD diagnosis, and the occurrence of cholangiocarcinoma, LT, and death after PSC diagnosis among patients with PSC-IBD. Temporal trends were assessed across 5 diagnostic eras of PSC.**

RESULTS: **Among 51,314 patients with IBD, 474 had PSC (0.92%), with a prevalence of 1.4% in ulcerative colitis and 0.13% in Crohn's disease. Among 375 Asian patients with PSC-IBD, 9.1% developed colorectal neoplasia, 7.2% developed cholangiocarcinoma, 24% underwent LT, and 16% died. In more recent diagnostic eras, patients presented with fewer symptoms, lower alkaline phosphatase levels, and better liver function scores. The use of magnetic resonance cholangiopancreatography has increased over time. Symptomatic PSC and low serum albumin were significantly associated with a shorter time to LT, which was significantly longer in recent eras ($P = .016$).**

CONCLUSIONS: **PSC is less prevalent among Asian patients with IBD than in Western populations. The increased use of magnetic resonance cholangiopancreatography may enable earlier detection, contributing to milder disease severity and improved clinical outcomes in recent years. umin.ac.jp, Number UMIN000054487.**

Keywords: Asia; Epidemiology; Inflammatory Bowel Disease; Primary Sclerosing Cholangitis.

Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), is an immune-mediated inflammatory disease of the gastrointestinal tract.[1] Approximately one-third of patients with IBD develop extraintestinal manifestations involving other organs.[2] Primary sclerosing cholangitis (PSC) is a chronic and progressive cholestatic disease affecting the intra- and/or extrahepatic bile ducts, often characterized by the formation of concentric fibrotic layers—referred to as an "onion skin" pattern—surrounding the cholangiocyte lining.[3] The natural course of PSC is typically progressive, evolving from biliary fibrosis to liver cirrhosis and, ultimately, end-stage liver disease that often necessitates liver transplantation (LT).[3]

PSC frequently coexists with IBD, and its pathogenesis is thought to involve genetic susceptibility, impaired bile acid homeostasis, and gut microbiota dysbiosis.[4] A systematic review and meta-analysis estimated the pooled prevalence of PSC to be 2.16% among patients with IBD, with 2.47% in those with UC and 0.96% in those with CD.

Notably, the prevalence in Southeast Asia was particularly low—0.60% in IBD, 0.67% in UC, and 0.16% in CD.[5] Consistently, retrospective cohort studies from India,[6] Korea,[7] Taiwan,[8] and Japan[9] have reported a substantially lower prevalence of PSC among patients with IBD in Asia than in Western countries, highlighting potential geographic and clinical differences in the PSC-IBD phenotype.

Patients with PSC-IBD exhibit distinct disease phenotypes and clinical courses. For instance, they frequently present with endoscopic findings such as rectal sparing, backwash ileitis, and right-sided colitis.[10] Furthermore, the risks of colorectal neoplasia, cholangiocarcinoma (CCA), and all-cause mortality are significantly higher in patients with PSC-IBD than in those with IBD alone.[11–13] To improve survival outcomes and guide timely LT, several prognostic scoring systems, including the Child-Pugh Score,[14] Model for End-Stage Liver Disease (MELD) score,[15] and revised Mayo Risk Score for PSC,[16] have been developed to estimate LT-free survival and mortality risk in patients with PSC.

However, most studies on PSC-IBD have been conducted in Western countries,[5] whereas research on Asian populations—particularly in East Asia—remains limited. To improve clinical outcomes and establish region-specific guidelines, a deeper understanding of the epidemiology and clinical characteristics of PSC-IBD in Asian patients is essential. Therefore, we conducted an international multicenter study to investigate the prevalence of PSC among patients with IBD across Asia and to assess its impact on clinical outcomes in patients with PSC-IBD.

What You Need to Know

Background

Primary sclerosing cholangitis (PSC) is a progressive liver disease that frequently coexists with inflammatory bowel disease (IBD), yet large-scale data from Asian populations have been limited.

Findings

This multinational study is the first to characterize PSC-IBD across Asia, identifying a lower prevalence of PSC among patients with IBD (0.92%) and potentially more favorable clinical outcomes compared with Western populations.

Implications for patient care

Our findings support surveillance using magnetic resonance cholangiopancreatography in IBD, as early PSC detection may delay disease progression and improve outcomes, highlighting the need for region-specific, evidence-based PSC-IBD management.

Methods

The Epidemiology Committee of the Asian Organization for Crohn's and Colitis (AOCC) distributed a notice regarding this study to all AOCC members. Prevalence and individual-level data were collected from all participating institutions, each of which obtained ethical approval for this study from their respective Institutional Review Boards (IRB) (Supplementary Table 1). In accordance with institutional ethical policies in mainland China, individual-level data were not shared. Instead, aggregated prevalence data were used, based on their own IRB-approved studies reported as abstracts at AOCC2025 (Abstract Numbers O05-05, PO-055, and PE-124). The study was conducted in accordance with the Declaration of Helsinki. Because the research involved a retrospective analysis of existing clinical data without the collection of new samples, the ethics committees approved the use of an opt-out consent approach and waived the requirement for written informed consent. This study was registered with the University Hospital Medical Information Network (UMIN) Center (UMIN000054487).

