

# Hepatic and extrahepatic malignancies and primary sclerosing cholangitis

E Schruppf, K M Boberg

There is an increased risk of pancreatic carcinoma in patients with primary sclerosing cholangitis

The paper of Bergquist and colleagues<sup>1</sup> is important for several reasons. In addition to confirming the increased risk of cholangiocarcinoma/hepatobiliary carcinoma in primary sclerosing cholangitis (PSC), they provide data on the size and nature of this risk. But more importantly, for the first time they demonstrate an increased risk of pancreatic cancer in addition to the well established risk of colonic malignancies in these patients. Thereby they demonstrate that PSC is a premalignant condition predisposing to several gastrointestinal cancers.

PSC patients are undoubtedly at an increased risk of developing cholangiocarcinoma. The size of this risk is however not universally agreed upon.<sup>2</sup> The present finding of 13% of hepatobiliary malignancies is based on the largest cohort of patients examined so far: as two thirds of all Swedish PSC patients were included, it is also probably the least selected series of patients. The high rate (74 %) of histological examination of livers post mortem and after transplantation among patients without hepatobiliary malignancy is an additional marker of the quality of this study. Although it is not clearly stated, one assumes that most of these are cholangiocarcinoma cases, indicating a standard incidence ratio of more than 100 for cholangiocarcinoma development among PSC patients and a frequency of cholangiocarcinoma development of 10–15%.

One remarkable finding of the present study is that a large proportion of PSC patients who developed hepatobiliary malignancy did so within the first year after diagnosis of PSC, indicating that the development of hepatobiliary malignancy in PSC may bring to light previously unrecognised PSC. This was even more evident in a joint European study.<sup>3</sup>

Not surprisingly, a 10-fold increased risk of colorectal cancers was also found. This is obviously linked to the high frequency of ulcerative colitis and Crohn's colitis in patients with PSC and implies that these patients should have colonoscopy at regular intervals both to have their colitis diagnosed (it may often be asymptomatic) and to look for colonic malignancies. Whether colonic malignancies

**Bergquist A, Ekblom A, Olsson R, et al.** Hepatic and extrahepatic malignancies in primary sclerosing cholangitis. *J Hepatol* 2002;**36**:321–7.

**Background:** Although primary sclerosing cholangitis (PSC) has long been described as a strong risk factor for the development of cholangiocarcinoma, there are few good epidemiological studies which have examined its frequency. In addition, the risk of developing other malignancies is unknown. Excellent health information systems in Scandinavia provide the opportunity to examine such associations in rare diseases.

**Objective:** To assess the risk of hepatobiliary and extrahepatic malignancy in a large Swedish cohort of patients with PSC.

**Design:** Follow up of a large case series of patients with PSC comparing the frequency of malignancy with that in the general Swedish population.

**Patients:** A total of 609 patients with a clinical, biochemical, and cholangiographic diagnosis of PSC, identified by hepatologists from all Swedish university hospitals. Follow up was from the National Swedish Cancer Registry; clinical follow up and median follow up time was 5.7 years.

**Results:** Twenty eight per cent of cases died during follow up, 44% of malignancy. Cholangiocarcinoma occurred in 13% of the cohort, with an incidence of hepatobiliary carcinoma of 1.5% per year after the first year post diagnosis of PSC. The risk of pancreatic cancer was increased 14-fold compared with the general Swedish population.

**Conclusion:** The major cause of death in PSC patients (excluding those undergoing liver transplantation) was cancer. Not only was the increased risk of hepatobiliary cancer confirmed, but a new discovery of an increased risk of pancreatic cancer in patients with PSC was described.

were more often seen in PSC patients with colitis than in other colitis patients<sup>4</sup> was not examined in the present study.

The new finding of a 14-fold increased risk of development of pancreatic cancer among PSC patients is particularly interesting. The possible diagnostic overlap between cholangiocarcinoma and pancreatic carcinoma has been underlined by the authors and confirmation of the finding should be attempted. Nevertheless, this finding may support the idea that PSC patients are at risk of developing several different types of gastrointestinal malignancies. As pancreatitis-like changes are sometimes seen in PSC,<sup>5</sup> malignancy development in both the hepatobiliary system as well as in the colon-rectum and the pancreas could be secondary to chronic inflammation. One should also consider however that it may not be solely a predisposition to develop PSC that may be linked to specific genes but also the risk of developing gastrointestinal malignancy.<sup>6</sup> The study of Bergquist *et al* should stimulate further studies on the mechanism of cancer development in PSC.

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## Authors' affiliations

E Schruppf, K M Boberg, Medical Department A, Rikshospitalet, Oslo, Norway

Correspondence to: E Schruppf, Medical Department A, Rikshospitalet, N-0027 Oslo, Norway; erik.schruppf@rikshospitalet.no

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