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RESEARCH ARTICLE

Correlations of Laparoscopy with Histology and Laboratory Studies on Liver Diseases in Bariatric Patients

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Abstract
Background Non-alcoholic fatty liver disease is prevalent in obese patients. Liver biopsy remains the best diagnostic tool for confirmation. We evaluated the effectiveness of macroscopic parameters of laparoscopy in diagnosis of liver diseases. Moreover, correlations of laparoscopy with histology and laboratory data were also studied.
Methods From December 2004 to April 2006, 126 morbidly obese patients submitted to laparoscopic bariatric surgery at the En-Chu-Kong Hospital were prospectively studied.
Results There were correlations of histologic steatosis with liver surface fat spot density, liver margin shape, and liver size. Histologic inflammation was related to liver color, vascularity beneath hepatic capsule, liver margin shape, liver size, and liver surface nodularity. Histologic fibrosis had relations to liver color, liver surface nodularity, liver size, varices of ligamentum teres. Spleen size was related to liver surface nodularity and spleen congestion. Relationships of laboratory data with laparoscopic findings included: aspartate transaminase (AST) level with liver size, alanine transaminase (ALT) level with liver color and liver size, albumin level with liver margin shape and liver surface fibrosis and liver size, total protein level with liver size, alkaline phosphatase (ALP) level with liver surface fibrosis, blood glucose level with liver surface nodularity and spleen size, C-peptide with liver size. Besides, there were relations of γ-GT level with liver color, liver margin shape, liver and spleen size.
Conclusion Besides histology and laboratory studies, laparoscopic inspection of the abdominal cavity provides important and additional information, which contributed to the final diagnosis of chronic liver diseases and detection of possible pathology in patients.

Keywords Non-alcoholic fatty liver disease · Morbid obesity · Laparoscopy · Liver disease diagnosis · Liver biopsy

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Introduction

Non-alcoholic fatty liver disease describes a common clinicopathological condition characterized by significant accumulation of fat in the hepatic parenchyma, in a patient without a history of excessive alcohol ingestion (20 g per day) [1]. It is commonly seen in obese patients [2]. It can evolve to more advanced stages of hepatic damage such as steatohepatitis and cirrhosis [3–5]. The gold standard for diagnosis of these diseases is tissue examination [5–8]. However, the traditional percutaneous liver biopsy has a relatively high complication rate of 0.9–3.7%, and a mortality of 0.01–0.12% [9]. Because laparoscopy is a diagnostic tool of liver diseases, it is interesting to know the exact value of laparosocpy in the diagnosis of chronic liver diseases in patients receiving bariatric surgeries. In this study, we try to find out the correlation of liver and intraabdominal imaging characteristics from laparoscopy

with the severity of hepatic pathologic abnormalities. Besides, the relationship of laparoscopic findings with laboratory data was also studied.

Materials and Methods

Patients

This was a prospective study, from December 2004 to April 2006, in which patients were submitted to laparoscopic bariatric surgeries for morbid obesity at the En-Chu-Kong Hospital, Taiwan. Informed consents were obtained preoperatively. Exclusions were made for patients who refused the study, or with alcohol use in excess of 20 g per day. Moreover, patients with other known causes of liver disease, e.g., hepatitis C seropositivity, granulomatous liver disease, hereditary hemochromatosis, alpha-1-antitrypsin deficiency, and known use of methotrexate, tamoxifen, and corticosteroids were excluded from this analysis.

A total of 126 patients were included in this study on the basis of the exclusion criteria. There were 42 male and 84 female patients with mean age 31.3±5.3 years (range 21.0–52.3). The preoperative mean body weight was 122.4±22.1 kg (range 92.0–193.6). The body height was 166.9±23.1 cm (range 152.0–187.0) and the mean body mass index (BMI) was 43.8±4.3 kg/m^2 (range 37.8–62.9).

