Asian Biomedicine Vol. 10 Supplement 1 2016; S49 - S55 DOI: 10.5372/1905-7415.1000.521

Brief Communication (Original)

Accuracy of noninvasive scoring systems to assess advanced liver fibrosis in Thai patients with nonalcoholic fatty liver disease

Sombat Treeprasertsuk[a,c], Panida Piyachaturawat[a], Tanassanee Soontornmanokul[a], Naruemon Wisedopas-Klaikaew[b], Piyawat Komolmit[a], Pisit Tangkijavanich[c]

[a]*Department of Medicine, Faculty of Medicine, Chulalongkorn University, and King Chulalongkorn Memorial Hospital, Thai Red Cross, Bangkok 10330, Thailand*

[b]*Department of Pathology, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*

[c]*Liver Research Unit, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand*

Background: Liver biopsy is the criterion standard to assess liver fibrosis in patients with nonalcoholic fatty liver disease (NAFLD), which is important for prognosis, whereas noninvasive scoring systems showing promise for predicting fibrotic status include aspartate/alanine aminotransferase (AST/ALT) ratio, BARD score, fibrosis–4-score (FIB-4), and the NAFLD Fibrosis Score (NFS).

Objectives: To determine the accuracy of noninvasive scoring systems to predict advanced fibrosis in Thai patients with NAFLD.

Methods: A prospective cross-sectional study of Thai patients with liver biopsy-proven NAFLD during January 2009–October 2012 at King Chulalongkorn Memorial Hospital, Bangkok, Thailand. Baseline NFS, BARD, and FIB-4 calculations were used to distinguish patients with NAFLD with and without advanced liver fibrosis, using cutoffs for NFS ≥ −1.455, BARD ≥ 2, and FIB-4 >1.3 (http://gihep.com/calculators/hepatology/).

Results: We included 139 patients mean age 40.95 (SD 13.3) years (47% male). Impaired fasting glucose or diabetes mellitus was found in 75, 9 showed advanced fibrosis (≥F3) by liver histology. NFS with cutoff ≥ −1.455 was determined as the best system with the highest sensitivity for identifying patients with advanced fibrosis, followed by BARD ≥2, FIB-4 >1.45, and AST/ALT ratio >0.8. Liver biopsy could potentially be avoided in >38% of patients with BARD, 46% with NFS, 64% with AST/ALT ratio, and 81% with FIB-4.

Conclusions: Advanced fibrosis was prevalent in 6% of our Thai patients with NAFLD. NFS had the highest negative predictive value for excluding patients with advanced fibrosis. At least 38% of patients with NAFLD could avoid liver biopsy by using the BARD system.

Keywords: Advanced liver fibrosis, NAFLD, noninvasive scoring systems, validity

Nonalcoholic fatty liver disease (NAFLD) is one of the most common causes of chronic liver disease in western countries [1, 2]. The prevalence of NAFLD is increasing and varies significantly with ethnicity; from 24% in black and 33% in white, to 45% in Hispanic people [3]. An increasing prevalence of NAFLD is associated with the increasing incidence of obesity and in 2007, about a third of the population in the United States of America aged from 40 to 79 years was obese [2, 4]. The mortality rate of patients with NAFLD in the community was found to be higher than that in the general population in the United States [5]. During an average 8.4 years of follow up of patients with NAFLD, death occurred in about 10%. Cardiovascular disease and coronary heart disease (CHD) were the most common cause of death, followed by malignancy, and liver related causes [6]. The survival outcome of patients with nonalcoholic steatohepatitis (NASH) was reduced significantly and they more often died from CHD (P = 0.04) and liver-related causes (P = 0.04) [7]. Patients with more severe liver fibrosis tend to have more liver complications than those without liver fibrosis [7]. Liver biopsy is a criterion standard by which to diagnose the severity of liver fibrosis, but it has several limitations for clinical practice including the expense and the invasive nature of the procedure, which is associated with a number of complications [8].

