Table 1 The characteristics of 12 patients with major complications after liver biopsy

Patient no.	Sex/age	Complications	Time of occurrence (hrs)	In-hospital days
1	M/35	Haemoperitoneum	6	3
2	M/53	Haemoperitoneum	6	3
3	F/55	Haemothorax	12	1
4	M/52	Haemothorax with empyema	6	7
5	M/53	Massive subcapsular haematoma with shock	12	1
6	M/35	Haemoperitoneum	12	1
7	F/60	Haemoperitoneum with shock	6	7
8	F/53	Haemoperitoneum	5	5
9	F/55	Haemoperitoneum	5	5
10	F/42	Haemoperitoneum, haemobilia, shock, and transient obstructive jaundice	24	7
11	M/65	Haemoperitoneum with shock	6	5
12	F/53	Haemoperitoneum	4	3

setting that provides close observation for 1 hour after a biopsy. However, we keep a conservative and different view on the sufficiency and safety of 1 hour observation time after a liver biopsy. We have performed a total of 3806 liver biopsies using 18-gauge needle on 2980 patients (males 1817, females 1163, mean age was 41.3 years, range 17–72 years), performed in a medical centre and in a core regional hospital in southern Taiwan from Jan 1996 through Sep 2006. Our outpatient biopsy was assigned to a 6-hour observation time. The reasons for the liver biopsy studies on these patients, were either a result of chronic viral hepatitis or a surveillance of abnormal liver function tests. There was no clinical evidence of cirrhosis diagnosed by high-resolution ultrasound before a biopsy. Patients who have thrombocytopenia or the presence of oesophageal varices, ascites, splenomegaly, signs of portal hypertension, or encephalopathy by other imaging studies as well as bleeding tendencies, were excluded. These procedures have been done by six well-trained, board certified hepatologists. Apart from minor complications such as pain, nausea, and vomiting, a total of 12 patients (0.32%) suffered from haemorrhagic complications 4 to 12 hours after the biopsy (table 1). Our results were comparable with those of Beddy *et al* in terms of major complications and mortality. Although there was no death at follow up of one week, four patients did experienced hypovolemic shock. In one patient, haemobilia, presenting with insidious onset of tarry stool, obstructive jaundice, and hypovolemic shock, developed 24 hours after the biopsy. The total in-hospital days therefore were extended and ranged from 1 to 7 days. In rare occasions haemorrhagic complications such as haemoperitoneum, haemothorax, and haemobilia did occur with potential risk of morbidity and mortality after the procedure. Noteworthy is that those with poor performance such as liver cirrhosis and bleeding tendency were excluded from our study. Major complications occurred in four patients after the regular observation time. This does, indicate a possible need of a longer time of observation. Therefore, our study with a 6-hour observation time basis concluded that although ultrasound-guided liver biopsy is generally a safe procedure, major haemorrhage complications may occur more than one hour after liver biopsy. A longer time of observation may be more suitable with this potential risky procedure.

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The role of gender on clearance of hepatitis C virus: a different story in an area endemic for hepatitis B and C

We read with interest the article by Bakr *et al* (*GUT* 2006;55:1183–7). The authors recruited 4720 residents aged 18–65 years from a rural community in Egypt, a country hyperendemic for hepatitis C virus (HCV) infection, which might be attributed to mass campaigns for intravenous antischistosomal treatment.¹ They found that the HCV antibody (anti-HCV) was positive in 910 individuals (19.3%), and 38.5% of the anti-HCV-positive individuals were negative for serum HCV RNA. Interestingly, the authors concluded that women had a significantly higher HCV clearance rate (44.6% vs 33.7%, respectively; $p = 0.001$, adjusted OR 1.77) than men, which was similar to reports by Inoue *et al*² and Yamakawa *et al*³ from Japan.

We conducted a large-scale community-based study in southern Taiwan, a country hyperendemic for hepatitis B virus (HBV) infection (prevalence of hepatitis B surface antigen (HBsAg) 10–20%), and several villages were reported to be hyperendemic for anti-HCV (prevalence of anti-HCV 17–50%).^{4–6} Among the general population of the Kaohsiung area aged 40–65 years, 11 239 subjects were enrolled. The prevalence of HBsAg and anti-HCV (detected using a third-generation, commercially available ELISA kit (Abbott Laboratories, Chicago, Illinois, USA)) as 13.7% and 6.3%, respectively, and 84 (0.7%) participants were positive for both HBsAg and anti-HCV. In all, 642 anti-HCV-positive participants were tested for HCV RNA using a polymerase chain reaction assay (Cobas Amplicor Hepatitis C Virus Test, V.2.0; Roche Diagnostics, Branchburg, New Jersey, USA; detection limit: 50 IU/ml), and 478 (74.5%) of them were positive for HCV RNA. In addition to the manufacturer's instructions, which suggest rechecking for anti-HCV if the data are <20% (0.8–0.99 signal to cut-off (SCO)) of

Figure 1 Proportions of clearance hepatitis C virus (HCV) RNA in 642 anti-HCV-positive participants grouped by positive (+) and negative (–) hepatitis B surface antigen (HBsAg) are shown. Individuals with positive HBsAg had a significantly higher proportion of HCV RNA clearance than these negative for HBsAg, men and women. There was no significant difference in the proportions of clearance of HCV RNA between male and female patients in HBsAg-positive and HBsAg-negative groups.

