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The serum Gamma Glutamyl Transferase(GGT) levels among Iranian Patients with Coronary Artery Disease: A Systematic Review and Meta-analysis

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Abstract

Objective
The aim of this systematic review and meta-analysis was to evaluate the serum levels of GGT among Iranian patients with Coronary Artery Disease (CAD).

Methods
Systematically, all articles published in PubMed, Embase and the Cochrane Library after October 2, 2016, without language restriction were searched. The following medical titles were used to search for related texts: (GGT or Liver enzymes or Glutamyl transferase or gamma GT or GT or non-alcoholic fatty liver disease) and (Group or OR observation/Longitudinal) and (cardiovascular mortality / cardiovascular disease / myocardial infarction / ischemic heart disease / CAD/heart disease / CAD or mortality / CVD or heart death / sudden death or cause of death/ cause of heart death or CV death or death). Statistical analysis was performed using version 12.0 STATA.

Results
Three studies were included in this meta-analysis.The overall mean serum GGT levels among Iranian patients with coronary artery disease was 41.8 ± 14.3 compared to 20.77 ± 11.9 in healthy patients($p<0.05$).

Conclusion
Overall, this meta-analysis was compatible with the relationship between GGT levels and the risk of cardiovascular disease in other studies. These results showed that GGT in the normal range might become an individual predictor in cardiovascular screening. However, potential mechanisms are still limited. Further research is essential to clarify the mechanisms and to examine the potential correction of the GGT cardiovascular mortality.

Keywords: Gamma Glutamyl Transferase, GGT, Coronary Artery Disease

Introduction

Coronary Artery Disease (CAD) is a complex multifactorial status that begins with a severe inflammatory response in various forms of impairment, which results in endothelial dysfunction in the arterial wall and ultimately leads to atherosclerosis [1].

Early CAD, defined as the existence of coronary artery atherosclerotic lesion in 45 years men and 55 years women, is growing in developing countries such as Iran. At least one of the four classic cardiovascular risk factors - smoking, diabetes, hypertension and dysylipidemmia- are in the majority (approximately 90 %) of patients with early CAD [3]. Some cardiovascular risk factors, such as family history, smoking, hypertension and diabetes [2, 4], in contrast to other factors, are strong predictions for early CAD [5]. Since coronary angiography remains the golden standard for the diagnosis of CAD [6], the identification of early CAD patients remains a challenge until they are affected by cardiovascular disease. Therefore, early prediction of this serious condition can help reduce mortality and cardiovascular complications. Finding tools for identifying people at risk and identifying new predictors, including biomarkers, can greatly help identify this disease in its early stages [2].

Increasing gamma glutamil transferase (GGT), an important liver enzyme, is the intermediary of amino acid to intracellular glutathione and also contributes to the destruction of extracellular glutathione [7]. Glutathione decomposition as the most important non-cellular protein antioxidant in various conditions, such as low-density lipoprotein oxidation, has the prooxidant role [8], which is evidence of the pathological impact of GGT enhancement on stimulating oxidative processes and regulating the antioxidant, immune system. Therefore, it can be assumed that GGT may be effective in the inflammatory process of atherosclerosis. Previous studies have proved serum GGT's relationship with cardiovascular disease, diabetes and metabolic syndrome [9]. In addition, it is proposed as a predictor for CAD and cardiovascular deaths [12, 13]. However, there is insufficient information about early GGT and CAD communication. The aim of this systematic review and meta-analysis was to evaluate the serum levels of GGT among Iranian patients with CAD.

Materials and Methods

To analyze and report the corresponding results in this meta-analysis, the instructions of chosen cases were selected for systematic Meta-analysis (Prisma) (Fig. 1). Systematically, all articles published in PubMed, Embase and the Cochrane Library after October 2, 2016, without language restriction were searched. The following medical titles were used to search for related texts: (GGT or Liver enzymes or Glutamyl transferase or gamma GT or GT or non-alcoholic fatty liver disease) and (Group or OR observation/Longitudinal) and (cardiovascular mortality / cardiovascular disease / myocardial infarction / ischemic heart disease /CAD/heart disease /CAD or mortality / CVD or heart death /sudden death or cause of death/ cause of heart death or CV death or death). In addition, the main authors were contacted to obtain further information and the reference list of other relevant studies which were not in the Databasewas examined.

Data Collection

One researcher extracted the data from qualified studies, and the other researcher confirmed the data to evaluate accuracy independently with a standard form as follows: First Author's Name, Year of Publication, Participant Country, Study or Participants', Base Review period, follow -up time (year), age (average or range), gender (female, male), mean or mean range of GGT levels per category.

Data Analysis

Statistical analysis was performed using version 12.0 STATA (Stata Corp LP, College Station, Texas). P <05 was considered a meaningful range for all results.