Correspondence to: Sombat Treeprasertsuk, Department of Medicine, Faculty of Medicine, Chulalongkorn University, Bangkok 10330, Thailand. E-mail: sombat.t@chula.ac.th

Patients with NASH showed progression of fibrosis in about 5%–32% during a 4.3-to-6 year follow-up period [9-11]. Several simple noninvasive scoring systems for assessment of liver fibrosis have been proposed for use in general clinical practice. NAFLD Fibrosis Score (NFS), which is a composite score of age, hyperglycemia, body mass index, platelet count, albumin, and aspartate aminotransferase/alanine aminotransferase (AST/ALT) ratio [12]. These factors were found to be independent indicators of separating NAFLD patients with and without advanced fibrosis at the initial diagnosis of NAFLD. The BARD score is a simple clinical score based on **B**MI ≥28 kg/m^2 (1 point), **A**ST/ALT **R**atio ≥0.8 (2 points), and **D**iabetes mellitus (1 point) [13]. If the total score ranges from 2–4, the chance of liver fibrosis is high with an odds ratio (OR) of 17 [13]. However, the BARD score had some limitations; for example, it has no predictive capacity for patients with higher BMI or higher ratio of AST/ALT, while the NAFLD Fibrosis Score can be applied to a different range of BMI or AST/ALT ratios. Fibrosis–4-score (FIB-4) was used initially in chronic hepatitis C infected patients with or without human immunodeficiency virus infection [14, 15]. It is a composite score of patient's age, AST, ALT, and platelet count, which are simple blood tests and showed a high negative predictive value (NPV) of 90% to exclude advanced fibrosis in NAFLD patients [16]. To our knowledge, these noninvasive scoring systems have not been validated in any population of Thai patients with NAFLD. We sought to determine the accuracy of these 4 existing noninvasive scoring systems for predicting patients with advanced fibrosis (≥F3) in a population of Thai patients with NAFLD.

Methods

The study was approved by the Institutional Review Board (IRB) of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand (IRB Nos. 248/50 and 249/54).

Patients

All patients included provided their written informed consent to participate in the present study. We prospectively included 139 consecutive patients with liver biopsy-proven NAFLD patients in King Chulalongkorn Memorial Hospital (KCMH) from January 2009 to October 2012. The inclusion criteria included patients at least 18 years old with NAFLD was diagnosed by liver biopsy with standard criteria. Exclusion criteria were incomplete data needed for the 4 noninvasive scoring system calculations. Patients who met the inclusion criteria were admitted for liver biopsy using standard procedures with ultrasonography guidance. Data of all patients were recorded, including demographic data, anthropometric data and biochemical tests on the day of liver biopsy or within 2 weeks of the procedure. All patients were followed-up with the results of liver histological findings within the following 2 weeks. We used the histological findings of liver fibrosis as the criterion standard or index diagnosis.

Definition

The diagnosis of NAFLD was based on the following criteria: (1) liver biopsy showing steatosis in at least 5% of hepatocytes, or (2) fatty infiltration of the liver confirmed on imaging studies (ultrasound, computed tomography, or magnetic resonance imaging), and (3) exclusion of liver disease from other etiologies including alcohol-induced (history of excessive alcohol consumption defined as >20 gm/day), drug-induced liver disease, autoimmune or viral hepatitis, and cholestatic or metabolic/genetic liver disease [17]. The staging of liver inflammation and fibrosis in patients with NAFLD was based on that proposed by Kleiner et al. [18]. The presence of metabolic syndrome (Mets) was defined by using the 2001 National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) criteria and the new definition, which required the presence of at least 3 of the 5 features [19], BMI was calculated as weight divided by height squared (kg/m^2). Because waist circumference (WC) measurements were not taken from the majority of patients, we defined obesity using BMI >30 kg/m^2 in accordance with the World Health Organization (WHO) definition of insulin resistance syndrome [20, 21]. The histological liver fibrosis stages 1–2 (F1–F2) were classified as "mild liver fibrosis" and those with histological fibrosis stages 3–4 (F3–F4) were classified as "advanced liver fibrosis" according to standard criteria [18]. Baseline NAFLD Fibrosis Scores, BARD, and FIB-4 calculations were used to distinguish NAFLD patients with and without advanced liver fibrosis, for which the cutoff NFS at > −1.455 (web-based calculation; http://gihep.com/calculators/hepatology/nafld-fibrosis-score/), BARD score with the cutoff >2 (web-based calculation; http://gihep.com/calculators/hepatology/bard/), and FIB-4 with the cutoff >1.3 (web-based calculation;

http://gihep.com/calculators/hepatology/fibrosis–4-score/) predict the advanced liver fibrosis or F3–F4.

