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Systematic review

Prognostic factors for the evolutionary changes of hypertensive heart disease from mild diastolic dysfunction to depressed systolic function. A systematic review with meta-analysis

Cardiopathy hypertensive heart disease: from mild diastolic dysfunction to depressed systolic function. Systematic review with meta-analysis

Prognostic factors for the evolutionary alterations of hypertensive heart disease, from mild diastolic dysfunction to depressed systolic function. Systematic review with meta-analysis

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Summary

Introduction:Hypertensive heart disease stands out among target organ damage caused by high blood pressure, due to its high morbidity and disability.

Aim: to evaluate the prognostic capacity of the different factors associated with the evolutionary changes of hypertensive heart disease up to depressed systolic function.

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MethodsA systematic review with meta-analysis of analytical case-control, cohort, and meta-analysis studies was conducted. An electronic literature search was performed for various studies related to the topic from April 10 to May 24, 2024.

ResultsThe meta-analysis demonstrated that the factors most strongly associated with the progression of hypertensive heart disease were: the presence of microalbuminuria (HR: 3.978; 95% CI: 2.131–7.428), C-reactive protein (HR: 2.141; 95% CI: 1.247–3.675), and the effects of hypertension itself (HR: 2.105; 95% CI: 1.647–2.692). Models used to assess cardiovascular risk did not demonstrate adequate calibration and discrimination for predicting the progression of hypertensive heart disease.

ConclusionsA significant association was demonstrated between different prognostic factors and the evolutionary changes of hypertensive heart disease. The need for a new prognostic tool based on these factors is evident in order to improve the accuracy and precision of this risk assessment.

KeywordsHypertensive heart disease; Prognostic factors; Systematic review; Meta-analysis.

ABSTRACT

Introduction:hypertensive heart disease stands out among the target organ lesions caused by arterial hypertension, due to its high morbidity and disability.

Objective:to evaluate the prognostic capacity of the different factors associated with the evolutionary changes of hypertensive heart disease up to depressed systolic function.

Method:a systematic review with meta-analysis of case-control, cohort and meta-analysis studies was carried out. For which an electronic literature search was performed for the various studies related to the subject from April 10 to May 24, 2024.

Results:it was demonstrated in the meta-analysis that the factors with the greatest association with the evolutionary changes of hypertensive heart disease were: the presence of microalbuminuria (HR: 3.978; 95% CI: 2.131-7.428), C-reactive protein (HR: 2.141; 95% CI: 1.247-3.675) and the effects of arterial hypertension (HR: 2.105; 95% IQ: 1,647-2,692). The models for assessing cardiovascular risk did not show useful

calibration and discrimination for predicting changes in the evolution of hypertensive heart disease.

Conclusions:a significant association was demonstrated between the different prognostic factors and the evolutionary changes of hypertensive heart disease. The need for a new prognostic tool based on these factors is evident in order to improve the accuracy and precision of risk assessment.

Keywords: Hypertensive heart disease; Prognostic factors; Systematic review; Meta-analysis.

SUMMARY

Introduction: Hypertensive heart disease stands out among other organ lesions due to arterial hypertension, due to its high morbidity and disability.

Aim: To evaluate the prognostic capacity of two different factors associated with the evolutionary alterations of hypertensive heart disease for depressed systolic function.

Methods:A systematic review was carried out with meta-analysis of analytical studies of cases and controls, cohort and meta-analysis. For this reason, an electronic search was carried out in the literature for two different studies related to the topic in the period from April 10 to May 24, 2024.

ResultsThe meta-analysis showed that the factors most associated with the evolutionary changes of hypertensive heart disease were: the presence of microalbuminuria (HR: 3.978; 95% CI: 2.131-7.428), C-reactive protein (HR: 2.141; 95% CI: 1.247-3.675), and the effects of high blood pressure itself (HR: 2.105; 95% CI: 1.647-2.692). The cardiovascular risk assessment models do not show the calibration and discrimination used to predict the evolutionary changes of hypertensive heart disease.

Conclusions:A significant association between the different prognostic factors and the evolutionary alterations of hypertensive cardiopathy was demonstrated. It is evident that a new prognostic tool is needed based on the above factors mentioned, in order to improve the accuracy and precision of the above mentioned risk.

