the power of our analysis. We agree with the authors' statement that larger and prospective assessments of this potentially fascinating association between fatigue and mortality in patients with PBC are warranted.

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Authors' reply

We appreciate the interest shown in our work by Zein and McCullough. In their series of 241 patients with primary biliary cirrhosis (PBC), they found that the presence of self-reported fatigue at clinical presentation was associated with an increased risk of death during follow-up on univariate analysis, but that, in contrast with our earlier report (*Gut* 2006;**55**:536–41), this was not independent of other previously identified prognostic factors in PBC, such as age and bilirubin. There are a number of important differences between the Zein and McCullough study and our original study. We think that two of these are likely to be of importance in explaining the differences in the conclusions reached by these two studies.

The first important difference is that Zein and McCullough used self-reporting of the presence of fatigue, as opposed to formal fatigue impact assessment, as the criterion for the presence of fatigue. This reflects the fact that their cohort dates from the early 1990s, an era that pre-dated the validation and application of formal fatigue impact scoring systems in PBC. In our experience, self-reporting of fatigue is very unreliable in predicting the presence of actual fatigue-associated lifestyle change. In the Newcastle population, self-reporting of the presence of fatigue tends to overestimate the true prevalence and impact of fatigue (>60% of our patients self-report the presence of fatigue, but significant increase in fatigue scores is seen in only ca 35–40% of patients). If also true of the Cleveland population included in the Zein and McCullough study, the implication is that their population actually has quite a low degree of fatigue, a potentially interesting observation in its own right.

The second important difference between the two studies is that the death rate in the Zein and McCullough patient cohort is significantly lower than that in our cohort (a crude death rate of 1% of patients per year of follow-up compared with 5.1% per year of follow-up). The most probable explanation for this difference would seem to be the ages of the cohorts at the outset of the follow-up period described in each of the studies (65 years in the Newcastle cohort compared with 53 years in the Cleveland cohort). This difference is likely to reflect the fact that the Cleveland cohort was an incident cohort of patients, whereas the Newcastle cohort was a geographically defined prevalent cohort (ie, the Cleveland cohort were followed up from the point of disease diagnosis, whereas the Newcastle patients were followed up from a fixed time point and were therefore typically several years into their disease time course). Other potential differences could result from either different referral patterns in the two centres or differences in the natural history of the disease in different continents.

We found, however, the low death rate, and apparent absence of an independent association between fatigue and mortality in the younger Cleveland population to be of great interest and reanalysed our data to explore further the impact of age on fatigue-associated mortality. Strikingly, when we split our patient cohort into those aged <65 and >65 years at the point of study, we found that those <65 years (mean age 53 years) had a death rate comparable to the Cleveland cohort (1.4% per year of subsequent follow-up), with no significant association between mortality and fatigue at the study outset (fig 1A). In marked contrast, the patients aged >65 years at the point of study (mean age 74 years) had a significant increase in their mortality (9.3% per year of follow-up). It was in this cohort that there was a significant association between fatigue at the study outset (defined as Fatigue Impact Scale >40) and subsequent mortality (fig 1B). Furthermore, when looking at the individual ages of the patients who died during follow-up, increase in the death rate was present at all ages from 65 years upwards, with age 65 years seeming to act as a natural cut-off point for increased mortality (eg, mortality in patients aged 60–64 years at study was 1.3% per year of follow-up compared with 5.5% per year for the 65–69-year group, 5% per year for the 70–74-year group and so on).

In conclusion, we value the contribution of Zein and McCullough to this important discussion. We support their view that further long-term studies are required and suggest that particular attention should be focused, in these studies, on the cohort aged 65–75 years where the effects of fatigue-associated mortality seem to have a disproportionate impact.

