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Surveillance for cholangiocarcinoma in PSC: MRI, ERCP, both—or neither?

Vincenzo Giorgio Mirante*

Gastroenterologia A, Azienda Ospedaliera Universitaria Integrata di Verona, 37126 Verona, Italy

***Correspondence:** Vincenzo Giorgio Mirante, Gastroenterologia A, Azienda Ospedaliera Universitaria Integrata di Verona, Piazzale Stefani 1, 37126 Verona, Italy. v.mirante@libero.it

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Cholangiocarcinoma (CCA) is an aggressive malignancy, accounting for around 15% of all primary hepatic tumours. It often presents at an advanced stage and has a poor prognosis [1]. Identifying high-risk populations and implementing effective surveillance strategies are, therefore, priorities in hepatobiliary oncology. High-risk groups for CCA include individuals with primary sclerosing cholangitis (PSC), choledochal cysts, cirrhosis, chronic hepatitis B or C infection, and metabolic/behavioral factors such as obesity, harmful alcohol use, and tobacco smoking [2]. Among these, PSC confers the highest lifetime risk of CCA and is also associated with smaller increases in gallbladder and hepatocellular cancers. Current society guidelines broadly endorse surveillance in adults with PSC, but the optimal modality and interval remain unsettled, and practice patterns vary widely across centers [3–5].

PSC is a chronic, immune-mediated cholangiopathy characterized by multifocal strictures along the intra- and extrahepatic biliary tree, affecting more than 16.2 per 100,000 population globally [6]. It is more frequent in men (65–70%), most often diagnosed between the ages of 30 and 40 years, common in non-smokers, and it is tightly associated with inflammatory bowel disease, particularly ulcerative colitis: approximately 70% of people with PSC have inflammatory bowel disease, and about 5–10% of people with UC develop PSC [6]. A geographical gradient in the prevalence of PSC has been observed, with the highest disease prevalence found in northern Europe, while the disease is less common in southern Europe and Asia [6]. Conversely, PSC appears to be equally prevalent among African Americans and white Americans, with no race/ethnicity predominance. These epidemiological features make generalization across regions difficult and highlight the need for pragmatic, 'real-world' data to improve surveillance pathways outside of tertiary hepatobiliary units.

Guidelines recommend imaging-based surveillance, typically annual magnetic resonance imaging/cholangiopancreatography (MRI/MRCP), while discouraging routine endoscopic retrograde cholangiopancreatography (ERCP) because of its invasiveness and complications. ERCP plus brush cytology (BC) is reserved for new or progressive dominant strictures, biochemical deterioration, or persistent suspicion of malignancy despite non-invasive workup [3, 4]. Importantly, biliary brushing alone has limited sensitivity for detecting CCA, though adjunctive techniques such as fluorescence in situ hybridization (FISH) or cholangioscopy-guided sampling can improve diagnostic yield. However, these advanced methods are not universally available, limiting the feasibility of routine ERCP surveillance.

In this context, Barner-Rasmussen et al. [7] compared three surveillance strategies across 1,629 PSC patients followed for a median period of eight to eleven years. The following strategies were employed: scheduled ERCP with systematic BC and endoscopic management of strictures when indicated; annual MRI/MRCP; and on-demand ERCP per guideline-driven triggers. The primary composite endpoint was hepatobiliary malignancy, liver transplantation, or liver-related death. The data showed that the cumulative incidence of this endpoint was lowest in the scheduled ERCP group [14.1%, 95% confidence interval (CI) 12.0–16.4%] and highest in the ERCP on demand group (35.0%, 95% CI 28.4–42.0%), $p < 0.001$. No statistically significant difference was observed in the cumulative incidence of CCA between the scheduled ERCP and MRI/MRCP surveillance groups, whereas it was higher in the on-demand ERCP group ($p < 0.001$). No differences in liver-related deaths were observed between the different surveillance strategies. While the findings favour a more proactive endoscopic surveillance approach, selection bias and protocol heterogeneity—for instance, the MRI/MRCP group still underwent ERCP per EASL-triggered indications—limit causal inference.

Given the inherent risks of selection bias, the results of this study should be treated with caution. Firstly, this is an observational study that compares centers as much as it compares strategies. Furthermore, the cohorts differed in terms of baseline disease activity, biochemistry, and access to structured endoscopy protocols (including BC and endoscopic dilations). Although the adjusted models included key demographics, they could not fully account for PSC severity metrics, inflammatory activity, or differences in multidisciplinary care pathways. As the authors acknowledge, selection and center effects cannot be excluded, so these data are intended to generate hypotheses rather than change practice.

Secondly, the safety record is incomplete. Routine ERCP exposes patients to risks, most notably post-ERCP pancreatitis and cholangitis, that may be significant in PSC and could offset the benefits of earlier detection or stricture control if the program is implemented outside of high-volume units. These realities argue for risk-adapted, resource-sensitive pathways, potentially integrating ultrasound or biomarker-driven algorithms in low-resource settings. Explicit, audited safety outcomes are essential.

Thirdly, while some registry analyses suggest an association between regular surveillance imaging and improved overall survival [8], prospective evidence that surveillance per se detects CCA early enough to alter disease-specific outcomes in unselected PSC remains limited and heterogeneous. A recent prospective program involving yearly MRI/MRCP and CA19-9 testing found a low incidence of CCA and failed to demonstrate a clear survival advantage from the timing of detection [9]. This highlights the critical need for validated, risk-adapted pathways rather than ‘one-size-fits-all’ schedules. Furthermore, emerging approaches, based on genomics, metabolomics, microbiome signatures, and DNA-methylation profiling, may in the future enhance early detection in PSC. In particular, methylation-based assays in bile or plasma have shown potential to identify CCA up to a year before radiological diagnosis [10].

Additionally, questions remain regarding cost, access, and global equity. In fact, the approach of these authors may be difficult to implement in developing countries and in places where limited resources are allocated to healthcare. Both ERCP + BC and MRI are costly and time-consuming techniques. The diversity of health systems suggests that risk-adapted, resource-sensitive pathways are preferable to prescriptive, uniform schedules. Ultrasonography is probably more cost-effective, and it is also universally available. It should be used in future studies alone or in combination with biomarkers.

Finally, additional unmeasured confounders, such as program size, inclusion/exclusion criteria, adherence rates, and patient experience, likely influenced outcomes. Understanding adherence is crucial, as many PSC patients are young and may be less inclined toward long-term surveillance adherence—a major barrier to effective screening.

In conclusion, Barner-Rasmussen et al. [7] contribute valuable comparative data but do not establish a one-size-fits-all model. The decision-making process for ERCP should rely on individualized risk stratification, ensuring that endoscopy is reserved for clinically or radiologically discordant cases and delivered in experienced centres that audit outcomes. Until stronger evidence emerges, annual MRI/MRCP

remains the default pathway, with ERCP as a targeted escalation step. Novel molecular tools may soon refine surveillance, provided they prove cost-effective and externally validated.

Abbreviations

BC: brush cytology

CCA: cholangiocarcinoma

ERCP: endoscopic retrograde cholangiopancreatography

MRCP: magnetic resonance cholangiopancreatography

MRI: magnetic resonance imaging

PSC: primary sclerosing cholangitis

Declarations

Author contributions

VGM: Conceptualization, Writing—original draft, Writing—review & editing. The author read and approved the submitted version.

Conflicts of interest

Vincenzo Giorgio Mirante, who is an Editorial Board Member of Exploration of Digestive Diseases, had no involvement in the decision-making or review process of this manuscript.

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