Key words: Hypertensive heart disease; Prognostic factors; Systematic review; Meta-analysis.

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Introduction

Hypertension (HTN) is the most prevalent chronic disease affecting humankind. It is considered a progressive cardiovascular syndrome caused by multiple complex and interrelated etiologies, in which some early markers of the disease, such as nocturnal blood pressure dips, mild left ventricular hypertrophy (LVH), microalbuminuria, increased atrial filling pressure, and increased stiffness of small and large arteries, appear before the sustained increase in blood pressure. (1,2)

Hypertensive heart disease stands out among the target organ damage caused by hypertension. It is defined as a complex and variable set of effects that hypertension causes in the heart and is characterized by the presence of anatomical or biochemical signs of left ventricular hypertrophy or diastolic or systolic ventricular dysfunction, myocardial ischemia, and cardiac rhythm disturbances. (2,3)

Despite advances in the diagnosis and treatment of hypertensive heart disease, it has high rates of prevalence, mortality, and disability; (4) for example, the age-standardized global prevalence in 2017 was 217.9 per 100,000 people. Among all causes of heart failure, it had the second highest age-standardized prevalence rate (26.2%) that year. (5)

In this sense, a diagnostic and therapeutic approach based on the detection and prevention of lesions affecting the different histological compartments of the myocardium is necessary.

It is a fact that its progression is variable and cardiomyocyte size is the sine qua non of LVH, but in the epidemiological or clinical setting, it is not feasible to document this alteration. LVH is an intermediate phenotype in the progression to hypertensive heart disease. So much so, that the progression from hypertension to concentric LV

hypertrophy is an essential step in the development of heart failure, ultimately leading to systolic depression. (2,6,7)

However, not only hemodynamic factors are responsible for the progression of hypertensive heart disease, but also non-hemodynamic factors. But their value in estimating the progression of hypertensive heart disease from mild diastolic dysfunction to depressed systolic function is unknown. (2,8)

Furthermore, although numerous prognostic markers exist, the progression of hypertensive heart disease remains a challenge. Therefore, identifying these factors will allow for the prediction of further organ deterioration and will also be useful for creating prognostic tools with practical applications.

Soluble aspect if the present research answers the following clinical question:What factors are associated with the evolutionary changes of hypertensive heart disease from mild diastolic dysfunction to depressed systolic function, and at the same time could be useful for the construction of a prognostic scale with applicability in the care of these patients?

To answer this question, a systematic review with meta-analysis was conducted with the objective of evaluating the prognostic capacity of the different factors associated with the evolutionary changes of hypertensive heart disease up to depressed systolic function.

Methods

A systematic review with meta-analysis of case-control, cohort, and meta-analysis studies was conducted. An electronic literature search was performed for various studies related to the topic from April 10 to May 24, 2024, using the search engines PubMed, Google Scholar, MEDLINE, Embase, LILACS, WHO, and SciELO. The reference lists of the included studies were also reviewed.

No limits were set based on language, country, or publication date. Reference lists of previous systematic reviews or relevant original research articles were searched to identify studies not found in the initial database search.

The selected studies were those that reported updated theoretical aspects that should be included in this systematic review, including epidemiological, historical, procedural, evaluative, and conceptual aspects.

Non-original studies, studies with a descriptive design, those that were not directly related to the title of the systematic review, and those that did not list an author or Digital Object Identifier System (DOI) were excluded.

Results Management The search results were imported into the Zotero reference manager, version 5.0.94. Duplicate articles were identified using Zotero and manually by independent reviewers. All duplicate articles were removed.

Selection of studies The authors independently screened the titles and abstracts identified by the planned search strategies. Research eligible based on the title or abstract was retrieved in full. Studies potentially eligible based on at least one author were assessed in full-text versions. Articles meeting the inclusion criteria were independently assessed by the researchers, and discrepancies were resolved through discussion of the inclusion or exclusion criteria.

To increase the reliability and safety of the process, the degree of agreement between reviewers was measured by calculating the kappa statistic for each item on the selection sheet. This statistic, simply put, measures the degree of agreement between reviewers that exceeds what would be expected by chance. In cases where there were discrepancies between the two reviewers regarding the decision to include or exclude an article, a third researcher (a subject matter expert) was appointed to arbitrate the disagreement and ultimately make the decision.

