Updating the Meta-Analysis of Perceived Stress and its Association with the Incidence of Coronary Heart Disease

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Abstract

Introduction: During the last few decades, substantial research have been carried out identifying factors that contribute to the etiology and progression of Coronary Heart Disease (CHD). This systematic review and meta-analysis has been conducted to update and summarize the results of the published articles that examine the effect of perceived stress and its association with the incidence of CHD.

Methods: In order to carry out this study, five electronic databases including PubMed, Scopus, Web of Science, Science Direct, and ProQuest were used to search for potentially relevant articles. Articles published from 1948 to November 2018 were investigated in this research. All cross-sectional, prospective observational cohort, and case – control studies were selected which had measured self-reported perceived stress and had assessed the incidence of CHD. From among all the potentially identified relevant articles, 10 articles met the criteria (n=165819). The incidence of CHD was defined as a new diagnosis of, Ischemic Heart Diseases (IHD) for, or Cardiovascular Disease (CVD) and mortality secondary to CHD.

Results: Meta-analysis yielded a risk ratio of 1.382% [CI 95% (1.056-1.808), and P=0.019] for CHD, and an aggregate IHD risk of 1.206% [CI 95% (1.112-1.308), and P<0.0001]. Pooled estimate were 1.455% [CI 95% (1.088-1.944), and P<0.011] for mortality, which showed that perceived stress had a significant increasing effect on mortality.

Conclusion: This systematic review and meta-analysis revealed that high levels of stress increases the risk of CHD, IHD and mortality. Lifestyle changes play an essential role in the clinical prevention of CVD.

Keywords: Coronary Heart Disease, Meta- Analysis, Perceived Stress, Stress

Citation: Vahedian-Azimi A, Moayed MS. Updating the meta-analysis of perceived stress and its association with the incidence of coronary heart disease. Int J Med Rev. 2019;6(4):146-153. Doi:10.30491/IJMR.2019.101968.

Introduction

Recent studies have profoundly converted the current view of CHD. Until a few years ago, atherosclerosis was considered as a "lipid storage disease" that was a major factor in the incidence of coronary heart disease. Nevertheless, CVD remains the first cause of death worldwide with an increasing prevalence in developing countries, despite the intensive effort against conventional risk factors.[1]

Annually, about 25 million deaths are expected to occur by 2020 from cardiac events in the worldwide,[2] which underlies the continuing need to identify new supplementary goals for prevention.[3] Chronic stress is believed to contribute to both the progression and sequence of CVD and cardiovascular death.[4] Most of the time, the added risks of smoking, high serum cholesterol levels, obesity, high blood pressure, or multiple severe stressful experiences in childhood are over noticed compared to the risks associated with CVD related to stress.[3,5,6]

In a large study which had investigated 52 countries in the world, it was proven that those who had experienced severe financial stress, were under stress at home or at work, had experienced stressful life events in the past year, or were depressed, were at higher risk of myocardial infarction.[7] In fact, the complex network links the heart, brain and the main biological systems.[8]

The diagnosis of Myocardial Infarction (MI) with normal coronary arteries has increased, constituting 5–25% of total myocardial infarction diagnoses.[9] Mac Coon (2012) showed that anxiety, depression and perceived stress are predictive factors of adverse outcomes such as CHD.[10] Richardson in a meta-analysis included six articles, the results showed that yielded a summation risk ratio of 1.27 for the amount of the correlation between high perceived stress and incidence of CHD, that meaning high perceived stress is correlated with a moderately increased risk of incidence of CHD.[11]

This systematic review and meta-analysis was conducted in order to update and summarize the results of published articles which had examined the effect of perceived stress and its association with the incidence of Coronary Heart Disease.

Methods

In the current systematic review and meta-analysis, studies which had reported a valid estimation of the association between perceived stress and the incidence of CHD diagnosis, hospitalization for CHD, MI, reMI or mortality secondary to CHD were found.

Eligibility Criteria

All studies must have been cross-sectional, prospective observational cohorts, and case- control with a self- report assessment of perceived stress. Only studies which had used measurements specifically referencing "stress" and not symptoms of psychological disorders such as post-traumatic stress disorder, anxiety, or depression were included in this review.

Information Sources

The electronic databases such as PubMed, Scopus, Web of science, Science Direct, ProQuest were searched for potentially relevant articles. Articles which had been published during 1948 to November, 2018 were included in this study. Searching the data were conducted by two researchers both in English and Persian languages, independently.

