The prevalence of bright liver echo pattern in patients with chronic hepatitis C: correlation with steatosis and fibrosis

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Abstract

Purpose To evaluate the prevalence of bright liver echo pattern (BLP) on ultrasonography and its correlation with liver steatosis (LS), and fibrosis in patients with chronic hepatitis C. The usefulness of detecting skip areas for steatosis diagnosis has also been evaluated.

Methods The study included 88 patients with chronic hepatitis C (55 men, 33 women, average age 45.7 ± 11.2 years). Ultrasound examination was performed in all patients before liver biopsy. The presence of BLP was assessed and graded from 1 to 3. Hypoechoic areas (skip areas) around the gallbladder or near the portal vein were also evaluated. Hepatic fibrosis was assessed using the Ishak fibrosis score. Steatosis was graded as follows: 1, 2, 3 (<30, 30–70, >70 % of hepatocytes affected, respectively).

Results Fifty-three of the 88 patients (60 %) showed BLP (40 grade 1, 13 grades 2 or 3). Skip areas were found in 14 patients (16 %). Histological steatosis was observed in 40 patients (45 %) and in 10 of them (25 %) was grades 2 and 3 (4 and 6 patients, respectively). As regards fibrosis, 2 patients showed F0, 34 F1, 28 F2, 20 F3, 4 F4, none of them F5 and F6. BLP of grades 2 or 3 and presence of skip areas were strongly correlated with LS ($P = 0.00007$ and $P = 0.00003$, respectively). No correlation was found between BLP and fibrosis. The sensitivity, specificity,

positive predictive value (PPV), negative predictive value (NPV) and accuracy of BLP for LS were 75, 50, 56, 68 and 61 %, respectively. When BLP of grades 2 and 3 and LS of 30 % or more were correlated, the sensitivity, specificity, PPV, NPV and accuracy of BLP were 72, 96, 61, 96 and 90 %, respectively. As regards skip areas the sensitivity, specificity, PPV, NPV and accuracy for LS were 35, 100, 100, 64 and 70 %, respectively.

Conclusions In a well-defined group of patients with chronic hepatitis C, the detection of BLP grades 2 and 3 has a good sensitivity and high specificity for high grades of steatosis. A high specificity but low sensitivity for liver steatosis was also found for skip areas, whereas mild fibrosis does not seem to correlate with the hyperechogenicity of the liver.

Keywords Liver steatosis · Ultrasonography · Bright liver echo pattern · Skip areas · Chronic hepatitis C

Riassunto

Scopo Scopo del lavoro è stato quello di valutare la prevalenza del “bright liver echo pattern” (BLP) all’ultrasonografia e la sua correlazione con la steatosi epatica (SE) e la fibrosi in un gruppo di pazienti con epatite cronica C. È stata valutata anche l’utilità della determinazione delle cosiddette “aree di risparmio” per la diagnosi di steatosi.

Metodi Lo studio ha incluso 88 pazienti con epatite cronica C (55 di sesso maschile, 33 di sesso femminile; età media 45.7 ± 11.2 anni). L’esame ultrasonografico è stato eseguito in tutti i pazienti prima di effettuare la biopsia epatica. La presenza di BLP è stata graduata da 1 a 3. È stata anche valutata la presenza o meno di aree ipoecogene (cosiddette “aree di risparmio”), adiacenti alla colecisti o in sede parailare epatica. La fibrosi epatica è stata stadiata

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istologicamente utilizzando la classificazione di Ishak. La steatosi epatica é stata graduata da un punto di vista istologico come segue: 1, 2, 3 (a seconda che il grado di interessamento degli epatociti era rispettivamente <30, da 30 a 70, >70 %).

