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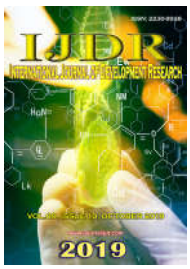

REVIEW ARTICLE OPEN ACCESS

THE FRAMINGHAM HEART STUDY - HYPERTENSION: SYSTEMATIC REVIEW

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ABSTRACT

This The Framingham Heart Study is a prospective longitudinal cohort study that began in 1948 with the enrollment of 5209 men. Women who were free of cardiovascular disease and between the ages of 28 and 62 years. As the largest and oldest cohort study ever produced, it has completed 70 years since its first data collection and has contributed in many ways to the scientific and academic community. The data produced by the FSH produced studies that proved the influence of some risk factors to predict the onset of illness, morbidity and mortality. Based on what was elucidated about the studies published by the FHS group, this systematic review aims to analyze and present the most relevant data about systemic arterial hypertension and its problems. The search for scientific articles on the proposed theme was made from the last 10 years of publications, taking into consideration the research terms "hypertension", "hypertension" and "blood pressure". No text will be discarded as it is believed to be important for understanding.

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INTRODUCTION

The Framingham Heart Study is a prospective longitudinal cohort study that began in 1948 with the enrollment of 5209 men and women who were free of cardiovascular disease and between the ages of 28 and 62 [1]. The work performed very efficiently by the Framingham Heart Study (FHS) group of researchers has helped to unravel several pathologies and systemic chronic conditions that were previously obscure because of the lack of understanding of the main causes of the disease, as they were always involved. a wide range of risk factor possibilities that confused understanding [2]. As the largest and oldest cohort study ever produced, it has completed 70 years since its first data collection and has contributed in many ways to the scientific and academic community[2].

The data produced by the FSH produced studies that proved the influence of some risk factors to predict the onset of illness, morbidity and mortality [2]. The guiding objective was based on the search for clarifications on the emergence of cardiovascular risk factors and their aggravating factors, because little was known about its pathophysiology and what would be the motivators for the onset of the disease, as well as its effects on the human body. The willingness of researchers has modified knowledge and intensified the search for knowledge, providing important information for prevention and treatment [2]. Based on what was elucidated about the studies published by the FHS group, this systematic review aims to analyze and present the most relevant data about systemic arterial hypertension and its problems. The search for

scientific articles on the proposed theme was made from the last 10 years of publications, considering the search terms "hypertension", "hypertension" and "blood pressure". No text will be discarded as it is believed to be important for understanding. However, the selected texts were also revised in pairs so that in fact their content did not deviate from the article selection rules. More information about the Framingham Heart Study can be found at *https://www.framinghamheartstudy.org/*, especially about the history, objectives, mission, methodology, and cohort studied.

