

# Evaluating the Role of Fibrinogen as an Independent Risk Factor in Coronary Heart Disease

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**Abstract:** *The involvement of fibrinogen in the etiology of cardiovascular diseases, such as coronary heart disease, is gaining attention. The significance of plasma fibrinogen as an independent cardiovascular risk factor has come to light in recent years. It is widely established that the majority of cases of unstable angina pectoris, abrupt cardiac ischemia mortality, and acute myocardial infarction (MI) are associated with occlusive thrombi. The primary mechanism underlying these atherosclerotic consequences is thrombosis. An increased risk of stroke and coronary heart disease is linked to an elevated amount of plasma fibrinogen. We address fibrinogen as an independent and changeable risk factor for cardiovascular disease, despite its association with other well-known risk factors like age, diet, and smoking. Long-term increases in fibrinogen levels can cause cardiovascular events, particularly atherosclerotic ones. These include fibrinogen infiltration of the vessel wall, increased platelet aggregation and thrombus formation, increased fibrin formation, and effects from increased blood viscosity. It also predicts accelerated coronary atherosclerosis and increases the risk of death or recurrent myocardial ischaemia in patients who have had a prior coronary incident. In fact, research indicates that the positive correlation between elevated levels of plasma fibrinogen and cardiovascular events is as predictive as elevated levels of cholesterol.*

**Keywords:** Fibrinogen, Coronary Heart Disease, Cardiovascular Risk Factors, Atherosclerosis, Thrombosis

## 1. Introduction

An increased risk of stroke and coronary heart disease is linked to an elevated amount of plasma fibrinogen. This research addresses fibrinogen as an independent and changeable risk factor for cardiovascular disease, despite its association with other well-known risk factors like age, diet, and smoking. Acute or long-term increases in fibrinogen levels can cause a variety of cardiovascular events, particularly atherosclerotic ones. These include fibrinogen infiltration of the vessel wall, increased platelet aggregation and thrombus formation, increased fibrin formation, and rheological effects from increased blood viscosity. In healthy individuals, elevated fibrinogen is a potent primary risk factor for cardiovascular disease. It also predicts accelerated coronary atherosclerosis and increases the risk of death or recurrent myocardial ischaemia in patients who have had a prior coronary incident. In fact, research indicates that the positive correlation between elevated levels of plasma fibrinogen and cardiovascular events is as predictive as elevated levels of cholesterol. (16)

The 'recognized' cardiovascular risk factors are now widely known to us. Its implementation in clinical practice has begun to significantly lower cardiovascular mortality and morbidity in a number of nations. It is estimated that only approximately 30% of cardiovascular events, can be "explained" using "accepted" risk factors. This means that there are probably more risk factors out there. Fibrinogen is a strong contender, according to a growing amount of data. The purpose of this review is to provide an overview of recent, significant findings from clinical and epidemiological studies that connect fibrinogen to cardiovascular risk. (17)

The molecular mass of human fibrinogen is 340 000 daltons and it is a lengthy, dimeric protein. It has a trinodular structure made up of three distinct pairs of polypeptide chains joined by disulphide linkages. The molecule is thus made up of two major subunits, each of which is made up of three polypeptide chains. Several genes on chromosome 4 (FOA, FOB, and FOe) encode them. The rate-limiting step, which is also impacted by interleukin-6, is the synthesis of the B chain. It is therefore possible for genetic and environmental elements to interact. (18)

Fibrinogen is produced by parenchymal liver cells and then transported into the bloodstream. The blood plasma contains eighty to ninety percent of the body's fibrinogen. The range of "normal" plasma levels is 200-400mg/dl. Three to six days is the molecule's half-life. The cytokines, especially interleukin-I, generated by activated macrophages and the products of fibrinogen's plasma breakdown are thought to be in feedback control over fibrinogen synthesis. (19,20)

Although fibrinogen serves a variety of purposes, its roles as an acute phase protein and clotting factor are the most well-known. It's a crucial cofactor for platelet aggregation, a strong influencer of blood's rheological behavior, and an inducer of the migration and proliferation of smooth muscle cells. Its potential to be a cardiovascular risk factor may be related to these and other phenomena. (21,22) The purpose of this review is to analyze the role of fibrinogen as an independent risk factor in coronary heart disease and its implications for cardiovascular health.

