福岡大医紀（*Med. Bull. Fukuoka Univ.*）：34(1)，1–7，2007

Sensitivity and Specificity Analysis of Hepatic Enzyme Blood Tests for the Diagnosis of Nonalcoholic Fatty Liver

Shinichi TANIHARA[1)], Yoshiharu HOSHIYAMA[2)] and Takeshi KAWAGUCHI[3)]

[1)] *Department of Hygiene and Preventive Medicine, School of Medicine, Fukuoka University*

[2)] *Department of Human Sciences, University of Human Arts and Sciences*

[3)] *Managing director, All Japan Labor Welfare Foundation*

Abstract：Background/Aims：Hepatic enzyme blood tests including analyses of serum aspartate aminotransferase（AST）and alanine aminotransferase（ALT）and gammaglutamyl transpeptidase（γ–GTP）levels are widely performed as screening tests, however, the performance of such tests remains controversial. The aim of this study was to evaluate the sensitivity and specificity for a diagnosis of nonalcoholic fatty liver by AST, ALT, γ–GTP and the body mass index（BMI）. Methods：Among the 5901 subjects without overt liver diseases who were confirmed by health checkups provided by a commercial health care center in 1995 and 2000, a receiver operating characteristic（ROC）analysis was performed to evaluate the performance of AST, ALT, γ–GTP and BMI for a diagnosis of fatty liver based on ultrasonography findings. Subjects with hepatitis as diagnosed by HBs antigen positive or HCV antibody positive and excess alcohol drinkers with a daily alcohol intake more than 180 ml of Japanese sake or equivalent and were thus excluded from the analysis. Results：The area under the ROC curve of ALT was largest among the four indexes. The area under the ROC curve of ALT was significantly greater than that of the BMI for men. The cutoff values that minimized the misclassification for a diagnosis of fatty liver of AST, ALT and γ–GTP were lower than the current cutoff values used in health checkups in both males and females. Conclusion：Based on our findings, ALT had better performance for a diagnosis of fatty liver than BMI. The evaluation of the results of hepatic enzyme blood tests must be reconsidered.

Key words：Fatty liver, Receiver operating characteristic curve, Screening test, Hepatic enzyme blood test

Introduction

The efficacy of health checkups using hepatic enzyme blood tests remains controversial. Infection with hepatitis B and C（HBV and HCV respectively), alcoholic hepatitis and fatty liver are considered to be the target diseases in the current liver function screening program, Hepatic enzyme blood tests including analyses of serum aspartate aminotransferase（AST）and alanine aminotransferase（ALT）and gammaglutamyl transpeptidase（γ–GTP）levels to detect HBV, HCV, alcoholic hepatitis and fatty liver have a very low sensitivity among Japanese male workers.[1)2)] However, the reference values for hepatic enzyme blood tests usually used in a health checkup were established in the 1980s but no such values have yet been made for persons with nonalcoholic fatty liver disease alone.[3)]

It is assumed that the prevalence of nonalcoholic fatty liver disease is greater than that of hepatitis

Corresponding author：Shinichi TANIHARA, MD
Department of Hygiene and Preventive Medicine, School of Medicine, Fukuoka University, 7–45–1 Nanakuma, Jonan-ku, Fukuoka 814–0180, Japan
Phone：(+81) 92–801–1011 ext. 3301　Fax：(+81) 92–863–8892　E-mail：taniyan@fukuoka-u.ac.jp

C virus infection in the United States.[4] Non-alcoholic steatohepatitis (NASH) tends to occur in obese patients and most cases of steatosis are also totally asymptomatic.[5)–7)] However, nonalcoholic steatosis may progress to liver fibrosis and cirrhosis.[5)6)8)9)] Many cross-sectional studies have shown the associations between fatty liver and the metabolic syndrome.[10)–14)] In addition, subjects with metabolic syndrome have a 4 to 11 times higher risk for nonalcoholic fatty liver disease according to a longitudinal study.[15] A proper screening test for fatty liver is important to avoid a possible future epidemic of nonalcoholic fatty liver disease and the metabolic syndrome. The aim of this study was to evaluate the sensitivity and specificity of hepatic enzyme blood tests for the diagnosis of fatty liver.

