# CORRELATION BETWEEN HEPATIC STEATOSIS AND LIVER FIBROSIS WITH CAROTID INTIMA-MEDIA THICKNESS AND CAROTID PLAQUES IN PATIENTS WITH NON-ALCOHOLIC LIVER DISEASE

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## ABSTRACT

**Background:** Nonalcoholic fatty liver disease (NAFLD) is currently the leading cause of chronic liver disease. Approximately 10 to 30% of patients with NAFLD progress to Nonalcoholic steatohepatitis (NASH). NASH can lead to liver fibrosis, progression to cirrhosis and hepatocellular carcinoma, and eventually death. In addition, NAFLD also increases the risk of cardiovascular diseases such as angina, myocardial infarction and stroke 1.64 times higher than patients without NAFLD. Determining the correlation between NAFLD and carotid intima-media thickness will indirectly contribute to demonstrating the association between NAFLD and cardiovascular risk factors. **Objectives:** Determine the proportion of NAFLD patients with carotid intima-media thickness (CIMT) ≥ 0.8 mm. Investigation of the correlation between the hepatic steatosis and liver fibrosis by FibroScan - CAP with CIMT in NAFLD patients. Determination of predictive risk factors of CIMT ≥ 0.8 mm in NAFLD patients. **Method:** Prospective study on 182 NAFLD patients aged 18 years and older who visited Dai Phuoc General Clinic from January 2023 to June 2023. **Results:** The proportion of NAFLD patients with CIMT ≥ 0.8 mm was 45.1%. The proportion of NAFLD patients with carotid atherosclerosis was 44.0%. There was a positive, strong correlation (r = 0.61) between the hepatic steatosis measured by FibroScan - CAP and CIMT in NAFLD patients. There is a positive, weak correlation (r = 0.37) between liver fibrosis measured by FibroScan and CIMT in NAFLD patients. Age, hypertension, central obesity, and hepatic steatosis were independent risk factors predicting CIMT ≥ 0.8 mm in NAFLD patients. **Conclusion:** There is a strong positive correlation between the hepatic steatosis measured by FibroScan - CAP and CIMT in NAFLD patients. Carotid doppler ultrasound to measure CIMT, evaluate carotid atherosclerosis should be undergone in NAFLD patients with risk factors such as older age, hypertension, central obesity and hepatic steatosis.


***Key words:*** *Nonalcoholic fatty liver disease, carotid intima-media thickness, FibroScan*

## I. BACKGROUND

Non-alcoholic fatty liver disease (NAFLD) is now becoming the leading cause of chronic liver disease. The prevalence of NAFLD worldwide accounts about ¼ of the global population. Approximately 10 to 30% of NAFLD patients progress to non-alcoholic fatty hepatitis (NASH)[2] which can lead to hepatic fibrosis, progress to cirrhosis and hepatocellular carcinoma and eventually lead to death. In addition, NAFLD also increased the risk of cardiovascular diseases such as chest pain, heart attack and stroke 1.64 times higher than patients without NAFLD[3]. NAFLD is currently identified as an independent risk factor of cardiovascular events and deaths from all causes. Numerous studies have shown a link between NAFLD and subclinical cardiovascular markers such as markers of endometrial dysfunction[5], ankle-brachial pulse wave propagation

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speed[6], left ventricular systolic dysfunction, and increased carotid intima-media thickness (CIMT). This contributes to making NAFLD an important marker that helps predict cardiovascular risk in the future.

In the world, there have been many studies showed that increased CIMT was closely associated with the risk of myocardial infarction, sudden death, death from coronary heart disease or a combination of the above events[8]. However, in Vietnam there are very few researches on this issue. Therefore, we decided to carry out the study " Correlation between hepatic steatosis and liver fibrosis with carotid intima-media thickness and carotid plaques in patients with non-alcoholic liver disease" with the following objectives: Determine the proportion of NAFLD patients with carotid intima-media thickness (CIMT) ≥ 0.8 mm, investigation of the correlation between the hepatic steatosis and liver fibrosis by FibroScan - CAP with CIMT in NAFLD patients, and determination of predictive risk factors of CIMT ≥ 0.8 mm in NAFLD patients.

## II. RESEARCH METHODS

**Study Design**: Cross-sectional Study

**Study subjects**: NAFLD patients aged 18 years or older who visited Dai Phuoc General Clinic from January 2023 to June 2023.