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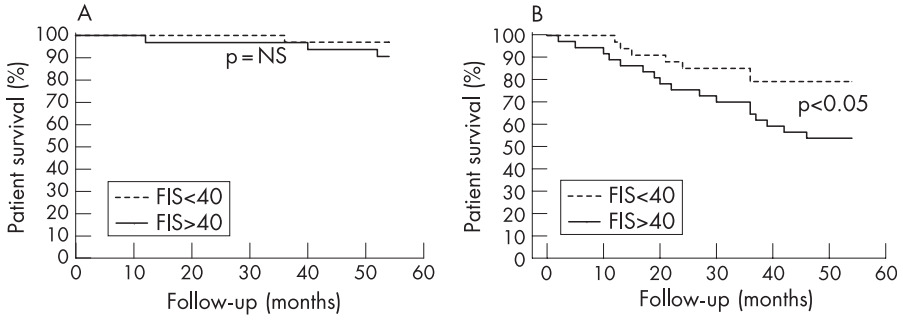

Figure 1 Survival analysis of patients with high (Fatigue Impact Scale (FIS) >40, solid line) and low (FIS<40, broken line) baseline fatigue scores who were (A) aged <65 years at the outset of our previously reported study (Gut 2006;**xx**:xxx) and (B) aged >65 years at the outset of the study. Curve comparison was by the log rank test. Fatigue-associated excess mortality was, in this population, restricted entirely to the patients aged >65 years at the outset of the study. NS, not significant.

Right liver lobe diameter:albumin ratio: a new non-invasive parameter for prediction of oesophageal varices in patients with liver cirrhosis (preliminary report)

Portal hypertension commonly accompanies liver cirrhosis, and development of oesophageal varices is among the major complications of portal hypertension. Patients with cirrhosis should be screened for the presence of oesophageal varices when portal hypertension is diagnosed. To reduce the increasing burden of endoscopy units, some studies have attempted to identify parameters for non-invasive prediction of the presence of oesophageal varices.

We read with great interest the article by Giannini *et al* (*Gut* 2003;**52**:1200–5). Besides the confirmation of proposed platelet count: spleen diameter ratio in predicting the presence of oesophageal varices in patients with liver cirrhosis, we introduced a new measurement for predicting oesophageal varices. Our preliminary study included 58 patients with cirrhosis who underwent a complete biochemical investigation, upper digestive endoscopy and ultrasonographic examination. Right liver lobe diameter:albumin ratio has been calculated and correlated with the presence and grade of oesophageal varices. All patients gave

Table 1 Clinical data of study patients with cirrhosis

Sex (M/F)	40/18
Mean (SD) age (years)	53.07 (13.09)
Age range (years)	17–79
Aetiology of liver disease (alcoholic/infective/immune/other)	26/13/12/7
Child–Pugh class (A/B/C)	31/23/4
Mean (SD) size of the right liver lobe	156 (22.72)
Mean (SD) albumin concentration	30.84 (7.28)
Mean (SD) albumin:right liver lobe diameter ratio	5.43 (1.79)
Oesophageal varices (grade 0/I/II/III/IV)	14/11/20/12/1

Table 2 Values of the right liver lobe diameter:albumin ratio

	Right liver lobe diameter:albumin ratio		
Varices	**Mean (SD)**	**Minimum**	**Maximum**
Grade 0	4.14 (1.29)	2.76	6.82
Grade I	5.25 (1.23)	3.92	7.63
Grade II	5.68 (1.29)	3.40	8.48
Grade III	6.66 (2.55)	4.07	11.44
Grade IV	6.86	—	—

their written consent, and the ethical committee of our institution permitted our study.

Table 1 lists the clinical features of the study patients. Right liver lobe diameter:albumin ratio and grade of oesophageal varices (table 2) seems to have a significant correlation (Spearman's test for non-parametric correlation $r = 0.441$; $p<0.01$).

Previously published studies reported that the platelet count:spleen size ratio is a good predictor of oesophageal varices. We investigated serum albumin concentration as a parameter of liver function in combination with right liver lobe size. Despite a good correlation of these ratios and grade of oesophageal varices, it is unlikely that these indexes could be used to exclude patients from initial screening endoscopy. Nevertheless, these indexes may serve for selection of patients in need for more frequent endoscopy. Using these indexes will enable identification of patients at higher risk for the development of oesophageal varices. It will provide insight into the relationships between clinical, biochemical, haematological and imaging abnormalities, and the development of clinically significant oesophageal varices.

The right liver lobe diameter:albumin and platelet count:spleen diameter ratios are non-invasive parameters that can provide accurate information pertinent to determining the presence of oesophageal varices and their grading in patients with liver cirrhosis.

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Competing interests: None.

Author's reply

I read with interest the study by Alempijevic and Kovacevic and wish to comment on their letter.