## 2. Literature Survey

S. No	Research	Outcome	References
1	Fibrinogen as a risk factor for coronary heart disease and mortality in middle-aged men and women	For both men and women, fibrinogen is a powerful predictor of coronary heart disease, whether it is deadly or not, new or recurring, and associated with death from an unknown cause. Smoking is the most significant coronary risk factor, accounting for only a portion of its effect.	M. Woodward et al.(1)
2	Overview of Referred Obstetric Patients and Their Outcome in Tertiary Care Hospital	Many different types of complex obstetric cases are sent to our tertiary care facility. The most frequent reasons for referrals are hypertensive diseases (preeclampsia, eclampsia), anemia, and postpartum or antepartum hemorrhage. All of these conditions require specific care. The primary care staff members ought to receive appropriate training. Women's health and social standing can be enhanced in our nation through health education and awareness campaigns run by non-governmental groups and the media.	Jyoti Bindal et al.(2)
3	Fibrinogen Is a Predictor of Mortality in Coronary Heart Disease Patients	The Framingham study solely examined the association between fibrinogen and CHD in the general population. This analysis did not include women due to the limited sample size. Even though women in our study population had greater levels of fibrinogen than men did, the death rate for women was lower—3.8% compared to 6.6% for men. Extended surveillance will enable us to make inferences about women as well.	Michal Benderly et al.(3).
4	Fibrinogen and coronary heart disease: test of causality by 'Mendelian randomization'	The incidence of coronary disease is not significantly influenced by genotypes that result in changes in fibrinogen concentrations throughout life. Since these genotype-dependent variations in fibrinogen were assigned at random during conception (Mendelian randomization), extraneous variables are unlikely to skew this connection. Thus, these genetic findings offer compelling proof that variations in fibrinogen concentration over the long term do not significantly influence the risk of coronary heart disease.	Bernard Keavney et al.(4)
5	Relationship Between Plasma Fibrinogen and Coronary Heart Disease in Women	The current results in this particular cohort show that plasma fibrinogen is linked to an increased risk of CHD in women, particularly when they are younger. Whatever the cause, it appears likely that elevated plasma fibrinogen levels significantly raise the risk of coronary thrombotic events in females.	Margita Eriksson et al (5).
6	Fibrinogen and cardiovascular risk	It is conceivable and likely that fibrinogen and atherothrombogenesis are related. According to epidemiological research, a plasma fibrinogen level above 3.0 g/l is a significant, independent risk factor for myocardial and/or cerebral infarction. Increased fibrinogen may potentially be a risk factor for the aftereffects of CVD, according to clinical data. Certain factors that influence the very varied quantity of fibrinogen in both health and sickness are currently understood. It would appear appropriate to conduct controlled intervention trials to investigate the "fibrinogen hypothesis." However, there is currently no perfect treatment to reduce fibrinogen on its own.	E Ernst" and W Koenig(6)
7	Does Elevated Plasma Fibrinogen Increase the Risk of Coronary Heart Disease?	FIB was independently associated with long-term all-cause and cardiac mortality among CAD patients	George Davey Smith et al.(7)
8	Plasma fibrinogen a major coronary risk factor	The results suggest that high plasma fibrinogen levels are an important coronary risk factor and should be included in profiles used to identify those at high risk of heart attacks.	M.C. Stone et al.(8)
9	a comparative study of plasma fibrinogen in male and female patients with coronary artery disease	The findings from our study provide evidence that plasma fibrinogen is associated with excess risk of CAD in women. But, the association between plasma fibrinogen and cardiovascular risk does not establish a cause-effect relationship. Further large scale studies are needed to establish the causal relationship of fibrinogen to coronary artery disease in both the sexes.	N.Sountharya et al.(9)
10	Fibrinogen Is a Predictor of Mortality in Coronary Heart Disease Patients	All-cause and CHD mortality rates increased with increasing fibrinogen levels.	Michal Benderly et al.(10)
11	Fibrinogen and Atherosclerotic Cardiovascular Diseases—Review of the Literature and Clinical Studies	Fibrinogen is a strong predictor of coronary heart disease, fatal or non-fatal, new or recurrent, and of death from an unspecified cause, for both men and women. Its effect is only partially attributable to other coronary risk factors, the most important of which is smoking.	Stanisław Surma et al.(11)
12	Observational study	Fibrinogen plasma concentration is a clinically useful biomarker that could characterise acute ischaemic stroke.	Peycheva et al(12)
13	Observational study	High-serum fibrinogen concentrations in high-risk individuals may be used as a predictor for the occurrence of acute ischemic stroke and mortality from stroke.	Samir et al(13)
14	Observational study	Plasma fibrinogen concentrations were independently associated with severity and complexity of CAD.	Tabak et al(14)
15	Observational study	Plasma fibrinogen concentrations at admission were independently associated with risk of death among subjects with acute MI.	Peng et al(15)

