Review Article

Caveolin Gene, a Possible Risk Factor for Metabolic Syndrome in Humans: A Systematic Review and Meta-Analysis

Abstract

Background: Studies show that caveolin genes are associated with metabolic disorders, so we aimed to systematically review the association between caveolin genes and metabolic syndrome in human studies. This systematic review is conducted based on the PRISMA 2020 checklist. **Methods:** A systematic literature search was done on electronic databases including Embase, Scopus, Medline (PubMed), and Web of Science until September 2023 and updated until June 2024. Human studies that were published in English were included without restricting other variables such as time, age, and gender. **Results:** At the first step, 10313 papers were found, and at the final step, nine studies were included in the systematic review, and four studies entered the quantitative analysis. The result showed that metabolic syndrome is significantly associated with minor alleles in the following genes: *CAV-1* rs1997623 (OR = 1.44 (95% CI: 1.2, 1.86)), *CAV-1* rs11773845, 22375–22375 del AC, and *CAV-1* rs3807992. No significant association was found for *CAV-1* rs926198 (OR = 1.61 (95% CI: 0.89-2.92)), and 22285 C>T. Caveolin mRNA level was increased in the cases of metabolic syndrome. *CAV-1* rs1997623 A allele changes the transcription factor binding site to increase the attachment of EBF1. **Conclusions:** This results in the enhancement of promoter activity and further transcription of the caveolin-1 gene. In conclusion, individuals carrying minor alleles for the *CAV-1* gene might have an increased risk for metabolic syndrome. With future studies focusing on the matter, this gene can be used as a screening tool for metabolic health to detect individuals with a higher genetic susceptibility to metabolic syndrome.

Keywords: *CAV1, Caveolin, MetS, metabolic syndrome, obesity*

Mohadeseh Arefian[1,2], Sadegh Mazaheri-Tehrani[1,2], Maryam Yazdi[2], Roya Kelishadi[2]

[1]Student Research Committee, Isfahan University of Medical Sciences, Isfahan, Iran, [2]Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran

Address for correspondence:
Dr. Roya Kelishadi, Department of Pediatrics, Child Growth and Development Research Center, Research Institute for Primordial Prevention of Non-Communicable Disease, Isfahan University of Medical Sciences, Isfahan, Iran.
E-mail: kelishadi@med.mui.ac.ir

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Introduction

Metabolic syndrome (MetS) is defined as a group of clinical factors including, hypertension, dyslipidemia, hyperglycemia, insulin resistance, and central obesity. Individuals with at least three of these components are classified as MetS.[1] Studies reported MetS as a risk factor for developing different non-communicable diseases such as cardiovascular diseases (CVD), diabetes mellitus, non-alcoholic fatty liver disease, and some types of cancers.[2] The prevalence of MetS varies within different regions and populations. According to the US national survey data, 34.7% of participants are classified as MetS,[3] while its prevalence is estimated to be 25% and 24.5% in the Middle East countries,[4] and China,[5] respectively. Moreover, diet and sedentary lifestyles are reported to be associated with developing MetS.[6] The mentioned factors demonstrated the role of the environmental factor in MetS. On the other hand, genetic factors also play an important role in developing MetS. For instance, non-obese people with MetS reported higher mortality rates due to associated diseases compared to obese MetS cases, which indicated the pivotal role of genetic factors.[7,8]

Caveolin-1 (*CAV-1*) is a cell membrane protein encoded by the *CAV-1* gene and involves cell migration, cholesterol distribution, and signaling.[9] Recently, *CAV-1* has been reported to play a role in developing metabolic pathways, including fatty acid metabolism, modulating insulin resistance, and glycolytic activities.[9] Caveolin-1 null mice were reported to develop insulin resistance, hypertension, and hypertriglyceridemia even without the influence of the environment.[10] Likewise, human studies revealed that lower expression of *CAV-1* due to gene mutations caused insulin resistance, diabetes mellitus,

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and hypertriglyceridemia.[11] On the other hand, studies up to date have assessed the effect of different single nucleotide polymorphisms (SNPs) of *CAV-1* on MetS incidence. Different SNPs affect *CAV-1* expression differently.[11] Therefore, this study aimed to conduct a systematic review and meta-analysis to summarize the association between different SNPs of *CAV-1* and MetS in humans.