The primary endpoint was the prevalence of PSC among patients with IBD in participating Asian hospitals. The diagnosis of PSC was based on biochemical evidence of cholestasis (eg, elevated alkaline phosphatase [ALP]) and cholangiographic findings of strictures and/or ectasias in the intrahepatic and/or extrahepatic bile ducts.[3,17]

The secondary endpoints included the incidence of colorectal neoplasia and IBD-related surgery (eg, total colectomy or other types of intestinal resection for IBD) after IBD diagnosis, as well as the occurrence of CCA, LT, and death following PSC diagnosis in patients with PSC-IBD. The inclusion criteria for this analysis were Asian patients with PSC-IBD aged $\geq$16 years with an available dataset. Colorectal neoplasia was defined as any dysplasia or carcinoma arising from an area with current or prior mucosal inflammation due to IBD, or exhibiting pathological features suggestive of IBD-associated neoplasia. Sporadic neoplasia, defined as neoplasia arising from areas without any evidence of current or past inflammation or explicitly described as sporadic in the pathology report, was excluded.[18] To evaluate the characteristics of IBD or PSC by year of diagnosis, the diagnostic era was categorized into 5 periods: Era 1 (before July 1, 2005) and 4 subsequent 5-year intervals, with Era 5 (July 1, 2020, to June 30, 2025) representing the most recent period.

We conducted a retrospective chart review using medical records, and the following variables were included in our datasheet: dates of birth and diagnosis of IBD and PSC, sex, race, country, most recent body mass index, history of smoking and alcohol use, family history of IBD, liver biopsy results, and current or past use of medications for IBD and PSC. The IBD phenotype based on the Montreal Classification,[19] endoscopic phenotypes (eg, rectal sparing, right-sided colitis, and backwash ileitis),[10] PSC disease location, presence of cirrhosis, and

extraintestinal manifestations (eg, arthritis, uveitis, pyoderma gangrenosum, and erythema nodosum), were determined based on representative findings over the clinical course. The following variables were assessed based on data obtained at the time of PSC diagnosis: liver function tests and components used in established prognostic scoring systems (eg, Child-Pugh Score,[14] MELD,[15] and revised Mayo Risk Score for PSC[16]), kidney function, PSC-related symptoms (eg, abdominal pain, fever, and jaundice), and imaging modalities used for PSC diagnosis.

Data were analyzed using standard statistical methods. Continuous variables are presented as medians with interquartile ranges (IQRs), and group comparisons were conducted using the Kruskal-Wallis or χ^2 test, as appropriate. Kaplan-Meier (KM) curves were constructed from the date of PSC diagnosis to the date of each outcome, and survival estimates were compared using the log-rank test. Data were censored at the date of the patient's last follow-up. Multivariate analysis for the risk of CCA, LT, or death was performed using the Cox proportional hazards model, including variables identified in the univariate analysis ($P < .10$), with preference given to those with the smallest P values and minimal correlation between covariates. Established prognostic scoring systems were not included in the model to avoid redundancy in their component variables. To assess the robustness of the findings, 2 sensitivity analyses were performed using the same set of covariates: (1) a Cox model with cluster-robust standard errors (SEs) by country to account for potential heterogeneity across sites, and (2) a Fine-Gray competing risk model to estimate subdistribution hazard ratios (HRs), considering CCA, LT, and death as competing events.

All statistical analyses were performed using R software (version 4.2.1). Cox models were fitted using the coxph function from the survival package, with country-level clustering specified through the cluster option. KM curves were plotted using the survminer package, and the Fine-Gray competing risk model was implemented with the crr function from the cmprsk package.

Results

Prevalence of PSC Among Patients With IBD in Asian Hospitals

We evaluated the data from 25 hospitals across 6 countries in Asia. Among 51,314 patients with IBD, 474 cases of PSC were identified, yielding an overall prevalence of 0.92%. The highest prevalence was observed in Mainland China (2.3%), followed by Malaysia (1.5%) and Japan (1.3%). Among 32,617 patients with UC, 450 (1.4%) had PSC, whereas 26 (0.13%) of 19,636 patients with CD had PSC (Table 1; Supplementary Table 1; Supplementary Figure 1). Excluding one center that evaluated only patients with CD, the dataset comprising centers with complete UC and CD denominators is summarized in Supplementary Table 2. Among 51,314 patients with IBD, 474 cases of PSC were identified (450 PSC-UC and 24 PSC-CD), yielding an overall prevalence of 0.92% (1.4% in UC and 0.13% in CD).

Clinical Characteristics of IBD in Asian Patients With PSC-IBD

To evaluate the clinical characteristics of PSC-IBD in Asian patients, we included 375 eligible individuals with available clinical data for this analysis (356 with PSC-UC and 19 with PSC-CD) (Supplementary Table 1; Supplementary Figure 2). The diagnoses of PSC and IBD were made between 1979 and 2025.

The median age at IBD diagnosis was 29 years (IQR, 20–43 years), and the median disease duration of IBD, which was equivalent to the follow-up duration after IBD diagnosis, was 9 years (IQR, 5–15 years) in PSC-IBD, 8 years (IQR, 5–14 years) in PSC-UC, and 13 years (IQR, 9–20 years) in PSC-CD. The median interval between IBD and PSC diagnoses was 1.1 years (IQR, 0.1–6.0 years), with 55% of patients diagnosed with IBD before PSC and 11% diagnosed with IBD at the time of PSC diagnosis. The proportions of current smokers and alcohol drinkers were 4.8% and 9.1%, respectively. Arthritis was the most common extraintestinal manifestation (4.1%) (Table 2).

