INPLASY PROTOCOL

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None declared.

The Visceral Adiposity Index in Non-Alcoholic Fatty Liver Disease and Liver Fibrosis — Systematic Review and Meta-Analysis

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Review question / Objective: **The objective of the study was to compare the mean difference and AUROC of Visceral Adiposity Index (VAI) in NAFLD/NASH/liver fibrosis patients and controls in observational studies.**
Condition being studied: **Nonalcoholic fatty liver disease (NAFLD) is a multi-system disease, being mainly a liver pathology involving excessive hepatic fat accumulation unrelated to alcohol consumption or other secondary causes of hepatic steatosis. It is an emerging cause of concern and increasing clinical burden, imposing a public health challenge. NAFLD is the most common chronic liver disease and is predicted to be the most common indication for a liver transplant in Western countries by 2030, owing to a prevalence of 25% worldwide. The visceral adiposity index (VAI) is a scoring system based on body mass index, triglycerides, high-density lipoproteins (HDLs), and waist circumferences (WCs).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 December 2021 and was last updated on 11 December 2021 (registration number INPLASY2021120056).

INTRODUCTION

Review question / Objective: **The objective of the study was to compare the mean difference and AUROC of Visceral Adiposity Index (VAI) in NAFLD/NASH/liver fibrosis patients and controls in observational studies.**

Rationale: **Currently, histopathological sampling is the gold standard for differentiating NAFL from NASH as well as for liver fibrosis staging. However, the procedure is invasive, with exposed sampling errors and inter-observer variability. The current guidelines agree that risk stratification can be performed by**

noninvasive methods. However, no acceptable noninvasive techniques were found to differentiate between bland steatosis and steatohepatitis. The current NAFLD diagnosis guidelines lack any recommendations regarding the visceral adiposity index (VAI), a scoring system based on body mass index, triglycerides, high-density lipoproteins (HDLs), and waist circumferences (WCs), probably due to inconclusive and insufficient data. Therefore, we conducted a systematic review and meta-analysis aiming to assess the VAI in NAFLD, including hepatic steatosis and NASH, as well as quantifying liver fibrosis. We also evaluated whether the VAI can differentiate between different hepatic steatosis grades and simple steatosis from NASH.

Condition being studied: Nonalcoholic fatty liver disease (NAFLD) is a multi-system disease, being mainly a liver pathology involving excessive hepatic fat accumulation unrelated to alcohol consumption or other secondary causes of hepatic steatosis. It is an emerging cause of concern and increasing clinical burden, imposing a public health challenge. NAFLD is the most common chronic liver disease and is predicted to be the most common indication for a liver transplant in Western countries by 2030, owing to a prevalence of 25% worldwide. The visceral adiposity index (VAI) is a scoring system based on body mass index, triglycerides, high-density lipoproteins (HDLs), and waist circumferences (WCs).

METHODS

Search strategy: We conducted a computerized search in PubMed, Embase, Scopus, and Cochrane Library electronic databases in order to identify observational studies assessing the VAI in NAFLD and liver fibrosis. The used search string is as follows: PubMed: (("visceral adiposity index") OR ("visceral adiposity index"[All Fields]) OR ("VAI")) AND (("Non-alcoholic Fatty Liver Disease"[Mesh]) OR ("Non-alcoholic Fatty Liver Disease"[All Fields])). EMBASE: ('visceral adiposity index'/exp OR 'visceral adiposity index' OR 'VAI') AND ('Non-alcoholic Fatty Liver Disease'/exp OR 'Non-alcoholic Fatty Liver Disease') Scopus (All fields): (("visceral adiposity index") OR ("visceral adiposity index"[All Fields]) OR ("VAI")) AND (("Non-alcoholic Fatty Liver Disease"[Mesh]) OR ("Non-alcoholic Fatty Liver Disease"[All Fields])) Cochrane Library: Visceral adiposity index AND Non-alcoholic fatty liver disease.

Participant or population: Various clinical settings.

Intervention: NAFLD/NASH/liver fibrosis.

Comparator: Controls.

Study designs to be included: Observational studies.

