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ORIGINAL ARTICLE

Screening for non-alcoholic fatty liver disease in community setting: A cohort study using controlled attenuation parameter-transient elastography

Nicha Teeratorn,*,†,‡ Panida Piyachaturawat,*,† Kessarin Thanapirom,*,† Roongruedee Chaiteerakij,*,† Kanokwan Sonsiri,*,† Piyawat Komolmit,*,† Pisit Tangkijvanich,†,§ Rungsun Rerknimitr,*,† Leon Adams¶ and Sombat Treeprasertsuk*,†,§

Departments of *Medicine, Division of Gastroenterology, Faculty of Medicine, §Biochemistry and Liver Research Unit, Faculty of Medicine, Chulalongkorn University, †Thai Red Cross Society, Bangkok, ‡Department of Medicine, Buddhachinaraj Hospital, Phitsanulok, Thailand and ¶Medical School, University of Western Australia, Nedlands, Western Australia, Australia

Key words
community-based, controlled attenuation parameter, liver fibrosis, non-alcoholic fatty liver disease, transient elastography.

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Correspondence
Sombat Treeprasertsuk, Professor of Medicine, Department of Medicine, Faculty of Medicine, Chulalongkorn University; Rama4 Road, Pathumwan District, Bangkok 10330, Thailand.
Email: sombat.t@chula.ac.th; battan5410@gmail.com

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Abstract

Background/Aim: The global problems of chronic liver disease and non-alcoholic fatty liver disease (NAFLD) are increasing. We examined the prevalence of NAFLD and significant liver stiffness in an asymptomatic population and identified the predictors of significant fibrosis in NAFLD.

Method: We prospectively enrolled Thai subjects, aged 18–80 years, from four regions (Bangkok, Central, North, South) of Thailand from March 2013 to November 2016. All participants underwent controlled attenuation parameter (CAP) measurement for liver fat quantification and transient elastography (TE) for liver stiffness measurement (LSM). NAFLD was defined as liver fat ≥10% (CAP ≥ 306 dB/m). Of 1145 participants, 782 (68.3%) were eligible for analysis.

Result: The mean age ± standard deviation (SD) was 53.1 ± 4.6 years, and 71.6% were female. The mean ± SD values of CAP and LSM of the overall cohort were 241.9 ± 61.4 dB/m and 5.5 ± 3.8 kPa, respectively. The prevalence of NAFLD was 18.0%, whereas 5.4% of the cohort had nonobese NAFLD (BMI < 25 kg/m^2), and 2.8% had lean NAFLD (BMI < 23 kg/m^2). The prevalence of significant liver fibrosis (≥F2) in NAFLD subjects was 18.4%. On multivariate analysis, the degree of significant fibrosis in NAFLD was significantly associated with male gender and a history of dyslipidemia.

Conclusion: NAFLD with significant fibrosis (≥F2) is prevalent in asymptomatic populations. The predictors of significant fibrosis in NAFLD were male gender and dyslipidemia. Screening for NAFLD using CAP/TE in asymptomatic populations should be considered in hospitals with available facilities.

Introduction

Deaths due to cirrhosis from etiologies other than hepatitis B, hepatitis C, and alcohol use have increased globally, from 232 800 cases in 2005 to 247 500 cases in 2015.[1] The problem of non-alcoholic fatty liver disease (NAFLD) is increasing over time in conjunction with the worldwide epidemics of obesity and diabetes and in the absence of effective pharmacotherapy.

In Asian countries, the prevalence of NAFLD is on the rise.[2] A recent large meta-analysis (48 studies and 356 367 subjects) from the mainland of China reported an overall pooled prevalence of 20.1%.[3] The estimated prevalence of NAFLD in Japan was 30% in men and 15% in women. Recently, a population-based study in Hong Kong showed a prevalence of 27.3% and an incidence of 13.5% after 3–5 years of follow up.[4,5] The pooled NAFLD incidence rate in Asia is estimated to be 52.3 per 1000 person-years (95% confidence interval [CI] 28.3–96.8).[6] The majority of NAFLD patients are asymptomatic, and a recent international, multicenter, retrospective cohort study of NAFLD patients has demonstrated that the fibrotic stage is independently associated with the overall and liver-related mortality.[7,8] Among NAFLD patients, the prevalence of Nonalcoholic steatohepatitis (NASH) and fibrosis stages 3–4 is significant, being found in 15–26% and 3–10% of patients, respectively.[9]