Subjects and Methods

1. Subjects

The subjects were selected from 17,082 persons who underwent health checkups provided by a commercial health care center in 1995 and 2000. We selected persons who took screening tests for both hepatitis B virus antigen and hepatitis C virus antibody in 1995. The number of eligible subjects was 8,847.

The results of AST, ALT, γ-GTP, hepatitis B virus antigen or hepatitis C virus antibody, abdominal ultrasound examination, body mass index (BMI), and self administrated questionnaires including drinking habits and past history of liver diseases were analyzed. BMI was calculated as body weight (kg) divided by the square of body height (m). Serum AST, ALT, γ-GTP levels were measured by an automatic biochemical analyzer and their quality control was approved by the Japan Society of Health Evaluation and Promotion.

The drinking habits for each subject were assessed by a questionnaire. The frequency of alcohol consumption during a typical week and the total alcohol intake on each occasion and type of beverage most often consumed. The total alcohol intake on each occasion was based on the Japanese quantity of one "GOU", a traditional Japanese drinking unit equivalent to 180 ml of Japanese SAKE, and its ethanol content is roughly equivalent to that of a bottle of beer (663 ml), two single shots of whiskey (70 ml). One GOU corresponds to 25 g of ethanol. We calculated the alcohol intake per week. This value was then divided by 7 to obtain the average alcohol intake per day.

The diagnosis of fatty liver was evaluated by a visual inspection of ultrasonography (US) images. The US examination is performed regardless of the results of the serum liver function test. Fatty liver is considered to exist if the subject meets at least two of the following three criteria:[16] 1) a bright liver, 2) increased echogenicity of the liver in comparison to the adjacent structure, such as in the renal cortex, and 3) an increased attenuation throughout the liver.

For the purpose of this study, those who met the following criteria were excluded from the analysis. 1) hepatitis virus carriers diagnosed by HBs antigen positive (n=184); 2) HCV antibody positive (n=310); 3) subjects with hematolysis in blood sample (n=2); 4) subjects with missing data (n=940); 5) excess alcohol drinkers with a daily alcohol intake more than one GOU of Japanese sake or equivalent (n=1496). 6) subjects with a history of known liver disease or US images of suspected neoplasms involving both the intrahepatic and extrahepatic bile ducts, gallbladder cancer, cholangiocarcinoma, cholangioma, and hepatocellular carcinoma (n=14). Finally, the number of subjects evaluated was 5,901 (male 3,674; female 2,227).

The names and the date of birth of subjects were deleted from the database at the commercial health care center to protect the confidentiality of the subjects' identities during the data analysis.

2. Data analysis

First, the proportion of subjects with abnormal BMI, AST, ALT, and γ-GTP levels by the current cutoff values used in the commercial health care center. The cutoff values of BMI was 25, AST and ALT were 40. In addition, the γ-GTP levels were 65 for males and 40 for females, respectively. Next, the receiver operating characteristic (ROC) curve was made for AST, ALT, γ-GTP, and BMI for a diagnosis of fatty liver as diagnosed by US. Finally, the area under the ROC curve was calculated and a cutoff value that minimized the misclassification was determined. The cutoff value that minimized the misclassification was defined so as to minimize the total number of false positive and false negative cases in the diagnosis of fatty liver as confirmed by a visual US images.

Two-sided values were used where a value of $p < 0.05$ was considered to be statistically significant. The analyses were performed using the SPSS software package (Version 13.0) and ROCKIT.[17]

Results

Among the 5,901 subjects, the number of subjects with nonalcoholic fatty liver was 989 (16.8%). Men had a higher prevalence of fatty liver than did women (22.6% vs. 7.2%). Table 1 shows the baseline characteristics for the subjects with and without fatty liver. The mean age of all subjects was 53.6±10.2 (men 53.7±10.2, women 53.5±10.2). For women, the mean age was significantly greater in the subjects with fatty liver although the mean age was significantly greater in the subjects without fatty liver for men. For both men and women, the mean body mass index and the hepatic enzyme blood tests were significantly greater in the subjects with fatty liver. The sensitivity and the false positive rate of BMI was the highest among the four indicators. The sensitivity of BMI exceeded 50% although those of AST and γ-GTP were less than 20%. Except woman's γ-GTP, the proportions of subjects with exceeded cutoff values were significantly higher among the subjects with fatty liver.

