



Risk of colorectal cancer in chronic liver diseases: a systematic review and meta-analysis

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Background and Aims: The risk of colorectal cancer (CRC) in various chronic liver diseases compared with the general population remains unclear. We performed a systematic review and meta-analysis to assess the risk of CRC in patients with chronic liver diseases before and after liver transplantation.

Methods: Electronic databases were searched for studies assessing the risk of CRC in patients with chronic liver diseases. The primary outcome was the pooled risk of CRC among studies that reported the risk as standardized incidence rate (SIR).

Results: Fifty studies that included 55,991 patients were identified. Among studies that included hepatitis and cirrhotic patients, the pooled SIR was 2.06 ($P < .0001$; 95% confidence interval (CI), 1.46-2.90) with moderate heterogeneity ($I^2 = 49.2\%$), which appeared to be because of the difference between subgroup of diseases and the power of studies. Three studies reported an increased risk of CRC in primary sclerosing cholangitis patients (pooled SIR 6.70; $P < .0001$; 95% CI, 3.48-12.91) with moderate heterogeneity ($I^2 = 36.3\%$), which appeared to be because of the difference between the power of studies. Among studies that included post-transplant patients, the pooled SIR was 2.16 ($P < .0001$; 95% CI, 1.59-2.94) with moderate heterogeneity ($I^2 = 56.4\%$). Meta-regression showed a correlation between the proportion of autoimmune-related liver diseases and the risk of CRC.

Conclusions: Patients with chronic liver diseases had an increased risk of CRC compared with the general population, which persisted after liver transplantation. A more intensive surveillance for CRC is warranted in this population. (Gastrointest Endosc 2017;86:93-104.)

Colorectal cancer (CRC) is a leading cause of death throughout the world. It is the third most common cancer diagnosis in males and females in the United States.¹

Abbreviation: AIH, autoimmune hepatitis; CRC, colorectal cancer; PBC, primary biliary cirrhosis; PSC, primary sclerosing cholangitis; SIR, standardized incidence rate; UC, ulcerative colitis.

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It affects all races and ethnicities but is generally seen in elderly people.¹ Its risk is increased in certain patient populations, such as hereditary nonpolyposis colorectal cancer,² inflammatory bowel disease,³ those with a family history of CRC,⁴ and African Americans.¹ Early detection and resection of adenomatous polyps by screening and surveillance colonoscopies have shown to be beneficial in reducing the risk of CRC.^{5,6}

Among various liver diseases, primary sclerosing cholangitis (PSC) is known to elevate the risk of CRC, which is mainly attributed to the concurrence of inflammatory bowel disease.⁷ Soetikno et al⁸ undertook a meta-analysis and showed that patients with PSC had a 4-fold increased risk of CRC compared with patients with ulcerative colitis (UC); however, the risk compared with the general population was not assessed. This study was undertaken more than a decade ago, and since then the risk of CRC in UC is not considered to be as high as initially reported.^{9,10} The risk of CRC in PSC patients compared with the general population is unclear, and