Methods

Search strategy and study selection

This systematic review was conducted based on the PRISMA (preferred reporting items for systematic reviews and meta-analysis) 2020 guideline.[12] The study was registered on PROSPERO (registration code: CRD42022332778). A comprehensive literature review was performed on electronic databases including Scopus, Web of Science, Medline database (PubMed), and Embase until September 2023. A weekly assessment of these databases was also done to include new articles, and the search was updated until June 2024. The search keywords were ("Caveolin" OR "Caveolin Protein" OR "Caveolin-3" OR "Caveolin-2" OR "Caveolin-1" OR "CAV1") AND ("Metabolic syndrome" OR "MetS" OR "syndrome X" OR "insulin resistance" OR "Diabetes" OR "obesity" OR "hypertension" OR "cardiovascular disease" OR "lipoprotein"). A limitation on the language (English) was applied. Moreover, in the Scopus database, to reduce irrelevant records, a search on the title-abstract-keywords was done. Letters, conference papers, erratums, and book chapters were excluded. The screening process was performed by two independent authors (M.A. and S.M-T), and disagreements were resolved using a group discussion about the subject. The reference list of relevant articles was also checked to find undetected associated articles. Supplementary File 1 shows the search string for each database.

Inclusion criteria

We included original articles to evaluate the association between caveolin genes and metabolic syndrome. Only studies written in English were included in the study. No restriction was added regarding age, gender, race, publication year, or the definition used for metabolic syndrome.

Exclusion criteria

Animal studies, duplicate publications, and studies that were not in full reports, such as letters, and conference abstracts, were excluded.

Data extraction

The following information was extracted by two independent reviewers (M.A and S.M-T): first author name, year of publication, and design of the study, characteristics of the samples, including country and ethnicity that the study occurred in, mean age, metabolic syndrome prevalence, percentage of the male sex, and total sample size, metabolic syndrome definition, genotyping method, type of SNP that is studied and results in the adjusted and non-adjusted models.

Risk of bias assessment

The quality of selected articles was assessed through the NIH checklist (National Institute of Health Quality Assessment Tool) for observational cohort and cross-sectional studies. NIH checklist is a list of 14 questions about the study population, inclusion-exclusion criteria, participation rate, and other potential defects in studies answered with yes or no or cannot determine (CD), not applicable (NA), not reported (NR). Afterward, the quality of included studies was classified as poor, fair, or good. Two reviewers (M.A and S.M-T) evaluate the quality of included records separately. Afterward, the result was checked by the third reviewer (RK).

Statistical analysis

Odds ratios and 95% confidence intervals were extracted as the effect size and pooled using random effects meta-analysis. The DerSimonian-Laird method was used to calculate the pooled effect size for those polymorphisms with available data. Heterogeneity between studies was assessed by I2 statistic. Due to the limited number of studies available for meta-analysis, publication bias tests were not performed. Meta-analyses were conducted using Stata version 17.

Results

Study selection process

According to the search strategy, 10313 records were found. After duplicate removal, 6422 articles remained. Based on the title and abstract screening, 6402 citations were excluded, and 20 articles were found to be eligible for full-text examination. After further assessment, 11 studies were excluded because they were conference papers, or they did not match the inclusion criteria. Therefore, nine records were ultimately entered into the systematic review [Figure 1]. Four study were eligible to enter the quantitative analysis.

Study characteristics

The primary characteristics of the included articles are shown in Table 1. Different *CAV-1* polymorphisms, including *CAV-1* rs926198, rs3807992, rs11773845, rs1997623, 22285 C>T, 22375–22375 ``del AC were assessed. Two study investigated caveolin mRNA level, and one study assessed *CAV-1* protein level. The total number of subjects was 6126, and the largest and smallest sample sizes were 1313 and 38. All of the studies were published after 2005, with the majority of the studies published after 2020. Two of the included studies were multinational, and the rest of them were conducted in Iran, Brazil, Kuwait, Colombia, and Spain. Different quantitative and qualitative definitions for MetS were used; two studies used joint interim statement criteria,[13] and one of the studies used AHA/NHLBI statement criteria.[14] One used Adult