Search Strategy

All relevant subject headings and free text terms were used to represent stress and CHD and the sets of terms were combined with "and." Terms for PubMed to represent stress included ("coronary heart disease" [Title] OR "ischemic heart disease" [Title] OR "myocardial ischemia" [Title] OR "myocardial infarction" [Title] OR "Acute coronary syndrome" [Title] OR "acute coronary disease"[Title] OR "chronic heart disease" [Title] OR "chronic arterial disease" [Title] OR "cardiovascular events" [Title] OR "cardiovascular mortality" [Title] OR "angina" [Title] OR "CVD"[Title] OR "CHD" [Title] OR "CAD" [Title] OR "Coronary artery disease"[Title]) AND "Perceived Stress"[Title]. The following words were used to search in Scopus: (TITLE "coronary heart disease" OR "ischemic heart disease" OR "myocardial ischemia" OR "myocardial infarction" OR "Acute coronary syndrome" OR "acute coronary disease" OR "chronic heart disease" OR "chronic arterial disease" OR" cardiovascular events" OR "cardiovascular mortality" OR "angina" OR "CVD" OR "CHD" OR "CAD" OR "Coronary artery disease") AND TITLE ("Perceived Stress"). In the Web of science TITLE: ("coronary heart disease" OR "ischemic heart disease" OR "myocardial ischemia" OR "myocardial infarction" OR "Acute coronary syndrome" OR "acute coronary disease" OR "chronic heart disease" OR "chronic arterial disease" OR "cardiovascular events" OR "cardiovascular mortality" OR "angina" OR "CVD" OR "CHD" OR "CAD" OR "Coronary artery disease") AND TITLE: ("Perceived Stress"). Also their key words were searched in SCIENCE DIRECT:TITLE ("coronary heart disease" OR "ischemic heart disease" OR "myocardial ischemia" OR "myocardial infarction" OR "Acute coronary syndrome" OR "acute coronary disease" OR "chronic heart disease" OR "chronic arterial disease" OR "cardiovascular events" OR "cardi") and TITLE ("Perceived Stress"). TITLE ("heart disease" OR "myocardial ischemia" OR "myocardial infarction" OR "Acute coronary "OR "chronic disease" OR "cardiovascular" OR "angina" OR "CVD" OR "CHD" OR "CAD" OR "Coronary artery disease") and TITLE ("Perceived Stress"). The ProQuest ti ("coronary heart disease" OR "ischemic heart disease" OR "myocardial ischemia" OR "myocardial infarction" OR "Acute coronary syndrome" OR "acute coronary disease" OR "chronic heart disease" OR "chronic arterial disease" OR "cardiovascular events" OR "cardiovascular mortality" OR "angina" OR "cud" OR "chad" OR "CAD" OR "Coronary artery disease") AND ti ("Perceived Stress").

Endnotes software (Thomson Reuters, X7.5, Bld 9325) was used to organize the studies. Additional records were identified by scanning the references lists of relevant studies and reviews and by employing the related article features in PubMed and the cited reference search in the ISI Web of Science.

Data Collection Process

The initial search yielded 61 articles, which was declined based on the PRISMA guideline. To determine the studies to be assessed further, 2 authors independently read the abstract and/or titles of every record retrieved for the selection criteria listed above (Table 1.). Ten articles with available texts were included in the synthesis. Sixteen risk factors were assessed in ten articles as four risk factors were observed in one article and two risk factors were observed in two articles. All potentially relevant articles were inquired as full text. Those studies describing the association of perceived stress to the incidence of CHD, IHD, CVD diagnosis, and mortality secondary to CHD, MI or Re-MI were studied. It is noteworthy to mention that the search was carried out from the 1st of July 1948 to the 20th of November 2018. This is while, based on the inclusion criteria the articles which had been published by 2015 were included in this research.

