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Gender difference in coronary artery disease

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Abstract. Background: Coronary artery disease (CAD) continues to exert a substantial impact on global health, being the main factor causing morbidity and mortality in North America and Europe. Men and women have different incidences of CAD and risk factors, which has been widely reported across populations. In light of a notable scarcity of studies examining the variation in CAD risk among different subgroups. We investigated how cholesterol, glucose, blood pressure, and age affect CAD risk in different sex and smoking groups. **Method**: Framingham Heart Study, a longest-running cardiovascular epidemiological investigation used furnishing valuable insights into CAD risk. Investigating the relationship between these characteristics and the occurrence of CHD involved using logistic regression. **Result**: For blood pressure variable among smoking group, there were significant increase in male group (β=0.0255, P<0.001) compared with non-smoking group (β=0.0164 in male, β=0.0162 among female group, P<0.001) and reduction among female group (β=0.0089, P<0.001). Within the female group, the age variable exhibited a notable reduction in smoking group (β=0.0460, P=0.0020) compared with the non-smoking group (β=0.0829, P<0.001). After adding the interactions between smoking and blood pressure, smoking and age. In the male group, both smoking and the interaction become insignificant, whereas in the female group the interaction is significant. **Conclusion**: Our study suggested that high level of glucose, total cholesterol and blood pressure increased the risk of CAD. By dividing into subgroup, we discovered that the combined presence of smoking and increased blood pressure, and of smoking and age could potentially exert a more adverse effect on pressure wave reflection in women compared to men.

Keywords: cardiovascular diseases, coronary disease, gender, smoking

1. Introduction

Coronary artery disease (CAD) continues to exert a substantial impact on global health, being the main factor causing adverse health outcomes and fatalities in Europe. Its complex nature, characterized by risk factors like hypertension, smoking, cholesterol profile (total cholesterol, LDL(low-density lipoprotein) cholesterol, HDL(high-density lipoprotein) cholesterol), and glucose level, underscores the challenge of detection [1]. These risk factors have significantly contributed to our understanding of CAD vulnerability. Population studies have facilitated predictive models that forecast CAD occurrence by integrating more factors.

Differences in CAD incidence and risk factors between genders have been extensively documented among various populations [2, 3]. Recent findings have highlighted the identification of novel cardiovascular disease risk factors specific to women. However, our comprehension of sex-specific risks remains limited, and the strategies for averting and handling stroke and cardiovascular risk elements are

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fundamentally indistinguishable for both sexes. This is the case despite an increasing body of evidence showcasing noteworthy sex-based variations in the occurrence of conventional CAD risk factors, as well as in how these factors influence CAD outcomes.

Another aspect related to gender is that the smoking habits of males and females are different. Across the general population, the frequency of smoking is greater among males compared to females, despite the fact that the recent reduction in the prevalence of smoking has been more conspicuous among men in comparison to women [4]. Nonetheless, smoking cigarettes undoubtedly stands as the most significant contributor to abrupt cardiac death among younger women, whose smoking prevalence is currently rising, as smoking is responsible for more mortality from CAD and stroke than any other medical conditions [5, 6].

In light of a notable scarcity of studies examining the variation in CAD risk among different subgroups, which potentially leading to missed opportunities for integrating subgroup-specific considerations into the design of CAD prevention strategies, we investigated how cholesterol, glucose, blood pressure, and age affect CAD risk in different sex and smoking groups.

2. Method

2.1. Data source

Our analysis drew on research information sourced from the Framingham Heart Study, a longest-running heart and circulatory epidemiological investigation initiated in 1948. National Institutes of Health and overseen by Boston University supported this study which encompasses three generations of well-characterized individuals of White ethnicity and two additional cohorts representing diverse racial and ethnic backgrounds. These cohorts are richly characterized, with extensive longitudinal monitoring, furnishing valuable insights into cardiovascular and noncardiovascular aspects of human physiology across the lifespan. Furthermore, they aid in the identification of significant factors contributing to the risk of cardiovascular disease.

The Institutional Review Board from the Boston Medical Center gave its approval to the study protocol after receiving the written informed consent of all participants.

2.2. Characteristics

There is a total of 4238 residents in this ongoing study. The extracted variables encompass both general information and personal history. In terms of general information, these variables include gender, age, and body mass index. Personal history, on the other hand, covers factors such as smoking, alcohol consumption, as well as other lifestyle and health-related behaviors.

