

Effect of Habitual Coffee Consumption on Cardiovascular Health: Protocol for a Review of Systematic Reviews of the Literature

Efecto del consumo habitual de café en la salud cardiovascular: protocolo de una revisión de revisiones sistemáticas de la literatura

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ABSTRACT

Introduction: Coffee is one of the most consumed beverages worldwide and its effect on health has not been clearly established. There is a special controversy about its effects on the cardiovascular system. The objective of this work is to synthesize the evidence on the effects of habitual coffee consumption on cardiovascular health. **Methods:** Review of systematic reviews of the literature published in English, Spanish, French and Portuguese in biomedical databases (Medline, Embase, Cochrane, and Lilacs). The search will be supplemented with manual searching of references of the included reviews. The information will be selected and extracted separately by two researchers, and disagreements will be resolved by consensus. The included reviews will be grouped by year of publication, outcomes, design of original studies and quality. The study will apply the Assessing Methodological Quality for Systematic Reviews checklists to assess the methodological quality of the systematic reviews. The information will be synthesized in systematized formats. **Discussion:** The review of reviews will synthesize the evidence of the effect of coffee on cardiovascular health and estimate the dose-response relationship.

Keywords

coffee; cardiovascular diseases; heart diseases; coronary disease; mortality.

RESUMEN

Introducción: El café es una de las bebidas más consumidas en el mundo, aunque no están claramente establecidos sus efectos en la salud. En particular, aún hay controversia sobre sus efectos cardiovasculares. El objetivo de este trabajo es sintetizar evidencia acerca de los efectos del consumo habitual de café en la salud cardiovascular. **Métodos:** Se llevó a cabo una revisión de revisiones sistemáticas de la literatura, de artículos obtenidos de las bases Medline, Embase, Cochrane y LILACS, publicados en inglés, español, francés o portugués. La búsqueda fue complementada manualmente con las referencias de las revisiones incluidas. Una pareja de

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investigadores seleccionó y extrajo información de manera independiente, y las discrepancias se resolvieron por consenso. Las revisiones incluidas se clasificaron según el año de publicación, desenlaces, diseño de los estudios primarios y calidad. Se utilizó el instrumento *Assessing Methodological Quality for Systematic Reviews* para calificar la calidad, y la información se sintetizó en formatos sistematizados. **Discusión:** La revisión sintetizó la evidencia del efecto del café sobre la salud cardiovascular y estimó la relación dosis-respuesta.

Palabras clave

café; enfermedades cardiovasculares; cardiopatías; enfermedad coronaria; mortalidad.

Introduction

Coffee is one of the most consumed beverages around the world (1,2), and its consumption is increasing. Reports show that between 2016 and 2017, nearly 159 million sacks of coffee were consumed globally, an increase of 2.2% over the previous year. In the last year (2016/2017), there was an increase in coffee consumption in coffee-producing (like Brazil, Colombia, Indonesia, Mexico) and in coffee-importing countries (Canada, European Union, Japan, United States, etc.), of 2.3% and 2.1%, respectively (3,4). In 2015, Holland and Finland were the top two coffee-consuming countries in the world (260.4 and 184.9 liters per capita per year). Seven of the top 10 coffee-consuming countries belong to the European Union. The top consumers in the Americas are Canada, the Dominican Republic and the United States (152.1, 119.5 and 115.2 liters per capita per year, respectively) (2,3). It is estimated that in 2015 in Colombia, people drank an average of 3.4 cups of coffee per day, a noteworthy level of consumption as compared to the average consumption in North America (3.1 cups/day). The cities with the highest level of coffee consumption in Colombia were Barranquilla, Bucaramanga, Bogotá, Manizales and Pereira (5).

Historically, coffee has been consumed to increase alertness and concentration, as well as to maintain wakefulness (6,7). On the other hand, its consumption has had a negative connotation, since it is associated with cigarette consumption, which negatively affects health (8).