The Cochrane Collaboration standardized extraction form was used, in this way the following data were extracted independently: study name (along with the name of the first author and the year of publication), country where the study was carried out, study design, number of participants, exposure, outcome and notification of bias.

When the data were insufficient or incomplete, this information was obtained from the text, from tables, or the utilization of the data included in the study was calculated.

Bias analysis. Risk of bias was assessed for selected studies through full-text reading, independently, in duplicate, and with blinding. Observational studies were assessed

using the Newcastle-Ottawa tool, and randomized controlled trials were assessed using the Cochrane RoB 2 tool. Methodological limitations described by the authors or identified by the authors' own analysis, as well as inconsistencies in the primary studies, were also taken into account.

Information analysis The meta-analysis was performed using Epidat software version 3.1. The dichotomous outcome was performed by calculating the relative risk (RR), the odds ratio (OR) or the hazard ratio (HR), as appropriate.

To estimate heterogeneity, the following were used: the Q statistic, the "between studies" variance, the "within studies" variance, the coefficient of variation between studies (variance between studies divided by the overall or weighted effect measure), and the RI coefficient, which represents the proportion of total variance due to the variance between studies and therefore takes values between 0 and 1.

Ethical considerations

In the present investigation it was not necessary to take it into account, since it is a review of articles, so contact with the patients was not required.

Strategy for searching for the most relevant articles:

The initial search was conducted in the most relevant databases (PubMed, Google Scholar, MEDLINE, Embase, LILACS, WHO, and SciELO). After excluding duplicate references, 520 were accepted. Of these, 363 were deemed ineligible for the next step (94 studies not conducted in humans and 247 were non-analytical studies). Thus, 199 studies were selected. After full-text review, 171 studies were excluded (due to methodological design issues, lack of clarity in objectives, and cross-sectional analytical studies). Additionally, of the remaining 28 studies, 4 were excluded for not clearly describing the event of interest. Finally, the sample consisted of 24 studies, as they met the objectives of this study.

Results

Result of the qualitative analysis of the prognostic factors of the evolutionary changes of hypertensive heart disease.

Effects of hypertension (lack of control, duration of evolution and stage)

- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 2.09; CI: 1.68-2.58; p: 0.000.
- ✓ Author, year of publication, country: Gu et al. (10) USA. 2010. Design: cohort. Population: 877. HR: 2.67 (CI: 1.71-4.19) p: 0.000.
- ✓ Author, year of publication, country: Kaczmarski et al. (11) USA. 2019. Design: Cohort. Population: 1522. HR: 1.43; CI: 1.05-1.94; p: 0.025.
- ✓ Author, year of publication, country: Hao et al. (12) China. 2019. Design: cohort. Population: 22,158. OD: 3.14; CI: 1.18-8.37; p: 0.025.
- ✓ Author, year of publication, country: Levy et al. (13) USA. 1996. Design: cohort. Population: 5209. Men HR: 2.07 (CI: 1.34-3.20) Women HR: 3.35 (CI: 1.67-6.73).
- ✓ Author, year of publication, country: Thomopoulos et al. (14) Italy. 2015. Design: meta-analysis. Population: 35 studies (146,810 patients). RR (0.97 (CI: 0.84–1.13) p< 0.001. Blood pressure control reduced the occurrence of heart failure.

Diabetes mellitus

- ✓ Author, year of publication, country: Dauriz et al. 2017. (15) Italy. Design: prospective cohort. Follow-up: 1 year. Population: 4,643. HR: 1.37; CI: 1.17-1.60; p: 0.001.
- ✓ Author, year of publication, country. Tovillas-Morán et al. (16) 2009. Spain. Design: cohort. Population: 265. HR: 1.67; CI: (1.03-2.69); p: 0.036.
- ✓ Author, year of publication, country: Levy et al. (13) 1996. USA. Design: cohort. Population: 5209. Men HR: 1.82 (CI: 1.28-2.58) Women HR: 3.73 (CI: 2.71-5.15).
- ✓ Author, year of publication, country: Aune et al. (17) 2018. USA. Design: prospective cohort. Follow-up: 1 year. Population: 401,495. RR: 2.06; CI: 1.73–2.46; p: 0.003.