Results

Using search strategies, a total of 373potentially relevant records were identified. Of the articles, 63 were repetitive research, and after reviewing titles and abstracts, 278 articles were eliminated.

The remaining 32 papers were recovered for accurate evaluation. After applying the entry criteria, 29 other articles were deleted for various reasons. The reasons for this removal are shown in Figure 1. Finally, 3 studies were included in this meta-analysis.
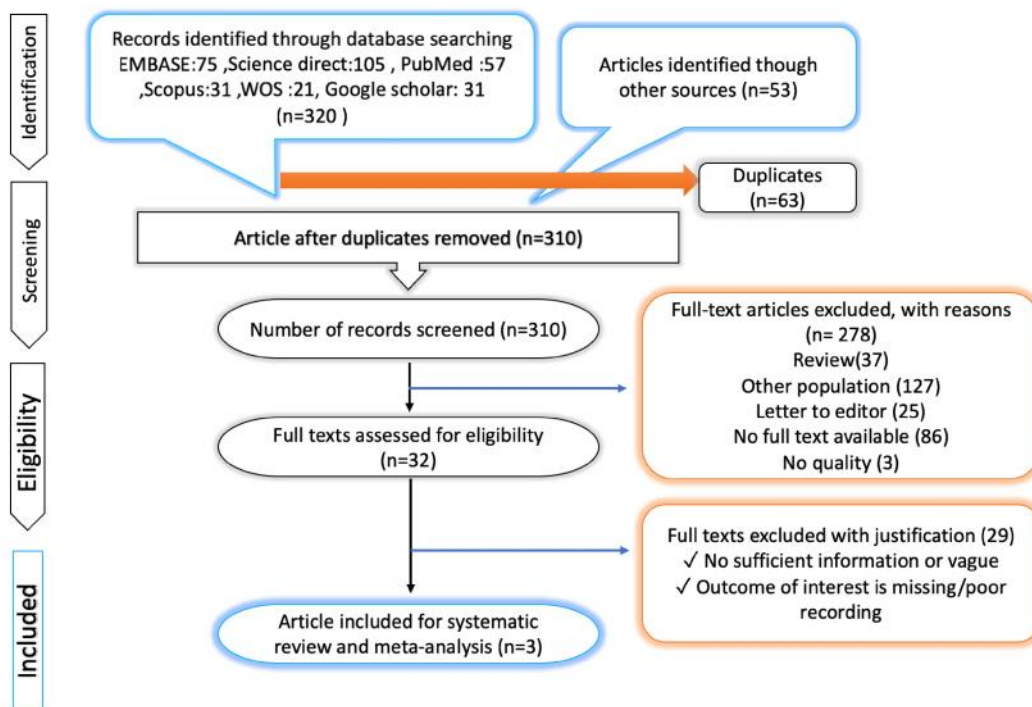

Figure 1. PRISMA flow diagram of study selection

Meta-analysis of the mean-serum GGT levels among Iranian patients with coronary artery disease

The overall mean serum GGT levels among Iranian patients with coronary artery disease was

41.8± 14.3 compared to 20.77± 11.9 in healthy patients (p<0.05).

Table1. Characteristics of the included studies regarding the GGT levels among Iranian patients with cardiovascular disease