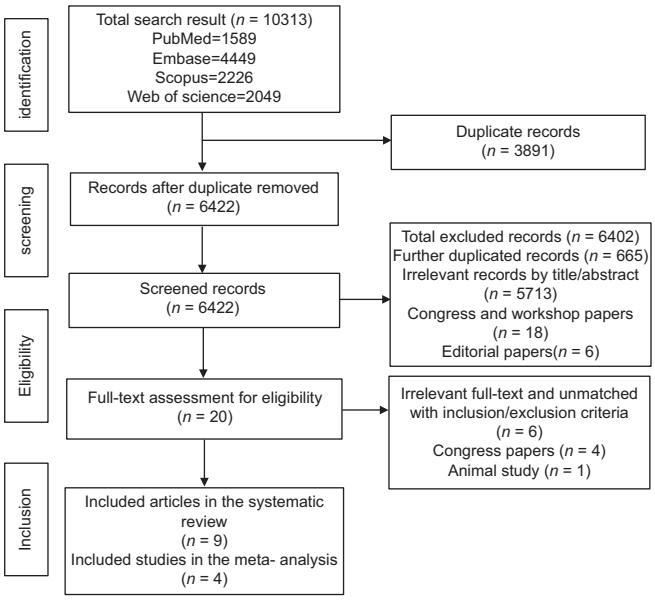

Figure 1: Flowchart for study selection

Treatment Panel III (ATP III) criteria.[14] IDF (International Diabetes Federation) criteria were also used by Grilo A and Al Madhoun A.[15] R Nizam utilized the metabolic syndrome score, which is defined as the number of presented risk factors in each individual.[16] The cMetS and siMS scores were other quantitative values that were used.[17-19] The cMetS score is calculated by a regression analysis of the risk factor's value.[18] Supplementary File 2 shows the quality of the studies. All the included studies have acceptable quality.

CAV-1 rs926198

Two studies investigated the relationship between *CAV-1* rs926198 and MetS. Baudrand *et al.*[11] have found a significant association between *CAV-1* rs926198 minor allele carrier (both CC homozygotes and CT heterozygotes group) and metabolic syndrome in Caucasian (OR = 2.83 (95% CI: 1.73–4.63)) and in the Hispanic background (OR = 1.61 (95% CI: 1.06–2.44)). Another study conducted by Mora-García G *et al.*[21] initially found the same outcome as the mentioned study. The result showed a significant difference between MetS prevalence in the *CAV-1* rs926198 minor allele carrier group (CC and CT group) and the TT homozygotes group. However, data entering logistic regression and adjusting for confounders, this association was not significant anymore (OR = 0.97 (95% CI: 0.67–1.42)).

Also, the pooled effect size for *CAV-1* rs926198 did not reach statistical significance (OR = 1.61 (95% CI: 0.89–2.92)) [Figure 2].

CAV-1 rs11773845

Mora-García *et al.*[21] assessed *CAV-1* rs11773845 polymorphism relation with metabolic disorders. The result suggests that this SNP is significantly associated with metabolic syndrome (OR = 1.58 (95% CI: 1.11–2.26)). CC and AC groups (minor allele carriers) had significantly higher MetS frequencies compared to AA homozygous (*P* value = 0.014).

CAV-1 rs3807992

Two studies evaluated *CAV-1* rs3807992 and MetS. Both investigations showed that *CAV-1* rs3807992 polymorphism dominant model-risk allele carriers (including AA and AG genotypes) had a significantly higher rate of metabolic syndrome compared to the GG homozygous group (*P* value = 0.01)[18] and (OR = 2.31 (95% CI: 1.16-4.61)).[20] Recessive model risk allele carriers also showed a higher metabolic syndrome rate, but the association was not significant (*P* value = 0.05).[18]