*Inclusion criteria*: Patients were included in the study when they had CAP > 233 dB/m (corresponding to the percentage of hepatic steatosis ≥ 5%) or had hepatic steatosis by abdominal ultrasound.

*Exclusion criteria*:

- Do not agree to participate in the study
- Secondary hepatic steatosis: Malnutrition BMI < 18.5 kg/m2, parenteral nutrition, drugs (amiodarone, methotrexate, tamoxifen, corticosteroids, valproate), pregnant women, significant alcohol consumption: ≥ 20 g/day for men or ≥ 140 g/week, ≥ 10 g/day or ≥ 70 g/week for women for at least 2 consecutive years[9].
- Other causes of hepatitis: Chronic hepatitis B and C; autoimmune hepatitis, drug-induced hepatitis, hemochromatosis, Wilson's disease
- Ascites, AST, ALT greater than 10 times ULN
- In valid FibroScan results IQR/Med > 30 % or success rate < 60%

**Variable definition**

- Central obesity when waist circumference ≥ 90 cm in men, waist circumference ≥ 80 in female[10]
- The patient is diagnosed with dyslipidemia based on a history of dyslipidemia being treated with lipid-lowering drugs or when the test results have an abnormality in one of the following lipid components[11]: Triglyceride ≥ 1.7 mmol/L (≥ 150 mg/dL), Cholesterol ≥ 5.2 mmol/L (≥ 200 mg/dL), HDLc < 1.05 mmol/L (< 40 mg/dL), LDLc ≥ 2.58 mmol/L (≥ 130 mg/dL)
- Patients are diagnosed with metabolic syndrome when there are at least 3 of the following criteria[12]: Central obesity: waist circumference ≥ 90 cm in men, ≥ 80 cm in women; Hypertriglyceridemia ≥ 150 mg/dL (≥ 1.7 mmol/L), decreased HDLc < 40 mg/dL (< 1.05 mmol/L) in men, < 50 mg/d (< 1.30 mmol/L) ) in women; Systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mm/Hg; Disorders of fasting blood sugar: fasting plasma glucose ≥ 100 mg/dL (≥ 5.6 mmol/L).
- ALT, AST increase when ≥ 33 U/L for men and ≥ 25 U/L for women [13]. GGT increases when > 32 U/L[14]. Fasting plasma glucose increases when ≥ 126 mg/dL[15]. Platelets decrease when < 150 K/µL[14].
- All patients would be asked to fast for at least 3 hours before their liver fibrosis test

**Table 1.** ***Liver stiffness value for liver fibrosis stages mearsured by FibroScan[16]***

| Liver stiffness (kPa) | Liver fibrosis stage |
|---|---|
| < 7 | F0 - F1 (mild or without fibrosis) |
| ≥ 7 | ≥ F2 ( significant fibrosis) |
| ≥ 8.7 | ≥ F3 ( advanced fibrosis) |
| ≥ 10.3 | F4 (cirrhosis) |

**Table 2.** ***The grade of hepatic steatosis mearsured by FibroScan- CAP[17]***

| Grade of hepatic steatosis | Liver fat percentage | CAP (dB/m) |
|---|---|---|
| S0 | 0 - 4% | 100 - 233 |
| S1 | 5 - 33% | 234 - 269 |
| S2 | 34 - 66% | 270 - 300 |
| S3 | 67 - 100% | ≥ 301 |

All patients underwent carotid doppler ultrasound using Versana Premier specialized ultrasound machine. The ultrasound process was performed by 2 experienced sonographers at Dai Phuoc General Clinic according to a protocol to measure CIMT, carotid atheroma.

**Statistical methods**

The collected data is managed and processed by the program SPSS 20, Microsoft Excel. Compare the mean of 2 groups using t-test, from 3 groups or more by analysis of variance (One way ANOVA). Compare 2 or more proportions (%) using chi-square test. Evaluation of the correlation between 2 continuous variables, namely liver elasticity and hepatic steatosis (CAP) with CIMT by correlation analysis, calculated Pearson correlation coefficient (r coefficient). Determine the predictive risk factor of CIMT ≥ 0.8 mm in NAFLD patients by logistic regression analysis.

## III. RESEARCH RESULTS

182 NAFLD patients aged 18 years or older who visited Dai Phuoc General Clinic between January 2023 and June 2023 were eligible to be included in the study.