Preoperative Laboratory Data Collection

After an overnight fast, venous blood was drawn to determine the liver function, including albumin, total protein (T-protein), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and γ-glutammyl transpeptidase (γ-GT). Metabolic profiles included fasting blood glucose, HbA1c, C-peptide, insulin, and insulin resistance (HOMA-IR). Insulin resistance was determined by the homeostatic model assessment (HOMA) method. There were other important biochemical data, e.g., cholesterol (CHO), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), uric acid (UA), and parathyroid hormone (PTH). Other data such as white blood cell count (WBC), hemoglobin (Hb), mean corpuscular volume (MCV), calcium level (Ca), and C-reactive protein (CRP) were also recorded.

Laparoscopic Exploration and Grading of Severity

The techniques of laparoscopic mini-gastric bypass and gastric banding that we followed have been detailed previously [10–12]. Pneumoperitoneum was established via a Veress needle with intraabdominal pressure up to 15 mmHg. The patient was put in a reverse Trendelenburg position. Five ports were used totally.

Each patient underwent routine laparoscopic exploration of the abdominal cavity, in which liver surface characteristics, including color (reddish-brown, yellowish, yellowish-white, and whitish), size of various degree (atrophic, normal, and hepatomegaly), irregularity of liver surface (smooth, uneven, granular, nodular, and circumferential scarring), dullness of liver edge, the presence of regenerative nodules, and subcapsular neovascularity were inspected. The presence of ascites, splenomegaly, peritoneal changes, and evidence of portal hypertension were also examined.

A systematic record was made of the degree of portal hypertension (size of the liver, congestion of liver and spleen, vascularity of the falciform ligament), the degree of fatty change (yellowish discoloration, margin of liver, and bulky liver), and the degree of inflammation (liver surface vascularity and redness). Fibrosis was graded and the presence or absence of cirrhosis and its type (nodularity, broken light reflex) were classified. Any focal lesion was also recorded and photographed. Criteria for macroscopic diagnosis of liver diseases were made with reference to those reported by Helt et al. [13] and Jalan et al. [9]. All of the laparoscopic (macroscopic) parameters were graded from none to severe, depending on the degree assessed by the same surgeon: none=0; minimal=1; moderate=2; severe=3.

Technique of Laparoscopic Liver Wedge Biopsy

Biopsy site was selected as the area with representative, the location of suspected mass lesion and accessibility for hemostasis. Wedge biopsy was obtained from the liver edge using laparoscopic scissors, including capsule on specimen surface. The specimen (about 0.4 cm in average) was retrieved through the port at the level of the umbilicus in the left anterior axillary line. Hemostasis was obtained by applying direct pressure on the biopsy site with a small piece of gauze and then electrocauterization. Bile leakage can also be checked (Fig. 1). Besides, any inadvertent injury to other organs must be confirmed before the ongoing procedures of bariatric surgeries.

Specimen Preservation and Histology Grading

After the specimen being fixed in 10% buffered formalin and embedded in paraffin, eight serial sections were cut for examination. These were stained with hematoxylin and eosin stain for steatosis evaluation. The periodic-acid Schiff with diastase stain was for the necroinflammatory grading and the Masson's trichrome and Sweet's reticulin stains

