Int. J. Curr. Res. Med. Sci. (2022). 8(8): 11-18

International Journal of Current Research in Medical Sciences

ISSN: 2454-5716

(A Peer Reviewed, Indexed and Open Access Journal)

www.ijcrims.com

Original Research Article

Volume 8, Issue 8 -2022

DOI: http://dx.doi.org/10.22192/ijcrms.2022.08.08.003

The association between fatty liver and coronary artery disease: a systematic review and meta-analysis among Iranian population

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Abstract

Objective

This study's objective was to examine any connections between NAFLD and CAD in people with ischemic heart disease.

Methods

Based on PRISMA, a systematic review and meta-analysis were carried out. Before August 2022, two authors independently searched PubMed, Medline, Cochrane, CINAHL, and Web of Science for prospective studies assessing the relationship between NAFLD and CVD. The following terms were entered into the search engine in various combinations: "NAFLD," "non-alcoholic steatohepatitis," "NASH," "non-alcoholic fatty liver disease," and "cardiovascular disease" STATA 13.1 (StataCorp. 2013. Stata Statistical Software: Release 13.) was used for all analyses (StataCorp LP, College Station, Texas).

Results

A total of 4 studies consisting of 953 cases were included in the current study. The total prevalence of NAFL among CAD patients was 60%(95%CI:57-63) out of which 32%(95%CI:29-35) were categorized in grade 1, and 9%(95%CI:7-11) had grade 2 fatty liver.

Conclusion

This meta-analysis demonstrated that NAFLD is linked to a higher risk of developing CAD. Prospective epidemiological research in several demographic groupings is required to confirm this connection. It is fair to aggressively evaluate NAFLD patients for cardiovascular risk factors and occult CVD in the interim and to start risk-reduction therapies (a healthy lifestyle, statins, etc.) as soon as possible.

Keywords: Fatty liver, coronary artery disease, ischemic cardiac disease

Introduction

One of the most prevalent liver illnesses is a non-alcoholic fatty liver disease (NAFLD) [1]. 10–30% of the general population has this disease, and both industrialized and emerging nations are seeing an increase in this incidence [2–5]. NAFLD is closely related to metabolic syndrome, insulin resistance, and both. The majority of patients had dyslipidemia, hypertension, poor glucose metabolism, and obesity—all of which are risk factors for NAFLD [6–8].

Coronary artery disease (CAD) ranks second in the middle- and low-income countries and first in wealthy nations as the leading cause of mortality [9]. Age, gender, diabetes [10–14], poor physical activity, smoking, hyperlipidemia, metabolic syndrome, and diet [9] are all CAD risk factors. NAFLD is regarded as a brand-new CAD risk factor. Inflammatory indicators, fibrinolytic, and hemostatic diseases are additional new risk factors.

Recent research revealed an increased risk of carotid intima and media thickness [20,21], impaired endothelial function [22], increased coronary artery calcification [23,24], and increased arterial stiffness [20] in NAFLD patients. Since NAFLD and CAD are thought to share several risk factors, such as dyslipidemia, hypertension, physical inactivity, insulin resistance, and inflammation, a probable connection between the two conditions might be theorized and assessed [8–25]. In addition, a proportion of CAD patients had abnormal liver function tests, and increased liver enzymes have been recognized as a separate risk factor for the disease [26]. NAFLD is the most frequent cause of high liver enzymes in Iran, and it has been demonstrated that raised liver enzymes are a risk factor for CAD.

This study's objective was to examine any connections between NAFLD and CAD in people with ischemic heart disease.

Method

Based on PRISMA, a systematic review and meta-analysis were carried out. BeforeAugust 2022, two authors independently searched PubMed, Medline, Cochrane, CINAHL, and Web of Science for prospective studies assessing the relationship between NAFLD and CVD. The following terms were entered into the search engine in various combinations: "NAFLD," "non-alcoholic steatohepatitis," "NASH," "non-alcoholic fatty liver disease," and "cardiovascular disease."