Table 2 shows the area under the ROC curve for males and females. For both males and females,

Table 1. Characteristics of the subjects

	Male			Female		
	Fatty Liver (+) (n=829)	Fatty Liver (−) (n=2845)	p-value	Fatty Liver (+) (n=160)	Fatty Liver (−) (n=2067)	p-value
	mean ± SD	mean ± SD		mean ± SD	mean ± SD	
Age (years)	52.8 ± 9.7	54 ± 10	0.030	57.9 ± 8.2	53 ± 10	<0.001
BMI (kg/m²)	25.8 ± 2.6	23 ± 2.4	<0.001	26.3 ± 3.3	22 ± 2.6	<0.001
AST (IU/L)	29.0 ± 12	22 ± 7.8	<0.001	28.8 ± 13	20 ± 6.5	<0.001
ALT (IU/L)	43.4 ± 25	25 ± 14	<0.001	36.9 ± 22	18 ± 11	<0.001
γ-GTP (IU/L)	44.8 ± 33	35 ± 36	<0.001	25.5 ± 15	17 ± 15	<0.001
	(sensitivity)	(false positive)		(sensitivity)	(false positive)	
High BMI (BMI>25)	482 (58.1%)	654 (23.0%)	<0.001	96 (60.0%)	258 (12.5%)	<0.001
High AST (AST>40)	103 (12.4%)	71 (2.5%)	<0.001	20 (12.5%)	26 (1.3%)	<0.001
High ALT (ALT>40)	364 (43.9%)	264 (9.3%)	<0.001	47 (29.4%)	51 (2.5%)	<0.001
High γ-GTP*	134 (16.2%)	331 (11.6%)	<0.001	15 (9.4%)	117 (5.7%)	0.055

BMI: body mass index; AST: aspartate aminotransferase; ALT: alanine aminotransferase;
γ-GTP: gammaglutamyl transpeptidase
*: High γ-GTP was defined separately for men (γ-GTP>65) and women (γ-GTP>40).

Table 2. Area under the receiver operating characteristic curve

		AUC	95%CI	difference	95%CI	p-value
Male	ALT	0.786	(0.768-0.804)	0.033	(0.011~0.053)	0.0026
	BMI	0.753	(0.735-0.771)	(reference)	−	−
	AST	0.709	(0.688-0.730)	−0.044	(−0.070~−0.022)	0.0002
	γ-GTP	0.658	(0.639-0.677)	−0.095	(−0.117~−0.070)	<0.0001
Female	ALT	0.867	(0.839-0.894)	0.019	(−0.020~ 0.050)	0.4014
	BMI	0.848	(0.820-0.876)	(reference)	−	−
	AST	0.783	(0.746-0.819)	−0.065	(−0.109~−0.023)	0.0025
	γ-GTP	0.792	(0.764-0.819)	−0.056	(−0.100~−0.024)	0.0014

AUC: Area under the receiver operating characteristic curve
95%CI: 95% confidence interval
BMI: body mass index; AST: aspartate aminotransferase;
ALT: alanine aminotransferase;
γ-GTP: gammaglutamyl transpeptidase

ALT had the largest area under the ROC curve among the three hepatic enzyme blood tests and BMI. For men, ALT had a significantly greater area under the ROC curve than the BMI. The area under the ROC curve of AST and γ−GTP were significantly smaller than that of BMI for both men and women.