Risultati Cinquantatré degli 88 pazienti (60 %) hanno mostrato BLP (40 di grado 1, 13 di grado 2 o 3). In 14 pazienti (16 %) sono state rilevate “aree di risparmio”. Istologicamente la steatosi é stata evidenziata in 40 % dei pazienti (45 %) e in 10 di loro (25 %) era di grado 2 e 3 (4 e 6 pazienti rispettivamente). Per quanto riguarda la fibrosi, 2 pazienti hanno presentato F0, 34 F1, 28 F2, 20 F3, 4 F4, nessuno F5 e F6. BLP di grado 2 o 3 e la presenza di “aree di risparmio” era strettamente correlata con SE ($P = 0.00007$ a $P = 0.0003$, rispettivamente). Nessuna correlazione é stata trovata tra BLP e fibrosi. La sensibilità, specificità, valore predittivo positivo (VPP), valore predittivo negativo (VPN) e accuratezza della BLP per SE sono stati rispettivamente 75, 50, 56, 68 e 61 %. Quando sono state messe in correlazione BLP di grado 2 e 3 e SE di 30 % o più, sensibilità, specificità, VPP, VPN e accuratezza della BLP sono stati rispettivamente 72, 96, 61, 96 e 90 %. Per quanto riguarda le “aree di risparmio” sensibilità, specificità, VPP, VPN e accuratezza per SE sono stati rispettivamente 35, 100, 100, 64 e 70 %.

Conclusioni In un ben definito gruppo di pazienti con epatite cronica C, la determinazione di BLP di grado 2 e 3 ha mostrato una buona sensibilità ed un’alta specificità per la steatosi epatica di grado elevato. Un’alta specificità per SE, associata a bassa sensibilità, é stata anche riscontrata per le cosiddette “aree di risparmio”, mentre la fibrosi moderata non sembra correlare con l’ipercogenicità del fegato.

Introduction

Liver needle biopsy is probably the most reliable method of detecting liver steatosis (LS) [1]. Unfortunately, it is invasive and associated with a small but definite morbidity and mortality [2–5]. Therefore, the use of non-invasive methods such as ultrasonography could be advantageous in LS assessment especially when frequent controls are necessary or in those situations where needle biopsy is contraindicated. Nevertheless, the ability of ultrasound to evaluate the presence and degree of LS remains debatable. In fact, although some authors have shown that the bright liver echo pattern (BLP) is strongly correlated with the diagnosis of hepatic steatosis [6–13], other authors think that this pattern is non-specific because the liver echogenicity on ultrasonography also increases with liver fibrosis [14–20]. Recently, the simultaneous presence of BLP,

posterior attenuation, and/or areas with different patterns of fat infiltration (so-called skip areas) around gallbladder or near the portal vein [21] have been identified as distinctive signs of steatosis involving a number of hepatocytes in a microscopic field >30 % [11].

The aim of this study was to retrospectively evaluate the prevalence of BLP on ultrasonography and its correlation with liver steatosis and fibrosis in patients with chronic hepatitis C, considered to be at high risk for steatosis. The usefulness of detecting skip areas for steatosis diagnosis was also taken into account.

Materials and methods

The study included 88 patients with chronic hepatitis C (55 men, 33 women, mean age 45.7 ± 11.2 years), examined in the Liver Unit of University of Cagliari and referred to the Sonography Unit for sonographic examination of the abdomen. Each patient was subjected to echo-assisted liver biopsy for diagnostic purposes or before entering therapeutic trials. The diagnosis of chronic hepatitis was based on abnormal serum aminotransferase levels (greater than or equal to 1.5 times the upper limit of normal) for at least 6 months. None of the patients showed clinical or biochemical signs of cirrhosis. All patients were positive for anti-HCV antibody by the third-generation ELISA (Abbott Laboratories, North Chicago, IL, USA). Infection was confirmed by detection of circulating HCV RNA by polymerase chain reaction using the COBAS AMPLICOR hepatitis C virus test, version 2.0 (Roche, Branchburg, NJ, USA). Exclusion criteria were coinfection with either hepatitis B virus or human immunodeficiency virus. Seventy-eight patients (88 %) were treatment-naïve, while ten (12 %) were non-responders to a previous treatment with standard alpha interferon. The following clinical and laboratory data were recorded from all patients at the time of liver biopsy: sex, age, body mass index (BMI), presence or absence of diabetes, hypertension, history of intravenous drug use, past and current alcohol intake (none, <50, or 50 g or more daily), current cigarette smoking status, liver function tests, cholesterol and triglycerides levels, HCV genotype (performed by Versant HCV Genotype 2.0 Assay, LiPa-Siemens, Erlangen, Germany), serum HCV RNA (detected by real-time PCR assay, COBAS AmpliPrep/COBAS TaqMan 48-Roche, with lower limit of detection of 15 IU/ml).