Synthesis of Results

Meta-analysis was performed using "Metan", publication bias by "Metabias", and "Metafunnel" commands in STATA 11 software. This command Calculate the pooled estimate after Log effect size (Ln) of the estimations. In the study, the meaning of effect size was equal to the Risk Ratio (RR), Hazard Ratio (HR), and Odd Ration (OR). According to the existence of heterogeneity between studies, data was pooled using a fixed or random effects model. The heterogeneity of studies were assessed by Cochran Q statistic. The statistical heterogeneity were tested with the Q test (Chi² and the I² and Tau-squared statistics). The findings were supposed heterogeneous in case the P-value was less than 0.1. Moreover, I² was utilized to provide a model of the degree of inconsistency between the results of the studies. A value of 0% indicates no observed heterogeneity, whereas larger values show increasing heterogeneity.
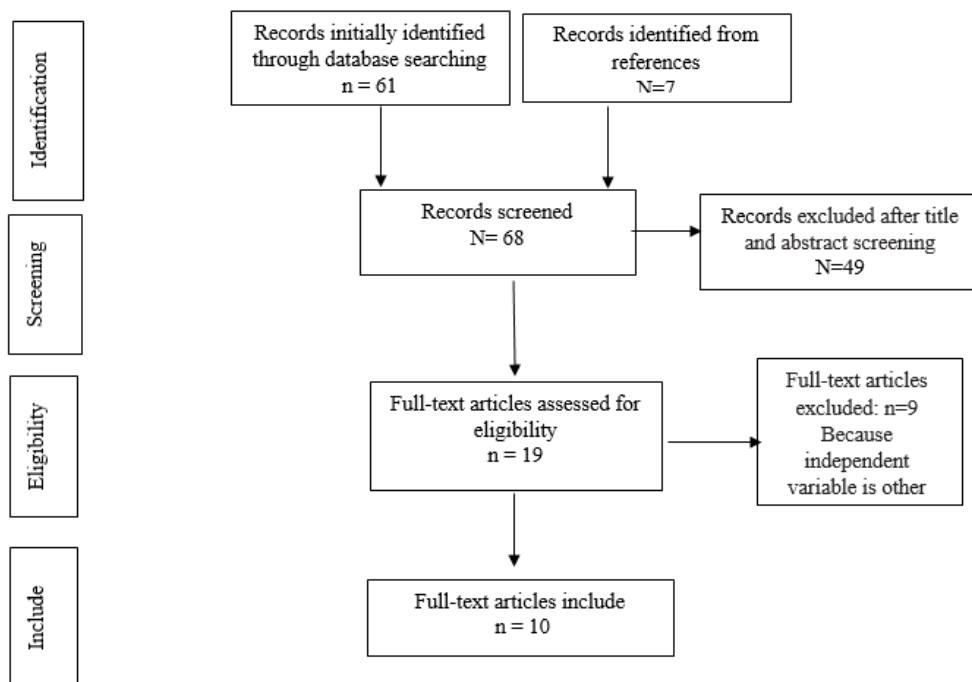
Figure 1. Screening and selecting the articles for meta-analysis based on PRISMA guidelines.

Table 1. Characteristics of included studied

Study and year	Risk Approximation	Follow-Up (years)	Outcome	Gender	Sample
Esben Strodl, 2003 [12]	OR 1.67 (1.17-2.37)	3	CHD	Female	6994
Naja Rod Nielsen, 2006 [13]	HR 1.23 (1.01-1.51)	17-19	IHD	Female	6543
Naja Rod Nielsen, 2006 [13]	HR 1.25 (1-1.56)	17-19	IHD	Male	5296
Suzanne V. Arnold, 2012 [14]	OR 1.42 (1.15-1.76)	2	Mortality	Both	4202
Amir vahedian-azimi, 2012 [15]	OR 1.2 (1.01-1.42)	0	Re MI	Both	3200
Nicole Redmond, 2013 [16]	HR 1.44 (1.05-1.98)	4.2-6.9	CHD (Low income)	Both	9966
Nicole Redmond, 2013 [16]	HR 0.72 (0.48-1.08)	4.2-6.9	CHD (High income)	Both	11442
Alexia Katsarou, 2014 [17]	OR 1.15 (1.11-1.18)	0	ACS	Both	500
You Yang, 2015 [18]	OR 1.81 (1.23-2.66)	0	CHD	Both	359
Iso, 2002 [19]	RR 1.08 (0.59-1.97)	7.9	Death CHD	Male	30180
Iso, 2002 [19]	RR 2.28 (1.17-4.43)	7.9	Death CHD	Female	43244
Nielsen, 2006 [13]	HR 1.23 (1.01-1.51)	18	IHD	Female	11839
Nielsen, 2006 [13]	HR 1.25 (1-1.56)	18	IHD	Male	11839
Rosengren, 1991 [20]	OR 1.5 (1.2-1.9)	11.83	CHD	Male	6935
Ohlin, 2004 [21]	RR 1.17 (1.02-1.33)	21.25	IHD	Male	10621
Ohlin, 2004 [21]	RR 1.04 (0.66-1.63)	21.25	IHD	Female	2659