Figures 1 and 2 show the ROC curve of the hepatic enzyme blood tests and the BMI among males and females, respectively. The distances between the upper left corner and ROC curve obtained by each index were arranged from smallest to largest

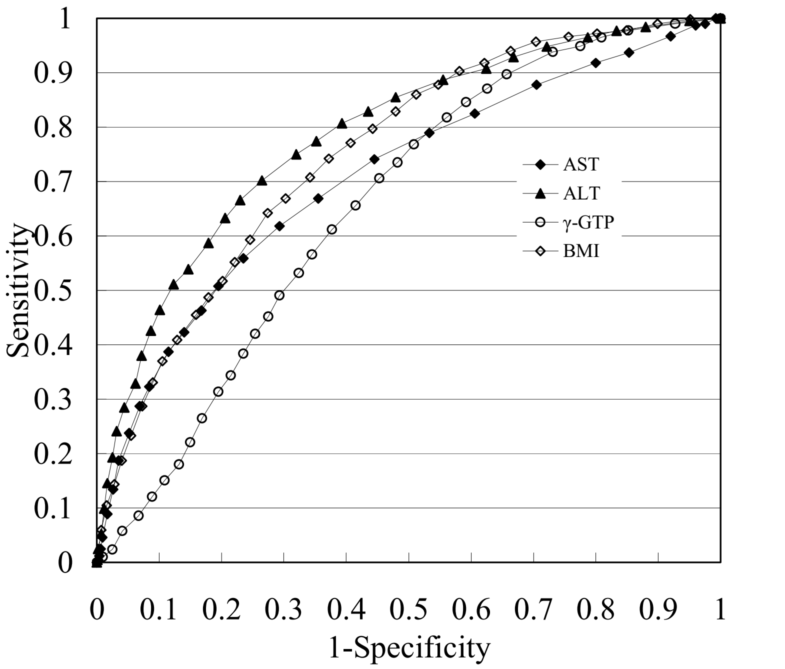

Figure. 1. ROC curve of the hepatic enzyme blood tests and the BMI (males)

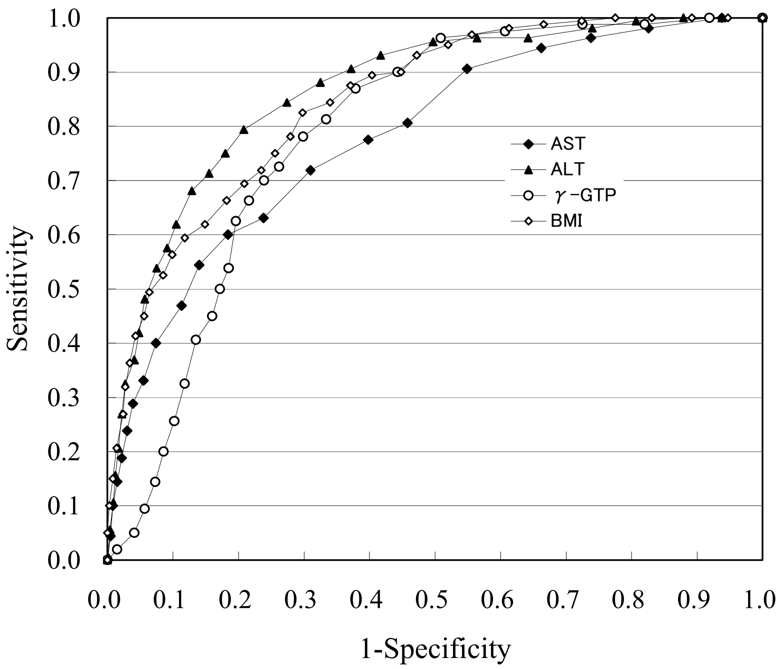

Figure. 2. ROC curve of the hepatic enzyme blood tests and the BMI (females)

as follows : ALT, BMI, AST, γ-GTP for males and ALT, BMI, γ-GTP, and AST for females. For each index, the distance between the upper left corner and the ROC curve of females is shorter than that of males. The cutoff values that minimized misclassification defined so as to minimize the sum of false positive and false negative of BMI, AST, ALT and γ-GTP were 24.4, 23, 26, 26 for male and 23.2, 21, 21, 15 for female, respectively. For each hepatic enzyme blood tests, the cutoff value which minimized the misclassification for diagnosis of fatty liver was around half of the current cutoff values.

Discussion

The current study revealed the following three points regarding the efficacy of hepatic enzyme blood tests to detect fatty liver : 1) ALT showed a significantly higher efficacy to detect fatty liver than did the BMI for males ; 2) The BMI showed a significantly higher efficacy to detect fatty liver than γ-GTP or AST for both males and females ; and 3) the cutoff line of hepatic enzyme blood tests currently used in general health checkups[1)-3)18)] is higher than the cutoff line which minimized misclassification for the diagnosis of fatty liver for both males and females.