**General characteristics of the study subjects**

Participant characteristics are summarized in table 3

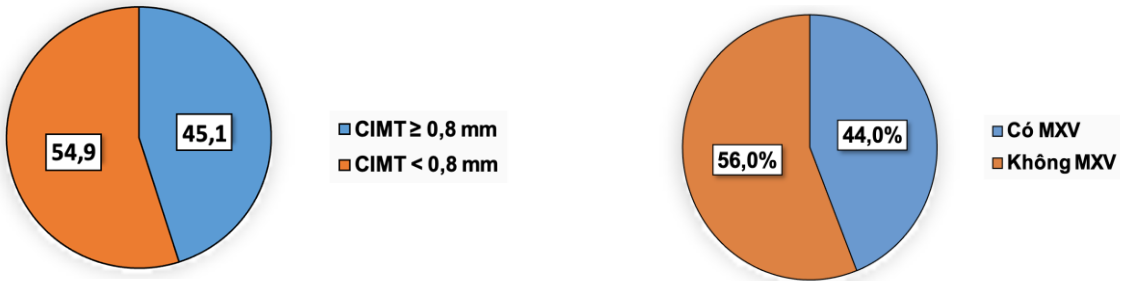
**Table 3.** ***General characteristics of the study subjects***

| Characteristics | N (%) | Mean ±SD<br>Median (quartile) |
|---|---|---|
| **Men** | 94 (51.6%) | |
| **Age** | | 56.4 ± 10.4 |
| **Hypertension** | 79 (43.4%) | |
| **BMI**<br>Normal<br>Overweight<br>Obesity | 21 (11.5%)<br>68 (37.4%)<br>93 (51.1%) | |
| **Waist circumference** | | 85.5 ± 7.6 cm |

| Characteristics | N (%) | Mean ±SD<br>Median (quartile) |
|---|---|---|
| **Central Obesity** | 97 (53.3%) | |
| **Dyslipidemia** | 148 (81.3%) | |
| **Fasting glucose**<br>**Elevated fasting glucose** | <br>43 (23.6%) | 106 (95 - 124) mg/dL |
| **Elevated ALT and/or AST** | 146 (80,2%) | |
| **CAP**<br>S1<br>S2<br>S3 | <br>49 (26.9%)<br>51 (28.0%)<br>82 (45.1%) | 286.6 ± 36.1 dB/m |
| **Liver fibrosis**<br>F0-1<br>F2<br>F3<br>F4 | <br>168 (92.3%)<br>8 (4.4%)<br>1 (0.6%)<br>5 (2.7%) | |
| **CIMT (P)**<br>**CIMT (T)**<br>**Mean CIMT** | 0.9 ± 0.2mm<br>0.8 ± 0.2 mm<br>0.9 ± 0.2 mm | |

More than 50% of patients are obese. Mean waist circumference was high in both men and women, with 53.3% of central obesity. Most patients had dyslipidemia (81.3%). Patients with S3 accounted for the highest percentage (45.1%). Most patients had mild fibrosis (F0-1).

**Proportion of NAFLD patients with carotid intima-media thickness (CIMT) ≥ 0.8 mm and atherosclerotic plaque**




A B

**Chart 1.** ***A. Proportion of NAFLD patients with carotid intima-media thickness (CIMT) ≥ 0.8 mm and B. Atherosclerotic plaque***

**The correlation between the hepatic steatosis and liver fibrosis with CIMT in NAFLD patients**

**Table 4***: The correlation between the hepatic steatosis with CIMT*

| n = 182 | CAP | | |
|---|---|---|---|
| | **r** | **CI 95%** | **p** |
| **CIMT** | 0.61 | 0.47 – 0.73 | < 0.001 |