Controlled attenuation parameter (CAP) and transient elastography (TE) are noninvasive and time-saving diagnostic tools that are used to determine liver steatosis and fibrosis concurrently. A recent study of repeating liver stiffness measurement

(LSM) using TE in NAFLD patients showed high sensitivity on TE, with a cut-off value < 7.9 kPa demonstrating a 100% negative predictive value for septal or bridging fibrosis and cirrhosis.[10]

NAFLD is traditionally thought to be a disease of affluence that is predominant in Western countries; however, emerging data from Asia suggest that this paradigm may not be true. Thus, we aimed to determine the prevalence of NAFLD and NAFLD with significant liver stiffness in a local community using CAP and TE in an asymptomatic population at low risk of chronic liver disease, that is, chronic alcoholic liver disease, chronic viral hepatitis B, and hepatitis C, in Thailand. In addition, potential risk factors of significant liver fibrosis in NAFLD were also evaluated.

Materials and methods

Study participants. We publicized this project in advance using public information officers, general hospitals, and primary care centers in four regions (Bangkok, Central, North, South) of Thailand. The liver research team from King Chulalongkorn Memorial Hospital sets up a mobile unit at targeted community hospitals on a schedule basis 2–3 times a year. Asymptomatic, healthy Thai volunteers aged 18–80 years are invited to participate in our project and are screened by health-care personnel at local hospitals. Our mobile medical units enrolled prospective volunteers in 11 provinces of those four regions of Thailand from 1 March 2013 to 16 November 2016. The study protocol was approved by the institutional review board (IRB) of Chulalongkorn University, Bangkok, Thailand (IRB number 333/58). Written consent was obtained from all the participants. All volunteers provided their history using a self-reported questionnaire followed by a physical examination and health counseling by a physician. Volunteers with neither a history nor signs suspected of chronic liver disease were included in the project and underwent TE. Volunteers at any risk of chronic liver disease were advised and referred to local gastroenterologists.

Participants were required to report baseline demographic data and history of risks for liver diseases using a standardized self-reported questionnaire (IRB committee of Faculty of Medicine, Chulalongkorn University-approved questionnaire). Body mass index (BMI) was calculated as body weight (kilogram, kg)