The most common indication for colonoscopy at the time of IBD diagnosis was the presence of symptoms suggestive of IBD (72% of patients). Among patients with PSC-UC, extensive colitis was dominant (93%), and the frequencies of backwash ileitis, rectal sparing, and right-sided dominant colitis were 26%, 35%, and 38%, respectively. Among patients with PSC-CD, ileocolonic involvement was the most common (50%), with stricturing and penetrating phenotypes observed in 42% and 26% of patients, respectively. Exposure to advanced therapies was documented in 20% of the overall cohort (19% for PSC-UC and 42% for PSC-CD) (Table 2; Supplementary Table 3).

Analysis by diagnostic era revealed that the age at IBD diagnosis significantly increased over time, whereas the interval between IBD and PSC diagnoses became shorter. In terms of the indication for colonoscopy at the time of IBD diagnosis, the proportion of cases undergoing screening colonoscopy due to PSC diagnosis significantly increased from Era 1 (5.6%) to Era 5 (37%) (Supplementary Table 4).

Clinical Characteristics of PSC in Asian Patients With PSC-IBD

The median age at PSC diagnosis was 32 years (IQR, 22–44 years), and the median disease duration of PSC, which was equivalent to the follow-up duration after PSC diagnosis, was 7 years (IQR, 3–12 years) in PSC-IBD,

Table 1. Prevalence of PSC Among Patients With IBD in Asian Hospitals

Country	No. facilities	Total IBD, *n*	Total PSC, *n*	Total UC, *n*	PSC-UC, *n*	Total CD, *n*	PSC-CD, *n*	PSC among IBD, %	PSC among UC, %	PSC among CD, %
Japan	9	20,053	268	13,705	259	6348	9	1.30	1.90	0.14
Korea	6	22,513	120	13,332	118	9181	2	0.53	0.89	0.022
Mainland China	3[a]	955	22	618	19	1276	5	2.30	3.10	0.39
Hong Kong, China	3	1965	18	1214	12	751	6	0.92	0.99	0.80
Taiwan	2	3490	21	2318	21	1172	0	0.60	0.91	0.00
India	1	1747	16	1127	14	620	2	0.92	1.20	0.32
Malaysia	1	591	9	303	7	288	2	1.50	2.30	0.69
Total	25	51,314	474	32,617	450	19,636	26	0.92	1.40	0.13

CD, Crohn's disease; IBD, inflammatory bowel disease; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.
[a]One facility reported only PSC prevalence among CD (2/939); excluded from total IBD and PSC case counts.

7 years (IQR, 3–12 years) in PSC-UC, and 8 years (IQR, 2–12 years) in PSC-CD. At the time of diagnosis, the median values for ALP, albumin, and total bilirubin were 331 U/L (IQR, 162–704 U/L), 3.9 g/dL (IQR, 3.5–4.3 g/dL), and 0.80 mg/dL (IQR, 0.50–1.5 mg/dL), respectively. Forty percent of patients presented with symptoms such as abdominal pain, fever, and jaundice (ie, symptomatic PSC). The median liver function scores at PSC diagnosis were 5 (IQR, 5–6) for the Child-Pugh Score, 7 (IQR, 6–9) for the MELD score, and −0.26 (IQR, −0.94 to 0.61) for the Mayo Risk Score for PSC. During follow-up, 34% of patients developed cirrhosis (Table 3).

Magnetic resonance cholangiopancreatography (MRCP) was the most commonly used imaging modality for PSC diagnosis (76% of cases). The most prevalent disease distribution was involvement of both the intrahepatic and extrahepatic bile ducts (51%). Liver biopsy was performed in 46% of patients, and onion-skin lesions were identified in 17%. Intervention with endoscopic retrograde cholangiopancreatography (ERCP) for biliary stricture was performed in 37% of patients. At the time of the study, ursodeoxycholic acid and bezafibrate were being administered to 80% and 12% of patients, respectively (Table 3).

Analysis by diagnostic era showed that the age at PSC diagnosis significantly increased over time, whereas the interval between PSC and IBD diagnoses became shorter. Notably, the proportion of patients with symptomatic PSC was significantly lower in the more recent diagnostic eras than in the earlier eras. Serum ALP levels and liver function scores were also significantly lower in the recently diagnosed cases. There was a significant shift toward MRCP for PSC diagnosis in recent eras, whereas ERCP was more commonly used in the past (Supplementary Table 5), suggesting that the use of MRCP may facilitate the earlier detection of PSC with milder disease activity.

Clinical Endpoints of IBD and PSC in Asian Patients With PSC-IBD

Although no cases of colorectal neoplasia were observed in patients with PSC-CD, 9.6% of patients with PSC-UC developed colorectal neoplasia (UC-associated neoplasia; UCAN). KM analysis showed that the 10-year colorectal neoplasia-free survival rate after the diagnosis of IBD was 93.9% (95% confidence interval [CI], 90.8%–97.1%) (Supplementary Figure 3*A*). IBD-related surgery was performed in 12% of patients overall—10% in the PSC-UC group and 47% in the PSC-CD group. The 10-year IBD-related surgery-free survival rate following IBD diagnosis was 90.1% (95% CI, 86.4%–94.0%) (Supplementary Figure 3*B*). Among patients with PSC-UC who underwent surgery, the most common indication was UCAN (57%), and nearly 70% underwent total colectomy. In patients with PSC-CD who required surgery, one had small intestinal cancer, and nearly 70% underwent intestinal resection other than total colectomy (Table 4).