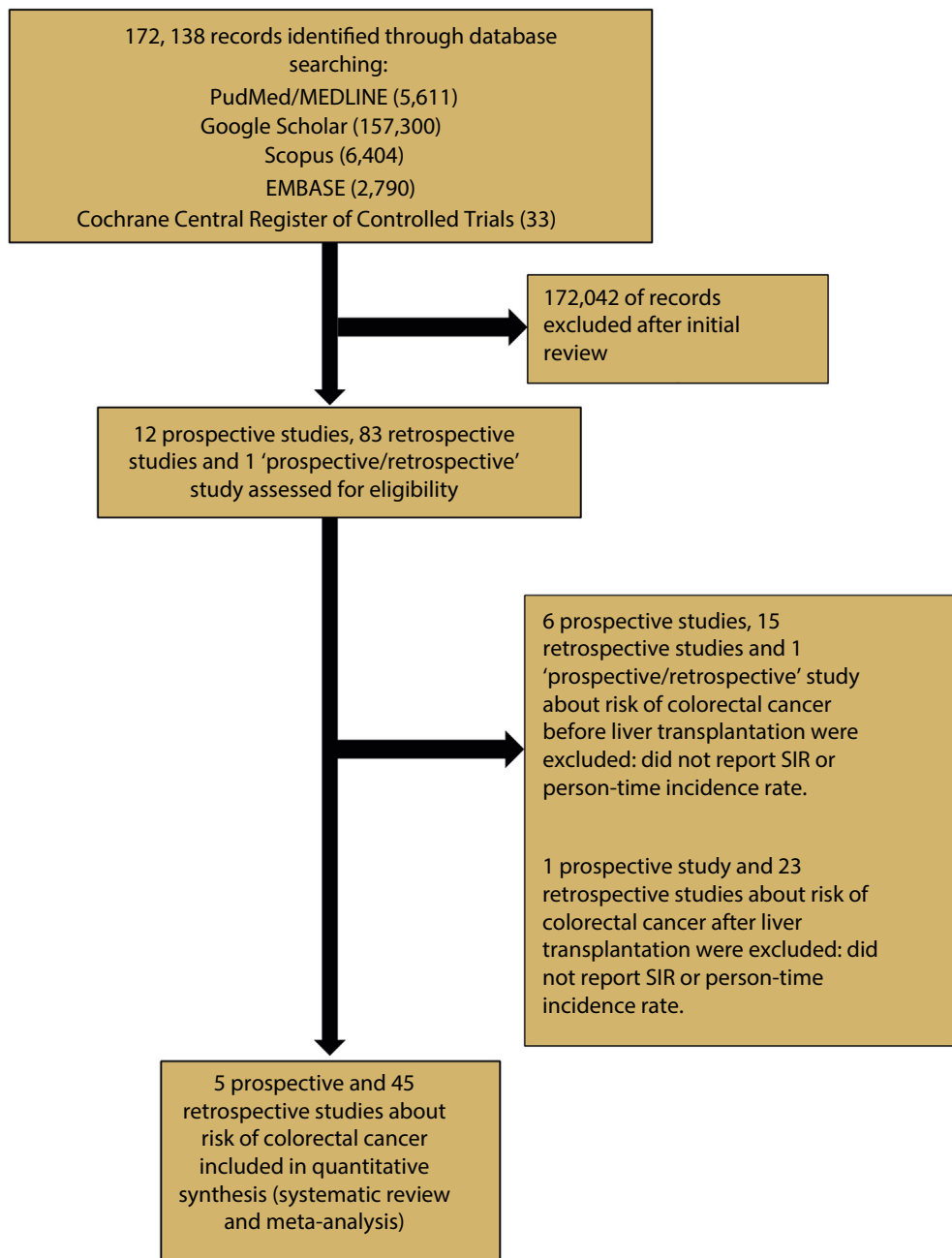


Figure 1. Flowchart of the assessment of the studies identified in the meta-analysis.

whether they remain at risk after transplant is controversial.¹¹ Two meta-analyses have shown increased incidences of CRC among liver transplant patients^{12,13}; however, many of the studies included in these meta-analyses were not matched by gender or age to the control population. Furthermore, it remains largely unknown whether patients with other chronic liver diseases are at risk for CRC. Increasingly, more liver transplants for end-stage liver diseases such as viral hepatitis/cirrhosis, alcoholic liver damage, and PSC are being performed, and the life expectancy of these patients is

improving.¹⁴ Exposure to immunosuppressive agents after transplantation is known to increase the risk of post-transplant malignancies,¹⁵ but the risk of CRC after liver transplantation remains unclear. Post-transplant malignancies can become a major cause of death, and it is important to determine the risk of CRC in these patients because it is one of the few that can be prevented by screening and surveillance. Current guidelines recommend age-appropriate screening colonoscopy for liver transplant candidates¹⁶; however, evidence supporting this recommendation is unclear.

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