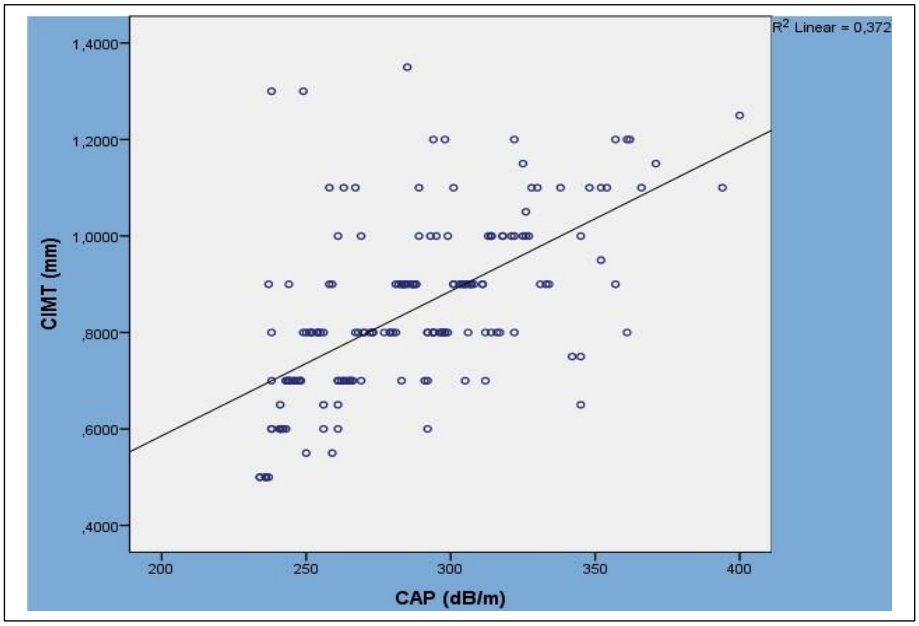



**Chart 2.** ***The correlation between the hepatic steatosis with CIMT***

There was a positive, strong correlation (r = 0.61) between the hepatic steatosis measured by FibroScan - CAP and CIMT

**The correlation between the hepatic fibrosis with CIMT**

**Table 5:** ***The correlation between the hepatic fibrosis with CIMT***

| n = 182 | Hepatic fibrosis | | |
|---|---|---|---|
| | **r** | **KTC 95%** | **p** |
| **CIMT** | 0.37 | 0.29 – 0.49 | < 0.001 |