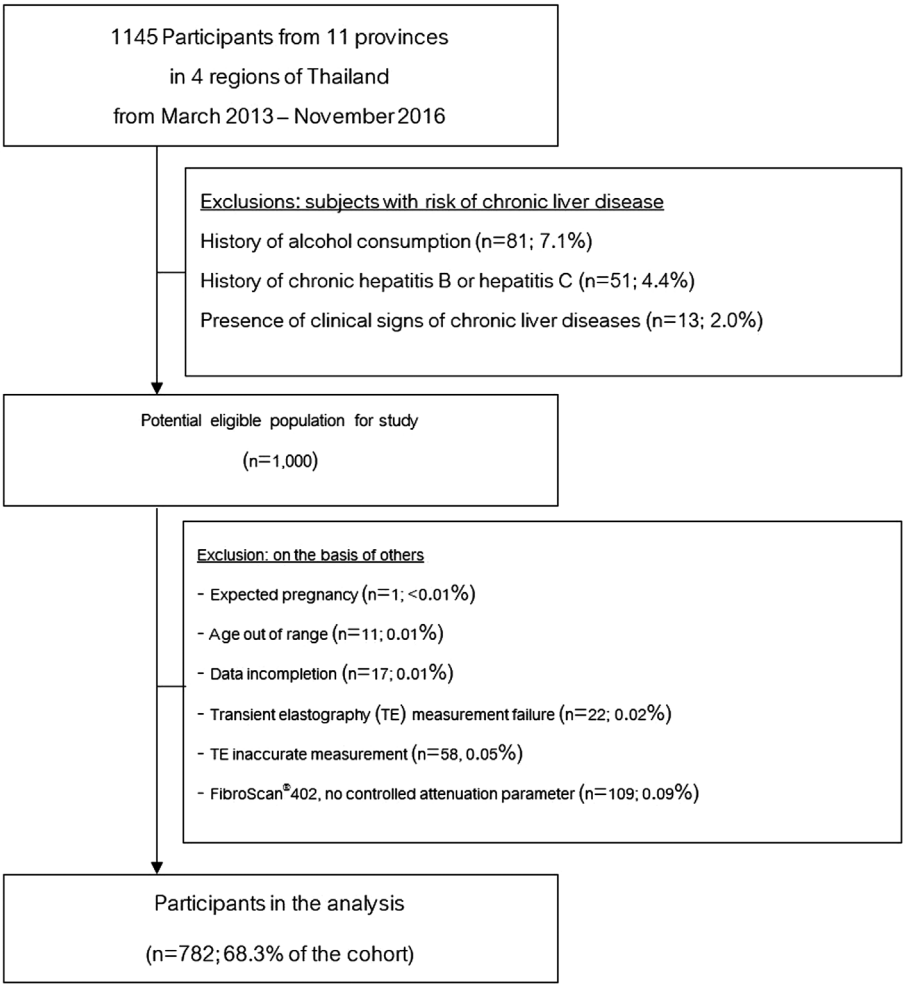

Figure 1 Diagram showing the inclusion and exclusion criteria of the enrolled participants.

Table 1 Characteristics of participants with NAFLD compared to those with normal liver fat

Characters (mean ± SD or number [%])	Overall (*n* = 782)	Liver fat ≥ 10% (*n* = 141)	Normal liver fat (*n* = 641)	*P*-value
Age (year)	53.1 ± 11.6	52.2 ± 10.8	53.3 ± 11.7	0.298
Age > 60	225 (28.8)	35 (24.8)	190 (29.6)	0.304
Gender (male)	222 (28.4)	47 (33.3)	175 (27.3)	0.150
BMI (kg/m^2)	25.1 ± 4.6	27.8 ± 5.6	24.5 ± 4.2	<0.001[1]
BMI < 23	248 (35.1)	22 (15.6)	226 (35.3)	<0.001[1]
BMI < 25	393 (50.2)	42 (29.8)	351 (54.7)	<0.001[1]
Waist circumference (cm)				
Male	86.4 ± 10.8	91.5 ± 0.5	85.2 ± 10.7	0.003[1]
Female	83.2 ± 12.7	89.0 ± 11.2	82 ± 12.6	<0.001[1]
Above norm	300 (38.4)	72 (51.1)	228 (35.6)	<0.001[1]
Comorbidities				
Dyslipidemia	221 (28.3)	50 (35.5)	171 (26.7)	0.038[1]
Hypertension	184 (23.5)	43 (30.5)	141 (22.0)	0.036[1]
Metabolic syndrome	117 (15.0)	37 (26.2)	80 (12.5)	<0.001[1]
Diabetes mellitus	110 (14.1)	29 (20.6)	81 (12.6)	0.015[1]
Liver fat (dB/m)	241.9 ± 61.4	335 ± 25.5	221.2 ± 45.6	<0.001[1]
Liver stiffness (kPa)	5.5 ± 3.9	6.7 ± 4.2	5.3 ± 3.7	<0.001[1]

[1] Statistical significance.
BMI, body mass index; NAFLD, non-alcoholic fatty liver disease.

divided by height (meter, m) squared. Waist circumference (WC) was measured at the midpoint between the lower rib margin and the iliac crest in the horizontal position, with cut-off normal WCs of <90 and <80 centimeters (cm) for men and women, respectively. Male WC > 90 cm or female WC > 80 cm was defined as high WC. Comorbidities (history of diabetes mellitus, essential hypertension, dyslipidemia, and metabolic syndrome), amount of alcohol consumption (cut-off < 30 g/day in male, <20 g/day in female), history of viral hepatitis B or hepatitis C or human immunodeficiency virus (HIV) infection, body piercings or tattoos with nonsterile instruments, intravenous drug use, donated blood products or organ recipients, hemodialysis, jaundice, ascites, variceal bleeding, hepatic encephalopathy, and history of viral hepatitis B of first-degree relatives and partners were included. For all participants, physical examination by a physician was performed, and patients with signs of chronic liver disease, suspicions of opportunistic infection, and presence of tattoos or pruritic papular eruptions were excluded.