At the time of the sonographic examination, the operator had no knowledge of clinical, biochemical or virological data. In all patients, hepatic echogenicity was assessed in comparison to the kidney, using the usual anterior approach, and graded as follows: grade 0, normal echogenicity; grade 1, slight, diffuse increase in fine echoes in

liver parenchyma with normal visualization of diaphragm and intrahepatic vessel borders; grade 2, moderate, diffuse increase in fine echoes with slightly impaired visualization of intrahepatic vessels and diaphragm; grade 3, marked increase in fine echoes with poor or non-visualization of the intrahepatic vessel borders, diaphragm, and posterior right lobe of the liver [12]. Grades 1, 2 and 3 were considered different degrees of BLP. The presence of hypo-echoic areas (skip areas) around the gallbladder or near the portal vein [4] was also evaluated. Ultrasound examination was performed by the same operator (ML), with 21 years of experience in abdominal sonography, using Sequoia 512 (Acuson Co., Mountain View, CA, USA) with a multifrequency convex electronic transducer set at 5 MHz frequency. Intraobserver variability, tested by dividing the number of occasions of complete agreement by the total number of occasions, showed a substantial agreement degree (K 0.80).

Liver specimens were obtained from the right hepatic lobe using 16-gauge Menghini modified needles inserted through the intercostals space. The biopsy specimens were fixed in buffered formalin, embedded in paraffin and routinely processed for histological analysis. Hepatic fibrosis was assessed using the Ishak fibrosis score [22]. Significant fibrosis was defined as Ishak score of 3 or more (presence of bridging fibrosis) and cirrhosis as Ishak score of 5 or 6 [23]. Steatosis was graded as follows: 1 (<30 % of hepatocytes affected), 2 (30–70 % of hepatocytes affected), or 3 (>70 % of hepatocytes affected) [24]. Histological evaluation was performed by a single pathologist without knowledge of patient's clinical or laboratory data.

Statistical comparisons were carried out by Student's t test, Chi-square, and linear regression. Multivariate stepwise regression analyses were performed, with both LS and LS more 30 % serving as dependent variable and age, gender, BMI, genotypes, alcohol consumption, cigarette smoking, staging, grading, ultrasound pattern, viral load, liver function tests, cholesterol and triglycerides level serving as independent variables. A P value of <0.05 was considered significant. Sensibility, specificity, positive predictive value (PPV), negative predictive value (NPV) test and accuracy for LS of BLP and skip areas were calculated.

Results

Clinical findings, histological and sonographic features of the 88 patients are illustrated in Table 1. Fifty-three of the 88 patients (60 %) showed BLP, in 40 (75 %) of these patients the degree of hyperechogenicity was slight (BLP grade 1), in 13 (25 %) moderate or marked (BLP grades 2 or 3; 12 and 1, respectively). Skip areas were found in 14

Table 1 Characteristics of the study population (88 patients)

Age: years	45.71 $\pm$ 11.2
Male/female	55/33
BMI (kg/m ²)	23.73 $\pm$ 2.8
Diabetes: n (%)	7 (7.9 %)
Hypertension: n (%)	14 (15.9 %)
History of intravenous drug use: n (%)	23 (26.1 %)
Past history of alcohol intake >50 g/day: n (%)	31 (35.2 %)
Present alcohol intake >50 g/day: n (%)	0 (0 %)
Present alcohol intake <50 g/day: n (%)	26 (29.5 %)
Cigarette smoking: n (%)	58 (65.9 %)
Genotypes	
1 n (%)	38 (43.2 %)
2 n (%)	10 (11.4 %)
3 n (%)	25 (28.4 %)
4 n (%)	15 (17 %)
Sonography	
BLP grades 1, 2 and 3: n (%)	53 (60 %)
BLP grades 2 and 3: n (%)	13 (15 %)
BLP grade 1: n	40
BLP grade 2: n	12
BLP grade 3: n	1
Skip areas: n (%)	14 (16 %)
Histological findings	
Steatosis	
Grade 1, 2 and 3: n (%)	40 (45.4 %)
Grade 1: n	30
Grade 2: n	4
Grade 3: n	6
Staging (fibrosis score)	
F0: n	2
F1: n	34
F2: n	28
F3: n	20
F4: n	4
F5: n	0
F6: n	0
Significant fibrosis (Ishak score of 3 or more): n (%)	24 (27 %)
Cirrhosis: n (%)	0 (0 %)