Some medical studies carried out in the sixties and seventies associated acute caffeine exposure with elevated blood pressure and the occurrence of arrhythmias (9). It should be noted that such studies were criticized for using very high caffeine doses and for not controlling for the effect of other coexisting factors such as smoking, alcohol consumption and hypercholesterolemia. In addition, it is now known that although acute caffeine consumption has a positive chronotropic and inotropic effect, this effect is attenuated with chronic consumption. On the other hand, it has been demonstrated that caffeine produces relaxation of the vascular smooth muscle, through endothelium-dependent and -independent mechanisms, particularly in tissues with intact membranes, which could partly explain its beneficial effects on the cardiovascular system (10).

Recent research has shown the role of other substances present in coffee, such as phenols, within which chlorogenic and caffeic acids have been shown to have an important antioxidant effect both *in vitro* and *in vivo* (11). In contrast, some studies have linked coffee consumption with increases in plasma homocysteine concentrations, which, in turn, has been correlated with an increased incidence of coronary heart disease and cerebrovascular and peripheral disease. However, this has not been adequately confirmed in subjects without a history of cardiovascular disease (12). Emerging studies on the effects of coffee on health in general have shown that it favorably affects metabolism (prevents type 2 diabetes mellitus) (13) and cognitive performance (prevents dementia and Parkinson's disease) (14), and improves concentration and attention and, above all, has a protective effect on the cardiovascular system (15,16,17,18).

Despite these findings, the medical community is currently unclear as to what recommendation should be issued regarding coffee consumption. There is no certainty as to whether its consumption should be restricted in people with certain diseases, and in case its consumption should be recommended, the appropriate amount is uncertain. The purpose

of this study is to summarize the evidence on the effects of coffee on cardiovascular risk and mortality, on the risk of cerebrovascular events and on the onset of arterial hypertension, considering the dose-response relationship.

Methods

The purpose of this review is to search, analyze, compare and synthesize evidence from the available systematic reviews of the literature on the effect of habitual coffee consumption on cardiovascular health, and establish the dose-response relationship. The specific objective is to analyze and summarize the available evidence on the effect of habitual coffee consumption and its dose-response relationship on general mortality, cardiovascular mortality and mortality due to coronary heart disease, as well as on the onset of cardiovascular disease, cerebrovascular disease and hypertension in the same population.

The review protocol was designed in accordance with the Cochrane Collaboration guidelines and with an adaptation of the checklist for protocols of systematic reviews of the literature and meta-analysis (Prisma-P) (19,20). The protocol was approved by the Ethics and Research Committee of the Pontificia Universidad Javeriana and Hospital Universitario San Ignacio (approval 2018/06).

The inclusion criteria considered systematic reviews of the literature that summarized information regarding the effect of habitual coffee consumption on cardiovascular health and mortality, compared to non-consumption or consumption of lower doses. These studies must have been conducted in populations of men and women over 18 years of age, with or without a diagnosis of cardiovascular disease. Manuscripts in English, Spanish, French and Portuguese were considered, according to the availability of translations in these four languages for the research team. We did not consider review articles that considered pregnant or breast-feeding women, people with mental health disorders or dependence on psychoactive substances, cancer, regular users of caffeine-

containing drugs or drinks (other than coffee), like tea, energy drinks, soft drinks, chocolate, etc. We also excluded studies conducted on animals.

The primary outcomes are the relative reduction in overall mortality, cardiovascular mortality, cardiovascular risk, onset of cerebrovascular disease and arterial hypertension.

The literature search was carried out in the Medline (via PubMed), Embase, Cochrane Collaboration and LILACS databases, from their creation until December 2017. To this end, search structures were designed that included MeSH or Emtree terms, text words and other terms corresponding to the selected topics (Table 1). In addition, a secondary search was made in the references contained in the selected articles; the search was done manually and by snowball sampling.