Results

In the initial search, sixty-one articles selected. By searching in the article references, seven articles identified. After the title and abstract screening, 49 articles removed. Full-text articles assessed for eligibility; in this step 9 articles excluded. In the final step, ten articles remained (Figure 1). The average of follow up was 88.2 months. Studies were conducted in Iran, U.S., Australia, Denmark, Greece, and Sweden. The total sample size contained 165819 men and women which were included in the meta-analysis.

The perceived stress was assessed with the Perceived Stress Scale. Six studies among the included studies used the Perceived Stress Scale, which has been designed to measure the degree to which subjects appraise situations in their lives as stressful. The Perceived Stress Scale takes about 5 minutes to complete, uses paper-and-pencil self-report, and evaluates the degree to which subjects find life unpredictable, incontrollable, or overloaded. The validity and reliability were evaluated in a large national probability sample (n=2038) in the US. Another study used the Reeder Stress Inventory, which consists of 4 statements about feelings of tension, strain, exhaustion, and stress in association with daily activities. Respondents rate the extent to which each of these 4 statements is true using a 4-point Likert format. The

other studies were exemplified as the sensation of tension, nervousness, impatience, anxiety, or sleeplessness, and no time frame was specified for the stress reporting. The stress score was then categorized into low (0–1 points), medium (2–4points), and high (5–6 points) stress.

For publication bias, Begg,s test [z= 1.62 , P-value=0.105] showed that there was no publication bias in results but the eager test demonstrated a low evidence of significance [t= 2.38 , P-value=0.032] (Figure 2)

CVD Outcomes

Eleven studies (five studies reported two risk ratio for subgroups) scrutinized CVD outcomes risk ratio the following perceived stress. According to the test of heterogeneity [Chi2= 30.28, dF=15, P=0.011] and heterogeneity indexes [I2=50.5% and Tau-squared=0.0085]. A random-model was used to calculate the pooled effect size. The pooled approximately risk ratio of CVD outcomes in these studies was 1.285% [CI 95% (1.167-1.357), and P<0.0001]. The results showed that perceived stress had a significant increasing effect on the CVD risk (Figure 3).
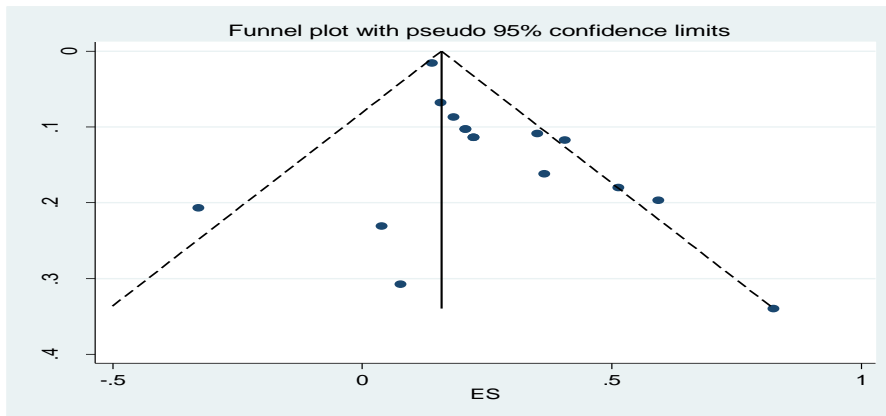

