Table 2 Allele frequencies for the -403, -28, in1.1 and 3'222 RANTES polymorphism in primary sclerosing cholangitis, inflammatory bowel disease and healthy controls

	PSC total n = 124 (%)	PSC without IBD n = 63 (%)	PSC CD n = 25 (%)	PSC UC n = 31 (%)	IBD total n = 595 (%)	CD without PSC n = 418 (%)	UC without PSC n = 160 v(%)	HC n = 362 (%)
RANTES-403A	18.1	14.9	25.0	20.0	18.6	19.1	17.9	19.7
RANTES-28G	5.9	3.4	10.4	6.5	3.3	3.0	4.2	2.2
RANTES in1.1C	15.3	12.9	22.9	14.5	13.8	15.0	10.6	14.6
RANTES 3'222C	0.0	0.0	0.0	0.0	0.7	0.9	0.3	0.0

CD, Crohn's disease; IBD, inflammatory bowel disease; PSC, primary sclerosing cholangitis; RANTES, Regulated on Activation Normal T Expressed and Secreted; UC, ulcerative colitis.

association between the RANTES -28G allele and PSC could be that an increased inflammatory response in the gut predisposes to bacterial translocation through the bowel wall.

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Increased risk of colorectal neoplasia in asymptomatic liver-transplant recipients

Liver-transplant recipients (LTRs) are known to carry an increased risk of cancer, including tumours of the skin and lymphoproliferative disorders.¹ Whether the risk of colorectal cancer (CRC) is increased after orthotopic liver transplantation (OLT) is controversial.² There is

also no consensus whether screening for colorectal neoplasia in asymptomatic LTRs is warranted, except for those with primary sclerosing cholangitis (PSC) with associated ulcerative colitis (UC).² In a previous study, we found an increased risk of CRC in patients after OLT compared with the general population.³ In this report, we examined the prevalence of colorectal adenomas and carcinomas in asymptomatic LTRs.

Between 1979 and 2001, 381 adult patients underwent OLT at the University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. For this retrospective study, all patients were included in which a colonoscopy had been performed for screening purposes, at least 5 years after OLT. Patients with symptoms suggestive of colorectal neoplasia and patients with previous colorectal neoplasia were excluded. Only complete colonoscopy reports including caecal inspection were included. Data on the presence, location and number of colorectal neoplastic lesions were collected. Patients with more than one lesion were categorised according to the most advanced lesion. All pathological specimens were reviewed by the study pathologist for assessment of the degree of dysplasia and the presence of villous architecture according to the World Health Organization criteria.⁴ Advanced neoplasia was defined as an adenoma of at least 1 cm in size, and/or (tubulo) villous architecture, and/or high-grade dysplasia, or cancer, in accordance with the literature.

In all, 92 asymptomatic patients, including 20 with PSC, had undergone colonoscopy at a median (range) age of 53.5 (35.8-71.2) years, after a median (range) interval of 11.1 (5.0-23.2) years after OLT. One or more adenomas were found in 20 of 92 (21.7%) patients (9 men, 11 women). Of these 20 patients, 4 had PSC, including 1 with concomitant UC. In 9 of 20 patients, one or more adenomas were located in the proximal colon. Advanced adenomas were found in 8 of 92 (8.7%) patients. Cancer was found in none of the patients.

These prevalence data in patients with OLT were compared with six asymptomatic cohorts from the literature (table 1). Although the prevalence of all neoplasia was comparable with other cohorts, advanced neoplasia was more often found in our population than in most studies. In addition, the relative proportion of advanced neoplasia, expressed as a ratio of all neoplasia, was 0.40 in our study, which is higher than in any other report. As the prevalence of colorectal neoplasia increases with age, data from our population were compared with data from the literature stratified in three groups (<50, 50-59 and >60 years). For patients aged <50 years and 50-59 years, the prevalence of advanced

neoplasia was higher in our study population than in any other study (table 1). Our data are probably best compared with the only other available Dutch study that was performed in a relatively young asymptomatic population.⁵ In patients aged <50 years, the relative risk in the population which underwent OLT was 3.6 (p<0.05) for overall neoplasia and 8.9 (p<0.01) for advanced neoplasia. Taken together, our data suggest that LTRs have a higher risk of colorectal neoplasia, particularly advanced neoplasia, compared with average-risk populations. The absence of a gender- and age-matched control group limits the strength of this retrospective study. We suggest designing larger and prospective studies including adequate control groups to better assess the risk of colorectal neoplasia in LTRs.

Currently, CRC screening is recommended in many countries worldwide for all patients aged ≥50 years. It was recently recommended that for the asymptomatic liver transplant population, CRC screening should be offered to those aged >50 years and those with PSC associated UC.² The results from our preliminary study suggest that CRC screening could be considered in all adult LTRs.