Liver stiffness and CAP measurements. All participants underwent TE for LSM (unit in kPa) and CAP (unit in dB/m) for liver fat percentage using a Fibroscan® 402 or Fibroscan® 502 touch (Echosens, Paris, France) by experienced operators who had performed at least 500 prior exams. The 3.5 MHz standard M probe was used. A minimum 2-h fast before the exam was required.[11]

Measurements were taken of the right lobe of the liver through the 9–11th intercostal spaces, with the participant lying in the dorsal decubitus position with the right arm in maximal abduction. The final liver stiffness result was the median value of 10 measurements performed between depths of 25 and 65 mm. Only results with 10 successful measurements, with a success rate > 70% and interquartile range/median (IQR/median) liver stiffness ratio < 30%, were included. An examination without successful measurements after at least 10 attempts was defined as a failure. Significant fibrosis (F2–F4) and cirrhosis (≥F4) were defined as LSM > 8 kPa and >13 kPa, respectively.[12,13] The CAP value was the median of 10 measurements obtained at the same time as the valid LSM. For a sensitivity of 78.6% and specificity of 82.5%, a cut-off CAP value of 306 dB/m was used for the diagnosis of NAFLD.[14] Among participants with NAFLD, we defined nonobese NAFLD as BMI <25 kg/m^2 and lean NAFLD as BMI <23 kg/m^2.[15]

Statistical analysis

All participants were assigned a numerical code that was used in the study. Statistical tests were performed using the IBM SPSS Statistics for Windows, version 23.0. (IBM® Corporation,

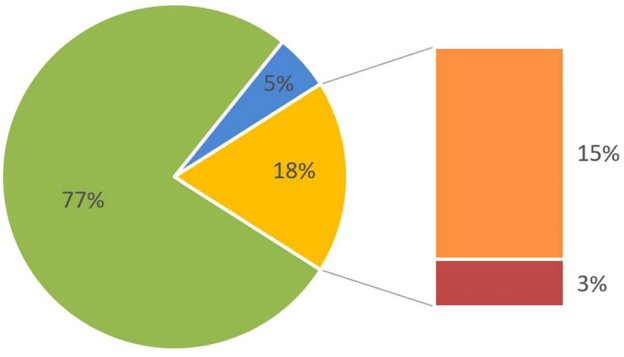

Figure 2 The prevalence of NAFLD in this cohort (*N* = 782). ■ Normal liver fat and liver stiffness; ■ Normal liver fat with TE > 6 kPa; ■ NAFLD with normal liver stiffness; ■ NAFLD with significant fibrosis

Table 2 Characteristics of participants with liver fat ≥10% with significant liver fibrosis (≥F2) compared to those with normal/insignificant liver stiffness

Characters (mean ± SD or number [%])	Significant liver fibrosis (≥F2) (*n* = 26)	Normal/insignificant liver stiffness (F0–F1) (*n* = 115)	*P*-value
Age (year)	51.4 ± 13.7	52.3 ± 10.1	0.692
Age > 60 years	9 (34.6)	26 (22.6)	0.215
Gender (male [%])	13 (50.0)	34 (29.6)	0.064
BMI (kg/m^2)	27.6 ± 6.7	27.9 ± 5.3	0.808
BMI < 23 kg/m^2 (%)	6 (23.1)	16 (13.9)	0.373
Waist circumference (cm)			
Male	95.3 ± 11.3	90.1 ± 8.7	0.196
Female	89.4 ± 9.5	88.9 ± 11.5	0.913
Comorbidities (%)			
Dyslipidemia	13 (50.0)	37 (32.2)	0.115
Hypertension	11 (42.3)	32 (27.8)	0.168
Metabolic syndrome	7 (26.9)	30 (26.1)	1.000
Diabetes mellitus	9 (34.6)	20 (17.4)	0.057
Liver fat (dB/m)	343.3 ± 28.6	334.1 ± 24.6	0.097
Liver stiffness (kPa)	12.4 ± 7.3	5.3 ± 1.0	<0.001

BMI, body mass index.