CAV-1 rs1997623

CA genotype was related to an increased risk of MetS (OR = 1.88 (95% CI: 1.21–2.93) *P* value = 0.005). For the AA genotype, they couldn't find a possible association with metabolic syndrome (OR = 0.45 (95% CI: 0.085–2.59). However, CA+AA (dominant model) pooled frequencies compared to CC homozygous were significantly associated with a higher metabolic syndrome risk score (OR = 1.806 (95% CI: 1.170–2.789).[16] The result of the second study exerted that *CAV-1* rs1997623 minor allele(A) was associated with a higher siMS score (effect size in adjusted model = 0.18, *P* value = 0.035) and MetS prevalence (aOR = 1.811 (95% CI: 1.25–2.61)) only in the Arab population. However, the association for South Asians (aOR = 1.189 (95% CI: 0.880–1.600)) and South East Asians (aOR = 1.118 (95% CI: 0.673–1.850)) was insignificant.[16]

Meta-analysis of available data showed a significant association between CAV-1 rs1997623 polymorphism and an elevated risk of Mets (OR = 1.44 (95% CI: 1.2, 1.86)) [Figure 2].

One study assessed the possible pathophysiology behind the *CAV-1* rs1997623 polymorphism that could explain its association with metabolic syndrome. This study showed that *CAV-1* A-allele creates a transcription factor binding site in favor of early B-cell factor 1 (EBF1) attachment (*P* value < 0.01). The promoter activity was also enhanced in the presence of the A-allele and the connection of exogenous or endogenous EBF1 (*P* value = 0.001).[19]

2285 C>T and 22375–22375 del AC

The two polymorphisms and haplotype analysis of 2285 C>T and 22375–22375 del AC were done in one study. This study had three groups: a healthy control group, a non-MetS high blood pressure group, and a MetS group with high blood pressure. For the 2285 C>T (C and T allele) polymorphism, they found no significant association between the genotypic distribution of the healthy control group vs. metabolic syndrome group or the hypertensive group vs. metabolic syndrome group. However, for 22375–22375 del AC polymorphisms (i and d alleles) a significant

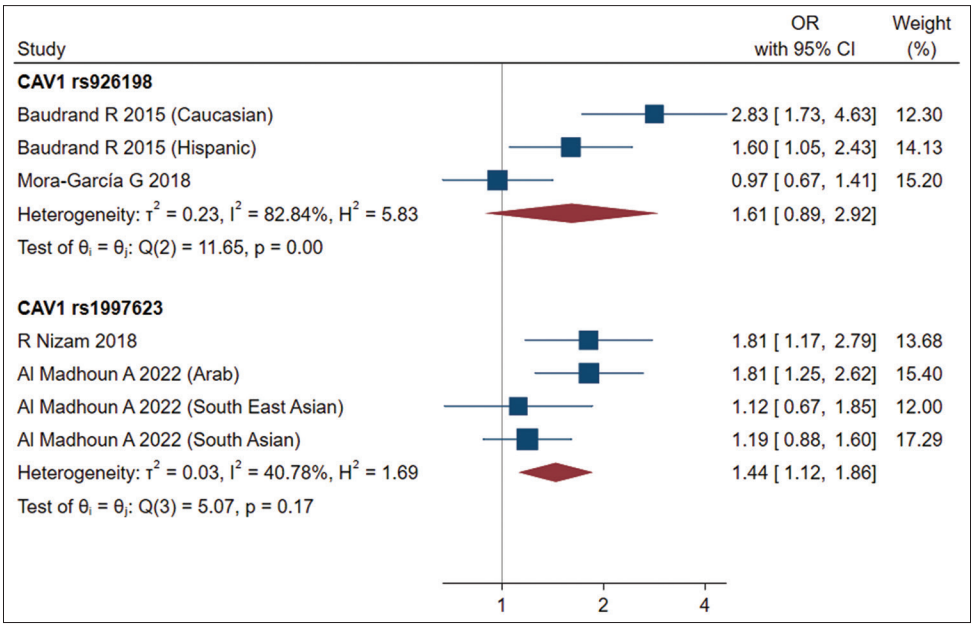

Figure 2: Forest plot depicting the association between polymorphisms and MetS

association was found between the genotypic distribution of the healthy control group and the MetS group (OR = 0.45, *P* value = 0.00075) and also, the MetS group and the non-MetS high blood pressure group (OR = 0.49, *P* value = 0.017), suggesting the preventive effect of allele d and identifying the i allele as a risk allele.[22]