Statistical analyses

Thai NAFLD patients were categorized by the severity or staging of liver fibrosis into 2 groups of the mild and advanced liver fibrosis based on histological diagnosis. Continuous outcomes are presented as mean (standard deviation, SD) and categorical data are presented as numbers (percentage). Differences between groups were tested by independent *t* tests for continuous variables, and were tested by χ^2 tests for proportions. Differences with $P < 0.05$ were considered significant. The overall accuracy of the NAFLD Fibrosis Score in identifying the mild or advanced stage of liver fibrosis was analyzed using the area under the receiver operating characteristic (ROC) curves. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated.

The analyses in this study were performed using SPSS for Windows (version 15.0.1.1; SPSS Inc, Chicago, IL, USA).

Results

Baseline characteristics

We included 139 Thai patients with liver biopsy-proven NAFLD with mean age of 40.95 (13.3) years, and 47% were male. There were 75 (54%) patients with impaired fasting glucose or diabetes mellitus and 73% of Thai NAFLD patients had a BMI >28 kg/m^2. Baseline characteristics are shown in **Table 1.**

Table 1. Baseline characteristics of 139 Thai patients with nonalcoholic fatty liver disease

Variable	Total (n = 139)	No/mild fibrosis (F0-F2) (n = 130)	Advanced fibrosis (F3-F4) (n = 9)	*P*
Age (years)	40.9 (13.3)	40.3 (13.0)	48.8 (15.5)	0.07$^+$
Male sex (%)	65 (47%)	61 (47%)	4 (44%)	1.00^t
BMI (kg/m^2)^a	36.1 (14.7)	40.6 (14.8)	29.4 (8.6)	0.01$^+$
BMI >28 (kg/m^2)	102 (73%)	97 (75%)	5 (56%)	0.23^t
Diabetes mellitus (DM)	53 (38%)	47 (36%)	6 (67%)	0.08^t
IFG/DM	75 (54%)	67 (52%)	8 (89%)	0.04^t
AST (IU/L)^a	38.0 (39.4)	38.0 (34.6)	39 (81.2)	0.24*
ALT (IU/L)^a	56.0 (47.2)	56.0 (47.7)	59.0 (40.7)	0.29*
Albumin (g/L)	4.4 (0.4)	4.4 (0.4)	4.4 (0.3)	0.84$^+$
Platelet ($\times 10^9$/L)	267 (64.2)	270 (64.3)	222 (43.7)	0.02*
Total cholesterol (mg/dL)	198 (46.6)	197 (45.5)	214 (60.8)	0.44*
Triglyceride (mg/dL)	146 (60.8)	145 (60.9)	164 (59.6)	0.31*
HDL (mg/dL)	45.6 (12.1)	45.5 (12.4)	46.8 (8.1)	0.53*
LDL (mg/dL)	125 (42.1)	125 (41.1)	135 (56.2)	0.61*
FPG (mg/dL)	112 (33.2)	109 (30.9)	142 (49.2)	0.01*
HbA1C (%)	7.38 (8.7)	7.36 (9.0)	7.59 (1.7)	0.08$^+$
AST/ALT ratio	0.78 (0.37)	0.78 (0.38)	0.85 (0.38)	0.59$^+$
BARD score				0.48$^+$
0	10 (7%)	10 (8%)	0 (0)	
1	45 (32%)	43 (33%)	2 (22%)	
2	41 (30%)	37 (29%)	4 (44%)	
3	26 (19%)	24 (19%)	2 (22%)	
4	17 (12%)	16 (12%)	1 (11%)	
FIB-4 score	0.98 (0.79)	0.91 (0.61)	1.9 (1.9)	0.17$^+$
NAFLD Fibrosis Score	−1.37 (1.70)	−1.418 (1.748)	−0.772 (0.668)	0.03$^+$