Participants in the heart research had a variety of evaluations during each visit, including physical exams, anthropometry measurements, measurements of blood pressure, and phlebotomy to evaluate factors associated with vascular risk. Participants were asked to place their left arm against the sphygmomanometer, which had a mercury column, and a cuff that was the right size. The examination blood pressure was determined using the average of two measures taken by doctors. Standardized enzymatic techniques were used to measure serum total cholesterol levels. Self-reporting was used to establish smoking status. Higher fasting glucose readings, specifically 126 mg/dL for the offspring cohort and 140 mg/dL for the original cohort, were recognized as signals of diabetes. Additionally, the administration of insulin or oral hypoglycemic drugs to regulate blood sugar levels was also considered indicative of the condition. During the heart investigation, the examining physician relied on self-report to identify whether antihypertensive drug use was present.

The occurrence of CAD episodes and mortality were continuously tracked for all research participants. As indicated by the findings of the Framingham Heart Study, CAD encompasses a range of cerebrovascular incidents including ischemic stroke, hemorrhagic stroke, and transient ischemic attack. Additionally, it involves various events linked to coronary heart disease (CHD) such as fatal coronary outcomes, myocardial infarction, instances of coronary insufficiency, and episodes of angina. Additionally, heart failure and peripheral artery disease (intermittent claudication) were included. A

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thorough strategy, including medical histories, clinic-based physical examinations, hospitalization records, and correspondence with personal physicians, was used to collect information concerning CAD episodes during follow-up. A team of three skilled investigators carefully evaluated any possible new incidents after carefully going through all pertinent medical information. A neurologist from the heart research team analyzed the majority of participants who were thought to be stroke suspects, and cases of cerebrovascular events were reviewed by a separate review committee involving a neurologist.

2.3. Statistical analysis

Logistic regression was applied to examine the association between cholesterol, glucose, blood pressure, age and occurrence of CHD. All models were first adjusted for known determinants of CHD risk as shown in Table 1. For the final model selection, we used a subset of different gender and smoking situation subjects data from FHS to derive the logistic model with five-fold cross-validation, recall value and roc_auc score. We added interactions term between blood pressure, hypertension, glucose and diabetes and evaluated whether they improved the model performance. R software, version 4.3.0 (R Foundation for Statistical Computing, Vienna, Austria), was used for all analyses.

3. Result

A total of 4238 participants were subject to continuous monitoring for the occurrence of CAD events and mortality. Among smokers, with a sensitivity of 0.75, a specificity of 0.64 and an ROC-AUC of 0.74, the model demonstrated its performance. In the nonsmoking group, the model attained a sensitivity of 0.7, specificity of 0.73, and an ROC-AUC of 0.79.

Table 1. Clinical characteristics in study subjects in male and female

	Male(n=1819)	Female(n=2419)
Current smoker(n)		
No	713	1431
Yes	1106	988
Prevalent stroke(n)		
No	1809	2404
Yes	10	15
Prevalent hypertension(n)		
No	1209	1673
Yes	570	746
Diabetes(n)		
No	1767	2362
Yes	52	57
	Male(n=1819)	Female(n=2419)
Age	49±9	50±9
Total cholesterol	233±42	239±46
Systolic blood pressure	131±19	133±24
BMI	26.2±3.4	25.5±4.5
Glucose	82±24	82±22

Table 1 shows the distribution of characteristics of the study population. More than half of the population were women. Non-smoking rates among women (59.16%) are significantly higher than among men (39.20%).

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Table 2. Results of logistic regression analysis to assess the relationships of risk factors and occurrence of CAD in four groups classified by gender and smoking

	Male			Female		
	β	95% CI	P	β	95% CI	P
Smoking						
Total cholesterol	0.0025	-0.001,0.0060	0.1636	0.0016	-0.0032,0.0063	0.5119
Glucose	0.0078	0.0012,0.0146	0.0215	0.0063	-0.0014,0.0138	0.0948
Blood pressure	0.0255	0.0176,0.0336	<0.001	0.0089	-0.0007,0.0182	0.0652
Age	0.0595	0.0400,0.0792	<0.001	0.0460	0.0168,0.0753	0.0020
nonsmoking						
Total cholesterol	0.0043	-0.001,0.0096	0.1084	0.0002	-0.0035,0.0038	0.9218
Glucose	0.0093	0.0031,0.0162	0.0048	0.0068	0.0011,0.0125	0.0188
Blood pressure	0.0164	0.0068,0.0261	<0.001	0.0162	0.0098,0.0227	<0.001
Age	0.0617	0.0365,0.0877	<0.001	0.0829	0.0594,0.1071	<0.001

Table 2 presents the associations between total cholesterol, glucose, blood pressure, age and occurrence in different subjects. For blood pressure variable among smoking group, there were significant increase in male group (β=0.0255, P<0.001) compared with non-smoking group (β=0.0164 in male group, β=0.0162 among female group, P<0.001<0.001) and reduction among female group (β=0.0089, P<0.001). In the female group, the age variable exhibited a considerable reduction in smoking group (β=0.0460, P=0.0020) compared with the non-smoking group (β=0.0829, P<0.001).