Chronic kidney disease

- ✓ Author, year of publication, country: Nielsen et al. 2019. (18) Australia. Design: analytical cross-sectional. Follow-up: 6 months. Population: 144. OR: 1.55. 95% CI. 0.97 to 2.47. p = 0.067.
- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. RR: 3.503; CI: 2.931-4.187; p: 0.000.
- ✓ Author, year of publication, country: Hao et al. (12) China. 2019. Design: cohort. Population: 22,158. RR: 4.24 (CI: 2.75-6.54) p< 0.001.
- ✓ Author, year of publication, country: Collins et al. (19) USA. 2003. Design: cohort. Population: 1100,000. RR: 2.23 (CI: 2.13–2.34).

Microalbuminuria

- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 1.623 (CI: 1.321-1.996); p: 0.000.
- ✓ Author, year of publication, country: Liu et al. (20) China. 2018. Design: prospective cohort. Population: 213. HR: 2.95 (CI: 1.46-5.96) p: 0.003.
- ✓ Author, year of publication, country: Okin et al. (21) USA. 2008. Design: cohort. Population: 7876. HR 2.8 (CI: 1.8-4.4) p< 0.001.
- ✓ Author, year of publication, country: Bailey et al. (22) USA. 2019. Design: cohort. Population: 779. HR: 6.20 (CI: 4.15-9.26) p: 0.005.

C-reactive protein

- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 1.330 (CI: 1.084-1.632); p: 0.006.
- ✓ Author, year of publication, country: Maio et al. (23) Italy. 2021. Design: cohort. Population: 812. HR: 7.699 (CI: 4.407-13.451) p: 0.000.
- ✓ Author, year of publication, country: Chivite et al. (24) Spain. 2018. Design: cohort. Population: OR: 2.55 (CI: 1.71-3.80) p: < 0.001.
- ✓ Author, year of publication, country: Lakhani et al. (25) China. 2021. Design: meta-analysis. Population: 19 publications (51,196 patients). HR: 1.08 (CI: 1.00-1.16; p: 0.04.

Pulse pressure

- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 1.321 (1.074-1.625); p: 0.008.
- ✓ Author, year of publication, country: Jackson et al. (26) European Union. 2015. Design: cohort. Population: 2040.HR: 1.50 (CI: 1.20-1.88) p: 0.001.
- ✓ Author, year of publication, country: Mancusi et al. (27) Italy. 2018. Design: cross-sectional. Population: 7336. HR: 1.689 (CI: 1.147-2.487) p: 0.008.
- ✓ Author, year of publication, country: Qiu et al. (28) China. 2022. Design: cohort. Population: 1581. HR: 2.00 (CI: 1.15-3.48) p: 0.014.
- ✓ Author, year of publication, country: Haider et al. (29) USA. 2003. Design: cohort. Population: 2040. HR: 2.56 (1.75-3.74) p: 0.001.

Smoking

- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 1.268 (1.199 1.342); p: 0.006.
- ✓ Author, year of publication, country: Hao et al. (12) China. 2019. Design: cohort. Population: 22,158. OD: 0.50 (CI: 0.22-1.13) p: 0.091
- ✓ Author, year of publication, country: Hippisley-Cox et al. (30) United Kingdom. 2017. Design: prospective cohort. Population: 189,000,000. Men: HR: 2.20 (CI: 2.14-2.27) p: 0.000; women HR: 2.34 (CI: 2.25-2.43) p: 0.000.

Total cholesterol greater than 4.8 mmol/L

- ✓ Author, year of publication, country: Hao et al. (12) China. 2019. Design: cohort. Population: 22,158. OD: 0.84 (CI: 0.42-1.68) p: 0.595.
- ✓ Author, year of publication, country: Álvarez-Aliaga et al. (9) Cuba. 2020. Design: prospective cohort. Population: 1637. HR: 1.067 (CI: 1.039-1.096) p: 0.000.
- ✓ Author, year of publication, country: Hippisley-Cox et al. (31) United Kingdom. 2008. Design: prospective cohort. Population: 1,280,000. HR: 1.530 (CI: 1.487-1.574) p: 0.000.

- ✓ Author, year of publication, country: Hippisley-Cox et al. (30) United Kingdom. 2017. Design: prospective cohort. Population: 1,890,000. Men: HR: 1.19 (CI: 1.18-1.19) p: 0.000; women HR: 1.17 (CI: 1.16-1.17) p: 0.000.