2009 - 2019 Articles Frame - Framingham Heart Study			
No.	Year	Author	Title
1	2009	William B. Kannel, MD, MPH, FACC	Hypertension: Reflections on Risks and Prognostication [3]
2	2009	Daniel Levy	Genome-wide association study of blood pressure and hypertension [4]
3	2009	Ravi Dhingra, M. D	Relationships of Matrix Remodeling Biomarkers to Blood Pressure Progression and Incidence of Hypertension in the Community [5]
4	2011	Meredith C. Foster, MPH	Fatty Kidney, Hypertension, and Chronic Kidney Disease[6]
5	2011	Andrew D Johnson	Association of hypertension drug target genes with blood pressure and hypertension in 86 588 individuals[7]
6	2012	Susan Cheng, MD	Blood pressure tracking over the adult life course: Patterns and correlates in the framingham heart study[7]
7	2012	Dr. Bernhard M ., Kaess	Aortic Stiffness, Blood Pressure Progression, and Incident Hypertension [8]
8	2012	Chunyu Liu, PhD	Association of Genetic Variation in the Mitochondrial Genome With Blood Pressure and Metabolic Traits [9]
9	2012	George Thanassoulis, MD	Relations of exercise blood pressure response to cardiovascular risk factors and vascular function [10]
10	2012	Pauline Maillard	in the Framingham Heart StudyEffects of systolic blood pressure on white-matter integrity in young adults in the Framingham Heart Study : A cross-sectional study [11]
11	2013	Connie W. Tsao, MD	Relationship of arterial stiffness and endothelial function to brain aging in the Community [12]
12	2013	Vanessa Xanthakis, PhD	Aldosterone and the Risk of Hypertension [13]
13	2013	E. Victor Adlin	Bimodal aldosterone distribution in low-renin hypertension[14]
14	2014	Jeannette Simino	Gene-age interactions in blood pressure regulation: A large-scale investigation with the CHARGE, global BPgen, and ICBP consortia[15]
15	2014	Connie W.	Cross-Sectional Relations of Arterial Stiffness, Pressure Pulsatility, Wave Reflection, and Arterial Calcification [16]
16	2015	Katherine A. Sauder	Endothelial function, arterial stiffness and adherence to the 2010 Dietary Guidelines for Americans: A Cross-sectional Analysis [17]
17	2015	Tianxiao Huan	A Meta-analysis of Gene Expression Signatures of Blood Pressure and Hypertension [18]
18	2015	Jacob Basson	Influence of Smoking Status and Intensity on Discovery of Blood Pressure Loci Through Gene-Smoking Interactions [19]
19	2015	Anthony Bonifonte	Antecedent blood pressure as a predictor of cardiovascular disease [20]
20	2015	Arvind Nishtala	Midlife Hypertension Risk and Cognition in the Non-Demented Oldest Old: Framingham Heart Study [21]
21	2017	Emer R. McGrath,	Blood pressure from mid-to late life and risk of incident dementia[22]
22	2017	Teemu J Niiranen	Heritability and risks associated with early onset hypertension: Multigenerational, prospective analysis in the Framingham He art Study
23	2018	Ramachandran S. Vasan, MD	High Blood Pressure in Young Adulthood and Risk of Premature Cardiovascular Disease: Calibrating Treatment Benefits to Potential Harm [23]
24	2018	Lindsay R. Pool, PhD, MPH	Use of Long-term Cumulative Blood Pressure in Cardiovascular Risk Prediction Models [24]
25	2018	Vasilis Tsimihodimos	Hypertension and diabetes: co-prediction and time trajectories Vasilis [1]
26	2019	Teemu J	Relative contributions of pulse pressure and arterial stiffness to cardiovascular disease: The framingham heart study [25]
27	2019	Giri, Ayush	Trans-ethnic association study of blood pressure determinants in over 750,000 individuals [26]

REVIEW

Arterial hypertension

Arterial hypertension is one of the most prevalent chronic diseases in the world, and its main characteristic is its gradation as you age [1]. Blood pressure is sometimes high in people with other conditions such as diabetes and obesity [27]. High blood pressure levels are well documented as an important point for the onset of cardiovascular disease and target organ damage throughout life [28]. Changes in living standards, advances in medicine and scientific research have been able to document hypertension very well, however the risk of its onset may be increasing mainly due to the increase in life expectancy, since age is the highest. main risk factor [25]. Although the elderly has the highest prevalence of disease, their vascular physiology itself causes a natural increase in vascular resistance due to decreased elasticity and compliance of vessels and arteries [29]. On the other hand, the risk may also have decreased since the cataloging of risk factors led to the emergence of educational, behavioral and medication preventive measures, imbued with attention to avoid the disease and its diseases [5,30]. However, it is still a highly prevalent disease with an extremely high mortality burden, which keeps it in the ranking of the most dangerous and deadly diseases. This is why its continuous study is important [4].