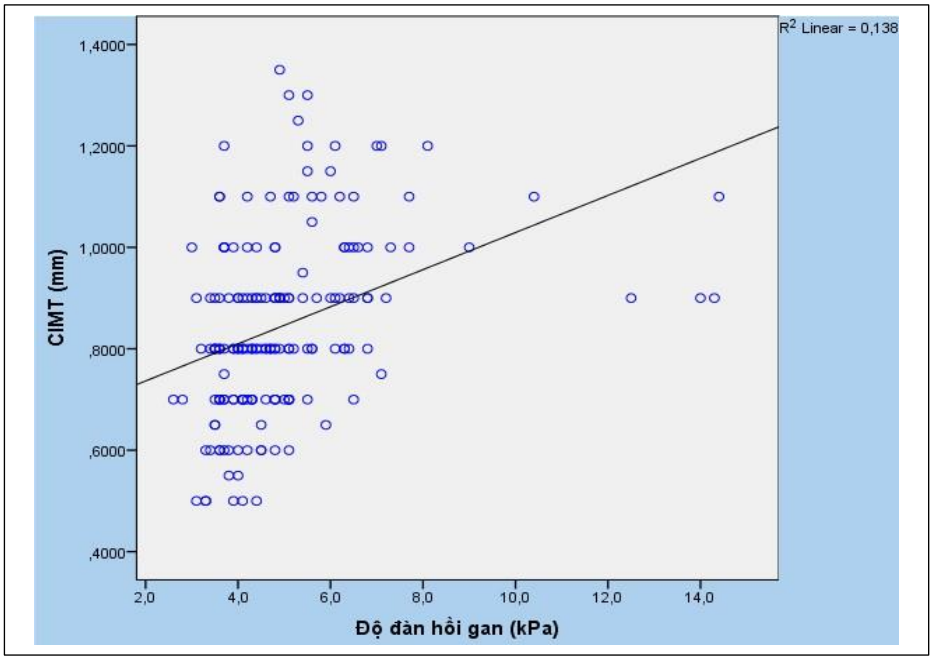



**Chart 3.** The correlation between the hepatic fibrosis with CIMT

***Predictive risk factors of CIMT ≥ 0.8 mm in NAFLD patients***

**Table 6.** ***Predictive risk factors of CIMT ≥ 0.8 mm in NAFLD patients***

| Risk factors | OR | CI 95% | p |
|---|---|---|---|
| **Age** | **1.13** | **(1.06 - 1,.20)** | **< 0.001** |
| **Hypertension** | **2.95** | **(1.03 – 8.44)** | **0.043** |
| BMI | 0.98 | (0.73 – 1.32) | 0.893 |
| Waist circumference | 0.98 | (0.88 – 1.10) | 0.744 |
| **Central obesity** | **6.28** | **(1.71 – 23.09)** | **0.006** |
| Metabolic syndrome | 0.86 | (0.30 – 2.48) | 0.774 |
| Cholesterol | 1.00 | (0.97 – 1.04) | 0.848 |
| LDLc | 0.99 | (0.94 – 1.03) | 0.561 |
| AST | 0,98 | (0,94 - 1,02) | 0,275 |
| **CAP** | **1.05** | **(1.03 – 1.07)** | **< 0.001** |
| Liver fibrosis | 1.38 | (0.86 – 2.20) | 0.180 |

*(Note: Multivariable logistic regression test)*

Multivariate analysis showed that age, hypertension, central obesity, and hepatic steatosis were independent risk factors predicting CIMT ≥0.8 mm in NAFLD patients.

## IV. DISCUSSION

**General characteristics of the study subjects**

Our study results showed that the mean age of NAFLD patients was 56.4, with an average BMI of 25.1 kg/m$^2$ higher than normal. Waist circumference was shown to be a better predictor of visceral fat status than BMI and waist-buttock index[18]. Increased visceral adipose tissue and body fat are correlated with components of metabolic syndrome. Visceral fat is also associated with hepatic steatosis, liver fibrosis, and atherosclerosis[19]. The prevalence of central obesity accounted for more than half of the patients (53.3%) with an average waist circumference of 85.5 cm, lower than in the Asian study by Eugene Choon-Li Tan, Jilin Zheng (96.9 cm) and 91.1 cm[20], respectively. Diabetes is not only one of the components in metabolic syndrome but also one of the leading risk factors for NAFLD. Indeed, NAFLD patients with type 2 diabetes accounts for nearly 70%[21]. In addition, dyslipidemia is also a risk factor for NAFLD, accounted for a very high rate of 81.3%, not significantly different from the study of Eugene Choon-Li Tan (80.6%)[22]. Our study showed that 45.1% of patients have the S3 steatosis level similarly, the study by Rupesh Shrestha et al[23]. NAFLD progression is very slow, it takes 20-30 years to progress to fibrosis and cirrhosis, so most patients have no cirrhosis or only mild fibrosis (92.3%), similar to the reseach of Shrestha (88%23)

**Proportion of NAFLD patients with CIMT ≥ 0.8 mm and atherosclerotic plaque**

According to the 2013 ESH/ESC and ASE guidelines, a CIMT ≥ 0.8 mm or 75th percentile is considered indicative of increased risk of cardiovascular disease. In addition, CIMT > 0.75 also increases the risk of future hypertension[24]. There were a lot of evidences that an association between NAFLD and subclinical atherosclerosis, such as coronary artery calcification, endothelial dysfunction is completely independent of other traditional risks and metabolic syndrom, especially in relation to CIMT[25].

In 182 NAFLD patients, the proportion of patients with carotid intima-media thickness ≥ 0.8 mm was 45.1%. Compared with other studies in the world, our results are similar to Jilin Zheng's study of 43.8%[20] and higher than those of Ali Mohammadzadeh's study of 15.3%[26]. In addition, in the study of Dong Hyun Sinn et al., found that old age, male gender, overweight/obesity, current or past smoking and the presence of metabolic syndrom were independently related factors to the carotid atherosclerotic plaque. Along with these risk factors, NAFLD is another important factor for carotid atherosclerotic plaque. Similarly in previous studies, it has been shown that NAFLD is not only associated with liver disease prognosis but also increases the risk of atherosclerotic cardiovascular disease. The proportion of NAFLD patients with carotid atherosclerotic plaque in our study was 44.0%. NAFLD patients with a CIMT ≥ 0.8 mm and or carotid atherosclerotic plaque need screening and prevention of cardiovascular events.