AST, aspartate aminotransferase; ALT, alanine aminotransferase; BARD, **B**MI ≥28 kg/m^2 (1 point), **A**ST/ALT **R**atio ≥0.8 (2 points), and **D**iabetes mellitus (1 point); BMI, body mass index; FIB-4 score, Fibrosis–4-score; FPG, Fasting plasma glucose; HbA1C, glycated hemoglobin (β-*N*-1-deoxyfructosyl); HDL, High density lipoprotein; IFG, Impaired fasting glucose; LDL, Low density lipoprotein; NAFLD, nonalcoholic fatty liver disease, ^{a}median, $^+$Student *t* test, *Mann–Whitney *U* test, *t*, χ^2 test

Advanced fibrosis (F3–F4) was found histologically in 9 patients (6%). Using the baseline AST/ALT ratio with a cutoff >0.8, NFS with a cutoff ≥ −1.455, BARD with a cutoff ≥2, and FIB-4 calculation with a cutoff >1.3, the prevalence of patients with a high risk of advanced liver fibrosis were 36%, 54.5%, 61.2%, and 19.1%, respectively.

Validation of the 4 noninvasive scoring systems for predicting advanced fibrosis (≥F3) in Thai patients with NAFLD

The sensitivity, specificity, positive-predictive values (PPV), and negative-predictive values (NPV) of the 4 noninvasive scoring systems were calculated. NFS with a cutoff ≥ −1.455 was found to be the best scoring system with highest sensitivity for identifying patients with advanced fibrosis, followed by BARD score ≥2, FIB-4 >1.45, and AST/ALT ratio >0.8, respectively **(Table 2).**

Patients with advanced fibrosis were significantly older and had higher blood glucose level than those with mild liver fibrosis. Using the area under the ROC curve of four noninvasive scoring systems at baseline, FIB–4 and NFS showed the highest AUROC in Thai NAFLD patients for predicting the advance liver fibrosis **(Figure 1)**. By using these 4 noninvasive scoring systems, liver biopsy could potentially be avoided in at least 38% of patients with BARD score, 45% with NFS, 64% with AST/ALT ratio, and 80% with FIB–4.

Discussion

We demonstrate that the NAFLD Fibrosis Score (NFS) with a cutoff ≥ −1.455 is the best scoring system with the highest sensitivity for identifying Thai patients with advanced fibrosis and a low PPV of 21%, whereas NFS <1.5 had high NPV of 91%, and can be used to exclude Thai patients with NAFLD and advanced fibrosis. The low prevalence (6%) of advanced liver fibrosis in Thai patients with NAFLD is critically associated with the drop-off in diagnostic ability of these 4 noninvasive scoring systems. The prevalence of advanced fibrosis in other studies of patients with Asian ethnicity ranged from 4% to 11% in China [22, 23], and together with 6% found in Thais in the present study was lower than that reported in studies conducted in western countries, which ranged from 23% to 27% as shown in **Table 3** [12, 16].

However, we can use the NFS or FIB-4 for excluding the advanced liver fibrosis because of its high AUROC (0.66–0.74) and high NPV of 96.4%–98.4%. This can reduce unnecessary liver biopsy in 67% of patients. With the limited sensitivity, specificity, and accuracy of these 4 scoring system for Thai patients with NAFLD, additional testing, for example, serum cytokeratin-18 fragments, liver stiffness measurement, or other biomarkers [24] may be used to add to the diagnostic yield for liver fibrosis assessment in these patients.

Our study has some limitations. First, we were only able to include a relatively small number of patients with NAFLD and advanced liver fibrosis (6%) within the time available for this prospective cohort study, which may affect the diagnostic ability. Second, we had limited information of long-term follow up and the serial liver biopsy, which may add new information on the natural history of liver histology and the change in scoring systems during the follow up period.

Table 2. Comparison of the 4 noninvasive scoring systems for the diagnosis of advanced fibrosis in 139 Thai patients with nonalcoholic fatty liver disease

Non-invasive scoring system	Cutoff ≥	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy	Patients avoiding liver biopsy	False negative result
AST/ALT	0.8	44.4	64.6	8.0	94.4	63	89 (64%)	5 (4%)
BARD score	2.0	77.8	40.0	8.2	96.3	42	54 (39%)	2 (1%)
FIB-4 score	1.3	55.6	83.5	19.2	96.4	79	110 (81%)	4 (3%)
NAFLD Fibrosis Score	–1.455	88.9	48.0	11.0	98.4	48	61 (46%)	1 (1%)