Selection of articles

Studies were chosen for inclusion in the systematic review and quantitative analysis if they assessed the relationship between NAFLD and clinical CVE in Iranian patients and satisfied the established inclusion and exclusion criteria. The following criteria must be met to be included: 1) a prospective assessment of clinical CVE in patients with NAFLD, 2) the presence of a control group free of NAFLD, 3) a precise description of both CVE and NAFLD, and 4) adult participants (more than 18 years). Retrospective studies, studies evaluating alternative endpoints (non-clinical), studies comparing disease rates in milder and more severe NAFLD without a control group, studies defining NAFLD by elevated transaminases without confirmation by imaging, and studies that use non-English or Farsi language publications are all excluded. Clinical CVE is defined as the following: 1) myocardial infarction or angina; 2) stroke/transient ischemic attack (cerebral hemorrhage excluded); 3) cardiovascular mortality; 4) requirement for coronary or peripheral revascularization; 5) symptomatic peripheral vascular disease, and 6) defined.

Statistical analysis

DerSimonian and Laird technique was used to do the analysis using a random effects model. The fixed effect model was applied when the level of heterogeneity was minimal. For each endpoint, the heterogeneity of the included trials was evaluated using Cochran's Q statistics. STATA 13.1 (StataCorp. 2013. Stata Statistical Software: Release 13.) was used for all analyses (StataCorp LP, College Station, Texas).

Results

All eligible studies were included in the data collection after systematic review and the data were integrated using the accumulation diagram. The random effects model was evaluated based on the overall prevalence of the disease among the participants. The heterogeneity of the initial studies was assessed using the I^2 test.

Study selection

A total of 542 articles were extracted through initial searches in various databases. Out of 421 essential studies identified by analyzing titles and abstracts, 239 studies were omitted due to irrelevant titles.Out of 178 deleted studies, 90 articles did not have full text, 46 articles were review articles, 4 articles were letters to the editor and 38 articles did not meet the study criteria. finally, 4 studies met the study criteria.

Meta-analysis

A total of 4 studies consisting of 953 cases were included in the current study. The four studies were conducted in the Isfahan, Lorestan, Mashhad, and Birjand provinces of Iran. Out of four included studies, 3 were case-control studies and one had a prospective design.

The total prevalence of NAFL among CAD patients was 60%(95%CI:57-63)out of which 32%(95%CI:29-35)were categorized in grade 1, and 9%(95%CI:7-11)had grade 2 fatty liver (Table1, figure 1-3).

Table1. The characteristics of included studies regarding the prevalence of NAFL among CAD patients

Author	Province	Year	Sample size	Design	Prevalence of NAFL			
					Total	Grade1	Grade2	Grade3
Adibi	Isfahan	2013	82	Case-control	45.12%	21%	7.2%	1.4%
Ahmadi	Lorestan	2014	170	Case-control	49.1%	38.2%	10.9%	N/A
Gholoobi	Mashhad	2022	187	Case-control	140/187	99/187	41/187	N/A
Saghafi	Birjand	2004	514	prospective	59.1%	27.36%	7.1%	0.4%

Figure1. Meta-analysis of the overall prevalence of fatty liver among CAD patients