**Correlation between hepatic steatosis and liver fibrosis with CIMT**

Our study found that there was a strong positive correlation (r = 0.61) between hepatic steatosis and CIMT. The higher the degree of hepatic steatosis in NAFLD patients, the higher the CIMT. The study of Abid Rasool et al on 200 NAFLD patients and 100 control groups also showed that the CIMT of NAFLD patients was higher than that of the control group and increased gradually according to the degree of hepatic steatosis. Furthermore, there was a weak positive correlation (r = 0.37) between liver fibrosis and CIMT. NAFLD patients with higher hepatic steatosis and fibrosis had an increased CIMT. Therefore, it is necessary to investigate both hepatic steatosis and fibrosis for NAFLD patients. Patients with high degree of hepatic steatosis or liver fibrosis should be screened for atherosclerotic cardiovascular disease and carotid doppler ultrasound

**Predictive risk factors of CIMT ≥ 0.8 mm**

Multivariate analysis showed that age, hypertension, central obesity, and hepatic steatosis were risk factors predicting CIMT ≥ 0.8 mm in NAFLD patients, in which central obesity was the highest predictive risk factor. NAFLD patients with central obesity had a 6-fold increased risk of carotid intima-media thickness ≥ 0.8 mm compared with NAFLD patients without central obesity. Similarly, Mohammadzadeh et al.[26] study showed that age, BMI, dyslipidemia were independent risk factors with OR 1.08; 0.86; 2.74 respectively and the presence of NAFLD was the highest risk factor with the strongest OR 16.40 (95% CI = 5.9 - 45). NAFLD patients had a 16-fold increased risk of CIMT ≥ 0.8 mm compared with patients without NAFLD. Therefore, it is necessary to pay attention to screening CIMT and carotid atherosclerotic plaque in elderly, overweight, obese patients, dyslipidemia, metabolic syndrome in NAFLD patients.

## V. CONCLUSION

There is a strong positive correlation between the hepatic steatosis measured by FibroScan - CAP and CIMT in NAFLD patients. Carotid doppler ultrasound to measure CIMT, evaluate carotid atherosclerosis should be undergone in NAFLD patients with risk factors such as older age, hypertension, central obesity and hepatic steatosis.

REFERENCES


1. **Younossi Z. M., Koenig A. B., Abdelatif D., et al.** Global epidemiology of nonalcoholic fatty liver disease-Meta-analytic assessment of prevalence, incidence, and outcomes. Hepatology. Jul 2016;64(1):73-84. doi:10.1002/hep.28431
2. **Fan J. G., Kim S. U., Wong V. W.** New trends on obesity and NAFLD in Asia. J Hepatol. Oct 2017;67(4):862-873. doi:10.1016/j.jhep.2017.06.003
3. **Targher G., Byrne C. D., Lonardo A., et al.** Non-alcoholic fatty liver disease and risk of incident cardiovascular disease: A meta-analysis. J Hepatol. Sep 2016;65(3):589-600. doi:10.1016/j.jhep.2016.05.013
4. **Stepanova M., Younossi Z. M.** Independent association between nonalcoholic fatty liver disease and cardiovascular disease in the US population. Clin Gastroenterol Hepatol. Jun 2012;10(6):646-50. doi:10.1016/j.cgh.2011.12.039
5. **Villanova N., Moscatiello S., Ramilli S., et al.** Endothelial dysfunction and cardiovascular risk profile in nonalcoholic fatty liver disease. Hepatology. Aug 2005;42(2):473-80. doi:10.1002/hep.20781
6. **Huang Y., Bi Y., Xu M., et al.** Nonalcoholic fatty liver disease is associated with atherosclerosis in middle-aged and elderly Chinese. Arterioscler Thromb Vasc Biol. Sep 2012;32(9):2321-6. doi:10.1161/atvbaha.112.252957
7. **Sert A., Aypar E., Pirgon O., et al.** Left ventricular function by echocardiography, tissue Doppler imaging, and carotid intima-media thickness in obese adolescents with nonalcoholic fatty liver disease. Am J Cardiol. Aug 1 2013;112(3):436-43. doi:10.1016/j.amjcard.2013.03.056
8. **Lorenz M. W., Markus H. S., Bots M. L., et al.** Prediction of clinical cardiovascular events with carotid intima-media thickness: a systematic review and meta-analysis. Circulation. Jan 30 2007;115(4):459-67. doi:10.1161/circulationaha.106.628875
9. **Wong V. W., Chan W. K., Chitturi S., et al.** Asia-Pacific Working Party on Non-alcoholic Fatty Liver Disease guidelines 2017-Part 1: Definition, risk factors and assessment. J Gastroenterol Hepatol. Jan 2018;33(1):70-85. doi:10.1111/jgh.13857
10. **Alberti K. G., Zimmet P., Shaw J.** Metabolic syndrome--a new world-wide definition. A Consensus Statement from the International Diabetes Federation. Diabet Med. May 2006;23(5):469-80. doi:10.1111/j.1464-5491.2006.01858.x
11. **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. Dec 17 2002;106(25):3143-421.
12. **Grundy S. M., Cleeman J. I., Daniels S. R., et al.** Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement. Circulation. Oct 25 2005;112(17):2735-52. doi:10.1161/circulationaha.105.169404
13. **Kwo P. Y., Cohen S. M., Lim J. K.** ACG Clinical Guideline: Evaluation of Abnormal Liver Chemistries. Am J Gastroenterol. Jan 2017;112(1):18-35. doi:10.1038/ajg.2016.517
14. **Trần Thị Khánh Tường.** Phân tích xét nghiệm sinh hóa gan và các dấu ấn virus viêm gan. Nhà xuất bản Đại Học Huế; 2018.
15. **Association American Diabetes.** 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2018. Diabetes Care. 2017;41(Supplement_1):S13-S27. doi:10.2337/dc18-S002
16. **Wong V. W., Vergniol J., Wong G. L., et al.** Diagnosis of fibrosis and cirrhosis using liver stiffness measurement in nonalcoholic fatty liver disease. Hepatology. Feb 2010;51(2):454-62. doi:10.1002/hep.23312
17. **Karlas T., Petroff D., Garnov N., et al.** Non-invasive assessment of hepatic steatosis in patients with NAFLD using controlled attenuation parameter and 1H-MR spectroscopy. PLoS One. 2014;9(3):e91987. doi:10.1371/journal.pone.0091987