CAV-1 gene expression level

One cross-sectional study compared the mRNA levels of *CAV-1* and metabolic syndrome. The outcome illustrated that *CAV-1* expression levels are higher in MetS patients (fold change (FC) =1.645 ± 1.2340 *P* value = significant). Patients with increased abdominal circumference had the highest mRNA level of *CAV-1* compared to healthy controls (FC = 3.643 ± 0.7724 *P* value = significant). Other factors that positively affected the expression level of *CAV-1* were dyslipidemia, obesity, increased systolic blood pressure, and patients with a mixture of these conditions.[7]

Al Madhoun A also showed similar results, individuals with higher siMS scores had higher *CAV-1* mRNA levels in subcutaneous adipose tissue (*P* value < 0.011). Following the mRNA level, the level of *CAV-1* proteins was also higher in these individuals (*P* value < 0.0001).[19]

Discussion

This systematic review aims to assess the relationship between different SNPs in the *CAV-1* gene and MetS in humans. MetS is a complex disorder that is influenced by a variety of genetic and environmental factors.[6] Studies have shown that there is a strong genetic component to the development of MetS, with certain genes being associated with an increased risk for the disorder.[23] These genes are involved in a variety of biological processes, including glucose and lipid metabolism, inflammation, and blood pressure regulation. Additionally, environmental factors such as diet and physical activity can also play a role in the development of MetS.[8] Understanding the genetic background of MetS is important for developing effective prevention and treatment strategies for this increasingly common disorder.

The *CAV-1* gene is found to be linked with the development of MetS, a cluster of conditions that increase the risk of heart disease, stroke, and type 2 diabetes. This gene is involved in the regulation of lipid metabolism and insulin signaling pathways, which are both critical for maintaining healthy blood sugar levels and preventing insulin resistance.[24] Studies have shown that variations in the *CAV-1* gene can affect the expression and function of proteins involved in these pathways, leading to dysregulation and an increased risk of metabolic syndrome.[20] While more research is needed to fully understand the role of this gene in MetS, the current findings suggest that targeting *CAV-1* may be a promising approach for preventing or modulating this condition.

As previously known, different locations of each SNP and its interaction with different regulatory parts affect the transcription of a certain locus.[25] Al Madhoun A did a relevant study that explains the possible cellular pathway that *CAV-1* rs1997623 functions.[19] This SNP is located in the proximal region of the locus, that is, the regulatory section. This location enables the A-allele to activate the transcription of this gene and altering the transcription binding site to facilitate the connection of EBF1 and enhancing the promoter activity.[19] EBF1 has proven to intervene in different inflammatory and metabolic pathways, including insulin sensitivity, lipogenesis, etc.[26,27]

Controversies related to *CAV-1* rs926198 results could be attributed to the selection of the samples; Baudrand R cohorts