Table 1
Search strategy for the effects of habitual coffee consumption on cardiovascular health (PubMed)

Subtopic	Terms related to coffee consumption	Terms related to cardiovascular outcomes	Terms related to type of publication
Cardiac arrhythmias		<ul style="list-style-type: none"> • Cardiac arrhythmias [MESH] • Cardiac rhythm [Title/Abstract] 	
Heart failure		<ul style="list-style-type: none"> • Heart* [Title/Abstract] • Heart diseases [MESH] • Heart failure [MESH] • Ventricular dysfunction [Title/Abstract] • Cardiomyopath* [Title/Abstract] 	
Coronary heart disease and cardiovascular risk	<ul style="list-style-type: none"> • Coffee [Title/Abstract] • Café [Title/Abstract] 	<ul style="list-style-type: none"> • Cardio* [Title/Abstract] • Cardia* [Title/Abstract] • Ischem* [Title/Abstract] • Angina [Title/Abstract] • Coronary [Title/Abstract] • Infarct* [Title/Abstract] • CVD [Title/Abstract] • Cardiac sudden death [MESH] • Endothelial dysfunction [Title/Abstract] • Myocard* [Title/Abstract] • Myocardial Ischemia [MESH] • Atherosclero* [Title/Abstract] • Coronary [Title/Abstract] • CHD [Title/Abstract] • Chest pain [Title/Abstract] 	<ul style="list-style-type: none"> • Systematic Review [All fields] • Methanalysis [All fields]
Cerebrovascular disease		<ul style="list-style-type: none"> • Stroke* [Title/Abstract] • Cerebrovasc* [Title/Abstract] 	
Arterial hypertension		<ul style="list-style-type: none"> • Hypertension [MESH] • Blood Pressure [MESH] 	
Mortality		<ul style="list-style-type: none"> • Mortality [MESH] • Cardiovascular mortality [Title/Abstract] • All-cause mortality [Title/Abstract] 	

A pair of researchers selected the manuscripts independently. First, they screened titles and abstracts, and then they applied eligibility criteria

to the full text of the article. The reviewers resolved the discrepancies by consensus.

Two other researchers extracted the data and classified it according to their outcome, and recorded the information in a standardized Excel file, version 2016. They also recorded general information on the title, author and year of publication, population, intervention, comparison group and outcome. They took into account the number and type of primary studies included, the search strategy used and its quality, results and potential biases (Table 2).

Table 2

Format to extract the information

Short reference	Surname of the author and initials of his/her name. Year of publication and magazine
PICO	Population, intervention, comparison and outcome
Searches	Databases, date and number of references. Date of the last search
Gray literature	Sources of unpublished literature consulted
Quality of the review	Quality scale used and quality level reported
Type and number of studies included	Primary studies of the review
Results and heterogeneity	Outcomes of interest in risk estimators (OR, RR, HR) and their confidence intervals. Heterogeneity estimator (I^2 or heterogeneity p)
Potential biases	Publication, selection, participation bias, etc.
Conflicts of interest	Report of conflicts of interest and funding sources

The duplication of primary studies in the different systematic reviews was taken into account. Two researchers evaluated the quality of the selected systematic reviews and meta-analyses with the *Assessing Methodological Quality for Systematic Reviews* (AMSTAR) tool (21). The information was extracted from systematic reviews and meta-analyses that had obtained an AMSTAR score greater than 60% (greater than 7). Disagreements between the reviewers were resolved by consensus, and when no agreement was reached, a third evaluator was used.

To evaluate the degree of agreement among the reviewers, the kappa coefficient was used. The results of the systematic reviews were summarized in tabular form for each of the outcomes of interest. The quality of the secondary studies is also presented in tables, and the heterogeneity of the results reported by the I^2 estimator was taken into account. A sensitivity analysis of the results was done by subgroups according to the quality of the studies included, and per dose of exposure to coffee consumption. Publication biases of the included secondary studies were evaluated. Figures were

designed to facilitate the understanding of the relevant results.

Discussion

Coffee is a drink that is consumed all over the world. In Colombia it is consumed frequently, since it is a custom rooted in our culture. Furthermore, given that Colombia is a coffee-producing country, knowledge about its effect on health could have consequences both for the health system and for the country's economy (5).

Despite the considerable evidence on the subject, it is unclear the actual effect of habitual coffee consumption on cardiovascular health in the adult population and, therefore, there are large discrepancies in the recommendations given by professionals in the field of clinical care, which includes cardiovascular health care (22,23). This is why it is important to review systematic reviews on this topic, to summarize and critically analyze the evidence on the effect of habitual coffee consumption on cardiovascular health. The objective is to identify all the important reviews on the subject, analyze and summarize them, to provide a clearer information to health professionals.

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Conflicts of interest

None of the authors declare conflicts of interest.

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