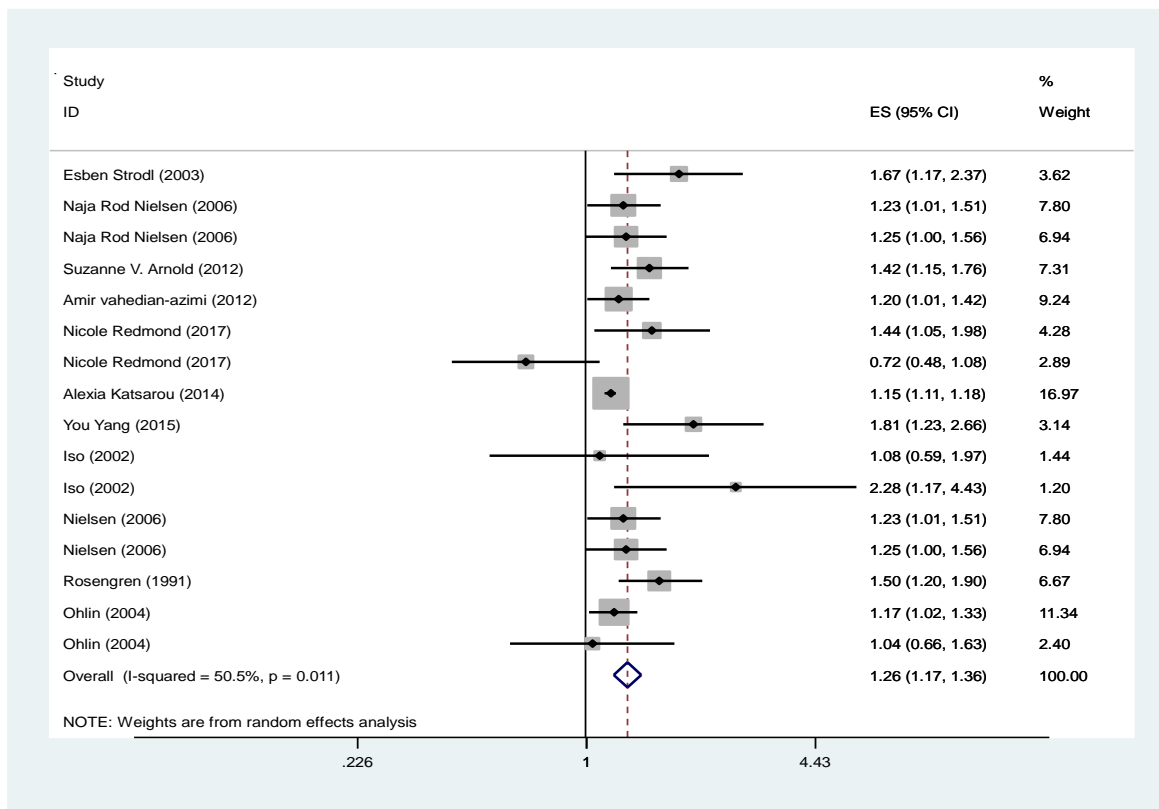**Figure 2.** Funnel plot to assess publication bias across incidence studies.

Figure 3. We estimated the associated with high perceived stress and coronary heart disease incidence. Each study's proportional weight (area of each square) in the meta-analysis and the confidence interval (lines) around the estimate and the aggregate (diamond) estimate and the confidence interval (lateral points) for this estimate are depicted

Different Effect Sizes

Following the analysis, the studies reported different ratio including RR, HR, and OR. According to the different ratio, the results of subgroups have been reported .The OR have been reported in the six studies. Pooled HR was 1.360% [CI 95% (1.179-1.570), and P<0.0001]. The results showed that perceived stress had a significant increasing effect on the CVD risk (Figure 3). The HR have been reported in three studies. Pooled HR was 1.209% [CI 95% (1.068-1.368), and P=0.003]. The results showed that perceived stress had a significant increasing effect on the CVD risk (Figure 3). In two studies, each reported their estimations of RR. The pooled RR was 1.211% [CI 95% (0.969-1.513), and P=0.093]. The results showed that perceived stress had a significant increasing effect on the CVD risk (Figure 4).

Disease

The studies reported risk ratio according to the different outcomes including disease. The incidence of CHD was reported in four studies (one study reported two estimations). The pooled estimation was 1.382% [CI 95% (1.056-1.808), and P=0.019]. The results showed that perceived stress had a significant increasing effect on the CHD risk (Figure 5).

The incidence of IHD was reported in three studies (all studies reported two estimations). The pooled estimation was 1.206% [CI 95% (1.112-1.308), and P<0.0001]. The results showed that perceived stress had a significant increasing effect on the IHD risk (Figure 5).

The incidence of mortality was reported two studies (one study reported two estimations). The pooled estimation was 1.455% [CI 95% (1.088-1.944), and P<0.011]. The results showed that perceived stress had a significant increasing effect on the risk of mortality (Figure 5).