AST and γ-GTP are less specific than ALT for liver disease. ALT is present at its highest concentration in the liver. AST is found, in decreasing order of concentration, in the liver, cardiac muscle, skeletal muscle, kidneys, brain, the pancreas, lungs, leukocytes, and erythrocytes. γ-GTP has been localized to the entire hepatobiliary tree, from hepatocytes to common bile duct, and to pancreatic acini and ductules.[19)] Our results indicate that ALT showed a significantly higher efficacy to detect fatty liver than γ-GTP and AST for both males and females it is thus considered to be an effective diagnostic parameter.

Based on our findings, ALT had a significantly better performance for the diagnosis of fatty liver than BMI for males. Among 326 male workers in a metal-working company, the area under the ROC curve for the diagnosis fatty liver of ALT was larger than that of BMI although it was not statistically significant.[2)] The study analyzed alcoholic fatty liver and nonalcoholic fatty liver simultaneously because the study excluded only excessive alcohol drinkers with a habitual daily alcohol intake comparable to or more than 540 ml of Japanese sake. To focus on nonalcoholic fatty liver, this study excluded excessive alcohol drinkers with a daily alcohol intake of more than 180 ml of Japanese sake or equivalent. For women, the area under the ROC curve of ALT was larger than that of BMI although it was not statistically significant. The number of female subjects with fatty liver is less than one fifth of the males with fatty liver. The absence of statistical significance in former study[2)] is due to their small sample size.

Since the data from the hepatic enzyme blood tests for the AST, ALT, and γ-GTP levels are continuous variables, there is no clear boundary regarding the shape of the distribution curve of hepatic enzyme blood tests between the subjects with fatty liver and those without. In this study, the cutoff line was determined to simply minimize the sum of false positives plus false-negatives. It is thus necessary to consider the characteristics of the disease to set the cutoff line in order to avoid either false-positive or false-negative which could be harmful for the screened subjects.[20)]

Furthermore, there have so far been few longitudinal studies about subjects with an abnormal liver function. The serum aminotransferase concentration has been reported to be associated with mortality from liver disease, even within the current normal range in Korea.[18)] A high AST or ALT level in annual health checkups were predictive factors for all cause, cancer and stroke death for men in Ibaraki prefecture, aged 40 to 79 years.[21)] A significant interaction between the serum ALT levels and the BMI was observed among Japanese National Health Insurance beneficiaries in Shiga prefecture.[22)]

It is important to consider the type of liver disease to interpret the results of hepatic enzyme blood tests because the distribution of AST, ALT and γ-GTP are different. From the results of this study, the optimal cutoff line for distinguishing fatty liver was determined to be 26 for ALT, which is much lower than the standard level usually used in general health checkups.[1)-3)18)] From the ROC curve for a fatty liver diagnosis, ALT is thus considered to be a better diagnostic factor than the BMI. When analyzing the hepatic enzyme blood tests during a health checkup as a screening test, a shifting cutoff level may change either the sensitivity or specificity. When determining the cutoff line for screening tests, the characteristics and natural history of the target disease should thus be considered.[3)18)20)23)–25)]

There are some limitations in this study. First, the subjects of this study were not necessarily representative of the general population. Moreover, only liver disease was investigated in the analysis. It cannot be ruled out that the subjects may have had other diseases which might have also caused hepatic dysfunction. However, it is assumed that the proportion of subjects with a serious disease was negligible since all subjects were confirmed to be alive five years after the screening. Therefore, no major problems are thought to have existed regarding the accuracy of the screening using hepatic enzyme blood tests in these subjects.

Next, ultrasonography may result in an incorrect diagnosis for fatty liver although it has a relatively high sensitivity (82% to 94%) and specificity (66% to 95%).[26)–30)] The US examination is performed regardless of the results of the serum liver function test so that any misclassification, if it occurs, is non-differential. If so, the efficacy of hepatic enzyme blood tests that has been computed must be smaller than the real value and it has no bearing on the conclusion of the present study, i.e., ALT is a useful method for detecting nonalcoholic fatty liver.