Eligibility criteria: The inclusion criteria of original articles in our systematic review and meta-analysis were as follows: (1) observational cohort, cross-sectional, or case–control studies assessing the VAI in NAFLD and liver fibrosis; (2) hepatic steatosis confirmed histologically through a liver biopsy, or evaluated by imagistic techniques such as ultrasonography, computed tomography (CT), and magnetic resonance imaging (MRI), or by noninvasive biomarkers and scores; (3) liver fibrosis confirmed histologically, or assessed by transient elastography (FibroScan), or noninvasive biomarkers and scores; (4) human studies with no restrictions to gender, race, or ethnicity; and (5) studies published in English, German, French, or Romanian. The exclusion criteria were as follows: (1) the presence of secondary causes of hepatic steatosis, significant alcohol consumption based on each study definition or any other cause of chronic liver disease (CLD); (2) liver cirrhosis of any etiology or end-stage liver disease patients who underwent or were awaiting liver transplantation; (3) hepatitis virus of any etiology; (4) HIV infection or use of antiretroviral therapy; (5) polycystic ovarian syndrome; and (6) editorials, letters, short surveys, commentaries, case reports, conference abstracts, review articles, practice guidelines, and abstracts published without a full article.

Information sources: We conducted a computerized search in PubMed, Embase, Scopus, and Cochrane Library electronic databases in order to identify observational studies assessing the VAI in NAFLD and liver fibrosis. Moreover, we performed a manual search for relevant missed publications through screening the references of included articles. The literature search was conducted from inception till the 19 October 2021 by two investigators (A.I. and D.C.L.) independently.

Main outcome(s): The principal summary outcomes were mean difference (MD) of Visceral Adiposity Index (VAI) in hepatic steatosis and NASH, as well as quantifying liver fibrosis. We also evaluated whether the VAI can differentiate between different hepatic steatosis grades and simple steatosis from NASH. Moreover, we assessed the area under the curve (AUC) of VAI in predicting NAFLD and NASH.

Data management: Bibliographic software was used to manage the references within the screening, selection, and data description. Data extraction was performed by one investigator (A.J.) and verified by another (S.L.P.), while any discrepancies were resolved by confronting the source article. The extracted data included author names, publication year, country, design of the study, studied population, total sample size, NAFLD percentage, mean age, sex distribution, body mass index (BMI), NAFLD diagnosis technique, mean ± SD or median (interquartile range), area under receiver operating characteristic (AUROC) curve, and study conclusion, which were collated, stored in a spreadsheet file, and presented in the manuscript text.

Quality assessment / Risk of bias analysis: Quality assessment of all included studies, evaluating the risk of bias and internal validity, was performed in a similar manner using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool by two investigators (A.I. and D.C.L.) independently. A consensus was reached through discussion in the presence of disagreement between the evaluations of the two investigators. The items assessed in the quality assessment tool were answered by either "yes", "no", or "unclear". The eligibility of the studies was not affected by the methodological quality assessment results.

Strategy of data synthesis: The data analyses of the systematic review and meta-analysis were performed using R with the Metafor package (OpenMeta [Analyst]). The principal summary outcomes of the VAI in NAFLD and liver fibrosis were the mean difference (MD) of the VAI and the area under the curve (AUC) evaluating the accuracy of the VAI. Between-study heterogeneity was evaluated by a $\chi 2$-based Q-test and I2. In studies reporting medians and interquartile ranges (IQRs), we calculated the mean and standard deviation (SD) based on them. The standard error of the AUC was calculated from the confidence interval (CI) and the point estimate. For all meta-analyses, we used restricted maximum likelihood random-effects models. We reported the data from each study as the estimated MD with 95% CI, lower bound, upper bound, standard error, and p-value, or the estimated AUC with 95% CI, lower bound, upper bound, standard error, and p-value.

Subgroup analysis: Subgroup analysis was conducted according to the diagnosis method of NAFLD, adults, pediatrics, the severity of hepatic steatosis, NASH, liver fibrosis grading, diabetic/prediabetic NAFLD patients, and sex, depending on the available values from the extracted data from included studies.

Sensitivity analysis: The sensitivity analysis assessed the leave-one-out effect on heterogeneity and effect estimate, excluding high-leverage studies or outliers, which were identified with dmetar package.

Language: Studies included had to be published in English, German, French, or Romanian.

Country(ies) involved: Romania.

Keywords: non-alcoholic fatty liver disease (NAFLD); non-alcoholic steatohepatitis (NASH); hepatic steatosis; liver fibrosis; visceral adiposity index (VAI); liver biopsy.

Dissemination plans: Publication in a peer-reviewed journal.

Contributions of each author:

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