BMI body mass index, n number of patients, BLP bright liver echo pattern

patients (16 %). Histological steatosis was observed in 40 patients (45 %), among them 30 with grade 1 (75 %), 4 with grade 2 (10 %), and 6 with grade 3 (15 %). As regards fibrosis, 2 patients (2.2 %) showed F0, 34 (38.6 %) F1, 28 (31.8 %) F2, 20 (22.7 %) F3, 4 (4.5 %) F4. None of the patients had F5 and F6. In Table 2, the characteristics of the patients with and without LS are compared. Steatosis correlated significantly with genotype 3 (P = 0.009) and with genotype 1 in patients with high BMI (P = 0.016) and

Table 2 Characteristics of 88 patients with chronic hepatitis C with and without histological steatosis

	Steatosis (<i>n</i> = 40)	No steatosis (<i>n</i> = 48)	<i>P</i>
Age: years	46.6 ± 10	44.9 ± 12	0.62 (ns)
Male/female	25/40	30/48	1 (ns)
BMI			
All genotypes	24.01 ± 2.85	23.51 ± 2.8	0.41 (ns)
Genotype 1	25.78 ± 2.47	23.66 ± 2.57	0.016 (s)
Diabetes: <i>n</i> (%)	2 (0.5)	5 (10.4)	0.45 (ns)
Hypertension: <i>n</i> (%)	7 (17.5)	7 (14.5)	0.97 (ns)
Present alcohol intake: <i>n</i> (%) (in all patients <50 g/day)	15 (37.5)	10 (20.3)	0.13 (ns)
Past history of alcohol intake >50 g/day			
All genotypes: <i>n</i> (%)	16 (40)	15 (32.2)	0.73 (ns)
Genotype 1: <i>n</i> (%)	7 (41)	2 (8)	0.016 (s)
Intravenous drug use: <i>n</i> (%)	12 (30)	11 (22.9)	0.47 (ns)
Cigarette smoking: <i>n</i> (%)	29 (72)	29 (60)	0.26 (ns)
Genotype 1: <i>n</i> (%)	15 (37.5)	23 (47.9)	0.39 (ns)
Genotype 2: <i>n</i> (%)	4 (10)	6 (12)	0.75 (ns)
Genotype 3: <i>n</i> (%)	17 (42)	8 (16)	0.009 (s)
Genotype 4: <i>n</i> (%)	4 (10)	11 (22)	0.15 (ns)
Serum HCV RNA level	1,146,000 ± 893,600	990,800 ± 944,000	0.43 (ns)
ALT	130 ± 66	104 ± 96	0.15 (ns)
AST	73 ± 36	58 ± 48	0.11 (ns)
GGT	69 ± 66	50 ± 46	0.12 (ns)
Cholesterol	174 ± 46	175 ± 37	0.83 (ns)
Triglycerides	94 ± 52	87 ± 37	0.46 (ns)
Sonography			
BLP: <i>n</i> (%)	30 (75)	23 (48)	0.017 (s)
BLP grades 2 and 3: <i>n</i> (%)	13 (32)	0 (0)	0.00007 (s)
Skip areas: <i>n</i> (%)	14 (35)	0 (0)	0.00003 (s)
Staging	1.95 ± 0.93	1.83 ± 0.95	0.56 (ns)

n number of patients, *ns* no significance, *BMI* body mass index, *s* significance, *ALT* alanine aminotransferase, *AST* aspartate aminotransferase, *GGT* γ-glutamyl transferase, *BLP* bright liver echo pattern