CCA developed in 7.2% of patients with PSC-IBD (n = 27), with a rate of 7.6% in PSC-UC and 0% in PSC-CD. The intrahepatic bile ducts were the most commonly involved (48%), and approximately one-half of the patients (52%) were deemed operable (Table 4). The KM curve demonstrated a 10-year CCA-free survival rate of 93.3% (95% CI, 90.0%–96.7%) following PSC diagnosis (Figure 1*A*). The time to CCA development was significantly shorter in patients diagnosed in more recent eras than in those diagnosed in earlier eras ($P = .016$) (Figure 1*B*). In the Cox proportional hazards model, older age at PSC diagnosis showed a trend toward a shorter time to CCA development ($P = .058$) (Table 5; Supplementary Table 6), whereas sensitivity analysis using cluster-robust SEs demonstrated that older age at PSC diagnosis was significantly associated with a shorter time to CCA development ($P < .001$) (Supplementary

Table 2. Clinical Characteristics of IBD in Asian Patients With PSC-IBD

Variables	N	N = 375	UC, n = 356	CD, n = 19
Sex	375			
Male		250 (67)	240 (67)	10 (53)
Female		125 (33)	116 (33)	9 (47)
Body mass index (most recent), kg/m^2	325	20.7 (18.8–23.1)	20.7 (18.8–23.1)	20.7 (20.2–22.7)
Type of IBD	375			
UC		356 (95)		
CD		19 (5.1)		
Age at IBD diagnosis, *y*	367	29 (20–43)	29 (20–43)	29 (15–36)
Disease duration of IBD, *y*	361	9 (5–15)	8 (5–14)	13 (9–20)
Interval between PSC and IBD diagnosis, *y*	363	1.1 (0.1–6.0)	1.0 (0.1–5.9)	2.2 (0.4–9.7)
Order of diagnosis	363			
PSC diagnosed before IBD		126 (35)	124 (36)	2 (11)
IBD diagnosed before PSC		198 (55)	182 (53)	16 (84)
IBD diagnosed at PSC diagnosis		39 (11)	38 (11)	1 (5.3)
Smoking	354			
Never		294 (83)	278 (83)	16 (84)
Former		43 (12)	41 (12)	2 (11)
Current		17 (4.8)	16 (4.8)	1 (5.3)
Alcohol	340			
Never		264 (78)	251 (78)	13 (76)
Former		45 (13)	43 (13)	2 (12)
Current		31 (9.1)	29 (9.0)	2 (12)
Family history of IBD	327	11 (3.4)	11 (3.6)	0 (0)
Extraintestinal manifestation	370			
Arthritis		15 (4.1)	13 (3.7)	2 (11)
Uveitis		0 (0)	0 (0)	0 (0)
Erythema nodosum		9 (2.4)	9 (2.6)	0 (0)
Pyoderma gangrenosum		1 (0.3)	1 (0.3)	0 (0)
Indication for colonoscopy at the diagnosis of IBD	327			
Symptoms suggestive of IBD		235 (72)	221 (71)	14 (93)
Screening colonoscopy (due to PSC diagnosis)		80 (24)	79 (25)	1 (6.7)
Others		12 (3.7)	12 (3.8)	0 (0)
Disease extent (UC)	333			
Proctitis		7 (2.1)	7 (2.1)	NA
Left-sided colitis		16 (4.8)	16 (4.8)	NA
Extensive colitis		310 (93)	310 (93)	NA
Backwash ileitis (UC)	318	82 (26)	82 (26)	NA
Rectal sparing (UC)	319	111 (35)	111 (35)	NA
Right-sided colitis (UC)	329	124 (38)	124 (38)	NA
Disease location (CD)	18			
Ileal disease		4 (22)	NA	4 (22)
Colonic disease		5 (28)	NA	5 (28)
Ileocolonic disease		9 (50)	NA	9 (50)
Isolated upper disease (CD)	18	2 (11)	NA	2 (11)
Stricturing disease (CD)	19	8 (42)	NA	8 (42)
Penetrating disease (CD)	19	5 (26)	NA	5 (26)
Perianal disease (CD)	19	5 (26)	NA	5 (26)
Biologic/Janus kinase inhibitor exposure	372	74 (20)	66 (19)	8 (42)

NOTE. Data are presented as number (%) or median (interquartile range).
CD, Crohn's disease; IBD, inflammatory bowel disease; NA, not applicable; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.