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Table 1 Prevalence of colorectal neoplasia in liver-transplant recipients, compared with selected studies from the literature in average-risk populations

	LTR	de Jong <i>et al</i> ^f	Strul <i>et al</i> ^f	Imperiale <i>et al</i> ^g	Soon <i>et al</i> ^f	Lieberman <i>et al</i> ^f	Schoenfeld <i>et al</i> ^o
Number of patients	92	342	1177	906	4859	3121	1463
All neoplasia (%)	21.7	6.1	20.9	11.0	18.9	37.5	20.4
Advanced neoplasia (%)	8.7	2.0	6.3	3.5	4.6	10.5	4.9
Ratio advanced/all neoplasia	0.40	0.33	0.30	0.32	0.24	0.28	0.24
Advanced neoplasia (%)							
<50 years	8.6	1.0	1.0	3.5	3.0	—	—
50–59 years	12.9	8.3	2.9	—	3.8	5.7	3.3

LTR, liver transplant recipients.

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Visceral leishmaniasis causes fever and decompensation in patients with cirrhosis

Infections and fever due to bacterial infections are well-known complications of liver cirrhosis, and often trigger decompensation and death.¹ Visceral leishmaniasis (VL), a protozoan infection endemic in the Mediterranean area, causes a febrile disease, the clinical and laboratory features (splenomegaly, pancytopenia, reduced serum albumin and increased γ -globulin concentrations) of which largely overlap with those of cirrhosis.^{2–3} Although the areas where VL is endemic coincide with areas where the prevalence of cirrhosis is high, no study has described VL in patients with cirrhosis.

During a 12-year period, all patients with cirrhosis admitted for decompensation and fever lasting more than 1 week, unresponsive to broad-spectrum antibiotics, underwent diagnostic procedures for VL. For each case diagnosed as VL, three consecutive cases of bacterial infection observed in the same period were enrolled. Cirrhosis was defined by liver histology or clinical, laboratory, ultrasonographic and endoscopic findings. VL was diagnosed by the immunofluorescent-specific antibody test (IFAT) and confirmed by the identification of *Leishmania* from Giemsa-stained smears of bone marrow or spleen

aspirates.⁴ Bacterial infections were diagnosed by standard clinical procedures. All patients were followed up for 6 months after diagnosis.

In total, 11 patients with VL and 33 with bacterial infections were enrolled. Table 1 summarises the main clinical and laboratory data at presentation.

Patients with VL received standard-dose liposomal-amphotericin B (l-AmB; nine cases)⁵ or meglumine antimoniate (two cases). Fever resolved within 72 h in patients receiving l-AmB and after 7 days in those receiving antimonials. No severe drug-related adverse reaction was recorded. Improvement in haematological parameters and reduction in liver enzymes, spleen diameter and anti-*Leishmania* antibody titre were recorded during the follow-up period in all patients with VL. The Child–Pugh class rapidly and stably improved in patients with VL (fig 1). The mortality was 17% for patients with bacterial infections and 0% for patients with VL.

VL was a troublesome diagnosis in patients with cirrhosis, as shown by the time from the onset of symptoms and diagnosis. This delay resulted from failure to consider this unusual diagnosis and was responsible for a progressive worsening in liver function. Indeed, once VL was cured, cirrhosis reverted to Child class A in all but one patient.

Apart from a long-lasting fever, there were no clear-cut clues to suspect VL. Some significant differences in the presentation data between VL and bacterial infections were found (table 1), but their clinical use is hampered by a substantial overlap of the laboratory values between VL and bacterial infection cases. Only white blood cell and γ -globulin data are of potential value.

IFAT serology is a sensitive and specific test for the diagnosis of VL in patients with cirrhosis; notably, IFAT was negative in all patients with bacterial infections and in 51 additional patients with cirrhosis without fever (table 1). In a series including 16 patients with

cirrhosis, a strip test using *Leishmania* K39 antigen was sensitive and specific.⁶ The diagnostic flow-chart for patients with cirrhosis with unexplained fever should include the anti-VL antibody test, thus avoiding the routine use of invasive diagnostic techniques. Once the diagnosis is established, l-AmB is a safe and effective treatment.

The study was not designed to assess whether the patients with cirrhosis are at a higher risk of acquiring VL than those without cirrhosis. Assuming that there are 10 000–20 000 patients with cirrhosis per year in our area, the annual incidence of VL among patients with cirrhosis was 0.5–1/10 000—that is, 8–17-fold higher than the incidence (0.06/10 000) among the adult population in the same area ($p < 0.001$).^{7–9}

Overall, the study underlines the need to consider this unusual cause of fever and decompensation in patients with cirrhosis when they are living in or have travelled through an area endemic with VL.

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Figure 1 Child–Pugh class before and after treatment for visceral leishmaniasis.

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