Table 3 Correlation between LS and sonographic aspects (BLP and skip areas)

	Steatosis (40 pt)	Absence of steatosis (48 pt)	<i>P</i>
BLP: <i>n</i> (%)	30 (75 %)	23 (48 %)	0.017
BLP grades 2 and 3: <i>n</i> (%)	13 (32.5 %)	0 (0 %)	0.00007
Skip areas: <i>n</i> (%)	14 (35 %)	0 (0 %)	0.00003

LS liver steatosis, *BLP* bright liver echo pattern, *pt* patients, *n* number of patients

past history of alcohol intake exceeding 50 g/day (*P* = 0.016). Current alcohol intake (however, in all patients below 50 g/day) was found in 15 (37.5 %) patients with LS and in 10 (20.8 %) without LS, but this difference

Table 4 Correlation between BLP and fibrosis

	Significant fibrosis	No significant fibrosis	<i>P</i>
All patients: <i>n</i>	24	64	
BLP/no BLP	13/11	40/24	0.6 (ns)
Patients without LS: <i>n</i>	12	36	
BLP/no BLP	7/5	16/20	0.6 (ns)

BLP bright liver echo pattern, *n* number of patients, *ns* no significance

did not reach statistical significance. Likewise, no significant difference was established for age, sex, diabetes mellitus and hypertension status, cigarette smoking, serum HCV RNA levels, staging, liver function tests, cholesterol and triglycerides levels. BLP correlated with LS

Table 5 Sensitivity, specificity, predictive values and accuracy of BLP and skip areas vs LS

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
All grades BLP vs LS	75	50	56	68	61
Grades 2 and 3 BLP vs LS	43	100	100	64	69
Grades 2 and 3 BLP vs LS = or >30 %	72	96	61	96	90
Skip areas	35	100	100	64	70

BLP bright liver echo pattern, LS liver steatosis, PPV positive predictive value, NPV negative predictive value

($P = 0.017$), especially for the grade of moderate or marked hyperechogenicity ($P = 0.00007$) (Table 3). The presence of skip areas was highly correlated with steatosis ($P = 0.00003$) (Table 3). No correlation was found between BLP and fibrosis, considering either all patients globally or exclusively the group of patients without LS (Table 4).

The sensitivity, specificity, PPV, NPV and accuracy of BLP for LS were 75, 50, 56, 68 and 61 %, respectively, when all the degrees of liver hyperechogenicity were considered; and 43, 100, 100, 64 and 69 %, respectively, when only BLP grades 2 and 3 were considered. When BLP grades 2–3 and skip areas were correlated with LS of 30 % or more, the sensitivity, specificity, PPV, NPV and accuracy were 72, 96, 61, 96, 90 and 35 %, 100, 100, 64, 70 %, respectively (Table 5). Table 6 provides the results of multiple regression analyses between LS and LS more 30 % with the various independent variables. The factors that were significantly associated with LS were skip area and genotype ($P = 0.0003$ and $P = 0.002$, respectively), while only skip area was associated with LS >30 % ($P = 0.0002$). When skip area was excluded as independent variable, BLP grades 2 and 3 and genotype 3 were independent factors correlated with LS ($P = 0.001$ and $P = 0.002$, respectively) and only BLP grades 2 and 3 were associated with LS >30 % ($P = 0.002$) (Table 7).