AST, aspartate aminotransferase; ALT, alanine aminotransferase; BARD, **B**MI ≥28 kg/m^2 (1 point), **A**ST/ALT **R**atio ≥0.8 (2 points), and **D**iabetes mellitus (1 point)); FIB-4 score, Fibrosis–4-score; NAFLD, nonalcoholic fatty liver disease; NPV, negative predictive value; PPV, positive predictive value

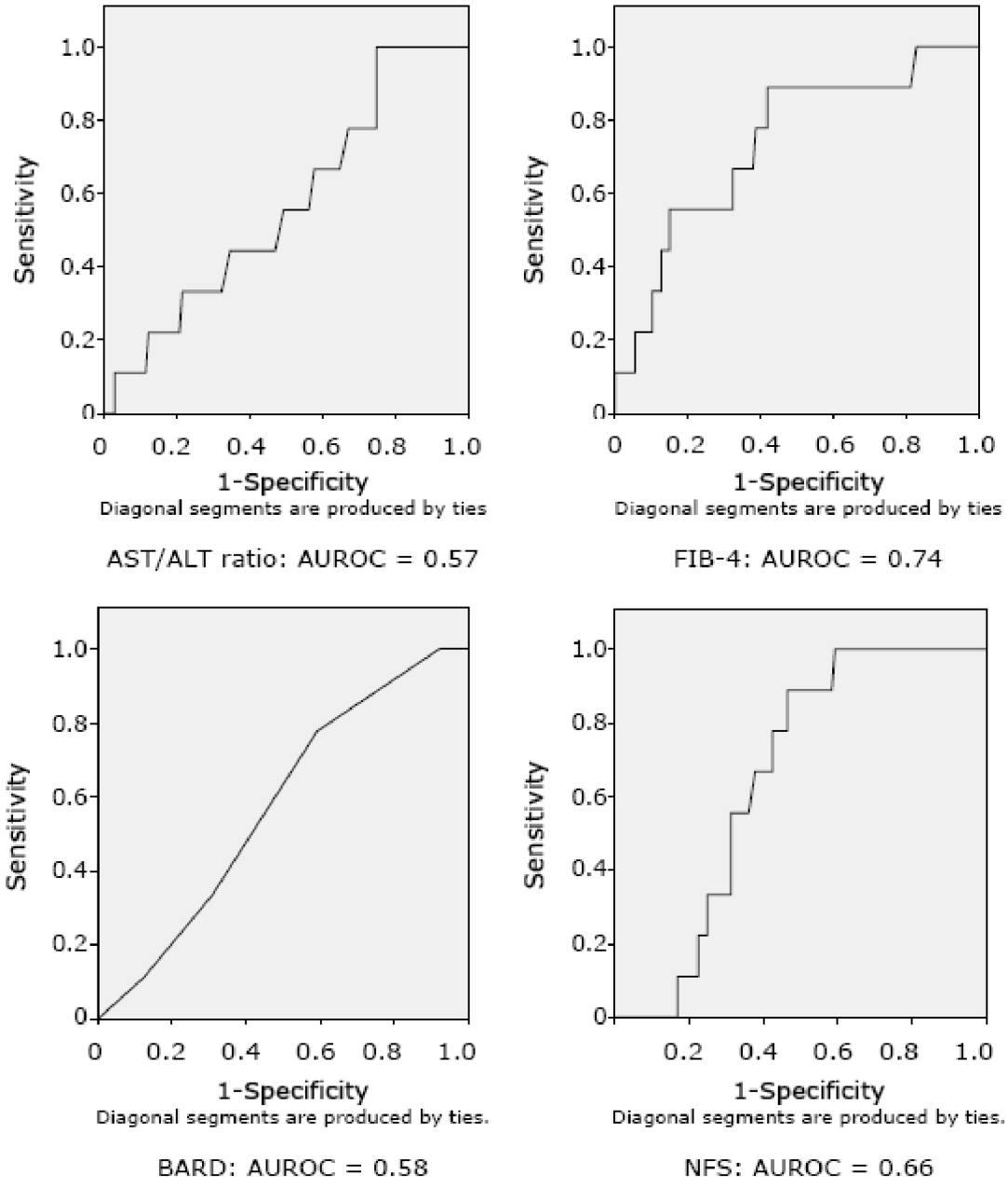

Figure 1. The area under the receiver operating characteristic curve (AUROC) of the 4 noninvasive scoring systems to identify Thai patients with nonalcoholic fatty liver disease with advance liver fibrosis (F3−4) at baseline. AST, aspartate aminotransferase; ALT, alanine aminotransferase; BARD, **B**MI ≥28 kg/m^2 (1 point), **A**ST/ALT **R**atio ≥0.8 (2 point); FIB-4 score, Fibrosis–4-score; NAFLD, nonalcoholic fatty liver disease; NPV, negative predictive value; PPV, positive predictive value