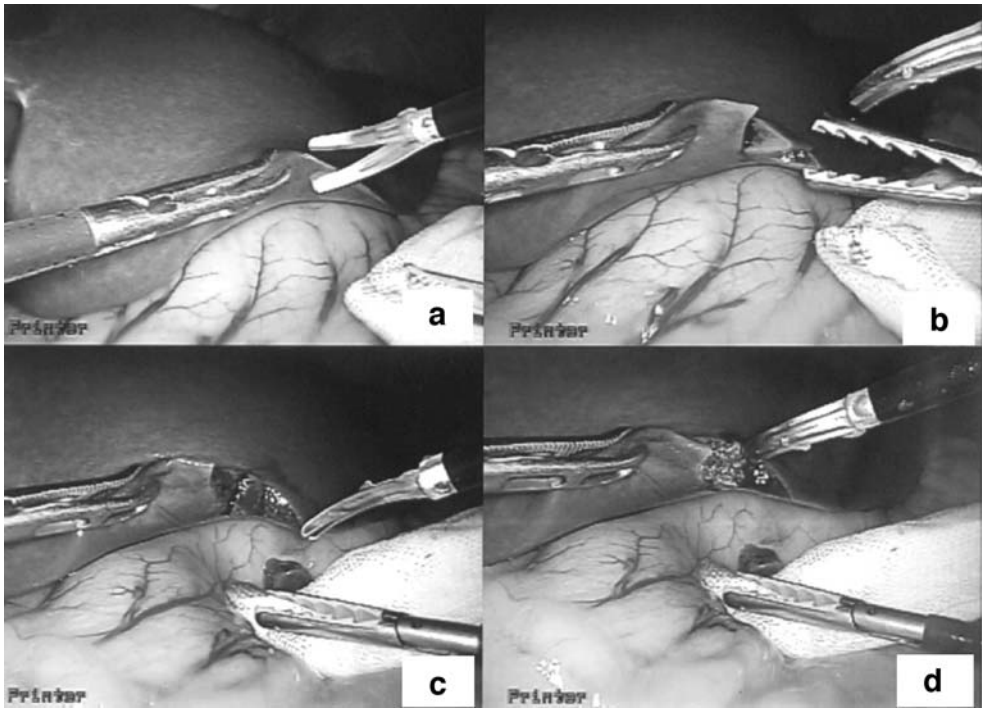

Fig. 1 Procedures of liver wedge biopsy under laparoscopy: **a**) Holding the selected hepatic tissue with a laparoscopic grasper, **b**) Cutting the specimen with a laparoscopic scissors, **c**) Prevention of missing the specimen with a piece of gauze, **d**) Electrocauterizing the liver cut surface for hemostasis and checking bile leakage with a piece of gauze

were reviewed for fibrosis and architectural changes. The biopsy specimens were coded and assessed by an experienced hepatopathologist unaware of the patient's clinical history, physical findings, laboratory data, or laparoscopic features. The histological diagnosis of fatty change, degree of inflammatory activity, fibrosis, and cirrhosis were based on conventional criteria [14, 15]. Additionally, all of the biopsies were scored from 0 to 3 on the basis of a grade for steatosis, inflammation and fibrosis: none=0; minimal=1; moderate=2; severe=3.

Statistical Analysis

The laparoscopic interpretation was compared with the histologic diagnosis of the biopsy material. Results were analyzed using multiple entry tables. Statistical evaluations were performed by Spearman's rank correlation; statistical significance was set at $p<0.05$. Besides, the laparoscopic and laboratory data were also compared.

Results

In Table 1, we noted some correlations of liver histology with laparoscopic findings. As histologic steatosis became more severe, the liver color appeared more yellowish and fat spots more diffuse in detail (Pearson coefficient of 0.548, $p=0.007$), the liver margin was more blunt (Pearson coefficient of 0.364, $p=0.017$). Besides, the liver size was more atrophic (Pearson coefficient of −0.736, $p=0.000$).

As the grade of histologic inflammation increased, we noted liver surface appeared more yellowish, even more reddish and congested (Pearson coefficient of 0.188, $p=0.000$), more vascularity beneath the hepatic capsule (Pearson coefficient of 0.330, $p=0.029$), liver margin more blunt (Pearson coefficient of 0.536, $p=0.000$), liver size smaller (atrophic) (Pearson coefficient of −0.477, $p=0.009$), surface nodularity more severe and diffuse (Pearson coefficient of 0.473, $p=0.011$).

When histologic fibrosis appeared more severe, we found that liver surface more reddish and congested (Pearson coefficient of 0.545, $p=0.000$), liver surface nodularity more evident (Pearson coefficient of 0.311, $p=0.014$), liver size smaller (Pearson coefficient of −0.263, $p=0.026$), more apparent varices of ligamentum teres (Pearson coefficient of 0.305, $p=0.000$).

There were other relationships among the laparoscopic findings. As the nodularity of liver surface appeared more severe, the spleen looked more enlarged in size (Pearson coefficient of 0.303, $p=0.019$). Meanwhile, when the spleen enlarged in size, its appearance became more congested (Pearson coefficient of 0.276, $p=0.007$).

Relationships of laboratory data with laparoscopic findings were demonstrated in Table 2. As AST level increased, the liver looked smaller (Pearson coefficient of −0.304, $p=0.000$). Likewise, ALT level had the same trend (Pearson coefficient of −0.323, $p=0.000$). Moreover, there was a positive correlation of ALT level with the degree of yellowish liver color and diffuse fat spots (Pearson coefficient of 0.177, $p=0.047$).