The results presented show a direct relationship with the risk of cardiovascular events, heart failure and hypertensive heart disease; however, there are differences in the effect, and in some cases such as cholesterol the results go in both directions, that is, increasing the adverse prognosis and other results towards protection.

In fact, one can appreciate the place occupied by the effects of high blood pressure, comorbidity (diabetes mellitus and chronic kidney disease), as well as the presence of microalbuminuria as the most important factors.

Result of the qualitative analysis of the prognostic models of the selected studies.

The models presented in the table are for evaluating the prognosis and risk of cardiovascular events in general, except for the model by Álvarez-Aliaga et al. (9), which was the only one found in the literature for predicting the evolution of hypertensive heart disease. These models have discrete areas under the receiver operating characteristic (ROC) curve and C-statistics, aspects that suggest they are not sufficiently useful for estimating the evolution of hypertensive heart disease from mild diastolic dysfunction to depressed systolic function.

Table. Forecast models of the selected studies.

Scale/Index	Author/Year	COR Curve/ C Statistic	Calibration
QRISK (30)	Hippisley-Cox/ 2008	Women 0.787 Men: 0.767	*Women 1.54 *Men: 1.39
Framingham		Women: 0.774 Men: 0.759	*Women: 1.44 *Men: 1.31
QRISK3 (28)	Hippisley-Cox/ 2017	Women 0.880 Men: 0.858	*Women 2.49 *Men: 2.26
Framinghamrisk score (32)	Saif Al-Shamsi/ 2020	0.83	p: 0.191**
Hypertensive model Cardiopathy (9)	Álvarez-Aliaga/ 2020	0.897	p: 0.716**

Durbin Watson statistic (autocorrelation)* Hosmer-Lemeshow $\chi 2$ statistic**

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Quantitative analysis

In the present investigation, the outcome considered in hypertensive patients with diastolic dysfunction was the development of hypertensive heart disease with depressed systolic function.

In the first group, the effects of hypertension (no control, duration, and stage) and progression to stage IV hypertensive heart disease were evaluated. An association was found between the effects of hypertension per se and a poor prognosis. HR: 2.105; 95% CI: 1.647–2.692. The coefficient of variation between studies was less than 0.5 (0.355), as was the RI coefficient: 0.5966 and the I^2: 36.48%; these findings support the low heterogeneity between studies (Figure 1).

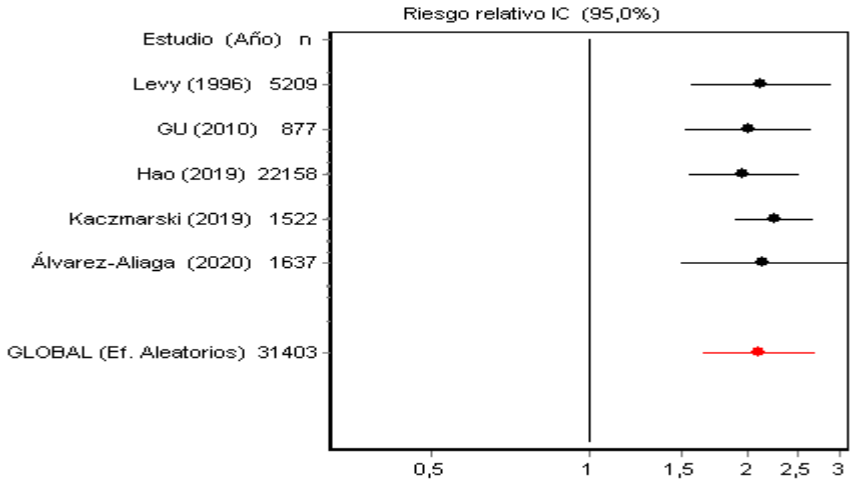

Figure 1. Meta-analysis on the association between the intrinsic effects of arterial hypertension and the progression to hypertensive heart disease with depressed systolic function.

The influence of diabetes mellitus (Figure 2) on the progression to stage IV hypertensive heart disease was demonstrated by the results of various researchers. ARR: 1.992; 95% CI: 1.428-2.779. The coefficient of variation between studies was 0.5846, the RI coefficient: 0.897 and the I2: 88.18%, these results show high heterogeneity between the results of the different studies.