Non-invasive indexes to identify the presence of oesophageal varices in cirrhotic patients may be a useful tool to decrease the number of digestive endoscopies that are performed in these patients. A ratio index can enhance the physiopathological meaning of the single variables, and therefore the specificity of the non-invasive evaluation. The clinical role of a non-invasive index depends on (1) the biological plausibility of the proposed ratio, (2) the reproducibility of the variables in the ratio, and (3) the accuracy of identifying or ruling out the presence of oesophageal varices. The right liver lobe diameter/albumin index would seem to be a biologically plausible link between hepatic function and portal hypertension owing to the role of the liver in the synthesis of albumin. However, this ratio lacks both the reproducibility of ultrasound measurement of the right liver lobe diameter and the accuracy at screening for the absence of oesophageal varices. It would be interesting to compare the accuracy of the right liver lobe diameter/albumin ratio with the platelet count/spleen diameter ratio to evaluate the presence or absence of oesophageal varices, considering that the reproducibility of ultrasound measurement of spleen bipolar diameter is well established (*Gut* 2003;**52**:1200–5) and that its accuracy in ruling out the presence of oesophageal varices has been confirmed in a multicentre study.[1] In particular, the reproducibility of the spleen bipolar diameter was high with an intraobserver expert ultrasound operator coefficient of variation for repeated measurements of 2% and interoperator coefficient of variation of 4%.

With regard to the suggestion that ''it is unlikely that these indexes could be used to exclude patients from initial screening endoscopy'', as stated by Alempijevic and Kovacevic, it must be pointed out that the non-invasive indexes should be used to screen for the presence or absence of oesophageal varices, and thus to provide an endoscopic evaluation in patients with a ratio index that is compatible with the risk of oesophageal varices. Furthermore, any non-invasive index, including liver stiffness measurement,[2] may reflect the various degrees of oesophageal varices, further stressing the role of non-invasive ratio indexes in preliminary screening to determine the presence or absence of oesophageal varices.

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Competing interests: None.

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Links between triglyceride levels, hepatitis C virus infection and diabetes

We read the interesting article by Marzouk *et al* (*Gut* 2007;**56**:1105–10). The authors enrolled 765 residents in Egypt and reported prevalences of hepatitis C virus (HCV) antibody (anti-HCV), chronic and past HCV infection of 23.5%, 14% and 8.8%, respectively. Patients with chronic HCV infection had lower triglyceride levels and those with past HCV infection had higher triglyceride levels than those never infected. With a diabetes prevalence of 5.4%, HCV infection status—but not triglyceride levels—was one of the independent factors associated with diabetes.

We have conducted a large-scale community-based study of 9932 residents aged 40–65 years in Kaohsiung City, Taiwan, a country endemic for hepatitis B virus (HBV) infection. The prevalences of anti-HCV, hepatitis B surface antigen (HBsAg) and diabetes were 6.5%, 13.1% and 12.5%, respectively. In 642 anti-HCV-positive residents the prevalences of HCV RNA (tested using the COBAS AMPLICOR HCV test Version 2.0; Roche, Branchburg, New Jersey, USA), HBsAg and diabetes were 74.5%, 11.7% and 15%, respectively. Subjects with positive HCV RNA had significantly lower triglyceride levels (115.7 (67.1) vs 133.3 (134.3) mg/dl, $p = 0.029$), a significantly lower proportion of abnormal triglyceride levels ($\geq$150 mg/dl) (18.6% vs 29.3%, $p = 0.004$) and a higher proportion of diabetes than HCV RNA-negative subjects (18.0% vs 6.1%, $p<0.001$). Clinical factors associated with diabetes and abnormal triglyceride levels by univariate analyses are shown in table 1. Higher levels of alanine aminotransferase and triglyceride and a higher proportion of abnormal triglyceride levels and positive HCV RNA were significantly associated with diabetes (all $p<0.005$). A higher body mass index (BMI), higher proportions of diabetes and negative HCV RNA were significantly associated with abnormal triglyceride levels (all $p<0.05$). Based on multivariate analyses, the HCV RNA status and abnormal triglyceride levels were independent factors associated with diabetes, and diabetes, BMI and HCV RNA status were independent factors associated with abnormal levels of triglyceride (table 2).

It is noteworthy that we enrolled 642 anti-HCV-positive subjects in whom the HCV RNA