deficiency was not observed. Moreover, in none of the 148 patients (0%, 95% confidence interval 0 to 2, 4%) endomysial antibodies were positive. In 32 patients, the treating physician ordered duodenal biopsy specimens as well. In two of them, histological examination of the biopsy specimens showed an increased number of intraepithelial lymphocytes but a normal villous morphology, in the other 30 patients, duodenal biopsy specimens showed normal mucosa.

To our knowledge, only two similar studies have been performed in the Western world.^{4,7} Our study is in contrast with a study performed in the UK that observed 11 cases of positive antiendomysial antibodies in 300 patients (3.6%).⁴ Furthermore, a study performed in the US found a prevalence of 4% (2/50 patients) when screening of patients with symptoms suggestive of irritable bowel syndrome was performed with antitissue transglutaminase antibodies, although none of these patients had positive antiendomysial antibodies.⁷ Most probably, our study is negative because of a low prevalence of coeliac disease in our examined population. In a recent Dutch survey, the overall prevalence of unrecognised coeliac disease in The Netherlands is 1:286.⁸ This is lower than the prevalence of 1:100 observed in the UK and of 1:133 observed in the US.^{9,10}

In summary, this study shows that in patients referred to a secondary care hospital in The Netherlands because of suggestive irritable bowel syndrome, the prevalence of coeliac disease is low and that screening for coeliac disease in this population is ineffective.

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Functional polymorphisms in the promoters of *MMP-1*, *MMP-2*, *MMP-3*, *MMP-9*, *MMP-12* and *MMP-13* are not associated with hepatocellular carcinoma risk

The matrix metalloproteinases (MMPs) play an important role in several steps of cancer development by regulating cancer-cell growth, differentiation, apoptosis, invasion, metastasis, angiogenesis and immune surveillance.¹ Several polymorphisms in the promoters of a number of *MMP* genes, which are thought to affect the respective *MMP* production in an allele-specific manner, have been well characterised.^{2–4} There is increasing evidence indicating that these functional polymorphisms may contribute to interindividual differences in susceptibility to a wide spectrum of cancers.^{2–7} The role of the *MMPs* polymorphisms in hepatocellular carcinoma (HCC), however, has never been specifically investigated. As *MMPs* are plausible HCC candidate genes, we sought to examine whether the *MMP* polymorphisms have any bearing on the risk of HCC. Among the candidate polymorphisms, we focused on seven in the promoters of six *MMP* genes. These polymorphisms were *MMP-1* -1607 1G/2G (rs1799750), *MMP-2* C-1306T (rs243865) and C-735T (rs2285053), *MMP-3* -1612 5A/6A (rs3025058), *MMP-9* C-1562T (rs3918242), *MMP-12* G-82A (rs2276109), and *MMP-13* G-77A (rs17860523), respectively.^{2–7}

We genotyped these seven polymorphisms in 434 incident patients with HCC and 480 controls enrolled at Fusui County and its surrounding regions at Guangxi province, a well-known high-risk region for HCC located in southern China. The diagnosis of cases, the inclusion and exclusion criteria for cases and controls and the definition of hepatitis B virus (HBV) carriers, smokers and drinkers were described previously.⁸ All seven polymorphisms were genotyped by DNA sequencing. The primers and conditions used for amplifying and sequencing the target region containing these seven polymorphisms are available on request. Haplotypes were assigned by the PHASE (<http://www.stat.washington.edu/stephens/>). The fitness to Hardy–Weinberg equilibrium was tested using the χ^2 test. The association between the genotypes/haplotypes and HCC risk was evaluated by multiple logistic regression analyses while controlling for confounding factors (including age, sex, status of smoking and drinking, pack-years of smoking and family history of HCC). Potential modification effect of the polymorphisms on HCC risk was assessed for the above risk factors by the addition of interaction terms in the logistic model and by separate analyses of subgroups of subjects determined by these factors.

The controls were comparable with cases with regard to age, status of smoking and drinking, and pack-years of smoking ($p>0.05$). However, more men ($p=0.005$), HBV carriers ($p<0.001$) and patients with a history of HCC in their first-degree biological relatives ($p<0.001$) presented in cases than in controls. The observed genotype frequencies for the seven polymorphisms conformed to the Hardy–Weinberg equilibrium in both cases and controls ($p>0.05$). On the basis of logistic regression analysis with adjustment for confounding factors, no significant association with the risk of HCC was observed with the seven polymorphisms in the overall sample, and HBV carriers and non-HBV carriers (table 1). The distribution of haplotypes based on the *MMP-2* C-1306T and C-735T polymorphism exhibited no significant difference between the cases and controls (data not shown). When the analyses were stratified by age, sex, status of smoking and drinking, pack-years of smoking and family history of HCC, no significant association was found between the *MMP* polymorphisms/haplotypes and the risk of HCC (data not shown).