Table 1 Correlation of histologic parameters (steatosis, inflammation, and fibrosis) with laparoscopic findings

	Variables	Histology findings			Laparoscopy findings										
		Steatosis	Inflammation	Fibrosis	Peritoneal vessel dilatation	Ascites	Spleen color	Spleen size	Liver size	Liver nodularity	Liver margin	Liver tumor	Liver color	Varices of Ligamentum teres	Vascularity beneath the hepatic capsule
Histology findings	Steatosis	1	0.507 (0.230)	0.222 (0.606)	–	–	0.132 (0.691)	0.245 (0.462)	− 0.736 (0.000)	0.241 (0.483)	0.364 (0.017)	–	0.548 (0.007)	0.165 (0.474)	0.259 (0.733)
	Inflammation	0.507 (0.230)	1	0.348 (0.338)	–	–	0.129 (0.950)	0.302 (0.622)	−0.477 (0.009)	0.473 (0.011)	0.536 (0.000)	–	0.188 (0.000)	0.213 (0.061)	0.330 (0.029)
	Fibrosis	0.222 (0.606)	0.348 (0.338)	1	–	–	0.108 (0.474)	0.257 (0.074)	−0.263 (0.026)	0.311 (0.014)	0.153 (0.222)	–	0.545 (0.000)	0.305 (0.000)	0.374 (0.647)
Laparoscopy findings	Peritoneal vessel dilatation	–	–	–	1	–	–	–	–	–	–	–	–	–	–
	Ascites	–	–	–	–	1	–	–	–	–	–	–	–	–	–
	Spleen color	0.132 (0.691)	0.129 (0.950)	0.108 (0.474)	–	–	1	0.276 (0.007)	−0.082 (0.645)	0.344 (0.071)	−0.071 (0.417)	–	0.103 (0.929)	0.011 (0.900)	0.049 (0.959)
	Spleen size	0.245 (0.462)	0.302 (0.622)	0.257 (0.074)	–	–	0.276 (0.007)	1	−0.392 (0.063)	0.303 (0.019)	0.232 (0.053)	–	0.340 (0.136)	0.176 (0.135)	0.278 (0.559)
	Liver size	−0.736 (0.000)	−0.477 (0.009)	−0.263 (0.026)	–	–	−0.082 (0.645)	−0.392 (0.063)	1	−0.384 (0.063)	0.582 (0.082)	–	0.538 (0.026)	0.238 (0.071)	0.236 (0.304)
	Liver nodularity	0.241 (0.483)	0.473 (0.011)	0.311 (0.014)	–	–	0.344 (0.071)	0.303 (0.019)	−0.384 (0.063)	1	0.259 (0.099)	–	0.651 (0.211)	0.397 (0.101)	0.688 (0.210)
	Liver margin	0.364 (0.017)	0.536 (0.000)	0.153 (0.222)	–	–	−0.071 (0.417)	0.232 (0.053)	0.582 (0.082)	0.259 (0.099)	1	–	0.341 (0.081)	0.027 (0.760)	0.208 (0.134)
	Liver tumor	–	–	–	–	–	–	–	–	–	–	1	–	–	–
	Liver color	0.548 (0.007)	0.188 (0.000)	0.545 (0.000)	–	–	0.103 (0.929)	0.340 (0.136)	0.538 (0.062)	0.651 (0.211)	0.341 (0.081)	–	1	0.864 (0.080)	0.382 (0.223)
	Varices of ligamentum teres	0.165 (0.474)	0.213 (0.061)	0.305 (0.000)	–	–	0.011 (0.900)	0.176 (0.135)	0.238 (0.071)	0.397 (0.101)	0.027 (0.760)	–	0.864 (0.080)	1	0.122 (0.592)
	Vascularity beneath the hepatic capsule	0.259 (0.733)	0.330 (0.029)	0.374 (0.647)	–	–	0.049 (0.959)	0.278 (0.559)	0.236 (0.304)	0.688 (0.210)	0.208 (0.134)	–	0.382 (0.223)	0.122 (0.592)	1