Some time ago hypertension was only perceived / identified when there were signs of active principle or target organ damage, but this negligent conduct identified the disease in an advanced state, because even before damaging some target organs, major changes were considered. in the vascular system, as well as ventricular hypertrophy [3]. The pressure levels of the elderly were identified by adding age plus 100mmHg, which imposes an excessively substantial cardiovascular risk. Currently, the risk classification strata are studied to avoid misdiagnosis and possible deaths due to treatment neglect [31]. The incremental risk of blood pressure observed within the prehypertensive range reflects the continuous gradual influence of blood pressure, without critical values that delineate the normality of "hypertension". The Framingham study found that 80% to 90% of the prehypertensive population sample had at least one additional cardiovascular risk factor. However, the risk for cardiovascular

in prehypertensive people is still modest and is significantly increased with the number of associated risk factors. Encouraging changes in behavioral and eating habits, and in some cases the use of drugs, may return blood pressure to the "ideal" level (> 120 / 80 mmHg) [31].

PHYSIOPATHOLOGY AND RISK FACTORS

Obesity and Excess Body Fat

Obesity has been a major risk factor for the emergence of chronic pathologies such as cardiovascular disease, kidney injury, hypertension can also complicate existing diseases. The uncontrolled increase in body composition has important physical and physiological repercussions. The focal concern is ectopic fat, as it presents in risky places such as the viscera, where its negative effect is accentuated [6]. Excess ectopic fat may compromise the functioning of important organs such as the kidney, which in turn has important functions in regulating blood pressure at local, systemic and central levels. Causing morphological changes in the systemic and renal vascular system, which increases the resistance of the blood flow along the vessels, requiring a greater heart effort associated with fluid and mineral elimination factors such as sodium [32,33]. Fighting excess weight, storing body fat, is essential to mitigate the risk of hypertension. Not only the FHS publications but also the WHO promote the idea of changing behavioral and eating habits to prevent and combat illness [34–40].

Age and Organic Aging

Naturally, blood pressure tends to increase linearly with age, mainly due to organic aging. The body begins to lose structural functions and elastic proteins like collagen [8]. Large arteries are beginning to lose elastic and resilient properties and a larger pressure pulse is now needed to eject the same amount of blood [41]. Thus, increasing blood pressure to maintain normal blood distribution [42,43]. However, it has been suggested by Cheng et al. That increasing blood pressure over the course of aging is not mandatory, and that it may modulate according to lifestyle and health conditions as well as cultural exposure as well as factors of risks [7,44]. However, the paper is also inconclusive because its results show that systolic blood pressure and pressure peaks are largely linear with increasing age, unlike mean blood pressure and diastolic blood pressure that appears to fall sharply. and nonlinear relationship with age [7]. Changes in blood pressure begin to appear at the onset of adulthood, with a greater predominance of diastolic blood pressure and mean arterial pressure, constant changes that are greater throughout adulthood. When compared with increased BMI and diastolic blood pressure, the ratio was higher in young than in older adults, leading to the understanding that body composition accumulation of adipose tissue could cause compression of vessels and arteries and raise return pressure [4546].

Brain Changes

Very recent findings that deduce that high blood pressure can cause changes in brain structure. One of the first findings was in 2012 when the article found that increased systolic blood pressure was linearly associated with decreased regional fractional anisotropy and increased mean diffusivity, especially in the anterior corpus callosum, in the fronto-occipital fascicles. And the fibers protruding from the thalamus into the upper frontal gyrus. It was also strongly associated with reduced gray matter volumes, particularly in the Brodmann 48 area on the medial temporal lobe surface and the Brodmann 21 area of the middle temporal gyrus [11]. Minimal vascular lesions can last for years until they become substantial problems.Therefore, lifelong blood pressure control is believed to be the best way to prevent the onset of changes and cerebral vascular problems and the reduction of accidents such as stroke. In addition to clinically evident vascular events, middle-aged hypertension is an important modifiable risk factor for cognitive decline, mild cognitive impairment, and dementia [22] at the end of life [12,17,30].