Author	Year	Province	Design	Sample size	Mean age	Female/male	GTT(case)	
							Case	Control
Arasteh	2018	Mashhad	Retro	500	54.5 ± 6.6	211/289	55.6±9.7	17±4.6
Hamzeh	2021	Kermanshah	Pros	7362	47.20 ± 8.33	3942/3420	26.63 ± 20.30	23.86 ± 18.58
Sheikh	2017	Tehran	Retro	84	67.51±12.90	40/44	43.3 ± 12.1	21.46 ± 12.8
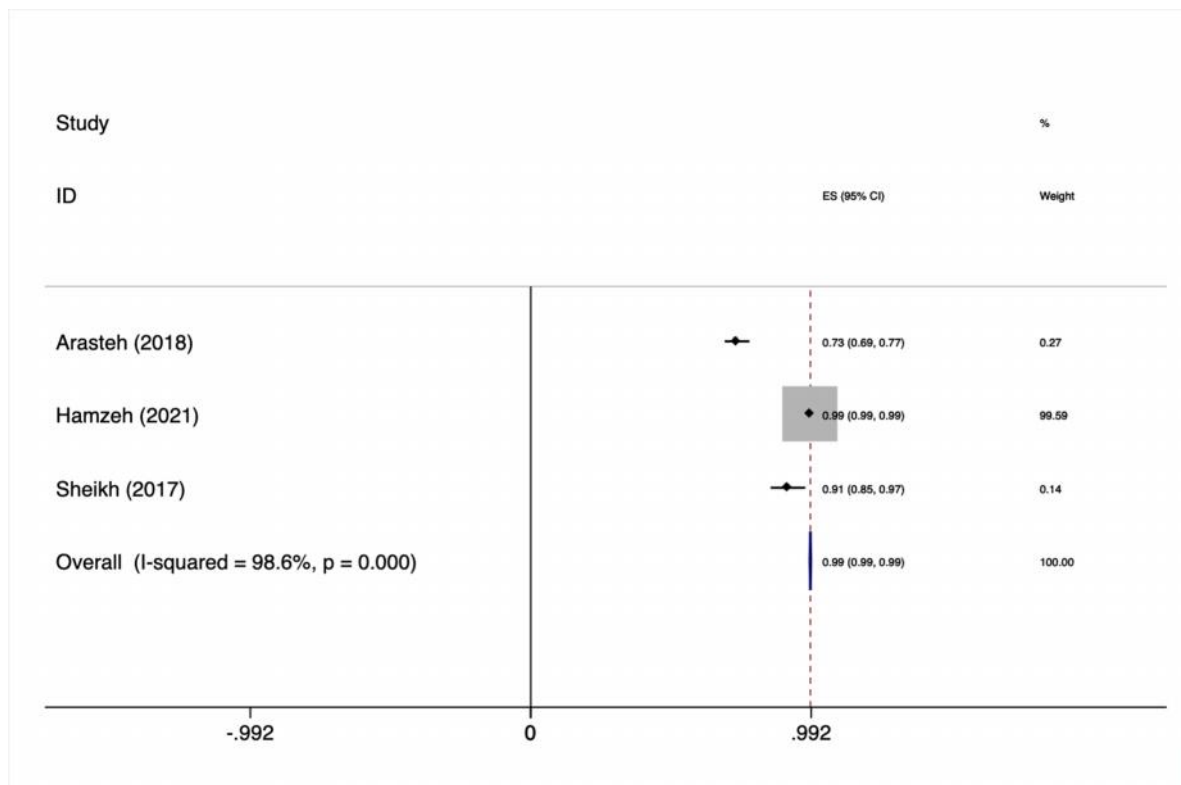
Discussion

The results of this study showed a strong relationship between serum GGT and CVD mortality; The population-based study also examined GGT's relationship with CVD or the risk of death. Lee and his colleagues were done one of the first epidemiological studies to investigate GGT's relationship with risk and cardiovascular disease. In the second cycle of the study, 3451 patients were selected between 1978 and 1982 and were followed up for 19 years. CAD was associated with body mass index, blood pressure, low-density lipoprotein (LDL) - cholesterol, triglycerides and glucose. In the follow-up phase, with every higher log GGT standard deviation, the risk of the outbreak of metabolic syndrome increased by 26 %. After adjusting the cardiovascular risk factors, every SD log GGT has created a 26% increase in CVD risk and 13% GGT. People in the highest GGT quarter showed a 67 % increase in CVD incidence. The study clearly showed that the increase in circulation GGT activity means the onset of metabolic syndrome isa CVD and mortality predictor, which refers to the role of GGT as a marker of metabolic and cardiovascular risk (1).

Amiroglu and his colleagues (15) conducted a comparative analysis of GGT and CRP with high sensitivity (hs -CRP) in a study with 219 patients with acute coronary syndrome (ACS) and 51 individuals as the control group. The results of their study showed that the serum levels of GGT and hs -CRP were higher in ACS patients, and there was a moderate but significant correlation between GGT and hs -CRP (15). In another prospective study that examined the clinical importance of serum GGT levels during the early period of myocardial infarction (16), the results indicated a significant positive correlation between serum GGT and hs -CRP and homocysteine levels. The left ventricle (LV) was independently associated with serum GGT activity on day five after acute myocardial infarction. Although the study was limited due to the small sample size, short -terms follow -up and uncontrolled study plan, the researchers stated that GGT has a potential role in predicting and dysfunction of LV during the initial period after myocardial infarction. The study of Emdin et al. (17) was also consistent with this conclusion.

They showed that GGT levels -similar to CRP and fasting glucose- were an independent risk factor in patients with CAD in research that 474 persons with angiography were evaluated. The lower levels of serum GGT were effective in identifying patients with the lowest risk of heart death (17).

Limitations

This Meta-analysis had several limitations. First, the major issues related to the possibility of confounding factors were not controlled. It is noteworthy that liver disease and alcohol consumption are associated with increased GGT, so the role of GGT predictor in individual studies may be partially distorted. Failure to adjust these factors may lead to excessive real risk. Second, the amount of increased GGT levels were different in various studies, and the optimal rate of GGT height was not determined.

Conclusion

Overall, the Meta-analysis of this study was compatible with the relationship between GGT levels and the risk of cardiovascular disease in other studies. These results showed that GGT in the normal range might become an individual predictor in cardiovascular screening. However, potential mechanisms are still limited. Further research is essential to clarify the mechanisms and to examine the potential correction of the GGT CV mortality.

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