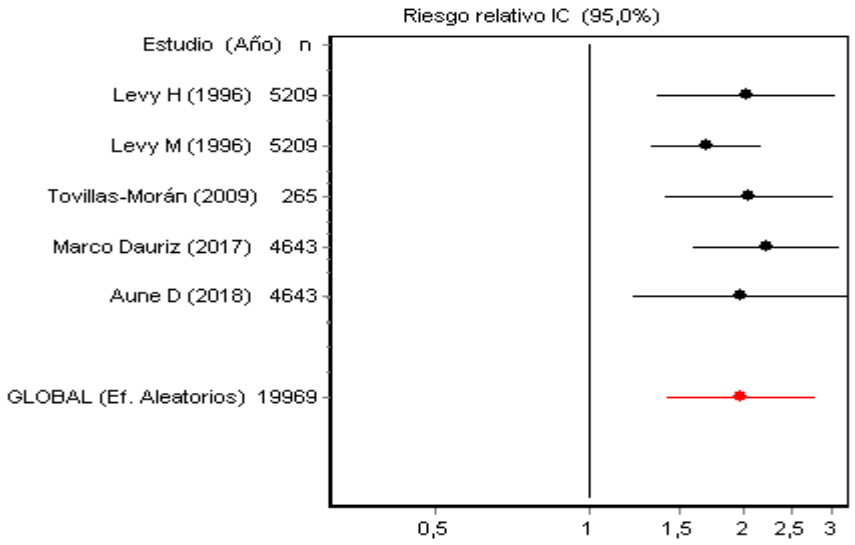

Figure 2. Meta-analysis on the association between diabetes mellitus and the progression to hypertensive heart disease with depressed systolic function.

Chronic kidney disease is one of the comorbidities most strongly associated with a poorer prognosis for cardiovascular diseases in general and hypertensive heart disease in particular, as demonstrated by the following result (RR: 2.1805; 95% CI: 1.6363-2.9057). The coefficient of variation between studies was 0.3847 and the I^2: 91.05%, indicating high heterogeneity among the studies (Figure 3).

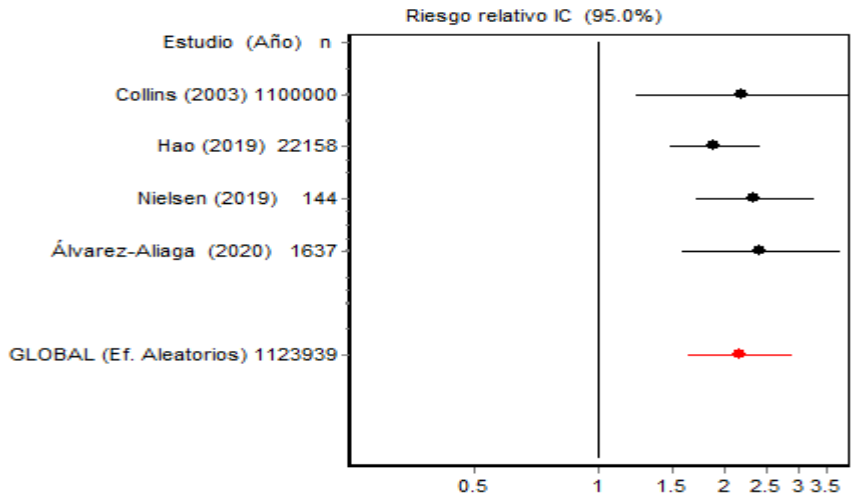

Figure 3. Meta-analysis on the association between chronic kidney disease and progression to hypertensive heart disease with depressed systolic function.

Figure 4 shows the evaluation of the influence of microalbuminuria on cardiovascular risk. It demonstrates that the presence of this biological marker was associated with a worse prognosis. HR: 3.978; 95% CI: 2.131–7.428. Furthermore, the coefficient of variation between studies was 0.3441 and the I^2 was 71.41%, demonstrating that, although microalbuminuria is a recognized cardiovascular risk factor, its pathogenic value varies according to the results of different studies.