Table 3. Clinical Characteristics of PSC in Asian Patients With PSC-IBD

Variables	N	N = 375	UC, n = 356	CD, n = 19
Age at PSC diagnosis, *y*	366	32 (22–44)	32 (22–44)	33 (23–51)
Disease duration of PSC, *y*	360	7 (3–12)	7 (3–12)	8 (2–12)
AST, *U/L*	283	51 (28–98)	51 (29–99)	34 (24–52)
ALT, *U/L*	296	60 (29–129)	61 (30–130)	23 (13–77)
ALP, *U/L*	296	331 (162–704)	346 (170–710)	174 (90–332)
Total bilirubin, *mg/dL*	293	0.80 (0.50–1.50)	0.80 (0.50–1.50)	0.70 (0.46–1.81)
γ-GT, *U/L*	281	239 (91–428)	239 (91–430)	165 (80–376)
CRP, *mg/dL*	264	0.36 (0.10–1.27)	0.34 (0.10–1.24)	0.51 (0.25–1.23)
Albumin, *g/dL*	292	3.90 (3.50–4.30)	3.90 (3.50–4.30)	4.00 (3.50–4.50)
PT-INR	241	1.01 (0.96–1.08)	1.01 (0.96–1.08)	0.95 (0.90–1.14)
Creatinine at the diagnosis of PSC, *mg/dL*	286	0.74 (0.60–0.84)	0.74 (0.60–0.84)	0.74 (0.59–0.87)
PSC-related symptoms at the diagnosis of PSC	337			
Asymptomatic PSC		202 (60)	189 (59)	13 (72)
Symptomatic PSC		135 (40)	130 (41)	5 (28)
Coma at the diagnosis of PSC	337	2 (0.6)	2 (0.6)	0 (0)
Ascites at the diagnosis of PSC	309	9 (2.9)	9 (3.1)	0 (0)
Variceal bleeding history at the diagnosis of PSC	336	4 (1.2)	4 (1.3)	0 (0)
MELD score	239	7 (6–9)	7 (6–9)	7.5 (6–10.5)
Mayo risk score for PSC	275	−0.26 (−0.94 to 0.61)	−0.26 (−0.92 to 0.61)	−0.51 (−1.58 to 0.13)
Child-Pugh score	228	5 (5–6)	5 (5–6)	6 (5–6)
Child-Pugh classification	228			
Class A		181 (79)	175 (80)	6 (75)
Class B		43 (19)	42 (19)	1 (13)
Class C		4 (1.8)	3 (1.4)	1 (13)
PSC imaging at the diagnosis of PSC	332			
MRCP		173 (52)	164 (52)	9 (53)
ERCP		68 (20)	63 (20)	5 (29)
Both MRCP and ERCP		80 (24)	78 (25)	2 (12)
Others		11 (3.3)	10 (3.2)	1 (5.9)
PSC disease location	358			
Intrahepatic bile ducts		148 (41)	138 (41)	10 (56)
Extrahepatic bile ducts		26 (7.3)	24 (7.1)	2 (11)
Both		184 (51)	178 (52)	6 (33)
Intervention with ERCP for biliary stricture	375	138 (37)	133 (37)	5 (26)
Liver biopsy	325	148 (46)	140 (45)	8 (47)
Onion skin lesion on liver biopsy	148	25 (17)	23 (16)	2 (25)
Ursodeoxycholic acid	364			
Current		290 (80)	281 (81)	9 (47)
None		35 (9.6)	29 (8.4)	6 (32)
Past		39 (11)	35 (10)	4 (21)
Bezafibrate	366			
Current		45 (12)	45 (13)	0 (0)
None		302 (83)	284 (82)	18 (95)
Past		19 (5.2)	18 (5.2)	1 (5.3)
Cirrhosis	351	118 (34)	113 (33)	5 (38)

NOTE. Data are presented as number (%) or median (interquartile range). Liver function parameters at PSC diagnosis.
ALT, alanine aminotransferase; ALP, alkaline phosphatase; AST, aspartate aminotransferase; CD, Crohn's disease; CRP, C-reactive protein; ERCP, Endoscopic retrograde cholangiopancreatography; γ-GT, gamma-glutamyl transferase; IBD, inflammatory bowel disease; MELD, Model for End-stage Liver Disease; MRCP, magnetic resonance cholangiopancreatography; PSC, primary sclerosing cholangitis; PT-INR, prothrombin time/international normalized ratio; UC, ulcerative colitis.

Table 4. Clinical Outcomes of IBD and PSC in Asian Patients With PSC-IBD

Variables	N	N = 375	UC, n = 356	CD, n = 19
IBD outcomes				
Colorectal neoplasia	375	34 (9.1)	34 (9.6)	0 (0)
Surgery for IBD	375	46 (12)	37 (10)	9 (47)
Indication for IBD surgery	46			
Cancer/dysplasia		22 (48)	21 (57)	1 (11)
Others		24 (52)	16 (43)	8 (89)
Surgery type for IBD	46			
Total colectomy		27 (59)	25 (68)	2 (22)
Intestinal resection excluding total colectomy		16 (35)	10 (27)	6 (67)
Others		3 (6.5)	2 (5.4)	1 (11)
PSC outcomes				
Cholangiocarcinoma	375	27 (7.2)	27 (7.6)	0 (0)
Type of cholangiocarcinoma	27			
Intrahepatic bile duct cancer		12 (44)	12 (44)	NA
Perihilar bile duct cancer		8 (30)	8 (30)	NA
Distal extrahepatic bile duct cancer		3 (11)	3 (11)	NA
Gallbladder cancer		2 (7.4)	2 (7.4)	NA
Intrahepatic bile duct cancer and gallbladder cancer		1 (3.7)	1 (3.7)	NA
Perihilar bile duct cancer and gallbladder cancer		1 (3.7)	1 (3.7)	NA
Stage of cholangiocarcinoma at the diagnosis	27			
Operable		14 (52)	14 (52)	NA
Inoperable		13 (48)	13 (48)	NA
Surgery for PSC	372	106 (28)	103 (29)	3 (16)
Indication for PSC surgery	104			
Cancer/cancer suspected		15 (14)	15 (15)	0 (0)
Others (eg, cirrhosis or cholecystitis)		89 (86)	86 (85)	3 (100)
Liver transplantation	373	88 (24)	86 (24)	2 (11)
Donor	85			
Deceased donor		18 (21)	18 (22)	0 (0)
Living donor		67 (79)	65 (78)	2 (100)
Immunosuppressive therapies after liver transplantation	88	84 (95)	83 (97)	1 (50)
Death	363	59 (16)	55 (16)	4 (21)
Cause of death	56			
Colorectal cancer		3 (5.4)	2 (3.8)	1 (25)
Cholangiocarcinoma		10 (18)	10 (19)	0 (0)
Cirrhosis		26 (46)	25 (48)	1 (25)
Others		17 (30)	15 (29)	2 (50)