The number above indicating "Pearson coefficient"
The number below indicating "*P* value", $P < 0.05$ meaning statistically significant

Table 2 Correlation of laboratory data with laparoscopic findings

Variables	Ascites	Spleen color	Spleen size	Liver size	Liver surface nodularity	Liver surface nodularity type	Liver margin	Liver tumor	Liver color	Liver surface fibrosis	Varices of Ligamentum teres
A1bumin	–	0.017	0.079	−0.255	0.044	0.602	−0.207	–	0.119	−0.203	0.025
		(0.851)	(0.376)	(0.004)	(0.622)	(0.050)	(0.019)		(0.183)	(0.021)	(0.775)
T-protein	–	−0.125	−0.067	−0.174	0.059	−0.182	−0.056	–	0.270	−0.044	0.006
		(0.158)	(0.452)	(0.049)	(0.507)	(0.593)	(0.529)		(0.102)	(0.623)	(0.947)
AST	–	−0.049	0.171	−0.304	0.073	−0.090	−0.086	–	0.162	0.060	0.008
		(0.584)	(0.053)	(0.000)	(0.412)	(0.793)	(0.331)		(0.069)	(0.496)	(0.932)
ALT	–	−0.042	0.137	−0.323	0.073	0.120	−0.138	–	0.177	−0.091	−0.008
		(0.640)	(0.122)	(0.000)	(0.412)	(0.726)	(0.119)		(0.047)	(0.305)	(0.924)
ALP	–	0.095	0.707	−0.316	0.577	0.014	−0.577	–	0.000	0.949	0.163
		(0.284)	(0.182)	(0.604)	(0.308)	(0.877)	(0.308)		(1.000)	(0.014)	(0.066)
γ-GT	–	−0.058	0.222	−0.315	0.117	−0.414	0.224	–	0.280	−0.037	−0.173
		(0.579)	(0.032)	(0.002)	(0.265)	(0.268)	(0.031)		(0.007)	(0.727)	(0.098)
Blood glucose	–	0.116	0.222	−0.113	0.238	−0.030	−0.053	–	0.041	0.037	0.201
		(0.189)	(0.012)	(0.202)	(0.006)	(0.930)	(0.549)		(0.650)	(0.673)	(0.223)
HbA1c	–	0.108	0.119	0.009	0.097	0.030	−0.091	–	−0.064	−0.124	0.073
		(0.222)	(0.181)	(0.922)	(0.275)	(0.930)	(0.305)		(0.475)	(0.163)	(0.414)
C-peptide	–	−0.063	0.051	−0.255	0.101	−0.060	−0.145	–	0.119	0.082	−0.137
		(0.482)	(0.576)	(0.004)	(0.264)	(0.861)	(0.107)		(0.188)	(0.366)	(0.128)
Insulin	–	−0.097	0.091	−0.140	0.024	0.120	−0.073	–	0.163	0.034	−0.128
		(0.275)	(0.307)	(0.115)	(0.784)	(0.726)	(0.410)		(0.068)	(0.699)	(0.150)
HOMA-IR	–	−0.107	0.160	−0.287	0.127	−0.181	−0.126	–	0.286	0.472	0.080
		(0.226)	(0.070)	(0.061)	(0.153)	(0.594)	(0.155)		(0.074)	(0.121)	(0.365)
CHO	–	−0.128	−0.164	0.026	−0.091	0.000	−0.082	–	−0.020	−0.117	−0.105
		(0.148)	(0.063)	(0.768)	(0.305)	(1.000)	(0.354)		(0.820)	(0.185)	(0.235)
TG	–	0.002	−0.051	−0.127	0.103	0.120	0.007	–	−0.014	0.088	−0.044
		(0.979)	(0.563)	(0.151)	(0.245)	(0.726)	(0.939)		(0.874)	(0.319)	(0.622)
HDL-C	–	−0.045	0.052	0.020	−0.048	0.332	−0.110	–	0.056	−0.047	0.049
		(0.612)	(0.555)	(0.820)	(0.591)	(0.318)	(0.213)		(0.528)	(0.596)	(0.582)
UA	–	−0.021	−0.003	−0.053	−0.049	0.719	−0.124	–	0.050	−0.195	−0.008
		(0.810)	(0.973)	(0.550)	(0.583)	(0.063)	(0.162)		(0.579)	(0.127)	(0.932)
PTH	–	0.095	−0.014	−0.126	−0.065	0.099	−0.022	–	0.244	0.090	−0.058
		(0.286)	(0.913)	(0.321)	(0.609)	(0.266)	(0.863)		(0.052)	(0.480)	(0.649)
WBC	–	−0.051	−0.042	−0.048	−0.019	−0.240	−0.076	–	0.012	−0.088	−0.187
		(0.566)	(0.636)	(0.591)	(0.828)	(0.478)	(0.393)		(0.896)	(0.324)	(0.134)
Hb	–	0.123	0.116	−0.147	0.106	0.150	−0.066	–	0.051	0.158	−0.008
		(0.163)	(0.190)	(0.097)	(0.230)	(0.660)	(0.454)		(0.571)	(0.073)	(0.924)
MCV	–	0.091	0.062	0.085	0.019	−0.179	0.026	–	−0.133	0.137	0.056
		(0.303)	(0.484)	(0.340)	(0.831)	(0.598)	(0.772)		(0.135)	(0.121)	(0.531)
Ca	–	0.167	−0.248	−0.042	−0.105	0.109	−0.089	–	0.159	−0.198	−0.036
		(0.058)	(0.145)	(0.735)	(0.399)	(0.223)	(0.477)		(0.203)	(0.111)	(0.774)
CRP	–	0.125	0.140	−0.108	0.052	−0.359	−0.079	–	0.103	0.057	−0.104
		(0.160)	(0.116)	(0.224)	(0.560)	(0.279)	(0.375)		(0.251)	(0.520)	(0.243)