Discussion

LS, defined by accumulation of lipids (mainly triglycerides) in the cytoplasm of hepatocytes, has been classified as alcoholic or non-alcoholic fatty liver disease (NAFLD). NAFLD includes non-alcoholic fatty liver alone and non-alcoholic steatohepatitis [25]. LS has been recognized by a BLP in 1979 [26]. Some authors consider this pattern as

Table 6 Correlation between LS and clinical, biochemical, histological and ultrasound pattern (BLP and skip areas) on multivariate analysis

Independent variable	Dependent variable	β coefficient	Standard error	P value
Age	LS	0.02	0.1	0.7
	LS >30 %	−0.15	0.11	0.2
Gender	LS	0.02	0.11	0.8
	LS >30 %	0.02	0.12	0.8
BMI	LS	0.13	0.09	0.17
	LS >30 %	0.05	0.11	0.6
Past history of alcohol intake	LS	0.1	0.09	0.2
	LS >30 %	0.11	0.11	0.3
Present alcohol intake	LS	−0.02	0.08	0.8
	LS >30 %	−0.06	0.1	0.5
Cigarette smoking	LS	−0.11	0.1	0.2
	LS >30 %	−0.18	0.1	0.1
Genotype 3	LS	0.31	0.09	0.002
	LS >30 %	0.12	0.1	0.2
Activity grade	LS	0.14	0.14	0.3
	LS >30 %	0.09	0.16	0.5
Fibrosis stage	LS	−0.15	0.12	0.2
	LS >30 %	0.01	0.14	0.9
Serum HCV RNA	LS	0.06	0.08	0.4
	LS >30 %	−0.02	0.1	0.8
BLP	LS	0.06	0.1	0.6
	LS >30 %	0.008	0.16	0.9
BLP 2 and 3	LS	−0.04	0.28	0.1
	LS >30 %	−0.04	0.38	0.2
Skip areas	LS	1.06	0.28	0.0003
	LS >30 %	1.05	0.33	0.002
AST	LS	0.12	0.19	0.52
	LS >30 %	0.11	0.23	0.62
ALT	LS	−0.14	0.20	0.48
	LS >30 %	−0.17	0.23	0.46
GGT	LS	0.13	0.11	0.22
	LS >30 %	0.08	0.13	0.5
Cholesterol	LS	0.06	0.11	0.58
	LS >30 %	0.01	0.13	0.9
Triglycerides	LS	−0.04	0.1	0.69
	LS >30 %	−0.04	0.12	0.7
Prothrombin time	LS	−0.17	0.11	0.06
	LS >30 %	−0.15	0.11	0.17
Platelets count	LS	−0.08	0.09	0.37
	LS >30 %	−0.1	0.1	0.31

highly correlated with LS [6, 7, 9, 10, 12, 13], especially if associated with a posterior beam attenuation and/or skip areas [10]. Nevertheless, other authors think that BLP might also indicate liver fibrosis [13, 17–20]. In this study, the prevalence of BLP, its correlation with LS and fibrosis,

Table 7 Correlation between LS and clinical, biochemical, histological and ultrasound pattern (BLP) on multivariate analysis

Independent variable	Dependent variable	β coefficient	Standard error	<i>P</i> value
Age	LS	−0.02	0.1	0.83
	LS >30 %	−0.2	0.12	0.11
Gender	LS	0.02	0.12	0.8
	LS >30 %	0.02	0.13	0.8
BMI	LS	0.13	0.1	0.19
	LS >30 %	0.05	0.11	0.6
Past history of alcohol intake	LS	0.12	0.1	0.25
	LS >30 %	0.11	0.11	0.3
Present alcohol intake	LS	−0.03	0.09	0.7
	LS >30 %	−0.06	0.1	0.5
Cigarette smoking	LS	−0.12	0.1	0.24
	LS >30 %	−0.18	0.1	0.1
Genotype 3	LS	0.33	0.1	0.002
	LS >30 %	0.12	0.1	0.2
Activity grade	LS	0.07	0.15	0.62
	LS >30 %	0.09	0.16	0.5
Fibrosis stage	LS	−0.13	0.13	0.3
	LS >30 %	0.01	0.14	0.9
Serum HCV RNA	LS	0.09	0.09	0.3
	LS >30 %	−0.02	0.1	0.8
BLP	LS	0.11	0.14	0.4
	LS >30 %	0.008	0.16	0.9
BLP 2 and 3	LS	0.51	0.14	0.001
	LS >30 %	−0.04	0.38	0.2
AST	LS	0.09	0.21	0.6
	LS >30 %	0.11	0.23	0.62
ALT	LS	−0.05	0.22	0.8
	LS >30 %	−0.17	0.23	0.46
GGT	LS	0.15	0.12	0.2
	LS >30 %	0.08	0.13	0.5
Cholesterol	LS	0.0004	0.12	0.9
	LS >30 %	0.01	0.13	0.9
Triglycerides	LS	−0.05	0.11	0.62
	LS >30 %	−0.04	0.12	0.7
Prothrombin time	LS	−0.17	0.11	0.06
	LS >30 %	−0.14	0.11	0.17
Platelets count	LS	−0.05	0.12	0.37
	LS >30 %	−0.1	0.1	0.31