### 3. Methodology

The most recent information acquired from a range of secondary sources, including published literature from numerous scholarly publications was used to conduct the literature review. Relevant articles were selected by an automated search on Google Scholar.

### 4. Results and Discussion

The study explores the role of fibrinogen in the etiology of coronary heart disease CHD, emphasizing its significance as an independent cardiovascular risk factor. Recent research establishes a correlation between elevated plasma fibrinogen levels and an increased risk of stroke and CHD. This review systematically evaluates the current literature, highlighting fibrinogen's impact on atherosclerosis, thrombus formation, and cardiovascular events. The findings underscore the need for further investigation into fibrinogen as a targetable risk factor in cardiovascular disease management.

### 5. Conclusion

In both men and women, thrombosis is a major factor in the development and clinical manifestation of CAD. Research has demonstrated a strong correlation between a higher risk of thrombosis, which impedes the advancement of coronary artery disease (CAD), and heightened levels of fibrinogen, one of the key proteins involved in the coagulation process. Regardless of conventional cardiovascular risk variables, fibrinogen elevated cardiovascular risk to a same degree. Furthermore, higher fibrinogen levels altered the risk associated with other variables such as elevated LDL or factor VII.

The majority of prospective cohort and observational studies that revealed fibrinogen correlations with higher risk of CAD did not conduct sub-analyses based on age and sex subgroups. Nonetheless, several studies suggest that men and women may have different roles for fibrinogen in the development of CAD. Since estrogens protect women naturally at a younger age by reducing inflammation and the activation of the RA system, other risk factors—fibrinogen being one of the most targetable—are probably to blame for premature CAD.

Women with premature CAD have a key role for fibrinogen in the formation of atherosclerotic plaque, especially in the early stages of the disease, as evidenced by decreased thrombus lysability and a higher level of fibrinogen in these women. By adsorbing LDL cholesterol, promoting monocyte chemotaxis, inducing smooth-muscle cell migration, and inducing the local inflammatory response, fibrinogen deposits in artery walls cause the formation of atherosclerotic plaque. In younger women, but not in men, local micro-thrombosis on degraded plaques with fibrin deposits is common. As a result, fibrinogen levels appear to be the primary factor influencing the development of atherosclerotic plaque in women who have early CAD.

The results above show how important it is to do additional research and clinical trials to evaluate the effect of

fibrinogen levels on cardiovascular risk in men and women differently based on age and other cardiovascular risk factors. These studies may serve as the foundation for new cardiovascular risk assessment instruments. The evaluation of fibrates' potential to lower cardiovascular risk should be the next course of action, in addition to the already advised optimal medical care and healthy lifestyle. By systematizing current cardiovascular information and risk assessment, these steps would probably improve patient outcomes and care.

### 6. Future Scope

This review establishes fibrinogen as a significant independent risk factor in coronary heart disease. The varying impact of fibrinogen levels on cardiovascular risk in different genders and age groups highlights the need for further research. Future studies should aim at developing targeted interventions to manage fibrinogen levels, enhancing cardiovascular disease prevention and treatment strategies.

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