The number above indicating "Spearson coefficient"
The number below indicating "*P* value", $P<0.05$ meaning statistically significant

As γ-GT increased, liver color appeared more yellowish, more diffuse fat spots on surface and even more reddish (Pearson coefficient of 0.280, $p=0.007$), liver margin more uneven (Pearson coefficient of 0.224, $p=0.031$), liver size smaller (Pearson coefficient of −0.315, $p=0.002$), and spleen looked more enlarged in size (Pearson coefficient of 0.222, $p=0.032$).

Whereas the albumin level decreased, the degree of uneven liver margin (Pearson coefficient of −0.207, $p=0.019$) and liver surface fibrosis (Pearson coefficient of −0.203, $p=0.021$) became more severe. Besides, liver size became smaller (Pearson coefficient of −0.255, $p=0.004$). Likewise, T-protein level had the same relationship with liver size (Pearson coefficient of −0.174, $p=0.049$).

When the level of ALP increased, liver surface fibrosis appeared more evident (Pearson coefficient of 0.949, $p=0.014$).

As blood sugar level became higher, surface nodularity of liver was more severe (Pearson coefficient of 0.238, $p=0.006$), spleen appeared more enlarged (Pearson coefficient of 0.222, $p=0.012$).

There was a negative correlation of C-peptide with the liver size (Pearson coefficient of −0.255, $p=0.004$).

In our study, there was no complication of laparoscopy-guided liver wedge biopsy.

Discussion

Obesity is a pan-endemic health problem in both developed and developing countries [10, 16]. Obese patients show a higher prevalence of chronic liver diseases compared to individuals with normal body weight [17, 18]. With the advent of new, potentially effective therapeutic treatment for certain chronic liver diseases, it is essential to have an accurate assessment of liver morphology and histological status before, during, and after experimental therapies to evaluate the efficacy and safety of these agents [19, 20]. Although laboratory abnormalities provide some information on liver damage, the sensitivity and specificity were doubted.

Liver biopsy is not only the best tool for non-alcoholic fatty liver disease confirmation, but also the most sensitive and specific means of providing important prognostic information. Some histologic features have been recognized as useful in determining the risk of deterioration to a more advanced stage [21]. Furthermore, liver biopsy is regarded as the best specific tool to assess the effect of medical treatment given the uncertain correlation between improvement of liver tests or imaging studies with histologic damage [6].