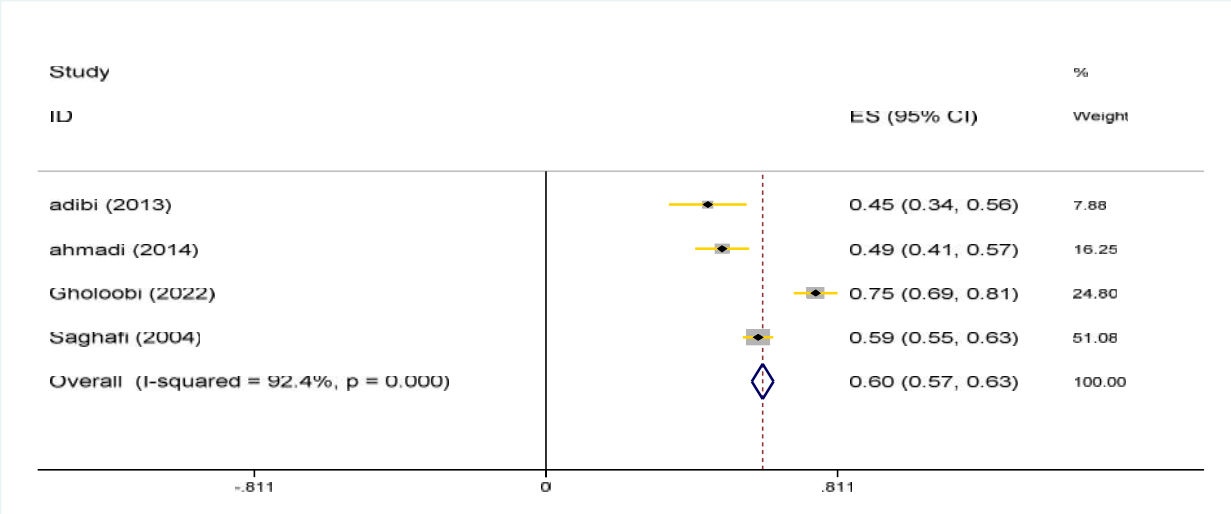


Figure 2. Meta-analysis of the overall prevalence of grade1fatty liver among CAD patients