Armonk, NY, USA). Continuous variables were analyzed as mean ± standard deviation (SD) and compared using the unpaired *t* test if they were normally distributed. Skewed variables were expressed as median (IQR) and compared using the Mann–Whitney *U* test. Categorical variables were compared using Fisher's exact test or the χ^2 test as appropriate. Binary logistic regression analysis, univariate analysis, and multivariate analysis were performed to identify factors associated with significant liver fibrosis. A *P*-value < 0.05 was considered statistically significant.

There were 1145 participants from 11 provinces (Bangkok, Chiang Mai, Chon Buri, Chumphon, Kamphaeng Phet, Nakhon Sawan, Pathum Thani, Phetchaburi, Phra Nakhon Si Ayutthaya, Prachuap Khiri Khan, and Samut Sakhon) in four regions of Thailand enrolled in the study. According to the inclusion criteria, 782 participants (68.3%) were eligible for data analysis (Fig. 1).

Results

Characteristics of participants. There were 782 participants with a mean age of 53.1 ± 4.6 years (age > 60 was 23.9%), and 71.6% were female. The mean BMI of participants was 25.1 ± 4.6 kg/m^2, of which those with BMI ≥23 kg/m^2 was 64.9% and BMI ≥ 30 kg/m^2 was 12.4%. The mean WCs were 86.4 ± 10.7 cm for men and 83.2 ± 12.7 cm for women. The prevalence of obesity (BMI > 25 kg/m^2 or high WC) in this cohort was 54.5%, and histories of dyslipidemia, essential hypertension, metabolic syndrome (modified NCEP III criteria), and type 2 diabetes mellitus were 28.4%, 23.7%, 16.8%, and 14.2%, respectively (Table 1).

CAP and LSM. The mean CAP and LSM values of this cohort were 241.9 ± 61.4 dB/m and 5.5 ± 3.8 kPa, respectively. Three fourths of the participants (76.7%) had normal liver fat and normal liver stiffness (CAP < 306 dB/m and LSM < 6 kPa). Their mean ± SD CAP and TE values were 219.2 ± 45.2 dB/m and 4.6 ± 1.2 kPa, respectively.

The prevalence of NAFLD patients (CAP ≥ 306 dB/m) was 18.0% (Fig. 2). There were 5.4% nonobese NAFLD (BMI < 25 kg/m^2) and 2.8% lean NAFLD (BMI < 23 kg/m^2) participants. Within the NAFLD population, approximately one in six (15.6%) had lean NAFLD, defined as a BMI < 23 kg/m^2. The prevalence of significant liver stiffness (≥F2, LSM > 8 kPa) was 8.6%, and 2.6% of this cohort had LSM >13 kPa, which resulted in a suspicion of cirrhosis (>F4). We found two factors associated with significant liver fibrosis: grade 3 hepatic steatosis and WC above the norm (>90 cm in men and >80 cm in women). In the NAFLD group, the prevalence of significant fibrosis was 18.4%, and 3.5% of these were suspected to have cirrhosis. Characteristics of participants in this cohort along with the stage of liver fibrosis are shown in Tables 1 and 2.

On multivariate analysis, the predictors of significant fibrosis in NAFLD were male gender (odd ratio [OR] 2.87, 95% CI 1.09–7.56, p < 0.033) and history of dyslipidemia (OR 2.75, 95% CI 1.05–7.21, p = 0.039) (Table 3). Of 392 participants without any comorbidities, the prevalence rates of NAFLD, significant fibrosis, and cirrhosis were 10.5%, 4.1%, and 2.3%, respectively.