Table 3. Results of logistic regression model to assess the effect of interaction between smoking and blood pressure, as well as smoking and age on risk of CAD in male and female

	Male		Female	
	β	P	β	P
Total cholesterol	0.0031	0.0357	0.0006	0.6845
Current smoker	0.5301	<0.001	0.2277	0.1029
Glucose	0.0085	<0.001	0.0065	0.0048
Blood pressure	0.0216	<0.001	0.0130	0.0652
Age	0.0612	<0.001	0.0666	0.0020
Interaction with blood pressure				
interaction	0.0087	0.1647	0.0119	0.0246
Total cholesterol	0.0030	0.0430	0.0006	0.6602
Current smoker	0.6672	0.4437	1.9034	0.0118
glucose	0.0085	<0.001	0.0065	0.0042
Blood pressure	0.0163	<0.001	0.0168	<0.001
Age	0.0607	<0.001	0.0684	<0.001
Interaction with age				
interaction	0.0016	0.9207	-0.0443	0.00877
Total cholesterol	0.0031	0.0339	0.0007	0.6398
Current smoker	0.4366	0.6164	2.5655	0.00467
Glucose	0.0085	<0.001	0.0065	0.0046
Blood pressure	0.0218	<0.001	0.0138	<0.001
Age	0.0598	<0.001	0.085	<0.001

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Table 3 shows how these four variables related to the occurrence of CAD after adding the interactions between smoking and blood pressure, smoking and age. In the male group, both smoking and the interaction become insignificant, whereas in the female group the interaction is significant.

4. Discussion

Our study suggested that high level of glucose, total cholesterol and blood pressure increased the risk of CAD. Smoking, blood pressure and age were identified as important factors contributing to risk of CAD. A potential disparity based on gender might exist in how these factors influence the level of risk. These factors might collaboratively amplify risk increase in females. In contrast, among males, these factors might independently raise incidence without interacting. Consequently, the combined presence of smoking and elevated blood pressure, and of smoking and age could potentially exert a more adverse effect on pressure wave reflection in women compared to men.

Previous research has demonstrated that smoking has a substantially more negative relative effect on CAD in women. Although men typically had a higher incidence of myocardial infarction, women who smoke heavily exhibited a greater frequency than men who had never engaged in smoking [7]. The mechanism of smoking is probably involving alterations to platelet function and clotting factors, as well as the acceleration of atherosclerosis and stimulation of the sympathetic nervous system. But the effect of smoking in females can be different. It is stated that women exhibited a higher propensity for plaque erosion than males were from the Burke study, and they also experienced less luminal narrowing and plaque calcification [8]. In our study, synergistic effect of smoking and blood pressure, smoking and age in women also suggest a different mechanism of smoking on female.

An increasing body of research indicates that women are less advantaged than men in numerous areas. According to epidemiological data, no variation is evident in the rate of CAD progression upon reaching menopause [9, 10]. There is no indication of a rise in the mortality rate due to CAD among women aged 45 to 55 years, nor is there evidence of a convergence of rates between women and men. Consequently, women might possess an unjustified sense of optimism concerning the level of protection against CAD attributed to estrogen, and this can cause people to overestimate their risk for cardiovascular disease. Although anecdotal evidence suggests that despite the regular emphasis on adopting a healthy lifestyle in women's periodicals and other platforms, many women may retain uncertainties about various factors related to the development of CAD [11]. further studies will be required for this potential lack of advocacy among women and the underlying mechanism.

While the current study uses reliable, standardized CAD incidence criteria and a sizable community-based sample under ongoing surveillance, it's important to acknowledge various limitations inherent to this study. Although medications for hypertension affect CAD risk, the present study did not examine the influence of these medications. A further study to examine the ethnical impact on the CAD risk factors is also proposed. Considering the predominantly white composition of the Framingham sample, it becomes essential to assess the applicability of the CVD risk function in different sample populations. It's worth noting that other risk functions from Framingham have demonstrated their applicability in diverse contexts [12].

5. Conclusion

In conclusion, our study suggested that high level of glucose, total cholesterol and blood pressure increased the risk of CAD. By dividing into subgroup, our findings revealed that combined presence of smoking and increased blood pressure, as well as smoking and age could potentially exert a more adverse effect on pressure wave reflection in women in contrast to men. It suggests a different mechanism of increase in risk. Subsequent investigations are necessary to explore the underlying mechanisms of these findings.

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