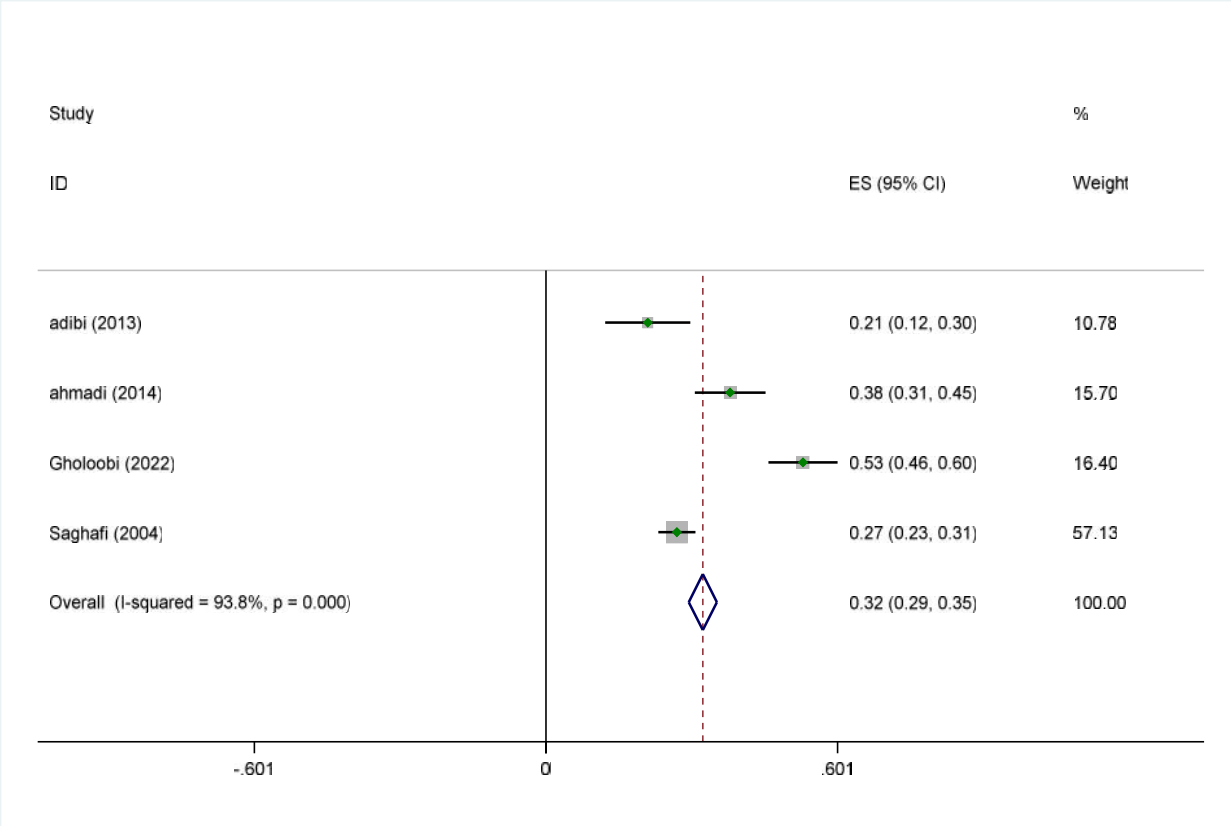
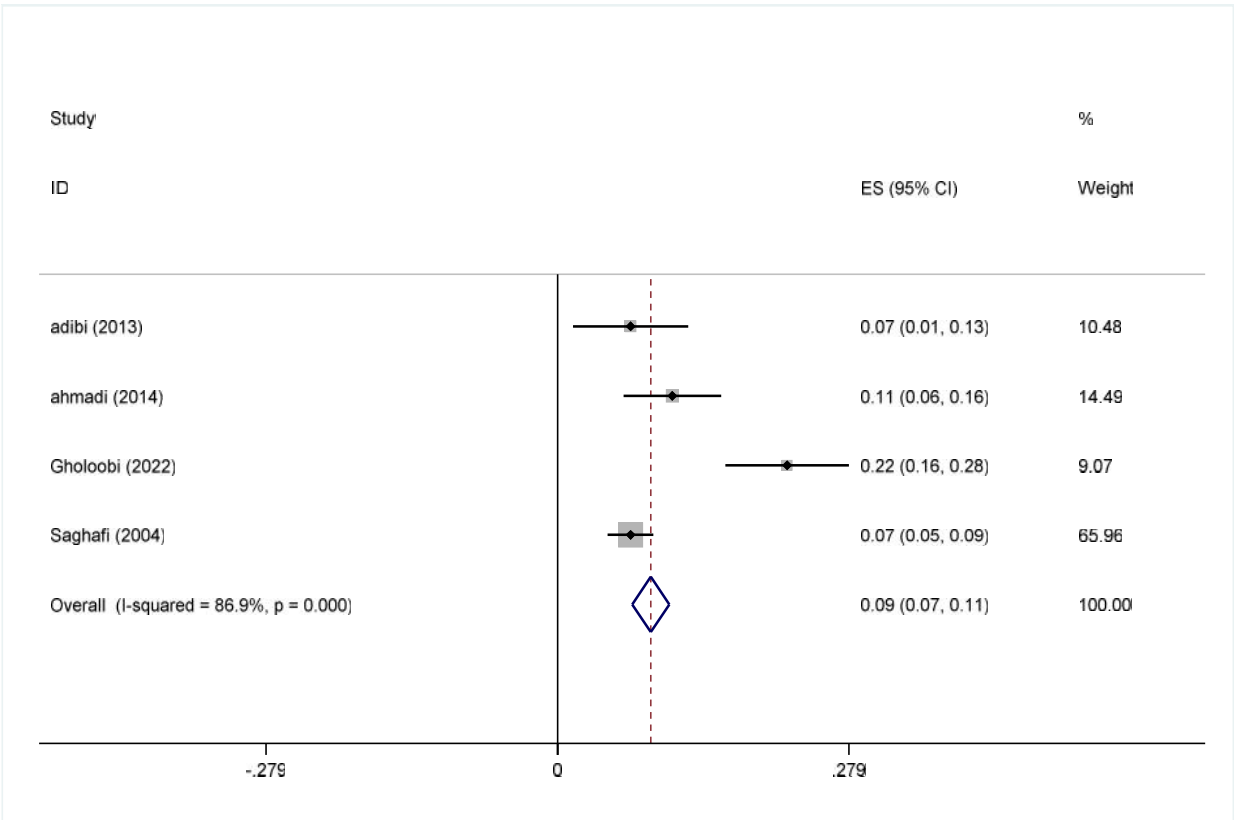


Figure 3.Meta-analysis of the overall prevalence grade2 fatty liver among CAD patients