There are several possible reasons for our negative results. First, inadequate power may be an explanation of our results. However, this study had >85% power at a significance of 0.05 to detect a recessive allele with a minor allele frequency of 0.20 that confers a risk of 1.4. Second, our findings could be the result of the different molecular mechanisms of HCC and other types of cancer. Alternatively, there may be population-specific differences in the contribution of these *MMPs* polymorphisms to HCC susceptibility. This might occur if there were population differences in linkage disequilibrium patterns or allele frequencies of *MMP* genes. Indeed, the allele and genotype frequencies of *MMP* polymorphisms vary with ethnicity. For instance, in this study with 480 control subjects, we found that the *MMP-2* -1306C allele frequency was 0.92 and that the C/C genotype accounted for 85.0% of the southern Han Chinese population studied, compared with around 0.75 and 60.0%, respectively, among Caucasians from France and the UK.^{4,9} Finally, our negative results may be due to inherent selection bias. As a hospital-based study, our patients with HCC were enrolled from the hospitals and the controls were selected from the community population, and therefore inherent selection bias cannot be completely excluded. However, by matching for age and residential area, potential confounding factors might have been minimised and any inadequacy in matching have been controlled in data analyses with further adjustment and stratification.

In conclusion, to the best of our knowledge, this is the first case-control study of *MMP* polymorphisms in relation to HCC. Our results suggest that the seven functional polymorphisms in the promoters of *MMP-1*, *MMP-2*, *MMP-3*, *MMP-9*, *MMP-12* and *MMP-13* do not significantly confer an increased risk of HCC. However, additional studies from larger populations among Chinese, and from diverse ethnic populations, are warranted before the importance of *MMP* polymorphisms in HCC risk can be fully ascertained.

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Table 1 Genotype and allele frequencies of MMPs polymorphisms among the cases and controls and adjusted ORs for HCC risk

Polymorphisms	Overall		HBV carriers		Non-HBV carriers	
	Cases/ controls	OR* (95% CI)	Cases/controls	OR* (95% CI)	Cases/controls	OR* (95% CI)
MMP-1 -1607 site						
2G/2G	169/183	1.00 (reference)	132/81	1.00 (reference)	37/102	1.00 (reference)
1G/2G	200/235	0.91 (0.68 to 1.21)	155/84	1.12 (0.76 to 1.67)	45/151	0.83 (0.51 to 1.37)
1G/1G	62/61	1.08 (0.71 to 1.64)	55/20	1.67 (0.93 to 3.03)	7/41	0.48 (0.21 to 1.15)
1G/2G+1G/1G	262/296	0.94 (0.72 to 1.24)	210/104	1.22 (0.85 to 1.77)	52/192	0.76 (0.48 to 1.22)
1G allele	0.38/0.37		0.39/0.34		0.33/0.40	
MMP-2 C-1306T						
C/C	358/402	1.00 (reference)	281/151	1.00 (reference)	77/251	1.00 (reference)
T/C	66/70	1.03 (0.72 to 1.49)	55/28	1.06 (0.63 to 1.75)	11/42	0.86 (0.43 to 1.75)
T/T	3/1	NA	3/0	NA	0/1	NA
T/C+T/T	69/71	1.16 (0.74 to 1.53)	58/28	1.12 (0.67 to 1.84)	11/43	0.84 (0.40 to 1.71)
T allele	0.08/0.08		0.09/0.08		0.06/0.08	
MMP-2 C-735T						
C/C	229/281	1.00 (reference)	176/104	1.00 (reference)	53/177	1.00 (reference)
T/C	167/167	1.20 (0.91 to 1.59)	138/70	1.18 (0.79 to 1.71)	29/97	1.00 (0.59 to 1.69)
T/T	35/30	1.55 (0.91 to 2.62)	28/10	1.64 (0.76 to 3.52)	7/20	1.16 (0.46 to 2.90)
T/C+T/T	202/197	1.26 (0.96 to 1.64)	166/80	1.21 (0.84 to 1.77)	36/117	1.04 (0.62 to 1.68)
T allele	0.28/0.24		0.28/0.25		0.24/0.23	
MMP-3 -1171 site						
6A/6A	360/399	1.00 (reference)	285/162	1.00 (reference)	75/237	1.00 (reference)
5A/6A	64/77	0.90 (0.63 to 1.30)	51/23	1.25 (0.73 to 2.15)	13/54	0.77 (0.38 to 1.46)
5A/5A	8/3	2.98 (0.78 to 11.46)	7/0	NA	1/3	NA
5A/6A+5A/5A	72/80	0.98 (0.69 to 1.40)	58/23	1.42 (0.84 to 2.42)	14/57	0.79 (0.40 to 1.48)
5A allele	0.09/0.09		0.10/0.06		0.08/0.10	
MMP-9 C-1562T						
C/C	338/369	1.00 (reference)	274/153	1.00 (reference)	64/216	1.00 (reference)
T/C	94/111	0.96 (0.70 to 1.32)	69/33	1.15 (0.72 to 1.86)	25/78	1.07 (0.62 to 1.85)
T/T	0/0	NA	0/0	NA	0/0	NA
T/C+T/T	94/111	0.96 (0.70 to 1.32)	69/33	1.15 (0.72 to 1.86)	25/78	1.07 (0.62 to 1.85)
T allele	0.11/0.12		0.10/0.09		0.14/0.13	
MMP-12 G-82A						
A/A	404/449	1.00 (reference)	317/173	1.00 (reference)	87/276	1.00 (reference)
A/G	29/30	1.02 (0.60 to 1.75)	27/12	1.22 (0.59 to 2.50)	2/18	0.36 (0.09 to 1.56)
G/G	0/1	NA	0/1	NA	0/0	NA
A/G+G/G	29/31	1.00 (0.59 to 1.70)	27/13	1.13 (0.56 to 2.24)	2/18	0.36 (0.09 to 1.56)
G allele	0.03/0.03		0.04/0.04		0.01/0.03	
MMP-13 G-77A						
G/G	116/129	1.00 (reference)	96/62	1.00 (reference)	20/67	1.00 (reference)
G/A	212/225	1.09 (0.79 to 1.49)	166/82	1.29 (0.85 to 1.99)	46/143	1.06 (0.58 to 1.98)
A/A	99/123	0.89 (0.62 to 1.29)	77/40	1.23 (0.74 to 2.06)	22/83	0.90 (0.45 to 1.77)
G/A+A/A	311/348	1.02 (0.76 to 1.37)	243/122	1.27 (0.86 to 1.91)	68/226	1.00 (0.56 to 1.80)
A allele	0.48/0.49		0.47/0.44		0.51/0.53	