Discussion

This present community-based study demonstrated the prevalence of NAFLD to be 18.0% in an asymptomatic Thai population without known risk factors for chronic liver disease using a cut-off CAP value of ≥306 dB/m. This high threshold of CAP correlated with liver fat content ≥10% by magnetic resonance imaging proton density fat fraction (MRI-PDFF) and showed

Table 3 Univariate and multivariate analyses of the predictors for significant liver fibrosis in participants with liver fat ≥10%

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age > 60 years	1.81 (0.72–4.54)	0.205		
Gender (male)	2.38 (1.01–5.67)	0.050	2.87 (1.09–7.56)	0.033[1]
BMI <23 kg/m^2	1.73 (0.60–5.02)	0.308		
Diabetes mellitus	2.62 (1.01–6.75)	0.047	2.59 (0.96–6.96)	0.060
Dyslipidemia	2.05 (0.87–4.87)	0.102	2.75 (1.05–7.21)	0.039[1]

[1] Statistical significance.
BMI, body mass index.

high sensitivity (85%) and high specificity (85%) to diagnosis grade 3 hepatic steatosis.[14,16] Among participants with NAFLD, 18.4% demonstrated significant liver fibrosis. Male gender and history of dyslipidemia were identified as predictors of significant liver fibrosis in NAFLD. Furthermore, we found that 8.6% of these volunteers had significant liver fibrosis, whereas 2.6% of this cohort were suspected to have liver cirrhosis. As CAP/TE is a good diagnostic tool for evaluating liver steatosis and liver stiffness, it is suggested to be considered for use in the screening of groups at risk of NAFLD. To our knowledge, this is the one of the largest Asian population studies to examine the prevalence of liver steatosis and liver stiffness by CAP/TE in a community-based setting. The obtained results of physical health status in the general population is essential for policy setting and tailor-made health-care service.

Regarding BMI, the prevalence of NAFLD increased and correlated with high BMI. In Japan, NAFLD was diagnosed in 2.7%, 34.6%, and 77.6% of adults with a BMI of <23, 23–25, and 25–30 kg/m^2, respectively. The prevalence of lean NAFLD (BMI < 23 kg/m^2) was similar to our cohort (2.8% overall), but we had a much lower rate of nonobese NAFLD (BMI < 25 kg/m^2) of 5.4% than Japan.[17] The prevalence of NAFLD in lean individuals was 8.9% and represented 22% of the total NAFLD population.

Our study showed a higher prevalence of significant liver fibrosis (8.6%) in the asymptomatic population compared to earlier studies.[12,13] From a study in Korea, 159 healthy subjects without a history of viral hepatitis with mean age of 56 years who underwent TE and CAP examinations during medical health check-ups had a small proportion of liver fibrosis of 6.9% using TE > 7 kPa, in which the cut-off was lower than that reported by our study.[18] In another large population-based study conducted in the Netherlands between 2011 and 2013, with a mean age of 66 $\pm$ 7.6 years, it was demonstrated that 5.6% of 3041 participants had TE > 8 kPa, and 0.6% of the cohort had TE > 13 kPa.[13] The TE cut-off in this study was similar to that used in our study, and the prevalence of significant liver fibrosis in the Netherlands was lower than those reported in our population.

In our cohort, 41 participants (5.3%) had high liver stiffness with normal liver fat (TE > 6 kPa and CAP < 306 dB/m). More than one-third of those (15/41) demonstrated significant liver fibrosis (TE > 8 kPa). A consideration should be made that they may have NAFLD that was not diagnosed by our high cut-off value of CAP or that may be caused by other pre-existing chronic liver diseases. Thus, we suggested that these patients consult the hepatologist at their local hospitals.

Because a diagnosis of early asymptomatic significant liver fibrosis had benefits, Ginès P et al. reported, in 2016, that there were 6–7% of liver fibrosis patients without known liver disease in population-based studies, which was supported by the results of our study.[19] Accordingly, screening CAP/TE in high-risk asymptomatic subjects should be considered in hospitals with available facilities. We identified male gender and dyslipidemia as risk factors that can help stratify subjects who should be screened using CAP/TE.