The diagnostic capabilities of such hepatic enzyme blood tests as AST, ALT and γ-GTP to diagnose fatty liver confirmed by US were evaluated in this study. ALT was found to be a better factor than the BMI from the ROC curve for a diagnosis of fatty liver. Analyzing the hepatic enzyme blood tests in a health checkup as a general screening test is therefore considered to have some efficacy. The evaluation of hepatic enzyme blood tests corresponding to the characteristics of the disease and the results of longitudinal study should thus be further discussed in the future.

Acknowledgments

This study was funded by a research grant from the Ministry of Health, Labour and Welfare Japan, 2001 entitled : "Ideal way and effective execution of health and welfare policy for the elderly" (Principal Investigator : Takeshi Kawaguchi).

The authors would like to thank Hidetoshi Kashihara and Masanori Tamura of PL Tokyo Health Care Center, Tokyo, Japan for help of arranging the data.

References

1) Yano E, Tagawa K, Yamaoka K, Mori M : Test validity of periodic liver function tests in a population of Japanese male bank employees. J Clin Epidemiol 54 : 945–51, 2001.

2) Nomura K, Yano E, Shinozaki T, Tagawa K : Efficacy and effectiveness of liver screening program to detect fatty liver in the periodic health checkups. J Occup Health 46 : 423–8, 2004.

3) Prati D, Taioli E, Zanella A, Della Torre E, Butelli S, Del Vecchio E, Vianello L, Zanuso F, Mozzi F, Milani S, Conte D, Colombo M, Sirchia G : Updated definitions of healthy ranges for serum alanine aminotransferase levels. Ann Intern Med 137 : 1–10, 2002.

4) Angulo P : Nonalcoholic fatty liver disease. N Engl J Med 346 : 1221–31, 2002.

5) Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, McCullough AJ : Nonalcoholic fatty liver disease : a spectrum of clinical and pathological severity. Gastroenterology 116 : 1413–9, 1999.

6) Angulo P, Keach JC, Batts KP, Lindor KD : Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. Hepatology 30 : 1356–62, 1999.

7) Ratziu V, Giral P, Charlotte F, Bruckert E, Thibault V, Theodorou I, Khalil L, Turpin G, Opolon P, Poynard T : Liver fibrosis in overweight patients. Gastroenterology 118 : 1117–23, 2000.

8) Fassio E, Alvarez E, Dominguez N, Landeira G, Longo C : Natural history of nonalcoholic steatohepatitis : a longitudinal study of repeat liver biopsies. Hepatology 40 : 820–6, 2004.

9) Dixon JB, Bhathal PS, O'Brien PE : Nonalcoholic fatty liver disease : predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology 121 : 91–100, 2001.

10) Bellentani S, Saccoccio G, Masutti F, Croce LS, Brandi G, Sasso F, Cristanini G, Tiribelli C : Prevalence of and risk factors for hepatic steatosis in