Traditionally, percutaneous liver biopsy with or without ultrasound guidance has become the preferred method for obtaining hepatic tissue in patients with hepatobiliary disease. This procedure is minimally invasive and is well tolerated by most patients. With this technique, all patients receive liver biopsy with Tru-cut introduced percutaneously, which permits evaluation of deep and less fragmented specimens. However, it cannot retrieve the superficial specimen and that with liver capsule [22]. Besides, this percutaneous introduction of a needle into the abdominal cavity may result in serious complications, such as bleeding, bile leakage, ascites leakage, pneumothorax, or visceral injury, especially when performed in high-risk patients [23]. Moreover, it has been reported previously by Nord et al. that even ultrasonography-guided percutaneous liver biopsy may miss the diagnosis of cirrhosis in 1 to 67% of 6,242 patients, with an average of 24%, secondary to sampling error [19, 24].

Surgery is the only method for the treatment of morbid obesity that is recognized as being effective and long-lasting [11, 17, 25–27]. The increased enthusiasm for bariatric surgeries coincides with the development and dissemination of the laparoscopic approach [10, 11, 25]. During operation, detection of associated pathologies in the abdominal cavity is easily performed, and only the bare area and the posterior surface of the liver are not visible by laparoscopy. Besides, the texture of the liver can be assessed visually and by palpating the surface with a probe. Accurate sonography and color Doppler examination can be proceeded with the flexible probes through laparoscopic ports. Aside from exploratory laparotomy, no other investigative modality provides as much concurrent information about gross appearance, extent of disease, histology, and associated intraabdominal pathology as does laparoscopy [23]. In addition, laparoscopy-guided liver biopsy has the advantages of direct biopsies in focal liver disease, with a specificity approaching 100% [9, 23]. It is more accurate than blind or ultrasonography-guided biopsy [28, 29]. Besides, complications of bleeding, bile leakage from the biopsy site can be monitored and managed immediately. In large collection studies, the risk of complications is about 0.095% and mortality varies between 0.014% and 0.076% [30].

Although histology is the “gold standard” [9], the value of laparoscopic diagnosis of diffuse and focal liver disease has been reaffirmed repeatedly over the years with surprisingly similar high levels of diagnostic accuracy [19]. One study reported their results of identifying pathological changes such as fatty change, fibrosis, and the degree of inflammatory activity. The relative sensitivities and specificities for diagnosing these laparoscopically were 96.4% and 100%, 100% and 95%, and 94% and 95.7%, respectively [9]. In another study, Poniachik et al. have recently shown that the macroscopic diagnosis of cirrhosis during laparoscopy is more accurate than the histological diagnosis [20, 31]. Thus, the diagnosis of cirrhosis can be made accurately by laparoscopic observation even when the liver biopsy is not conclusive for cirrhosis because of fragmentation, sampling error, or inadequate amount of tissue [20]. Our study demonstrated that laparoscopic exploration could provide essential and additional information in liver disease diagnosis, besides histology and laboratory data.

From our results in Table 1, we noted the severity of histologic steatosis of liver was positively correlated with the density of yellowish spots on liver surface (Pearson coefficient of 0.548, $p=0.007$). Besides, blunter margin

(Pearson coefficient of 0.364, p=0.017) and smaller liver size (Pearson coefficient of −0.736, p=0.000) were more often seen in patients with advanced fatty liver disease. Likewise, as the grade of histologic inflammation increased, liver surface appeared more yellowish, even more reddish and congested (Pearson coefficient of 0.188, p=0.000), more vascularity beneath the hepatic capsule (Pearson coefficient of 0.330, p=0.029), liver margin more blunt (Pearson coefficient of 0.536, p=0.000), surface nodularity more severe and diffuse (Pearson coefficient of 0.473, p=0.011). Liver size became smaller (atrophic) (Pearson coefficient of −0.477, p=0.009) finally. We had an initial assumption of these results. These changes represented the different stages and severity of liver change as fatty liver and inflammation reaction deteriorated. At first, fat deposits inside the liver cells and causes appearance of fatty spots on liver surface. It is widely accepted that fatty liver exhibits increased lipid peroxidation [32, 33], which becomes more pronounced when inflammation is present. Neovascularity happens as an adaptation of the initial alteration of liver structure when the inflammation persists. As the destruction of liver proceeds, focal or even diffuse surface nodularity is seen.