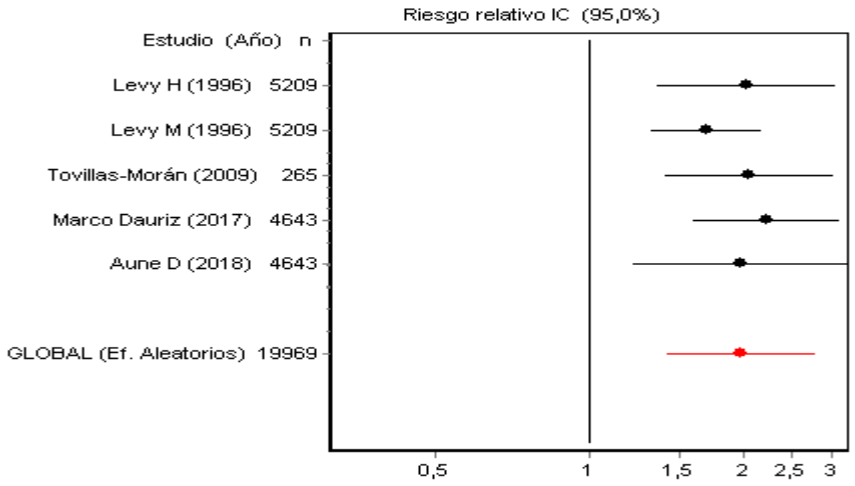

Figure 4. Meta-analysis on the association between microalbuminuria and the progression to hypertensive heart disease with depressed systolic function.

C-reactive protein stood out among the biological markers as shown by the HR values: 2.141; 95% CI: 1.247-3.675; the coefficient of variation between studies was 0.321 and the I2: 9.48% which indicates homogeneity between the studies.

Knowledge of the long-term effects of hypertension and atherosclerosis on the cardiovascular system has allowed researchers to identify the role of pulse pressure in the prognosis of cardiovascular diseases in general, and hypertensive heart disease in particular. In fact, the present study demonstrated that pulse pressure increases the aforementioned risk toalmost twice (HR: 1.678; 95% CI: 1.340-2.101). The coefficient of

variation between studies was 0.4295 and the I2: 68.18%; elements that show moderate heterogeneity.

Total cholesterol greater than 4.8 mmol/L was also associated with a worse prognosis (HR: 1.221; 95% CI: 1.1354–1.3148). The coefficient of variation between studies was 0.4101 and the I^2 was 98.74%, indicating the diversity of results.

Discussion

Hypertensive heart disease is characterized by alterations in cardiac morphology and function, particularly of the left ventricle. These conditions are caused by the increased left ventricular afterload induced by hypertension, along with remodeling of the atria, ventricles, and arterial system. The likelihood of adverse cardiovascular events, such as congestive heart failure, increases in these individuals. (33)

Thus, the current systematic review supports that the presence of a group of prognostic factors is associated with the evolutionary changes of hypertensive heart disease from mild diastolic dysfunction to depressed systolic function.

The effects of hypertension itself (lack of control, duration, and stage) are particularly noteworthy. So much so, that hypertension is considered the most important risk factor for heart failure. In fact, most patients with heart failure have a history of hypertension, which also causes left ventricular hypertrophy, with consequent diastolic dysfunction. This, in turn, is an important predictor of heart failure, even when left ventricular systolic function is normal and there has been no prior myocardial infarction. (33-35)

Hypertension-dependent fibrosis and structural alterations of large and small vessels (microvascular disease) also contribute. In fact, myocardial interstitial fibrosis is a distinctive histological feature of several heart diseases where hypertension is prominent. And these changes in myocardial architecture and function are associated with the progression of heart failure, especially in patients with uncontrolled hypertension. (35-37)

The presence of diabetes mellitus in hypertensive individuals increases the risk of myocardial dysfunction, as demonstrated in this research. Diabetes mellitus is one of the

main risk factors for cardiovascular disease in patients with hypertension. In fact, a higher incidence of heart failure with reduced ejection fraction has been demonstrated in diabetic and hypertensive patients. (9,13-17,38)

In patients with chronic kidney disease, resistant hypertension, masked hypertension, and elevated nocturnal blood pressure are common, and these are associated with a low glomerular filtration rate, higher levels of albuminuria, and organ damage. (9,39,40)

Undoubtedly, the strong connection between kidney and heart disease reflects the complex interaction between the heart and kidneys (the renin-angiotensin system, various inflammatory mediators, and reactive oxygen species cause histological and functional changes characteristic of hypertensive kidney and heart injury). This interaction may explain the findings in this series, creating a vicious cycle: higher blood pressure leads to greater kidney and heart damage. However, the pathophysiological mechanisms of this reciprocal relationship remain ambiguous. Therefore, further research in this area is necessary. (39,40)