Table 1: Characteristics of studies included in the systematic review

First author/year	Country/ race	Study design	Age (mean±SD)	Sex (male %)	Sample size	SNPs	MetS definition	MtS prevalence (%)	Genotyping data N (%) in cases vs. controls	Results
Baudrand R[11]/2015	Caucasian	Cross-sectional	45.1±10.4	55%	735	rs926198	Joint Interim Statement criteria	30%	NA	Minor allele carriers (CC+CT) are associated with MetS
	Hispanic	Cross-sectional	39.3±15.1	41%	810	rs926198	Joint Interim Statement criteria	24%	NA	Minor allele carriers (CC+CT) are associated with MetS
de Souza GM[7]/2020	Brazil	Cross-sectional/ case-control	NA	48.27%	87	CAV1 mRNA	AHA/ NHLBI statement criteria	NA	FC (fold change) =1.645±1.2340	Caveolin 1 mRNA level is higher in the MetS patient.
Abaj F[20]/2022	Iran	Cross-sectional	NA	0%	404	rs3807992	Adult Treatment Panel III criteria	NA	AA: 23 (34.8%) vs. 41 (24.7%) AG: 13 (19.7%) vs. 31 (18.4%) GG: 30 (45.5%) vs. 94 (55.2%)	Minor allele carriers increase the risk of developing MetS.
Mora-García G[21]/2018	Colombia	Cross-sectional	44.7±17.7	59.60%	605	rs926198	Joint Interim Statement criteria	39.70%	CC: 23 (37.7%) vs. 38 (62.3%) CT: 96 (38.9%) vs. 151 (61.1%) TT: 121 (40.7%) vs. 176 (59.3%)	Minor allele carrier (CC+CT/TT) don't have a significant relationship with MetS.
	Colombia	Cross-sectional	44.7±17.7	59.60%	695	rs11773845	Joint Interim Statement criteria	NA	AA: 95 (46.6%) vs. 109 (53.4%) AC: 103 (37.3%) vs. 173 (62.7%) CC: 42 (33.6%) vs. 83 (66.4%)	Minor allele carriers (CC+AC) are associated with increased risk of MS.
R Nizam[16]/2018	Kuwait	Cross-sectional	12.08±0.64	35.94%	1313	rs1997623	Metabolic syndrome score	18.70%	AA: 2 (1%) vs. 4 (2%) CA: 69 (28%) vs. 40 (17%) CC: 172 (71%) vs. 186 (81%)	CA+AA genotypes (mutant allele carriers) had higher rate of MetS.
Grilo A[22]/2006	Spain	Cross-sectional/ case-control	46.43±6.5	48.77%	285	22285 C>T	IDF criteria	NA	CC: 61/125 CT: 44/84 TT: 9/1	No significant association was found.
	Spain	Cross-sectional/ case-control	46.43±6.5	48.77%	285	22375–22375 del AC	IDF criteria	NA	ii: 91/135 id: 21/74 dd: 2/1	Existence of d allele has preventive effect on MetS.
Abaj F[18]/2021	Iran	Cross-sectional	36.67±9.1	0%	386	rs3807992	cMetS score	NA	NA	AA and AG genotypes (minor allele carriers) increase the risk of developing MetS.
Al Madhoun A[17]/2022	Kuwait/ Arab	Cohort	NA	54.72%	479	rs1997623	IDF criteria/ siMS score	35.90%	AA: 8/6 CA: 57/74 CC: 107/227	A allele (minor allele) was associated with MS and higher siMS score.

Contd...

Table 1: Contd...

First author/year	Country/ race	Study design	Age (mean±SD)	Sex (male %)	Sample size	SNPs	MetS definition	MtS prevalence (%)	Genotyping data N (%) in cases vs. controls	Results
	South East Asian	Cohort	NA	72.05%	362	rs1997623	IDF criteria/ siMS score	32.27%	AA: 1/3 CA: 31/35 CC: 113/179	No significant association was found.
	South Asian	Cohort	NA	34.52%	660	rs1997623	IDF criteria/ siMS score	40.05%	AA: 9/14 CA: 63/121 CC: 141/312	No significant association was found.
Al Madhoun A[19]/2022	Kuwait/ Arab	Cohort	NA	NA	38	rs1997623/ CAV1 mRNA and protein	IDF criteria/ siMS score	NA	NA	Caveolin 1 mRNA and CAV1 protein level is higher in patients with higher siMS score. CAV1 rs1997623 A-allele change transcription binding site in favor of EBF1 attachment and enhancement of the promoter activity.

both Hispanic and Caucasian ethnicities were hypertensive; however, in Mora-García G's study, hypertensive patients were infrequent. We could come to the conclusion that *CAV-1* rs926198 may affect MetS more in hypertensive individuals than in others[11,21] Moreover, Baudrand R[11] showed concordance between MetS diagnosis and *CAV-1* rs926198, C allele carriers in siblings. Concordant siblings had three times higher chances of carrying minor alleles, as the genetic background of siblings with different MetS outcomes was randomly distributed. This finding can show the domestic collection of the risk allele. This study also showed that the *CAV-1* rs926198 mutant allele (C allele) could be used as a perfect predictor of MetS occurrence in non-obese individuals compared to the obese ones, this polymorphism was associated with a 3-fold higher chance of MetS in non-obese individuals as the corresponding chance in obese individuals was only 1.7-fold higher.[11]