Aldosterone and Blood Pressure Modulation

Aldosterone is an important hormone linked to body sodium regulation and homeostasis, a protein produced in the adrenal glomerular zone, its synthesis is regulated by three main stimuli: local and systemic angiotensin II, circulating adrenocorticotropic hormone and levels serum potassium. Its action is renal, more precisely in the collecting ducts and in the tubular lumen, in which sodium and water reabsorption and potassium elimination occurs. Other adverse effects have been attributed to corticosteroid mineral, which is vascular remodeling, also causing a fibrotic process in cardiomyocytes (cardiac muscle cells) and a profibrotic, hypertrophic and inflammatory response in the vascular smooth muscle. Reducing nitric oxide bioavailability and consequently endothelial dysfunction [8]. Aldosterone negatively influences endothelial cell function, causing cells to swell and become rigid due to its effect on the antioxidant enzyme glucose-6-phosphate dehydrogenase and epidermal growth factor, activating phospholipase C and inhibiting the return of progenitor cells. endothelial 47. Therefore, aldosterone contributes to vascular remodeling, proinflammatory, atherosclerotic profile, endothelial dysfunction, and damage to target organs such as the heart, brain, and kidneys. Being able to influence the onset of diseases such as hypertension and its comorbidities, the main ones being cardiovascular diseases [48]. Its higher incidence is related to elevated blood aldosterone and suppressed renin levels. Some cases are related to primary hyperaldosteronism, which in many cases is related to some tumor in the adrenal or in the gland responsible for the release hormone - hypothalamus-pituitary-adrenal axis.

Genetic Polymorphisms

Arterial hypertension is multifactorial [49]. However, family / genetic issues are still unclear, much has been said about genetic polymorphisms linked to changes in blood pressure, but none hold long, or their contribution to illness is still very small in relation to external (environmental) factors)[18.50–56].
In a meta-analysis published in 2015 by the Framingham Heart Study group, the percentage that genetic factors (polymorphisms found) range from 5% to 9% of blood pressure variations. Being an interference slightly smaller than the environmental factors that coincide with all the remaining percentage [18]. Genetic variation for chronic illness has its burden in the pathology, however, because its prevalence is still an important but small part, it is noteworthy that environmental factors are imperative for such condition [49,57].

Prevention and treatment of systemic arterial hypertension

Widely recognized as the main form of prevention and treatment in relation to chronic diseases, the regular practice of

physical activity has also been recommended for the control and prevention of hemodynamic variations resulting from aging, and / or emergence of severe forms of hypertension [10,58]. Regular physical activity could improve cardiovascular health and functionality; however, well-planned, intensely progressive physical exercise programs have been shown to be effective in enhancing the positive effects already well established by usual exercise practice. physical activity [59]. Being associated with drug use, and depending on blood pressure levels, and according to the emergence of blood pressure variation [10,60]. It can lead to total pressure control, with the use of suspended medication, replaced by healthy habits, which in addition to behavioral will also include adequate nutrition [10,61]. Drug treatment is a very important ally for proper blood pressure control, especially in severe cases where blood pressure is unable to return to baseline homeostatic values, as there is a reorganization of what is "normal" for the body. So, it is a persistent and resistant hypertension that needs help to maintain constant and safe levels. There are various types of drugs with different effects whether to decrease the effect of aldosterone, renin angiotensin system, angiotensin converting enzyme inhibition, calcium channel blockers, diuretics. All with the purpose of better providing quality of life and health [31].

Final considerations

Arterial hypertension is a very common chronic disease worldwide, so it is important to develop ethical behaviors so that the disease can be prevented and that the disease be mitigated. Decreasing the use of blood pressure depressant medications.Regular physical activity was considered a protective effect against chronic illness, especially for disorders that affect the cardiovascular system. Being able to be the effective substitute for the drug. Thus, the Framingham Heart Study is still the best risk predicting tool for the onset of hypertension in adults. Used worldwide for its practicality and low cost. Also demonstrating what are the factors that are responsible for the increased risk and also the factors that can contribute to reducing the risk of the onset of illness in a period of 2 to 4 years.

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