Discussion

Our research demonstrates a continuous link between clinical CVE and NAFLD. People with NAFLD had a greater chance of developing CVE than people without NAFLD. This has significant ramifications because NAFLD is becoming more prevalent [27]. It is challenging to determine the real effect of NAFLD on CVE since prior meta-analyses and reviews incorporated clinical CVD and subclinical atherosclerosis indicators, such as 50% coronary stenosis without recorded clinical events and coronary artery calcium, carotid intimal thickness, etc. The relationship between NAFLD and the risk of cardiovascular mortality (CVM) was no longer significant after adjusting for major confounders (age, male sex, ethnicity, obesity, diabetes, smoking, and family history of myocardial infarction), according to two previous studies based on NHANES data [28,29]. However, CVD is one of the most common causes of death. Other studies that found high transaminase levels to be a predictor of CVE reported similar outcomes [30–32]. However, in these investigations, the diagnosis of NAFLD was made based on high transaminases and self-reported abstinence from alcohol use. There was no liver imaging or histology, which are presently advised for the diagnosis of NAFLD [33].

Co-morbid conditions including diabetes/insulin resistance, hypertension, and smoking might be causes of this connection. NAFLD patients have been found to have higher rates of traditional CAD risk factors than controls, including metabolic syndrome, dyslipidemia, hypertension, cigarette use, and physical inactivity [34,35]. It is now well accepted that, in addition to conventional joint risk factors, inflammation plays a critical role in the spread of atherosclerosis and clinical CVD [36–39]. Now that systemic inflammation is recognized to be linked to NAFLD; patients may be more susceptible to atherosclerosis and CVE. Finally, NAFLD patients have been demonstrated to have abnormalities in fibrinolytic pathways, increased platelet activation, and alterations in endothelial function, all of which can raise their risk of developing clinical CVD [40,41]. NAFLD and harmful cardiovascular events are associated in a variety of ways, according to recent research. NAFLD was linked to CVD in diabetic individuals, according to some researchers [42–44], although this conclusion was not supported by other researchers [45]. It is assumed that there are significant disparities across research populations, sample sizes, study designs, study durations, and illness detection techniques that account for this contradictory conclusion. Individual research' imprecision is usually made up for by the value of the present meta-analysis, an issue that was mitigated by combining data from all investigations.

A cohort analysis of 144 NAFLD patients who were tracked for more than 13.7 years revealed that their survival rates were comparable to those of the general Swedish population (matched for age and sex). However, their research revealed that individuals with NASH45 had a higher chance of dying. While two other studies [46,47] in England and Denmark likewise found no proof that those with NAFLD had a higher mortality risk compared to the general population.

Conclusion

This meta-analysis demonstrated that NAFLD is linked to a higher risk of developing CAD. Prospective epidemiological research in several demographic groupings is required to confirm this connection. It is fair to aggressively evaluate NAFLD patients for cardiovascular risk factors and occult CVD in the interim and to start risk-reduction therapies (a healthy lifestyle, statins, etc.) as soon as possible.

References

1. G. C. Farrell and C. Z. Larter, “Nonalcoholic Fatty Liver Disease: From Steatosis to Cirrhosis,” Hepatology, Vol. 43, No. 2, 2006, pp. 99-112. doi:10.1002/hep.20973
2. J. D. Browning, L. S. Szczepaniak, R. Dobbins, P. Nur- emberg, J. D. Horton, J. C. Cohen, et al., “Prevalence of Hepatic Steatosis in an Urban Population in the United States: Impact of Ethnicity,” Hepatology, Vol. 40, No. 6, 2004, pp. 1387-1395. doi:10.1002/hep.20466