It should be noted that increased albuminuria indicates a progressive loss of renal function and is an independent and cumulative predictor of increased cardiovascular risk. (8,9,21,22)

There is evidence that microalbuminuria is an important predictor of cardiovascular risk. Indeed, there is a high prevalence of subclinical left ventricular dysfunction in individuals with microalbuminuria. Reducing albuminuria has also been considered a therapeutic target. Analysis of clinical trial data has found that changes in urinary albumin excretion are predictors of renal and cardiovascular complications. (9,40,41)

However, it has not been resolved whether reducing albuminuria per se can be useful for the prevention of cardiovascular disease.

Several factors may explain the pathogenic importance of high C-reactive protein levels and the progression of hypertensive heart disease. These include the fact that this biological marker accelerates ventricular remodeling, increases the impairment of endothelial vasodilator function, activates platelets, increases hypoxia-induced apoptosis through a mitochondrial-dependent pathway, and is found at elevated levels in heart failure. (9,42-44)

C-reactive protein is definitely a biomarker of active vascular processes, which exerts a direct action on cardiac function and morphology and may causally contribute to the evolution to stage IV hypertensive heart disease. (9,42)

Pulse pressure is another factor influencing the decline in systolic function in hypertensive patients. It increases with age in both men and women, paralleling the increase in systolic blood pressure, especially in the population over 60 years of age. Increased pulse pressure is associated with greater cardiovascular morbidity and mortality, constituting an independent marker of cardiovascular risk. (27-29,45)

Although quitting smoking has not been shown to reduce the risk of heart failure of any etiology, its epidemiological association with the onset and prognosis of cardiovascular diseases is certain. Therefore, it is recommended not only to abstain from smoking but also to avoid exposure to secondhand smoke, as it significantly increases the risk of cardiovascular diseases. (12,30)

A review of the evidence shows that patients with hypercholesterolemia may benefit from statin therapy, particularly those with metabolic syndrome, diabetes mellitus, and multiple risk factors for atherosclerosis. This statement is somewhat consistent with our work, which found a higher risk of heart disease in patients with high cholesterol and high cholesterol/high-density lipoprotein ratios. (1)

However, elevated levels of low-density lipoprotein cholesterol are not common in heart failure with reduced ejection fraction. Patients with advanced heart failure may have low levels of low-density lipoprotein cholesterol, which is associated with a worse prognosis, although treatment did not reduce morbidity or mortality. (9,46)

There is a clear need for more specific and concrete studies to evaluate these factors.

Currently, several scales are available to predict overall cardiovascular risk. Among them, the most widely used are the Framingham Risk Score,30 and the more recent Cardiovascular Disease Risk Algorithm QRISK30 and later QRISK3,28 which includes other risk factors, such as a family history of early CVD. However, they have not proven useful in predicting the progression of hypertensive heart disease.

The hypertensive cardiopathy model showed an area under the curve and calibration far superior to the scales mentioned above, demonstrating that a specific tool for hypertensive cardiopathy is needed, and not a general cardiovascular risk tool.

The authors believe there is a need to create and validate scales specific to hypertensive heart disease, which, although it shares some pathogenic elements, has a different pathophysiological value; these elements would allow for better precision and therefore a more accurate evaluation.

Conclusions

A significant association was demonstrated between the different prognostic factors and the evolutionary changes in hypertensive heart disease. Furthermore, the need for a new prognostic tool based on these factors is evident in order to improve the accuracy and precision of the aforementioned risk assessment.

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Conflict of interest

The authors declare no conflicts of interest.

Authorship contribution

Liannys Lidia Naranjo Flores: participated in the conceptualization and curation of the data, in the formal analysis, research, methodology, in the drafting of the draft original and in the drafting, revision and final editing of the manuscript.

Dr. C. Alexis Álvarez Aliaga: participated in the data curation, in the formal analysis, research, methodology, in the drafting of the original draft and in the writing, final revision and editing of the manuscript.

Dr.C. Julio César González Aguilera: participated in the curation of the data, in the formal analysis, research and in the writing of the manuscript.

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