HBV, hepatitis B virus; HCC, hepatocellular carcinoma; MMP, matrix metalloproteinase.

The number of genotyped samples varies because of genotyping failure for some individuals. The carriers of HBV are subjects positive for both HBsAg and HBcAb for at least 6 months. OR, odds ratio; CI, confidence interval; NA, not applicable.

*ORs and 95% CIs were calculated by logistic regression and adjusted for age, sex, status of smoking and drinking, pack-years of smoking and family history of HCC.

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Octreotide LAR for severe obscure-overt gastrointestinal haemorrhage in high-risk patients on anticoagulation therapy

We read with interest the letter by Krikis *et al* (*Gut* 2005;54:171–2). We report on two patients with a poor clinical history (recurrent gastrointestinal haemorrhage, older age, severe comorbidity, anticoagulation, contraindication to β -blockers), successfully treated using only octreotide long-acting release (LAR).

A 73-year-old man was admitted six times (32 days of hospital stay) in the previous six months because of recurrent episodes of melaena. Medical history included type 1 diabetes, three myocardial infarctions and multivessel disease treated by triple-bypass graft surgery (left ventricular ejection fraction 35%), ischaemic stroke due to total occlusion of the right carotid artery, surgically solved, and occlusion of the left carotid artery of 40%, treated with acenocoumarol. Haemoglobin fell to 7–8 g/dl in all admissions developing stable angina pectoris, without overcoagulation, requiring a transfusion of 25 units of packed red blood cells. Three upper endoscopies, two colonoscopies with ileal intubation, small bowel series radiography, computed abdominal tomography, capsule endoscopy and radionuclide scanning did not find the source of bleeding.

A 69-year-old man was admitted ten times during 14 months for recurrent episodes of melaena (122 days of hospital stay). He smoked 30 cigarettes per day. His medical history included obesity, heart failure, chronic obstructive pulmonary disease on long-term oxygen therapy, obstructive sleep apnoea and atrial fibrillation on acenocoumarol therapy. Haemoglobin fell to 6–7 g/dl in all admissions, with exacerbation of previous diseases. No overanticoagulation was detected and a transfusion of 37 units of packed red blood cells was required. Two upper endoscopies, two colonoscopies, small-bowel series radiography, computed abdominal tomography and radionuclide scanning did not achieve diagnosis. Capsule endoscopy showed diffuse angiodysplasias from the jejunum to the ileum.