18. **Ross R., Rissanen J., Hudson R.** Sensitivity associated with the identification of visceral adipose tissue levels using waist circumference in men and women: effects of weight loss. Int J Obes Relat Metab Disord. Jun 1996;20(6):533-8.
19. **Trần Thị Khánh Tường.** Gan nhiễm mỡ. Nhà xuất bản y học, TP. Hồ Chí Minh; 2019.
20. **Zheng J., Zhou Y., Zhang K., et al.** Association between nonalcoholic fatty liver disease and subclinical atherosclerosis: a cross-sectional study on population over 40 years old. BMC Cardiovasc Disord. Jul 16 2018;18(1):147. doi:10.1186/s12872-018-0877-2
21. **Tilg H., Moschen A. R., Roden M.** NAFLD and diabetes mellitus. Nat Rev Gastroenterol Hepatol. Jan 2017;14(1):32-42. doi:10.1038/nrgastro.2016.147
22. **Tan E. C., Tai M. S., Chan W. K., et al.** Association between non-alcoholic fatty liver disease evaluated by transient elastography with extracranial carotid atherosclerosis in a multiethnic Asian community. JGH Open. Apr 2019;3(2):117-125. doi:10.1002/jgh3.12114
23. **Shrestha R., Kc S., Thapa P., et al.** Estimation of Liver Fat by FibroScan in Patients With Nonalcoholic Fatty Liver Disease. Cureus. Jul 2021;13(7):e16414. doi:10.7759/cureus.16414
24. **Takase H., Sugiura T., Murai S., et al.** Carotid intima-media thickness is a novel predictor of new onset of hypertension in normotensive subjects. Medicine (Baltimore). Aug 2017;96(31):e7710. doi:10.1097/md.0000000000007710
25. **Oni E. T., Agatston A. S., Blaha M. J., et al.** A systematic review: burden and severity of subclinical cardiovascular disease among those with nonalcoholic fatty liver; should we care? Atherosclerosis. Oct 2013;230(2):258-67. doi:10.1016/j.atherosclerosis.2013.07.052
26. **Mohammadzadeh Ali, Shahkarami Vahid, Shakiba Madjid, et al.** Association of non-alcoholic fatty liver disease with increased carotid intima-media thickness considering other cardiovascular risk factors. Iranian Journal of Radiology. 2019;16(3)
27. **Sinn D. H., Cho S. J., Gwak G. Y., et al.** Nonalcoholic Fatty Liver Disease for Identification of Preclinical Carotid Atherosclerosis. Medicine (Baltimore). Jan 2016;95(3):e2578. doi:10.1097/md.0000000000002578
28. **Rasool A., Dar W., Latief M., et al.** Nonalcoholic fatty liver disease as an independent risk factor for carotid atherosclerosis. Brain Circ. Jan-Mar 2017;3(1):35-40. doi:10.4103/bc.bc_28_16