3. J. A. Welsh, S. Karpen and M. B. Vos, "Increasing Prevalence of Nonalcoholic Fatty Liver Disease among United States Adolescents, 1988-1994 to 2007-2010," Journal of Pediatrics, Vol. 162, No. 3, 2013, pp. 496-500. doi:10.1016/j.jpeds.2012.08.043
4. Sheikh M, Ostadrahimi P, Salarzaei M, Parooie F. Cardiac Complications in Pregnancy: A Systematic Review and Meta-Analysis of Diagnostic Accuracy of BNP and N-Terminal Pro-BNP. Cardiology and Therapy. 2021 Dec;10(2):501-14.
5. X. Hu, Y. Huang, Z. Bao, Y. Wang, D. Shi, F. Liu, et al., "Prevalence and Factors Associated with Nonalcoholic Fatty Liver Disease in Shanghai Work-Units," BMC Gas- troenterology, Vol. 12, No. 1, 2012, p. 123. doi:10.1186/1471-230X-12-123
6. X. Ying, Y. Jiang, Y. Qian, Z. Jiang, Z. Song and C. Zhao, "Association between Insulin Resistance, Metabolic Syn- drome and Nonalcoholic Fatty Liver Disease in Chinese Adults," Iranian Journal of Public Health, Vol. 41, No. 1, 2012, pp. 45-49.
7. G. Musso, R. Gambino, S. Bo, B. Uberti, G. Biroli, G. Pagano, et al., "Should nonalcoholic Fatty Liver Disease Be Included in the Definition of Metabolic Syndrome? A Cross-Sectional Comparison with Adult Treatment Panel III Criteria in Nonobese Nondiabetic Subjects," Diabetes Care, Vol. 31, No. 3, 2008, pp. 562-568. doi:10.2337/dc07-1526
8. Sheikh M, Mahabadi BS, Ostadrahimi P. Prevalence of addiction in Iranian myocardial infarction patients: a systematic review and meta-analysis. Int. J. Curr. Res. Biol. Med. 2018;3(12):47-52
9. W. Nseir, A. Shalata, A. Marmor and N. Assy, "Mecha- nisms Linking Nonalcoholic Fatty Liver Disease with Coronary Artery Disease," Digestive Diseases and Sci- ences, Vol. 56, No. 12, 2011, pp. 3439-3449. doi:10.1007/s10620-011-1767-y
10. C. Ruhl and J. Everhart, "Epidemiology of Nonalcoholic Fatty Liver," Clinical Liver Disease, Vol. 8, No. 3, 2004, pp. 501-519. doi:10.1016/j.cld.2004.04.008
11. Sheikh M, Mahabadi BS, Ostadrahimi P. Infective endocarditis in Iranian children: A systematic review and meta-analysis in three age groups. Int. J. Adv. Res. Biol. Sci. 2019;6(5):110-7.
12. B. Neal, S. MacMahon and N. Chapman, "Effects of ACE Inhibitors, Calcium Antagonists, and Other Blood Pres- sure-Lowering Drugs," Lancet, Vol. 356, No. 9246, 2000, pp. 1955-1964. doi:10.1016/S0140-6736(00)03307-9
13. G. Donati, B. Stagni, F. Piscaglia, N. Venturoli, A. M. Morselli-Labate, L. Rasciti, et al., "Increased Prevalence of Fatty Liver in Arterial Hypertensive Patients with Nor- mal Liver Enzymes: Role of Insulin Resistance," Gut, 2004, Vol. 53, No. 7, pp. 1020-1023. doi:10.1136/gut.2003.027086
14. S. Yokohama, M. Yoneda, M. Haneda, S. Okamoto, M. Okada, K. Aso, et al., "Therapeutic Efficacy of an An- giotensin II Receptor Antagonist in Patients with Nonal- coholicsteatohepatitis," Hepatology, Vol. 40, No. 5, 2004, pp. 1222-1225. doi:10.1002/hep.20420
15. J. Stamler, O. Vaccaro, J. Neaton and D. Wentworth, "Diabetes, Other Risk Factors, and 12-Yr Cardiovascular Mortality for Men Screened in the Multiple Risk Factor Intervention Trial," Diabetes Care, Vol. 16, No. 2, 1993, pp. 434-444. doi:10.2337/diacare.16.2.434
16. A. Adlerberth, A. Rosengren and L. Wilhelmsen, "Dia- betes and Long-Term Risk of Mortality from Coronary ET AL. and Other Causes in Middle-Aged Swedish Men. A Gen- eral Population Study," Diabetes Care, Vol. 21, No. 4, 1998, pp. 539-545. doi:10.2337/diacare.21.4.539
17. R. de Marco, F. Locatelli, G. Zoppini, G. Verlato, E. Bo- nora and M. Muggeo, "Cause-Specific Mortality in Type 2 Diabetes. The Verona Diabetes Study," Diabetes Care, Vol. 22, No. 5, 1999, pp. 756-761. doi:10.2337/diacare.22.5.756
18. G. Marchesini, R. Marzocchi, F. Agostini and E. Bugia- nesim, "Nonalcoholic Fatty Liver Disease and Metabolic Syndrome,"