Gender

The studies reported the risk ratio according to gender .The incidence of CVD in female was reported in five studies. The pooled estimation was 1.318% [CI 95% (1.110-1.564), and P=0.002]. The results showed that perceived stress had a significant increasing effect on CVD (Figure 6). The incidence of CVD in male was reported in five studies. The pooled estimation was 1.243% [CI 95% (1.134-1.362), and P<0.0001]. The results showed that perceived stress had a significant increasing effect on the risk of CVD (Figure 6).

Discussion

This systematic review and meta-analysis was conducted in order to detect the relation between perceived stress and CHD, CVD, and IHD. The 165819 participants were included in this analysis. These results indicate that high perceived stress may be a causal factor for CHD. Based on the meta- analysis results, the perceived stress had a significant increasing effect on CVD outcome. Pooled RR was 1.211% [CI 95% (0.969-1.513). The mortality risk was 1.455 (1.088-1. 944), and the IHD risk was 1.206 (1.112-1. 308), respectively.
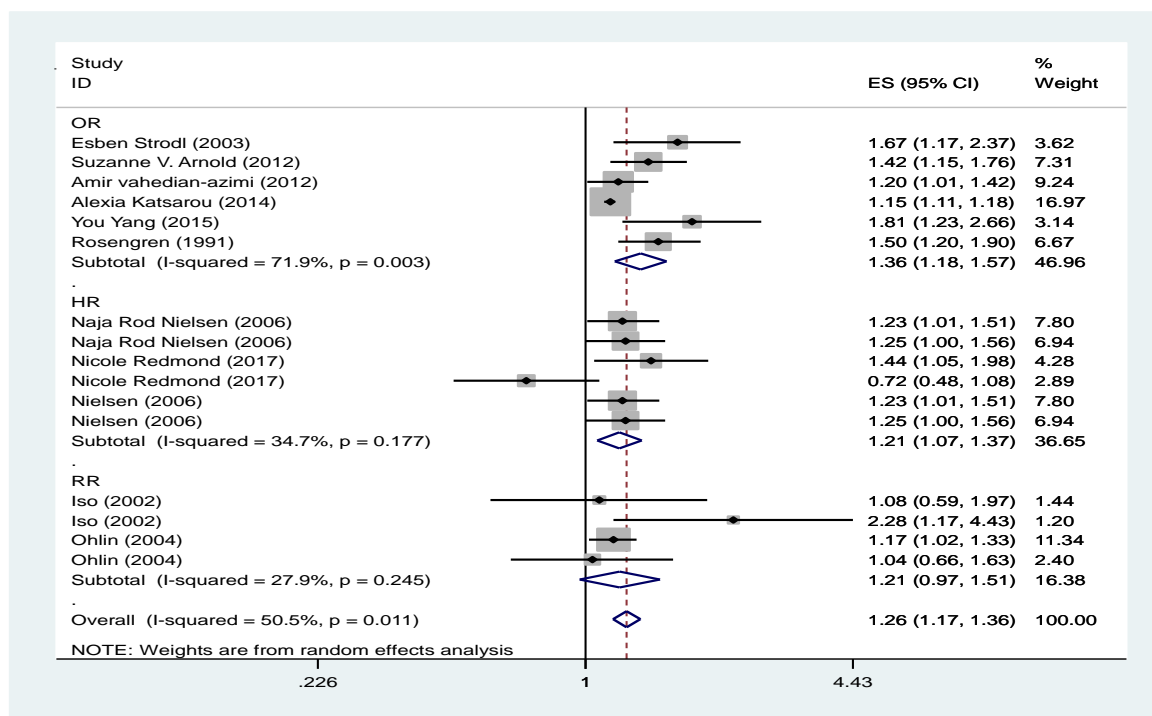
Figure 4. Compared to the three parameters, the OR value is higher than the other two parameters. This indicates that observational studies may slightly overestimate the risk of cardiovascular risk compared to follow-up studies.
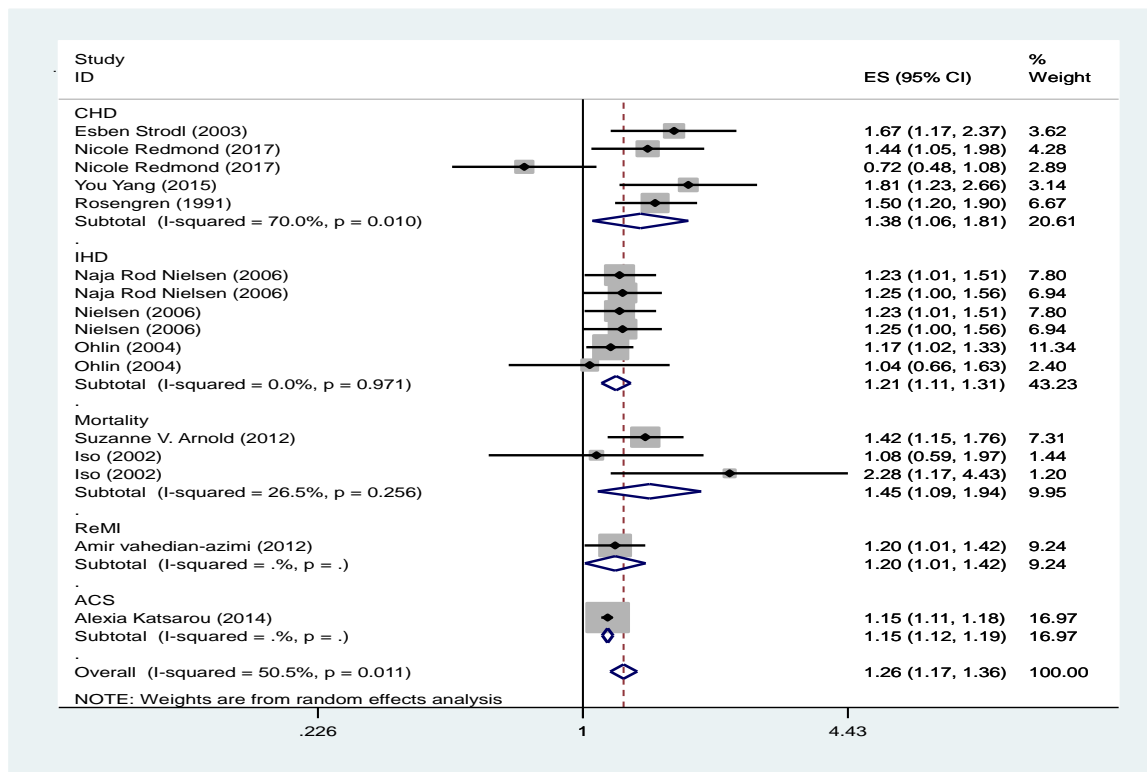