Table 3. Comparison of the diagnostic ability of the 4 noninvasive scoring systems for advanced fibrosis between 2 studies

	Shah et al. [16]	Present study
Baseline characteristics		
Impaired fasting glucose or DM	19.4%	54%
Body mass index (mean; kg/m^2)	34 (6.3)	36 (14.7)
%F3–F4	54%	6%
	AUROC of noninvasive scoring system	
AST/ALT	0.74	0.57
BARD score	0.70	0.58
FIB-4 score	0.80	0.74
NAFLD Fibrosis Score	0.77	0.66

AST, aspartate aminotransferase; ALT, alanine aminotransferase; area under the receiver operating characteristic curve (AUROC); BARD, **B**MI ≥28 kg/m^2 (1 point), **A**ST/ALT **R**atio ≥0.8 (2 points), and **D**iabetes mellitus (DM) (1 point)); FIB-4 score, Fibrosis–4-score; NAFLD, nonalcoholic fatty liver disease

Liver fibrosis in patients with NAFLD progresses slowly over time, and the changes of aminotransferase did not parallel changes in fibrosis stage [25]. This information was supported by a study of the natural history of histological changes, which was performed in 103 of the patients with NAFLD who had no effective treatment with mean interval between serial liver biopsies of 3.2 years (range 0.7–21.3) [25]. Fibrosis stage progressed in 37%, remained stable in 34%, and regressed in 29% [25]. The rate of fibrosis change ranged from −2.1 to 1.7 stages per year. Diabetes (P = 0.007) and low initial fibrosis stage (P < 0.001) were associated with higher rate of fibrosis progression [23]. In clinical practice, the serial liver biopsy may not be a practical tool to use to follow up and monitor the severity of liver fibrosis [8]. The noninvasive scoring system may play an important role for follow up, and requires further research to identify the correlation between the change of noninvasive scoring system and the degree of liver fibrosis progression over time [26].

Advanced fibrosis was prevalent in 6% of our Thai patients with NAFLD. NFS had the highest negative predictive value for excluding patients with advanced fibrosis. At least 38% of patients with NAFLD could avoid liver biopsy by using the BARD scoring system.

Acknowledgments

This study was supported by the grant of Ratchadapiseksompotch Research Fund and Liver Research Unit, Faculty of Medicine, Chulalongkorn University. The authors thank all patients from the liver clinic, King Chulalongkorn Memorial Hospital, and the Thai Red Cross. The authors express their appreciation to Professor Pinit Kullavanijaya, who initiated the idea of clinical research of fatty liver disease in Thailand.

Conflict of interest statement

The authors have no conflicts of interest to declare.

References

1. Adams LA, Lindor KD. Nonalcoholic fatty liver disease. Ann Epidemiol. 2007; 17:863-9.
2. Angulo P. GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther. 2007; 25:883-9.
3. Browning JD, Kumar KS, Saboorian MH, Thiele DL. Ethnic differences in the prevalence of cryptogenic cirrhosis. Am J Gastroenterol. 2004; 99:292-8.
4. Ogden CL, Yanovski SZ, Carroll MD, Flegal KM. The epidemiology of obesity. Gastroenterology. 2007; 132:2087-102.
5. Adams LA, Lymp JF, St. Sauver J, Sanderson SO, Lindor KD, Feldstein A, et al. The natural history of nonalcoholic fatty liver disease: a population-based cohort study. Gastroenterology. 2005; 129:113-21.
6. Ong JP, Pitts A, Younossi ZM. Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease. J Hepatol. 2008; 49:608-12.
7. Ekstedt M, Franzen LE, Mathiesen UL, Thorelius L, Holmqvist M, Bodemar G, et al. Long-term follow-up of patients with NAFLD and elevated liver enzymes. Hepatology. 2006; 44:865-73.
8. Oh MK, Winn J, Poordad F. Review article: diagnosis