Current Opinion in Lipidology, Vol. 16, No. 4, 2005, pp. 421-427. doi:10.1097/01.mol.0000174153.53683.f2

19. N. Sarraf-Zadgan, G. Sadri, H. Malek-Afzali, M. Bag- haei, N. Mohammadi-Fard, S. Shahrokhi, et al., "Isfahan Healthy Heart Program: A Comprehensive Integrated Community-Based Program for Cardiovascular Disease Prevention and Control," Acta Cardiologica, Vol. 58, No. 4, 2003, pp. 309-320. doi:10.2143/AC.58.4.2005288
20. A. Brea, D. Mosquera, E. Martín, A. Arizti, J. L. Cordero and E. Ros, "Nonalcoholic Fatty Liver Disease Is Associ- ated with Carotid Atherosclerosis: A Case-Control Stu- dy," Arteriosclerosis, Thrombosis, and Vascular Biology, Vol. 25, No. 5, 2005, pp. 1045-1050. doi:10.1161/01.ATV.0000160613.57985.18
21. C. H. Tsai, T. C. Li and C. C. Lin, "Metabolic Syndrome as a Risk Factor for Nonalcoholic Fatty Liver Disease," Southern Medical Journal, Vol. 101, No. 9, 2008, pp. 900-905. doi:10.1097/SMJ.0b013e31817e8af9
22. G. N. Ioannou, N. S. Weiss, E. J. Boyko, D. Mozaffarian and S. P. Lee, "Elevated Serum Alanine Aminotransfer- ase Activity and Calculated Risk of Coronary Heart Dis- ease in the United States," Hepatology, Vol. 43, No. 5, 2006, pp. 1145-1151. doi:10.1002/hep.21171
23. A. Ugur, T. Sedat, B. Serhat, T. Yusuf, K. Tarkan and C. Atiye, "Association between Nonalcoholic Fatty Liver Disease and Coronary Artery Disease," Coronary Artery Disease, Vol. 18, No. 6, 2007, pp. 433-436. doi:10.1097/MCA.0b013e3282583c0d
24. L. Pacifico, V. Cantisani, P. Ricci, J. F. Osborn, E. Schi- avo, C. Anania, et al., "Nonalcoholic Fatty Liver Disease and Carotid Atherosclerosis in Children," Pediatric Re- search, Vol. 63, No. 4, 2008, pp. 423-427. doi:10.1203/PDR.0b013e318165b8e7
25. I. S. Okosun, K. M. Chandra, A. Boev, J. M. Boltri, S. T. Choi, D. C. Parish, et al., "Abdominal Adiposity in US Adults: Prevalence and Trends, 1960-2000," Preventive Medicine, Vol. 39, No. 1, 2004, pp. 197-206. doi:10.1016/j.ypmed.2004.01.023
26. Y. Lin, H. Lo and J. Chen, "Sonographic Fatty Liver, Overweight and Ischemic Heart Disease," World Journal of Gastroenterology, Vol. 11, No. 31, 2005, pp. 4838- 4842.
27. Clark JM, Brancati FL, Diehl AM. Nonalcoholic fatty liver disease. Gastroenterology 2002;122(6):1649–57.
28. Lazo M, Hernaez R, Bonekamp S, et al. Non-alcoholic fatty liver disease and mortality among US adults: prospective cohort study. BMJ 2011;343:d6891.
29. Stepanova M, Younossi ZM. Independent association between nonalcoholic fatty liver disease and cardiovascular disease in the US population. Clin. Gastroenterol. Hepatol. 2012;10(6):646–50.
30.]Ong JP, Pitts A, Younossi ZM. Increased overall mortality and liver-related mortality in non-alcoholic fatty liver disease. J. Hepatol. 2008;49(4):608–12.
31. Dunn W, Xu R, Wingard DL, et al. Suspected nonalcoholic fatty liver disease and mortality risk in a population-based cohort study. Am. J. Gastroenterol. 2008;103(9):2263–71.
32. Schindhelm RK, Dekker JM, Nijpels G, et al. Alanine aminotransferase predicts coronary heart disease events: a 10-year follow-up of the hoorn study. Atherosclerosis 2007;191(2):391–6.
33. Chalasani N, Younossi Z, Lavine JE, 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(7):1592–609.
34. Misra VL, Khashab M, Chalasani N. Nonalcoholic fatty liver disease and cardiovascular risk. Curr. Gastroenterol. Rep. 2009;11(1):50–5.
35. Kim D, Choi SY, Park EH, et al. Nonalcoholic fatty liver disease is