In this study, we did not perform the liver biopsy because it was not ethical in a community-based study of such large numbers. A standardized self-reported questionnaire that was approved by an IRB committee of the Faculty of Medicine, Chulalongkorn University was used. The questionnaire included details of the risks of common chronic liver diseases in Thailand, that is, viral hepatitis B, viral hepatitis C, alcohol-related liver disease, and history of hepatic decompensation. Furthermore, physicians looked for signs of chronic liver disease. We can exclude those 145 participants with a history of alcohol consumption (7.1%), those with a history of chronic hepatitis B or hepatitis C (4.4%), or those with the presence of clinical signs of chronic liver diseases (2.0%). Due to the high prevalence of co-infection of HIV and HBV in a risk group of HIV patients, which accounted for 14–24% in Thailand, we excluded these subjects from our study.[20,21] Volunteers without those histories and signs were not assumed to have a normal liver, and this group was enrolled to determine if the participants had any undiagnosed liver disease, starting with non-invasive procedures such as CAP/TE. This screening model is adapted from the concept of a community outreach model suggested by the Asian Pacific Association for the Study of the Liver (APASL) clinical practice guidelines on the management of hepatitis B, a 2015 update.[22] However, our study has limitations. These screening tools are not a perfect to definitely diagnose the status of chronic liver diseases, but we use it as an available tool in local hospitals with limited resources in Thailand. In addition, the rate of the prevalence of hepatitis B and hepatitis C in Thailand is about 3 and 1%, respectively.[23] The lack of testing for viral hepatitis and serum biochemistry was due to limitations of budget; hence, we could not exclude hepatitis B and hepatitis C infections and were unable to calculate the noninvasive scoring system for liver fibrosis assessment. Although higher Alanine aminotransferase (ALT) may affect TE value, leading to an overestimate of significant fibrosis, age, gender, BMI, and fibrosis stage do not affect the performance of CAP.[24] Our study is one of the possible models to implement in local hospitals with limited resources, and such a model has to determine the outcomes in terms of the proportion of patients undergoing screening, proportion of patients that test positive, and proportion that requires treatment, which needs to be confirmed by other studies. Comorbidities in this study were previously diagnosed by local health-care providers and might be underdiagnosed due to recall bias. In addition, our study showed results of the predictors for significant liver fibrosis in participants with liver fat ≥10%, which are male gender and history of dyslipidemia and/or diabetes (Table 3). The proportions of diabetes and dyslipidemia in subjects with liver fibrosis are significantly higher than those without fibrosis, with equal BMI means. Furthermore, in this study, we used a new high cut-off CAP of 306 dB/m to diagnose NAFLD with a specificity of 82.5%, which was correlated with liver fat content ≥10% by MRI-PDFF to diagnosis grade 3 hepatic steatosis and found that 54.5% of participants had obesity and 28.4% had dyslipidemia, but 76.7% had normal liver fat.[14,16]

In conclusion, the prevalence of NAFLD in an asymptomatic population with low risk of chronic liver disease in this community-based study was observed in about one-fifth and has shown a significant liver fibrosis and cirrhosis rate of 18.4%. Predictors of significant liver fibrosis in NAFLD were male gender and history of dyslipidemia. Screening CAP/TE in a high-risk asymptomatic population, especially in men with dyslipidemia, should be considered.