Because of the medical conditions and a high rate of bleeding, rescue treatment in both patients was started with octreotide LAR 20 mg intramuscularly once a month. Neither blood transfusions nor admissions were needed after 9 months of follow-up, and no side effects or anticoagulant interaction was detected.

Obscure gastrointestinal haemorrhage represents 5% of gastrointestinal bleeding. Some patients are not suitable for endoscopic or

surgical management because of severe comorbidity, lack of diagnosis of the source of bleeding or diffuse lesions non-responsive to conventional treatments, and may be at high risk of re-bleeding, especially if active bleeding or lesions are detected in the small bowel.^{1,2} The effectiveness of hormonal treatment is unclear and burdened by adverse effects.^{3,4} Octreotide can control bleeding from the gastrointestinal angiodysplasia and variceal bleeding,^{5,6} probably by decreasing splanchnic and portal blood flow. Octreotide LAR, a depot formulation, is administered once monthly, with a similar efficacy and safety profile as octreotide, and does not require hospital admission. In addition to the report by Krikis *et al*, we found only two other reports on the usefulness of octreotide LAR for severe obscure gastrointestinal bleeding,^{7,8} but not in older anticoagulated patients with a poor prognosis. Moreover, the economic and medical resources saved and the psychological benefits for patients and families in an outpatient management make octreotide LAR an attractive, effective, safe and comfortable treatment for some specific cases of obscure gastrointestinal bleeding, like ours, thanks to conservative management.

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Acute surgical abdomen—an atypical presentation of *Plasmodium vivax* malaria

A search of the existing literature did not identify any previously reported cases of acute abdomen as atypical features of *vivax* malaria.

The case presented here illustrates the ubiquitous nature of this disease with its unusual clinical manifestations in the UK.

A 51-year-old Asian man presented to the acute surgical admissions unit with a 1 week history of left iliac fossa pain, malaise and non-bilious vomiting. No other bowel or urinary symptoms were present. His medical history included asthma, which was well controlled with inhalers. He had no history of any previous abdominal surgery.

On examination, he was found to be clammy and to have dry mucosal surfaces. Initial observations recorded a temperature of 40.1°C and a regular pulse of 133 beats/min, with a blood pressure of 108/51 mm Hg and a respiratory rate of 20 breaths/min. Pulse oximetry showed an oxygen saturation of 97% in room air. Cardiorespiratory examination was normal. Abdominal examination showed marked left iliac fossa tenderness with signs of peritonism. No evidence of hepatosplenomegaly was seen. Per rectal examination was normal. Chest and abdominal x rays were unremarkable, with no evidence of perforation. Urine analysis was negative. Blood tests gave 13.1 g/dl haemoglobin, 2.97×10⁹/l leucocytes, 115×10⁹/l platelets, 9.8 mmol/l urea, and 128 mmol/l creatinine. All other blood tests including serum amylase were normal. The initial clinical impression was sepsis secondary to diverticulitis with localised diverticulum perforation.

The patient was resuscitated with crystalloid, with a lack of response to resuscitation or deterioration in the clinical condition indicating an emergency laparotomy. However, over a period of observation with aggressive fluid resuscitation, he stabilised haemodynamically (pulse 80 beats/min and blood pressure 92/57 mm Hg). An abdominal/pelvic computed tomogram showed no evidence of diverticulitis or perforation. No focal small or large bowel abnormality was detected. A cardiac echo excluded infective endocarditis. Interestingly, blood films taken for haematology were reported to show *Plasmodium vivax* infestation. Further questioning revealed that the patient had returned from Pakistan 8 months before. He also admitted to not taking prophylaxis. Treatment for malaria was initiated with a 600 mg chloroquine stat dose, 300 mg once daily for 2 days. This was followed with primaquine, 30 mg once daily for 14 days. The patient was discharged 4 days later, having remained pain-free and afebrile.

This case report shows that increased global travel results in infections in non-endemic areas.¹ Therefore, doctors in non-endemic areas need to be familiar with the clinical features of this disease (fever, chills,² headache, myalgia, nausea, vomiting, cough,³ malarial paroxysm, migraine, urticarial rashes, bradycardia, postural hypotension,⁴ jaundice, cerebral involvement, anaemia, thrombocytopenia, pancytopenia,⁴ splenic rupture due to splenomegaly⁵), as diagnosis may not be straightforward and malaria presents in many atypical ways. Firstly, it is important to take a travel history. Secondly, symptoms and illness from *vivax* malaria may present many months after travel and exposure, possibly as a relapse from an earlier mild infection.⁶ Thirdly, malaria may cause abdominal pain.⁷ This patient presented with all the clinical features of localised peritonitis with concomitant dehydration and hypotension, and was being considered for an exploratory laparotomy. The diagnosis was made on the smear obtained for full blood