Northern Italy. Ann Intern Med 132 : 112–7, 2000.
11) Assy N, Kaita K, Mymin D, Levy C, Rosser B, Minuk G : Fatty infiltration of liver in hyperlipidemic patients. Dig Dis Sci 45 : 1929–34, 2000.
12) Gupte P, Amarapurkar D, Agal S, Baijal R, Kulshrestha P, Pramanik S, Patel N, Madan A, Amarapurkar A, Hafeezunnisa : Non–alcoholic steatohepatitis in type 2 diabetes mellitus. J Gastroenterol Hepatol 19 : 854–8, 2004.
13) Donati G, Stagni B, Piscaglia F, Venturoli N, Morselli–Labate AM, Rasciti L, Bolondi L : Increased prevalence of fatty liver in arterial hypertensive patients with normal liver enzymes : role of insulin resistance. Gut 53 : 1020–3, 2004.
14) Lee S, Jin Kim Y, Yong Jeon T, Hoi Kim H, Woo Oh S, Park Y, Soo Kim S : Obesity is the only independent factor associated with ultrasound–diagnosed non–alcoholic fatty liver disease : a cross–sectional case–control study. Scand J Gastroenterol 41 : 566–72, 2006.
15) Hamaguchi M, Kojima T, Takeda N, Nakagawa T, Taniguchi H, Fujii K, Omatsu T, Nakajima T, Sarui H, Shimazaki M, Kato T, Okuda J, Ida K : The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. Ann Intern Med 143 : 722–8, 2005.
16) Kojima S, Watanabe N, Numata M, Ogawa T, Matsuzaki S : Increase in the prevalence of fatty liver in Japan over the past 12 years : analysis of clinical background. J Gastroenterol 38 : 954–61, 2003.
17) Metz CE, Herman BA, Roe CA : Statistical comparison of two ROC–curve estimates obtained from partially–paired datasets. Med Decis Making. 18 : 110–21, 1998.
18) Kim HC, Nam CM, Jee SH, Han KH, Oh DK, Suh I : Normal serum aminotransferase concentration and risk of mortality from liver diseases : prospective cohort study. Br Med J 328 : 983, 2004.
19) Friedman LS, Martin P, Munoz SJ : Laboratory evaluation of the patient with liver disease. In : Zakim D and Boyer TD (ed), Hepatology 4th ed, Volume 1. pp. 661–708, Saunders (Philadelphia), 2003.
20) Steurer J, Fischer JE, Bachmann LM, Koller M, ter Riet G : Communicating accuracy of tests to general practitioners : a controlled study. Br Med J 324 : 824–6, 2002.
21) Noda H, Iso H, Sairenchi T, Irie F, Fukasawa N, Toriyama Y, Ota H, Nose T : Prediction of stroke, coronary heart disease, cardiovascular disease, cancer, and total death based on results of annual health checkups. Jpn J Public Health 53 : 265–76, 2006. (in Japanese)
22) Nakamura K, Okamura T, Kanda H, Hayakawa T, Okayama A, Ueshima H : The value of combining serum alanine aminotransferase levels and body mass index to predict mortality and medical costs : a 10-year follow–up study of National Health Insurance in Shiga, Japan. J Epidemiol 16 : 15–20, 2006.
23) de Ledinghen V, Combes M, Trouette H, Winnock M, Amouretti M, de Mascarel A, Couzigou P : Should a liver biopsy be done in patients with subclinical chronically elevated transaminases ? Eur J Gastroenterol Hepatol 16 : 879–83, 2004.
24) Sorbi D, Boynton J, Lindor KD : The ratio of aspartate aminotransferase to alanine aminotransferase : potential value in differentiating nonalcoholic steatohepatitis from alcoholic liver disease. Am J Gastroenterol 94 : 1018–22, 1999.
25) Pratt DS, Kaplan MM : Evaluation of abnormal liver–enzyme results in asymptomatic patients. N Engl J Med 342 : 1266–71, 2000.
26) Saverymuttu SH, Joseph AE, Maxwell JD : Ultrasound scanning in the detection of hepatic fibrosis and steatosis. Br Med J (Clin Res Ed) 292 : 13–5, 1986.
27) Needleman L, Kurtz AB, Rifkin MD, Cooper HS, Pasto ME, Goldberg BB : Sonography of diffuse benign liver disease : accuracy of pattern recognition and grading. Am J Roentgenol 146 : 1011–5, 1986.
28) Joseph AE, Saverymuttu SH, al–Sam S, Cook MG, Maxwell JD : Comparison of liver histology with ultrasonography in assessing diffuse parenchymal liver disease. Clin Radiol 43 : 26–31, 1991.
29) Mendler MH, Bouillet P, Le Sidaner A, Lavoine E, Labrousse F, Sautereau D, Pillegand B : Dual–energy CT in the diagnosis and quantification of fatty liver: limited clinical value in comparison to ultrasound scan and single–energy CT, with special reference to iron overload. J Hepatol 28 : 785–94, 1998.
30) Graif M, Yanuka M, Baraz M, Blank A, Moshkovitz M, Kessler A, Gilat T, Weiss J, Walach E, Amazeen P, Irving CS : Quantitative estimation of attenuation in ultrasound video images : correlation with histology in diffuse liver disease. Invest Radiol 35 : 319-24, 2000.

(Received on October 2, 2006,
Accepted on January 5, 2007)