Table 1 Comparison of clinical factors between 642 anti-hepatitis C virus (HCV)-positive participants with and without clearance of serum HCV RNA

Clinical factors	Clearance of HCV RNA		p Value
	Yes	No	
Case numbers, n (%)	164 (25.5)	478 (74.5)	
Sex			0.449
Male, n (%)	56 (23.8)	179 (76.2)	
Female, n (%)	108 (26.5)	299 (73.5)	
Mean (SD) age (years)	56.4 (5.9)	56.4 (5.9)	0.987
Mean (SD) BMI (kg/m ²)	24.7 (3.3)	24.7 (3.8)	0.961
>27, n (%)	32 (22.5)	110 (77.5)	0.351
≤27, n (%)	132 (26.4)	368 (73.6)	
Mean (SD) ALT (IU/l)	27.8 (28.3)	64.2 (60.5)	<0.001
>34, n (%)	33 (9.7)	306 (90.3)	<0.001
≤34, n (%)	131 (43.2)	172 (56.8)	
HBsAg			<0.001
Positive, n (%)	34 (45.3)	41 (54.7)	
Negative, n (%)	130 (22.9)	437 (77.1)	

ALT, alanine aminotransferase; BMI, body mass index; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus.

the cut-off value (= 1 SCO), in this study, the anti-HCV tests were also rechecked if the data were 1–2 SCO. For avoiding false-positive tests, anti-HCV was also rechecked for the participants with positive anti-HCV and negative HCV RNA. When comparing clinical factors between 642 anti-HCV-positive participants, with and without clearance of serum HCV RNA, we found that patients with positive HBsAg had a significantly higher proportion of HCV RNA clearance than those negative for HBsAg ($p < 0.001$; table 1). In a stepwise logistic regression analysis, positive HBsAg was the only independent factor significantly associated with negative HCV RNA in anti-HCV participants (OR 0.348; 95% CI 0.211 to 0.574, $p < 0.001$). HBV carriers were observed to have a significantly higher proportion of HCV RNA clearance than non-carriers among men and women (fig 1).

Viral interferences and reciprocal viral interactions have been observed between HBV and HCV dual infection.^{7,8} Our previous study also showed that there might be a reciprocal viral interaction between HBV and HCV in patients with dual viral infection treated with interferon/ribavirin combination.⁹ Reports from Egypt and Japan^{2,3} were conducted in countries endemic for HCV where the prevalence of HBV carriers was <8% and they did not elucidate the influence the HBV infection. In our large-scale community-based study in an area endemic for HCV infection in a country hyperendemic for HBV, the important role of HBV carriers on HCV clearance was noteworthy and especially demonstrated. Besides, we did not find the effect of gender on the HCV clearance observed in previous studies.^{2,3} It seems necessary to conduct prospective, longitudinal studies in clarifying roles of gender or concurrent HBV infection on the HCV clearance rate in patients infected with HCV.

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Relation between incidence of hepatic carcinogenesis and integration value of alanine aminotransferase in patients with hepatitis C virus infection

Alanine aminotransferase (ALT) activity is the most widely used laboratory parameter in the evaluation of necroinflammatory activity in liver disease.^{1–3} However, it is incorrect to evaluate the arithmetic or the annual mean values. If the ALT level is high, the measurement interval decreases, whereas if the ALT level is low, the interval increases. As a result, the arithmetic mean value increases in patients with increased ALT levels. We performed a more accurate evaluation by using the integration value of ALT. The aim of this study was to determine the utility of the integration value of ALT in predicting hepatic carcinogenesis in patients with the hepatitis C virus (HCV) infection.

A total of 1704 consecutive patients with follow-up periods of ≥3 years, with no evidence of hepatocellular carcinoma (HCC) for ≥3 years before the observation period, and interferon treatment completed ≥3 year before the detection of HCC during the period from January 1995 to December 2002 were included. In all, 594 patients received interferon treatment and 1110 patients did not. All patients were followed up at Ogaki Municipal Hospital, Ogaki, Japan, at least every 6 months. During each follow-up examination, liver-function tests, including ALT, were measured. We calculated the area of a trapezoid with ALT value and the measurement interval, and added the values. We divided the integration value of ALT by the observation period to obtain the average integration value. Patients were classified into five groups according to the average integration value of ALT: group A, 0–20 IU/l (n = 217); group B, 21–40 IU/l (n = 614); group C, 41–60 IU/l (n = 446); group D, 61–80 IU/l (n = 240); and group E, ≥81 IU/l (n = 187). The median (range) follow-up period was 7.9 (3.0–16.8) years. The total number of blood examinations was 90 211, and the median (range) number of blood examinations was 33 (6–222). Factors associated with the cumulative incidence of HCC were analysed using the Cox proportional hazard model with the forward selection method.

HCC occurred in 206 of 1704 (12.1%) patients during the follow-up period. According to univariate analysis, the following were significantly associated with the development of HCC:

- Age >65 years (relative risk (RR) 2.688 (95% CI 2.020 to 3.578); $p < 0.001$);