Figure 5. Perceived stress has the greatest effect on mortality, CHD, and IHD based on approximate RR.
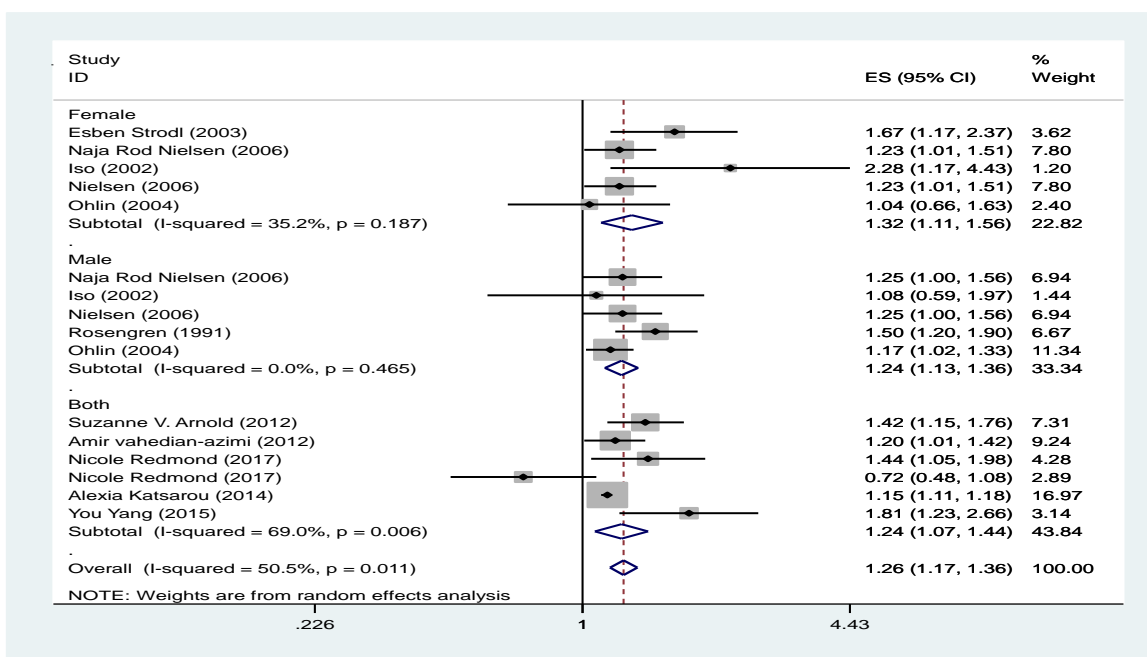