NOTE. Data are presented as number (%).
CD, Crohn's disease; IBD, inflammatory bowel disease; NA, not applicable; PSC, primary sclerosing cholangitis; UC, ulcerative colitis.

Table 7). In the Fine-Gray model, with LT and death treated as competing events, 24 patients who developed CCA as the first event were included in the analysis (Supplementary Table 8). The results were similar to those of the main analysis, suggesting that the increasing age at diagnosis in recent cases may have contributed to shorter CCA-free survival.

LT was performed in 24% of patients (n = 88), and 79% of them received a liver from a living donor (Table 4). After LT, almost all patients (95%) received immunosuppressants to prevent graft rejection. The 10-year LT-free survival rate after PSC diagnosis was 75.1% (95% CI, 69.4%–81.4%) (Figure 1*C*). The time to LT was significantly longer in patients diagnosed in more recent eras than in those diagnosed in earlier periods (P = .016) (Figure 1*D*). In the Cox proportional hazards model, symptomatic PSC, history of variceal bleeding, low serum albumin levels, and PSC diagnosed preceding IBD were significantly associated with a shorter time to LT (Table 5; Supplementary Table 9). Sensitivity analyses, including the Cox model with cluster-robust SEs and the Fine-Gray model that included 77 patients who experienced LT as the first event, also showed results similar to those of the main analysis (Supplementary Tables 10 and 11), suggesting that less severe disease in recent cases may lead to prolonged LT-free survival.

The overall mortality rate was 16% (n = 59), with cirrhosis being the most common cause of death (46%) (Table 4). The 10-year overall survival rate following PSC diagnosis was 87.3% (95% CI, 83.1%–91.8%) (Figure 1*E*). No significant differences were observed in the survival time across the diagnostic eras (Figure 1*F*). In the Cox proportional hazards model, older age, lower serum albumin levels, and higher ALP values at the time of PSC diagnosis were significantly associated with an increased risk of mortality (Table 5; Supplementary