Abaj F showed that the visceral fat level had a mediation effect on MetS and *CAV-1* rs3807992 relations.[18] This finding proposes the possible way that caveolin induces MetS; as we know, visceral fat is associated with insulin resistance and other metabolic disorder,[28] and the *CAV-1* gene has a high expression in adipose tissue and considerable interaction with other genes, so changes in the activity of *CAV-1* can easily affect the lipogenic pathways.[24]

Dietary fat intake may have an enormous effect on the formation of the MetS. Previous studies showed that saturated fatty acid (SFA) intake could induce metabolic disorders like high HDL, and LDL-C, while polyunsaturated fatty acid (PUFA) has a protective effect on the metabolic profile.[29] Abaj *et al.*[20] demonstrated that PUFA could attenuate the *CAV-1* rs3807992 minor allele carriers (AA+AG group) negative effect on developing MetS, and SFA intake could further deteriorate *CAV1* rs3807992 A allele carriers (AA+AG group) effect on MetS inducement.

Strengths and limitations

To the best of our knowledge, this is the first comprehensive review study regarding the association of the *CAV-1* gene with metabolic syndrome. We did not put any limitation on publication time, age, or other characteristics of the searched studies to include all the relevant studies. However, this study has some limitations. First, the low number of studies on the matter, on the one hand, and the great heterogeneity of included studies due to investigations of different *CAV-1* polymorphisms and different populations, on the other hand, persuade us not to conduct a meta-analysis on all of the available polymorphisms. Second, several studies that assessed the effect of knocking out the *CAV-1* gene were conducted in animal models. Although some of their symptoms were similar to MetS, like insulin resistance and dyslipidemia, we could not add these articles to our review due to the lack of selection criteria for MetS in animal models, so future studies could concentrate on developing proper criteria for MetS in experimental studies.

Conclusions

Our study manifested that caveolin-1 minor allele carriers are associated with MetS. However, the relationship varies with the different polymorphisms in this gene. Caveolin genes play a crucial role in glucose and lipid metabolism; therefore, they could be used as a screening tool for MetS occurrence in individuals. In order to confirm our findings, further research is needed to specifically show the relationship between caveolin-1 polymorphisms and MetS in humans.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary File1

EMBASE

('caveolin'/exp OR caveolin OR 'caveolin 1'/exp OR 'caveolin 1' OR 'caveolin 2'/exp OR 'caveolin 2' OR 'caveolin 3'/exp OR 'caveolin 3' OR 'cav1 gene'/exp OR 'cav1 gene') AND ('metabolic syndrome x'/exp OR 'metabolic syndrome x' OR 'syndrome x'/exp OR 'syndrome x' OR 'insulin resistance'/exp OR 'insulin resistance' OR 'diabetes mellitus'/exp OR 'diabetes mellitus' OR 'lipoprotein'/exp OR lipoprotein OR 'cardiovascular disease'/exp OR 'cardiovascular disease' OR 'obesity'/exp OR obesity OR 'hypertension'/exp OR hypertension)

4449 records

WEB OF SCIENCE

(ALL=(caveolin) OR ALL=("caveolin Protein") OR ALL=("caveolin-3") OR ALL=("caveolin-2") OR ALL=("caveolin-1") OR ALL=(CAV1)) AND (ALL=("metabolic syndrome") OR ALL=(MetS) OR ALL=("syndrome X") OR ALL=("insulin resistance") OR ALL=(diabetes) OR ALL=(obesity) OR ALL=(hypertension) OR ALL=("cardiovascular disease") OR ALL=(lipoprotein)) + English language

2049 records

SCOPUS

(TITLE-ABS-KEY (caveolin) OR TITLE-ABS-KEY ("caveolin Protein") OR TITLE-ABS-KEY ("caveolin-3") OR TITLE-ABS-KEY ("caveolin-2") OR TITLE-ABS-KEY ("caveolin-1") OR TITLE-ABS-KEY (cav1)) AND (TITLE-ABS-KEY ("metabolic syndrome") OR TITLE-ABS-KEY (mets) OR TITLE-ABS-KEY ("syndrome X") OR TITLE-ABS-KEY ("insulin resistance") OR TITLE-ABS-KEY (diabetes) OR TITLE-ABS-KEY (obesity) OR TITLE-ABS-KEY (hypertension) OR TITLE-ABS-KEY ("cardiovascular disease") OR TITLE-ABS-KEY (lipoprotein)) AND (LIMIT-TO (LANGUAGE , "English")) AND (EXCLUDE (DOCTYPE , "cp") OR EXCLUDE (DOCTYPE , "ch") OR EXCLUDE (DOCTYPE , "le")) AND (EXCLUDE (DOCTYPE , "er"))