and the utility of detecting BLP and skip areas for LS diagnosis were evaluated in a group of patients with chronic hepatitis C. Considering that steatosis, a frequent feature of chronic hepatitis C [27, 28, 30], is associated with progression of chronic HCV-related liver disease [24, 30–34], we thought that establishing a correlation between sonographic findings and LS could be of great usefulness in the management of these patients.

Our data confirmed the high prevalence of histological steatosis in chronic hepatitis C, as documented in 45 % of our patients, in analogy with previous studies [27–29]. The association between LS and genotype 3 presumably due to the direct action of HCV [35, 36] was also confirmed by both univariate and multivariate analysis. Besides, only in patients with genotype 1, LS was correlated with high BMI and past history of alcohol intake exceeding 50 g/day, in agreement with the pathogenic mechanism of steatosis, principally metabolic, postulated in the patients with this genotype [37]. As regards the correlation between histological steatosis and sonographic findings of steatosis, when all grades of hyperechogenicity were globally considered, BLP showed a relatively high sensitivity for LS (75 %), while the specificity was low (50 %), for the presence of a high number of false positives for LS in the patients with BLP grade 1. Excluding a possible mistake in the liver biopsy due to a sampling variation, our results showed that the reliability of BLP low grade was uncertain for LS. However, it is necessary to remark that the prevalence of ultrasound LS found in our study (in 60 % of patients in comparison to 30–47 % found from other authors always in patients with chronic hepatitis) [10, 11, 17, 19] could be overestimated from use of multifrequency transducer set at relatively high frequency (5 MHz) that increases the echogenicity of the structures in the superficial field, making the liver more echogenic in comparison to the kidney. The correlation between BLP of moderate or marked grade and LS showed a high specificity and a relatively high sensitivity (96 and 72 %, respectively) for LS >30 % and a high specificity and a low sensitivity (100 and 43 %, respectively) for all grades of LS. High specificity (100 %) and low sensitivity (30 %) for LS were also observed for the presence of skip areas. Whereas the presence of skip areas, together with the genotype 3, is considered to be independent predictor of LS by multivariate analysis; our data, in agreement with other authors [38] showed a high degree of certainty for the diagnosis of LS, just thanks to the identification of skip areas in patients with chronic hepatitis C. Nevertheless, the absence of skip areas does not exclude the LS as indicated by from their low sensitivity for histological finding of steatosis. No correlation between BLP and fibrosis has been found. These data are in agreement with those recently reported by other authors [11], although they must be confirmed on wider groups including patients with higher levels of fibrosis than those included in our study.

To sum up, our study, which combined the analysis of clinical, histological and sonographic features of a well-defined group of patients with chronic hepatitis C, showed that the detection of BLP grades 2 and 3 has a good sensitivity and high specificity for high grades of steatosis. Besides, the detection of skip areas around the gallbladder

or near the portal vein showed a high predictive value for LS.

Finally, it must be emphasized that our study is limited to the patients with chronic hepatitis C and that ulterior studies are necessary to establish their applicability in the general population and other groups of patients.

Conflict of interest Maurizio Loy, Giancarlo Serra, Luchino Chessa declare that they have no conflict of interest.

Informed consent All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000 (5). All patients provided written informed consent to enrolment in the study and to the inclusion in this article of information that could potentially lead to their identification.

Human and animal studies The study was conducted in accordance with all institutional and national guidelines for the care and use of laboratory animals.

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