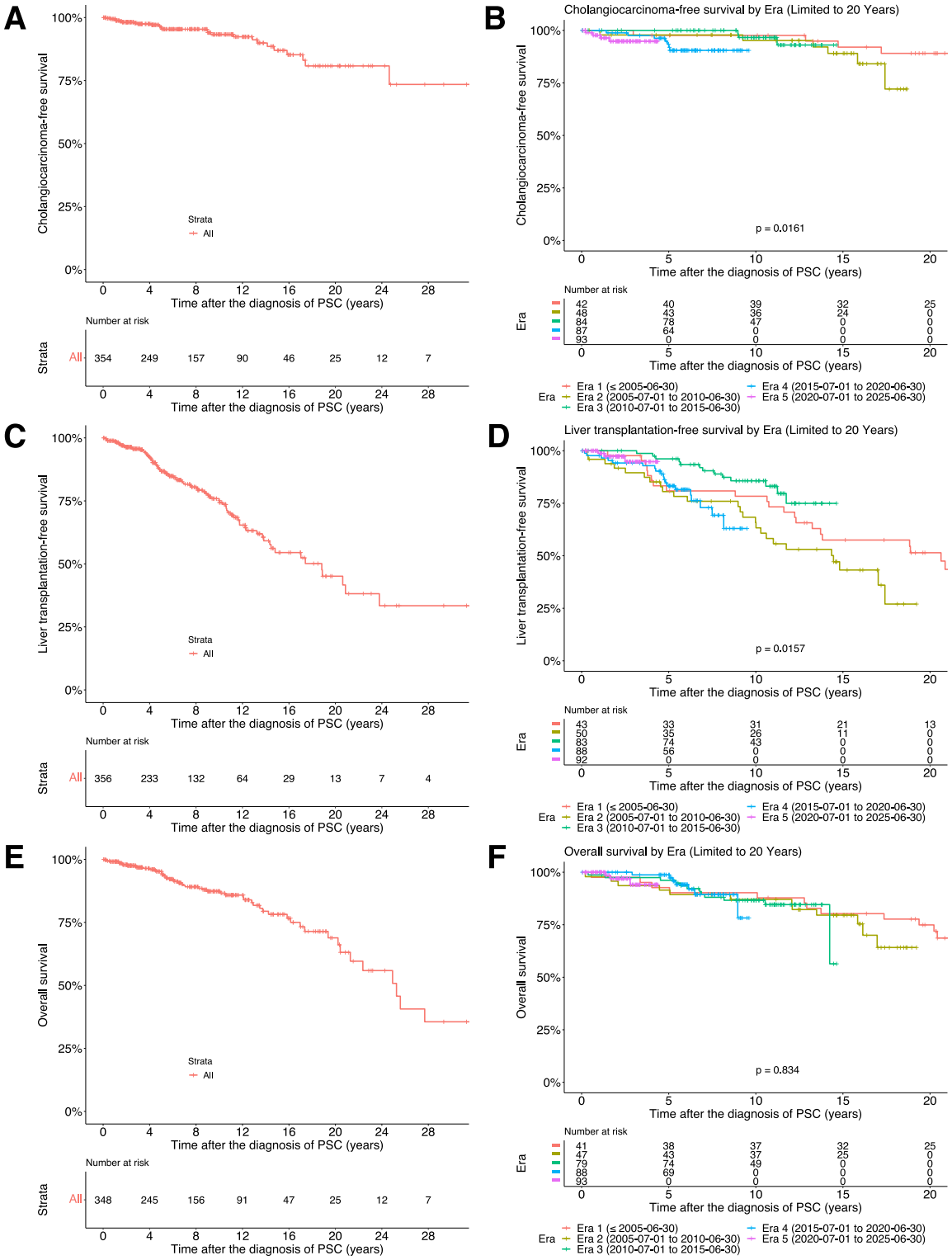

Figure 1. PSC-related clinical endpoints. KM curves illustrating event-free survival since PSC diagnosis: (*A*) risk of CCA; (*B*) risk of CCA stratified by diagnostic era; (*C*) risk of LT; (*D*) risk of LT stratified by diagnostic era; (*E*) risk of all-cause mortality; and (*F*) risk of all-cause mortality stratified by diagnostic eras.

Table 12). Similar findings were observed in the Cox model using cluster-robust SEs (Supplementary Table 13). Because only 17 deaths were identified as the first event, the Fine-Gray model included only 2 covariates—age at PSC diagnosis and serum albumin level—and showed that older age at PSC diagnosis was significantly associated with an increased risk of death (Supplementary Table 14).

Table 5. Cox Proportional Hazards Model for PSC Outcomes in PSC-IBD

Group/characteristic	HR	95% CI	*P* value
CCA			
Age at PSC diagnosis, *y*	1.03	1.00–1.05	.06
LT			
Order of diagnosis			
PSC diagnosed before IBD	–	–	
IBD diagnosed before or at PSC diagnosis	0.48	0.24–0.94	.03
Total bilirubin, *mg/dL*	0.99	0.91–1.08	.77
Albumin, *g/dL*	0.44	0.27–0.72	<.001
Variceal bleeding history at the diagnosis of PSC	5.78	1.21–27.70	.03
PSC-related symptoms at the diagnosis of PSC	2.33	1.16–4.69	.02
Death			
Age at PSC diagnosis, *y*	1.06	1.03–1.09	<.001
Order of diagnosis			
PSC diagnosed before IBD	–	–	
IBD diagnosed before or at PSC diagnosis	1.50	0.62–3.64	.37
ALP, *U/L*	1.00	1.00–1.00	.02
Albumin, *g/dL*	0.40	0.21–0.74	<.01
PT-INR	0.96	0.13–6.91	.97

NOTE. Liver function parameters at PSC diagnosis.
ALP, alkaline phosphatase; CCA, cholangiocarcinoma; CI, confidence interval; γ-GT, gamma-glutamyl transferase; HR, hazard ratio; IBD, inflammatory bowel disease; LT, liver transplantation; PSC, primary sclerosing cholangitis; PT-INR, prothrombin time/international normalized ratio.

Discussion

This multicenter study involving 25 hospitals across Asia demonstrated that the prevalence of PSC among Asian patients with IBD is lower than that reported in Western populations. In recent years, the age at PSC diagnosis has increased, and the risk of CCA has become more pronounced, underscoring the growing importance of routine surveillance for this biliary malignancy. Additionally, in more recent diagnostic eras, symptomatic PSC was less frequently observed, and liver dysfunction was significantly milder, likely reflecting earlier detection as a result of increased utilization of MRCP, which may also contribute to the prolonged time to LT. Although an older age at PSC diagnosis was associated with an increased mortality risk, the overall survival time did not differ significantly across the diagnostic eras. This may reflect appropriate disease management of PSC in IBD, including timely LT.

Several studies have shown that PSC and UC share only limited genetic overlap,[20] suggesting that nongenetic factors such as the gut microbiome may play a larger role in PSC pathogenesis in IBD. The "leaky gut" hypothesis proposes that IBD-related mucosal injury allows colonic bacteria to translocate to the liver, contributing to PSC development.[3] However, a recent multi-biome study found similar microbiome profiles in patients with IBD from Japan and Western countries, suggesting that different pathogenic mechanisms may underlie PSC-IBD in Asia.[21] Integrin $\alpha v\beta 6$ has recently emerged as a potential biomarker for both PSC and IBD,[22] indicating shared immunological pathways. As multi-omics and genome-wide association data from Asian patients with PSC remain scarce, further studies are needed to clarify the immunological mechanisms underlying the lower prevalence of PSC in this region.