Figure 6. High perceived stress has the greatest effect on gender based on approximate RR

The perceived stress is robustly associated with multiple types of CVD. Previous meta-analyzes estimated 1.27 (1.12 to 1. 45) the risk ratio of CVD in a population of 118,696.[11] Psychological factors play an important role in overtaken CHD.[22] In another study, sub diagnoses of ischemic heart disease were analyzed separately. High stress was associated with a higher incidence of angina pectoris for women (1. 83; 1.15–2. 91) and for men (2. 14; 1.32–3.47).

There was no association with myocardial infarction for both women (0. 80; 0. 56–1. 15) and men.[23] A 10-year study of patients with myocardial infarction showed that they had higher perceived stress levels in a year which end up with MI. One study also reported higher stress levels as a cause of

higher mortality in the first two years and a lower outcome in the first year after MI.[24,25] Although the estimated results of the data analysis reported a significant CVD incidence in both sexes following perceived stress; but the incidence of CVD in women following perceived stress was 1.318% and it was estimated to be 1.243% in men. This indicates a higher incidence of CVD in women due to perceived stress comparison to men. Psychological differences between men and women are one of the features that are controversial in the development of heart disease; because women use different ways of coping or confronting with stress. Women usually use ineffective self-control coping styles while men use ineffective direct confronting styles. This may be one of the causes of a higher incidence of CVD in women.[26] In addition, women tend to express and receive higher levels of stress compared to men as they accept multiple roles in their lives.[27-29] Also, gender differences are factors that affect the treatment and care of heart patients.[24]

Comparing the magnitude of the increased risk associated with high perceived stress to those of traditional cardiovascular risk factors is useful. However, risk factors independently have increased the incidence and progression of CHD, which is known as classical or conventional risk factors such as age, sex, race, smoking, hypertension, hyperlipidemia, insulin resistance, diabetes, physical activity, and obesity.[30] Yang (2015) compared high perceived stress with other risk factors for cardiac events. He stated that factors such as smoking was OR=3.12, hyperlipidemia was OR=1.42, C-reactive protein (hs-CRP) was OR=3.57 which were associated with a markedly higher incidence of CHD. Also, the estimated PSS score was OR= 1.81 in youth.[18] The incidence of MI was 5.7% in the highest quintile of ox-LDL compared with 2.6% in the lowest quintile. The risk ratio for those in the highest quintile was 2.25 (95% CI 1.22 4.15). The incidence rate for patients with the metabolic syndrome was 5.6% vs. 2.9% for those without the metabolic syndrome.[31]

The death due to IHD was 1.96 folds in ever hookah smokers with higher daily intensity of hookah smoking compared to those who had never smoked throughout their lives.[32] The inability of people to control and reduce perceived stress or not to use effective methods can widely and significantly increase the risk of heart disease. The results of this study and other studies indicate the role of perceived stress on the occurrence of painful events such as angina and infarction that directly cause disease and heart complications. In addition, perceived stress can lead to unhealthy behaviors that cause the disease or provide the conditions for the inflammatory process.[1] Given the increasing prevalence of cardiovascular complications, confirmation of the results of studies on predictors of CVD can be used in primary and secondary prevention planning by health authorities.

The findings regarding the relationship between positive psychological attributes and cardiac health are promising and suggest that positive psychology interventions may be worth studying.[33] It seems to be a good time to recognize emotional disorders and to help people cope with stressful events by supporting them to understand the influence of psychobiological risk factors, and to make plans in order to manage daily stress.[34]

Conclusion

This systematic review and meta-analysis demonstrated that high perceived stress is related to a moderately increased risk of CHD, IHD and mortality. Lifestyle changes play an essential role in the clinical prevention of CVD. Various, effective and useful stress intervention plans have been approved in heart patients, programs that provide formal psychotherapy, psychotropic medications, progressive relaxation training, meditation, time management training, or regular exercise. Progressively, such plans are tracking markers of cardiovascular risk such as different to cardiac events and find that the psychosocial intervention plans have positive effects.

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