and treatment of non-alcoholic fatty liver disease. Aliment Pharmacol Ther. 2008; 28:503-22.
9. Fassio E, Alvarez E, Dominguez N, Landeira G, Longo C. Natural history of nonalcoholic steatohepatitis: a longitudinal study of repeat liver biopsies. Hepatology. 2004; 40:820-6.
10. Harrison SA, Torgerson S, Hayashi PH. The natural history of nonalcoholic fatty liver disease: a clinical histopathological study. Am J Gastroenterol. 2003; 98:2042-7.
11. Powell EE, Cooksley WG, Hanson R, Searle J, Halliday JW, Powell LW. The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. Hepatology. 1990; 11:74-80.
12. Angulo P, Hui JM, Marchesini G, Bugianesi E, George J, Farrell GC, et al. The NAFLD fibrosis score: a noninvasive system that identifies liver fibrosis in patients with NAFLD. Hepatology. 2007; 45:846-54.
13. Harrison SA, Oliver D, Arnold HL, Gogia S, Neuschwander-Tetri BA. Development and validation of a simple NAFLD clinical scoring system for identifying patients without advanced disease. Gut. 2008; 57:1441-7.
14. Vallet-Pichard A, Mallet V, Nalpas B, Verkarre V, Nalpas A, Dhalluin-Venier V, et al. FIB-4: an inexpensive and accurate marker of fibrosis in HCV infection. comparison with liver biopsy and fibrotest. Hepatology. 2007; 46:32-6.
15. Vallet-Pichard A, Mallet V, Pol S. FIB-4: a simple, inexpensive and accurate marker of fibrosis in HCV-infected patients. Hepatology. 2006; 44:769.
16. Shah AG, Lydecker A, Murray K, Tetri BN, Contos MJ, Sanyal AJ. Comparison of noninvasive markers of fibrosis in patients with nonalcoholic fatty liver disease. Clin Gastroenterol Hepatol. 2009; 7:1104-12.
17. Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: practice guideline by the American Gastroenterological Association, American Association for the Study of Liver Diseases, and American College of Gastroenterology. Gastroenterology. 2012; 142:1592-609.
18. Kleiner DE, Brunt EM, Van Natta M, Behling C, Contos MJ, Cummings OW, et al. Design and validation of a histological scoring system for nonalcoholic fatty liver disease. Hepatology. 2005; 41:1313-21.
19. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation. 2002; 106:3143-421.
20. Alberti KG, Zimmet P, Shaw J. The metabolic syndrome—a new worldwide definition. Lancet. 2005; 366:1059-62.
21. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: diagnosis and classification of diabetes mellitus provisional report of a WHO consultation. Diabet Med. 1998; 15:539-53.
22. Wong VW, Wong GL, Chim AM, Tse AM, Tsang SW, Hui AY, et al. Validation of the NAFLD fibrosis score in a Chinese population with low prevalence of advanced fibrosis. Am J Gastroenterol. 2008; 103: 1682-8.
23. Wong VW, Chu WC, Wong GL, Chan RS, Chim AM, Ong A, et al. Prevalence of non-alcoholic fatty liver disease and advanced fibrosis in Hong Kong Chinese: a population study using proton-magnetic resonance spectroscopy and transient elastography. Gut. 2012; 61:409-15.
24. Kwok R, Tse YK, Wong GL, Ha Y, Lee AU, Ngu MC, et al. Systematic review with meta-analysis: non-invasive assessment of non-alcoholic fatty liver disease—the role of transient elastography and plasma cytokeratin-18 fragments. Aliment Pharmacol Ther. 2014; 39:254-69.
25. Adams LA, Sanderson S, Lindor KD, Angulo P. The histological course of nonalcoholic fatty liver disease: a longitudinal study of 103 patients with sequential liver biopsies. J Hepatol. 2005; 42:132-8.
26. Martinez SM, Crespo G, Navasa M, Forns X. Noninvasive assessment of liver fibrosis. Hepatology. 2011; 53:325-35.