associated with coronary artery calcification. Hepatology 2012;56(2):605–13.
36. Hansson GK. Inflammation atherosclerosis, and coronary artery disease. N. Engl. J. Med. 2005;352(16):1685–95.
37. Rajappa M, Goswami B, Balasubramanian A, Chakraborty B, Kumar S. Interplay between inflammation and hemostasis in patients with coronary artery disease. Indian J. Clin. Biochem. 2015;30(3):281–5.
38. Schror K, Huber K. Platelets, inflammation and anti-inflammatory drugs in ACS and CAD. Thromb. Haemost. 2015;114(3):446–8.
39. Paoletti R, Gotto AM, Hajjar Jr. DP. Inflammation in atherosclerosis and implications for therapy. Circulation 2004;109(23 Suppl. 1):III20–6.
40. Hui JM, Hodge A, Farrell GC, Kench JG, Kriketos A, George J. Beyond insulin resistance in NASH: TNF-alpha or adiponectin? Hepatology 2004;40(1):46–54.
41. Haukeland JW, Damas JK, Konopski Z, et al. Systemic inflammation in nonalcoholic fatty liver disease is characterized by elevated levels of CCL2. J. Hepatol. 2006;44(6):1167–74.
42. Targher, G. et al. Prevalence of nonalcoholic fatty liver disease and its association with cardiovascular disease among type 2 diabetic patients. Diabetes Care 30, 1212–1218 (2007)
43. Hamaguchi, M. et al. Nonalcoholic fatty liver disease is a novel predictor of cardiovascular disease. World J Gastroenterol. 13, 1579–1584 (2007).
44. Wong, V. W. et al. Coronary artery disease and cardiovascular outcomes in patients with non-alcoholic fatty liver disease. Gut. 60, 1721–1727 (2011)
45. McKimmie, R. L. et al. Hepatic steatosis and subclinical cardiovascular disease in a cohort enriched for type 2 diabetes: the Diabetes Heart Study. Am J Gastroenterol. 103, 3029–3035 (2008).
46. Dam-Larsen, S. et al. Long term prognosis of fatty liver: risk of chronic liver disease and death. Gut. 53, 750–755 (2004).
47. Teli, M. R., James, O. F., Burt, A. D., Bennett, M. K. & Day, C. P. The natural history of nonalcoholic fatty liver: a follow-up study. Hepatology 22, 1714–1719 (1995)

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How to cite this article:
Mahboobeh Sheikh, Pouya Ostadrahimi. (2022). The association between fatty liver and coronary artery disease: a systematic review and meta-analysis among Iranian population. Int. J. Curr. Res. Med. Sci. 8(8): 11-18.
DOI: http://dx.doi.org/10.22192/ijcrms.2022.08.08.003