2226 records

PUBMED

((caveolin) OR ("caveolin Protein") OR ("caveolin-3") OR ("caveolin-2") OR ("caveolin-1") OR (CAV1)) AND (("metabolic syndrome") OR (MetS) OR ("syndrome X") OR ("insulin resistance") OR (diabetes) OR (obesity) OR (hypertension) OR ("cardiovascular disease") OR (lipoprotein))

("caveolins"[MeSH Terms] OR "caveolins"[All Fields] OR "caveolin"[All Fields] OR "caveolin-1"[MeSH Terms] OR "caveolin-1"[All Fields] OR "caveolin Protein"[All Fields] OR "caveolin-3"[All Fields] OR "caveolin-2"[All Fields] OR "caveolin-1"[All Fields] OR "CAV1"[All Fields]) AND ("metabolic syndrome"[All Fields] OR "MetS"[All Fields] OR "syndrome X"[All Fields] OR "insulin resistance"[All Fields] OR ("diabete"[All Fields] OR "diabetes mellitus"[MeSH Terms] OR ("diabetes"[All Fields] AND "mellitus"[All Fields]) OR "diabetes mellitus"[All Fields] OR "diabetes"[All Fields] OR "diabetes insipidus"[MeSH Terms] OR ("diabetes"[All Fields] AND "insipidus"[All Fields]) OR "diabetes insipidus"[All Fields] OR "diabetic"[All Fields] OR "diabetics"[All Fields] OR "diabets"[All Fields]) OR ("obeses"[All Fields] OR "obesity"[MeSH Terms] OR "obesity"[All Fields] OR "obese"[All Fields] OR "obesities"[All Fields] OR "obesity s"[All Fields]) OR ("hypertense"[All Fields] OR "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR "hypertension s"[All Fields] OR "hypertensions"[All Fields] OR "hypertensive"[All Fields] OR "hypertensive s"[All Fields] OR "hypertensives"[All Fields]) OR "cardiovascular disease"[All Fields] OR ("lipoprotein s"[All Fields] OR "lipoproteine"[All Fields] OR "lipoproteins"[MeSH Terms] OR "lipoproteins"[All Fields] OR "lipoprotein"[All Fields]))

1589 records

Supplementary File 2: Details of the quality assessment process

Study	Questions of NIH quality assessment tool for cohort and cross-sectional studies[1]														Summary quality
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	
Baudrand *et al* 2015	Yes	Yes	Yes	Yes	No	Yes	NA	NA	Yes	No	Yes	NR	NA	Yes	Good
de Souza *et al* 2020	Yes	Yes	Yes	Yes	Yes	No	NA	Yes	Yes	No	Yes	NR	NA	Yes	Good
Abaj *et al* 2021	Yes	Yes	Yes	Yes	Yes	No	NA	Yes	Yes	No	Yes	NR	NA	Yes	Good
Mora-García *et al* 2018	Yes	Yes	Yes	Yes	Yes	Yes	NA	No	Yes	No	Yes	NR	NA	Yes	Good
Nizam *et al* 2018	Yes	Yes	Yes	Yes	Yes	No	NA	Yes	Yes	No	Yes	NR	NA	Yes	Good
Al Madhoun *et al* 2022	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Good
Abaj and Mirzaei 2020	Yes	Yes	Yes	Yes	No	No	NA	No	Yes	No	Yes	NR	NA	Yes	Fair
Grilo A	Yes	Yes	Yes	Yes	No	No	NA	Yes	Yes	No	Yes	NR	NA	Yes	Fair
Al Madhoun *et al* 2022	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	No	Yes	Yes	Good

Available online at: https://www.nhlbi.nih.gov/health-topics/studyquality-assessment-tools. NA: Not applicable, NR: Not reported