In recent diagnostic eras, the age at PSC diagnosis has increased. Consistently, a population-based retrospective study from Canada reported an increasing incidence of PSC-IBD among patients >30 years of age.[23] A nationwide study from England also demonstrated that the prevalence of PSC-IBD has been rising most rapidly in individuals aged 30 to 44 years, and that this age group is expected to remain the predominant demographic through 2027.[24] Notably, the age at IBD diagnosis has also risen in recent years, both in our Asian cohort and in global epidemiological studies.[25,26] In our cohort, 65% of patients with PSC-IBD were diagnosed with IBD before or at the time of PSC diagnosis, and the interval between the 2 diagnoses has shortened over time. These findings suggest that PSC is increasingly being diagnosed during routine follow-up after IBD diagnosis, typically prompted by abnormal liver function tests (eg, elevated ALP levels) and further evaluated using MRCP. Consequently, the age at PSC diagnosis has increased in parallel with the rising age at IBD diagnosis. These trends support the idea that improved diagnostic techniques and shifting patient demographics are contributing to the earlier and more frequent detection of PSC—particularly in asymptomatic or milder cases—and are reshaping the clinical presentation of PSC-IBD over time. In Japan, the diagnostic criteria for PSC were recently revised.[17] According to the updated criteria, PSC can now be diagnosed in patients with IBD based solely on typical MRCP findings, without the need for further invasive testing unless biliary

malignancy or other differential diagnoses are suspected. Furthermore, the criteria recommend routine colonoscopy for patients with newly diagnosed PSC, even those without gastrointestinal symptoms, to evaluate for concomitant IBD. Indeed, our data showed an increasing trend toward performing screening colonoscopy. Together, these updates are expected to facilitate earlier detection of both PSC and IBD, thereby enabling more timely and comprehensive management.

The presence of PSC has been identified as an independent risk factor for colorectal dysplasia and cancer in patients with UC.[27] A meta-analysis reported that 21% of patients with PSC-UC developed colorectal neoplasia, compared with only 4% of those with UC alone.[11] In contrast, the incidence of UCAN among patients with PSC-UC was lower in our Asian cohort (9.6%), which may be attributable to the increased rate of screening colonoscopy prompted by PSC diagnosis in the recent era. PSC is also a well-established risk factor for hepatobiliary malignancies.[28] A population-based cohort study in Norway and Sweden showed that 5.2% of patients with PSC-IBD developed biliary tract cancer, compared with 0.2% of non-PSC-IBD patients.[29] A multicenter retrospective cohort study from the Spanish ENEIDA registry found that 2.5% (7/277) of patients with PSC-IBD developed CCA.[30] These findings indicate that the incidence of CCA in PSC-IBD generally falls within the single-digit range, and the rate observed in our cohort (7.2%) is comparable to those previously reported.

Concomitant PSC is a recognized risk factor for chronic liver disease-related complications among patients with IBD. In a population-based, propensity score-matched analysis using the United States National Inpatient Sample database, the prevalence of cirrhosis was 30.2% in patients with PSC-IBD, significantly higher than in non-PSC-IBD patients (2.3%),[31] and comparable to the rate observed in our PSC-IBD cohort (34%). Regarding LT and mortality, a Canadian population-based cohort reported a 10-year LT-free survival rate of 59% among patients with PSC-IBD.[23] Meanwhile, a Swedish population-based study showed a 10-year overall survival of 71.8% in patients with PSC-IBD.[32] Compared with these reports, the outcomes observed in our Asian cohort were comparable or potentially more favorable, although our cohort was not population-based. This may reflect earlier diagnosis and improved disease management, including timely LT, in recent years.

A major strength of this study lies in its multicenter design, encompassing 25 leading hospitals across 6 Asian countries. This broad collaboration enabled us to examine not only the prevalence of PSC among patients with IBD, but also the impact of PSC on long-term clinical outcomes. To our knowledge, this is the first large-scale study to demonstrate both the lower prevalence of PSC among patients with IBD in Asia and the milder disease phenotype in recent diagnostic eras, with substantial representation from East Asia. However, this study has some limitations. First, the retrospective nature of the study introduces the possibility of selection and information bias, and the cohort was not population-based. Variability in diagnostic resources and management across Asian centers may have further contributed to under-ascertainment. In particular, small-duct PSC[33] was likely under-captured, as liver biopsy is not necessarily performed in patients without biliary abnormalities on imaging, and MRCP is not uniformly used as a first-line investigation for patients with IBD who have minimally elevated serum ALP levels, leading to possible under-recognition of mild cholestatic abnormalities. Second, because this study focused on the effect of PSC on outcomes in patients with PSC-IBD, the lack of detailed clinical data at the time of IBD diagnosis limited our ability to fully perform multivariate analyses of UCAN and IBD-related surgery. Therefore, prospective multinational studies with more granular data are required to validate and extend our findings.

In conclusion, the prevalence of PSC among Asian patients with IBD was lower than that reported in Western countries. Compared with earlier diagnostic eras, disease severity at the time of PSC diagnosis has become milder in recent years, likely due to the increased use of MRCP. Consequently, the overall prognosis of Asian patients with IBD appears more favorable than that in previous studies, suggesting that earlier detection and appropriate management have contributed to improved outcomes. These findings have direct implications for clinical practice and highlight the need for tailored surveillance protocols and evidence-based management guidelines for PSC-IBD, not only in Asia but also globally.

Supplementary Material

Note: To access the supplementary material and/or video(s) accompanying this article, visit the online version of *Clinical Gastroenterology and Hepatology* at www.cghjournal.org, and at https://doi.org/10.1016/j.cgh.2025.11.020.

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Conflicts of interest

The authors disclose no conflicts.

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Data Availability

All data generated or analyzed during this study are included in this published article and its Supplementary Material files.