Initially, histologic fibrosis appeared during the progression of hepatic fatty change and inflammation (Pearson coefficient of 0.545, p=0.000). It became more and more apparent as the subsequent course of macroscopic liver surface nodularity (Pearson coefficient of 0.311, p=0.014). Finally, at the predecompensated stage, severe histologic fibrosis was accompanied with macroscopic liver atrophy (Pearson coefficient of −0.263, p=0.026) and emergence of varices in ligamentum teres (Pearson coefficient of 0.305, p=0.000).

Although there was neither definite correlation between the size of spleen and the level of portal pressure, nor between splenomegaly and the presence of esophageal varices, it was widely accepted that an enlarged spleen was the most important clue of portal hypertension [22]. From our result, we noted that enlargement of spleen was positively related to the degree of liver surface nodularity (Pearson coefficient of 0.303, p=0.019). Meanwhile, as the spleen enlarged in size, it became more congested (Pearson coefficient of 0.276, p=0.007), so we made an initial deduction that splenomegaly may be regarded as an early indicator of liver cirrhosis and portal hypertension.

Abnormal liver functions were often seen in the course of gradual liver damage. One study concluded that a significant increase in the prevalence of fatty change of liver detected in patients with elevated ALT levels [34]. From Table 2, we also noted that when laparoscopic fatty liver change became more severe, elevation of ALT was noted (Pearson coefficient of 0.177, p=0.047). Liver size had a strongly negative coefficient with AST (Pearson coefficient of −0.304, p=0.000) and ALT level (Pearson coefficient of −0.323, p=0.000), whereas γ-GT increased, liver color appeared more yellowish, more diffuse fat spots on surface and even more reddish (Pearson coefficient of 0.280, p=0.007), liver margin more uneven (Pearson coefficient of 0.224, p=0.031), liver size smaller (Pearson coefficient of −0.315, p=0.002) and spleen more enlarged in appearance (Pearson coefficient of 0.222, p=0.032). As Albumin level decreased, the degree of uneven liver margin (Pearson coefficient of −0.207, p=0.019) and liver surface fibrosis (Pearson coefficient of −0.203, p=0.021) became more severe. Besides, liver was smaller (Pearson coefficient of −0.255, p=0.004). Likewise, T-protein level had the same trend about liver size (Pc of −0.174, p=0.049). We can explain this phenomenon by the following deduction. Initially, lipid peroxidation causes cell damage in fatty liver. Persistent elevated AST and ALT values reflect chronic liver damage. Increase in γ-GT was predictive of processing hepatic lobular inflammation and fibrosis, which was announced by Dixon et al. [35]. Later, severe liver damage causes deteriorated liver function, which is expressed in terms of decreased albumin and total protein production. Uneven liver margin looks more evident. More fibrosis is noted on liver surface. Finally, liver becomes atrophic.

In Table 2, we also noted the relationships of ALP, blood glucose, and C-peptide with liver and spleen findings under laparoscopy. Metabolic syndrome was once considered to be the possible causes, which was common in the obese individuals [36, 37]. However, the real mechanisms of these relationships were not fully understood.

Although laboratory data provide many vital clues to the diagnosis of chronic liver diseases, awareness by the pathologist of the clinical data and laparoscopic findings provides important and additional information to improve the accuracy of liver biopsy diagnosis. Meanwhile, we think when the clinician realizes the peritoneal characteristics (presence of collateral circulation and varices), macroscopic findings of liver and spleen, the accuracy of liver disease diagnosis would presumably improve. By that time, high-risk patients could receive medical treatment earlier before the pathologic change appeared.

In our study, some macroscopic parameters of abdominal cavity from laparoscopy seemed to provide high correlation values with histologic steatosis, inflammation, fibrosis, and cirrhosis. The combination of information gained on laparoscopy with histology provides the diagnosis in most patients. In future, laparoscopy may replace the need for liver biopsy in whom the etiological diagnosis is not in question and the biopsy is being performed only to stage the disease. However, a larger prospective study is needed to provide more reliable and accurate information.

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