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References

1 Wang H, Naghavi M, Allen C *et al*. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet*. 2016; **388**: 1459–544.
2 Koh JC, Loo WM, Goh KL *et al*. Asian consensus on the relationship between obesity and gastrointestinal and liver diseases. *J. Gastroenterol. Hepatol.* 2016; **31**: 1405–13.
3 Li Z, Xue J, Chen P, Chen L, Yan S, Liu L. Prevalence of non-alcoholic fatty liver disease in mainland of China: a meta-analysis of published studies. *J. Gastroenterol. Hepatol.* 2014; **29**: 42–51.
4 Wong VW, Chu WC, Wong GL *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.
5 Wong VW, Wong GL, Yeung DK *et al.* Incidence of non-alcoholic fatty liver disease in Hong Kong: a population study with paired proton-magnetic resonance spectroscopy. *J. Hepatol.* 2015; **62**: 182–9.
6 Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. *J. Hepatol.* 2016; **64**: 73–84.
7 Obika M, Noguchi H. Diagnosis and evaluation of nonalcoholic fatty liver disease. *Exp. Diabetes Res.* 2012; **2012**: 145754.
8 Angulo P, Kleiner DE, Dam-Larsen S *et al*. Liver fibrosis, but no other histologic features, is associated with long-term outcomes of patients with nonalcoholic fatty liver disease. *Gastroenterology*. 2015; **149**: 389–97 e10.
9 Mahady SE, Adams LA. Burden of non-alcoholic fatty liver disease in Australia. *J. Gastroenterol. Hepatol.* 2018; **33** (Suppl. 1): 1–11.
10 Chow JC, Wong GL, Chan AW *et al*. Repeating measurements by transient elastography in non-alcoholic fatty liver disease patients with high liver stiffness. *J. Gastroenterol. Hepatol.* 2019; **34**: 241–8.
11 Mikolasevic I, Orlic L, Franjic N, Hauser G, Stimac D, Milic S. Transient elastography (FibroScan®) with controlled attenuation parameter in the assessment of liver steatosis and fibrosis in patients with non-alcoholic fatty liver disease—where do we stand? *World J. Gastroenterol.* 2016; **22**: 7236–51.
12 de Ledinghen V, Wong VW, Vergniol J *et al*. Diagnosis of liver fibrosis and cirrhosis using liver stiffness measurement: comparison between M and XL probe of FibroScan®. *J. Hepatol.* 2012; **56**: 833–9.
13 Koehler EM, Plompen EP, Schouten JN *et al*. Presence of diabetes mellitus and steatosis is associated with liver stiffness in a general population: the Rotterdam study. *J. Hepatol.* 2016; **63**: 138–47.
14 Caussy C, Alquiraish MH, Nguyen P *et al*. Optimal threshold of controlled attenuation parameter with MRI-PDFF as the gold standard for the detection of hepatic steatosis. *J. Hepatol.* 2018; **67**: 1348–59.
15 Kim D, Kim WR. Nonobese fatty liver disease. *Clin. Gastroenterol. Hepatol.* 2017; **15**: 474–85.
16 Siddiqui MS, Vuppalanchi R, Van Natta ML *et al*. Vibration-controlled transient elastography to assess fibrosis and steatosis in patients with nonalcoholic fatty liver disease. *Clin. Gastroenterol. Hepatol.* 2019; **17**: 156–63.
17 Matsuura B, Nunoi H, Miyake T, Hiasa Y, Onji M. Obesity and gastrointestinal liver disorders in Japan. *J. Gastroenterol. Hepatol.* 2013; **28** (Suppl. 4): 48–53.
18 You SC, Kim KJ, Kim SU *et al*. Factors associated with significant liver fibrosis assessed using transient elastography in general population. *World J. Gastroenterol.* 2015; **21**: 1158–66.
19 Ginès P, Graupera I, Lammert F *et al*. Screening for liver fibrosis in the general population: a call for action. *Lancet Gastroenterol. Hepatol.* 2016; **1**: 256–60.
20 Jackson JB, Wei L, Liping F *et al*. Prevalence and seroincidence of hepatitis B and hepatitis C infection in high risk people who inject drugs in China and Thailand. *Hepat. Res. Treat.* 2014; **2014**: 296958.
21 Khamduang W, Ngo-Giang-Huong N, Gaudy-Graffin C *et al*. Prevalence, risk factors, and impact of isolated antibody to hepatitis B core antigen and occult hepatitis B virus infection in HIV-1-infected pregnant women. *Clin. Infect. Dis.* 2013; **56**: 1704–12.
22 Sarin SK, Kumar M, Lau GK *et al*. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. *Hepatol. Int.* 2016; **10**: 1–98.
23 Wait S, Kell E, Hamid S *et al*. Hepatitis B and hepatitis C in southeast and southern Asia: challenges for governments. *Lancet Gastroenterol. Hepatol.* 2016; **1**: 248–55.
24 Wong VW-S, Petta S, Hiriart J-B *et al*. Validity criteria for the diagnosis of fatty liver by M probe-based controlled attenuation parameter. *J. Hepatol.* 2017; **67**: 577–84.