INTRODUCTION

Accurate identification of individuals who will benefit most from cardiovascular risk reduction should result in a substantial reduction in morbidity and mortality. Although a number of risk prediction engines are available to predict atherosclerosis and cardiovascular events,[1] calculation of the Framingham Risk Score (FRS) is recommended for the initial assessment of the majority of patients in the primary prevention category.[2]

The updated FRS calculation has the ability to adjust certain risk factors such as total cholesterol, high-density lipoprotein-cholesterol, diabetic, and smoking status for age, gender and correct for the effect of blood pressure treatment.[3,4] However, additional genetic factors and other variables also influence the development of atherosclerosis [5,6] but are not included in the risk assessment by the FRS.

Thus, FRS predicts risk in large populations but may only have moderate or limited predictive value for an individual symptomatic or asymptomatic patient.[7]

This limitation of FRS highlights the potential utility of direct imaging modalities such as computed tomographic coronary angiography (CTA) for accurate identification of the presence and extent of coronary atherosclerosis in individual patients.

Coronary artery calcification (CAC) measured by electron beam computed tomography and multi-detector computed tomography has been demonstrated to have incremental prognostic value over traditional clinical predictors,[8,9] particularly in women with a low FRS.[10] Since CAC is an indirect measure of total coronary atherosclerosis, the absence of CAC does not preclude the presence of non-calcific atherosclerotic plaque. Thus CAC assessment may lead to the underestimation of the total atherosclerotic burden.

More accurate measures of total atherosclerotic burden may allow the identification of patients without CAC who may also be at risk of future cardiac events and may benefit from earlier application of various preventive strategies.

AIM OF THE WORK

To study the relationship between the cardiovascular risk as assessed by Framingham score and the extent of atherosclerotic affection among symptomatic patients with chest pain assessed by MDCT.

CHAPTER (1)

FRAMINGHAM RISK SCORE

History of the Framingham Heart Study:

Cardiovascular disease (CVD) is the leading cause of death and serious illness in the United States. In 1948, the Framingham Heart Study - under the direction of the National Heart Institute (now known as the National Heart, Lung, and Blood Institute or NHLBI) - embarked on an ambitious project in health research. At the time, little was known about the general causes of heart disease and stroke, but the death rates for CVD had been increasing steadily since the beginning of the century and had become an American epidemic. The Framingham Heart Study became a joint project of the National Heart, Lung and Blood Institute and Boston University.

The objective of the Framingham Heart Study was to identify the common factors or characteristics that contribute to CVD by following its development over a long period of time in a large group of participants who had not yet developed overt symptoms of CVD or suffered a heart attack or stroke.

The researchers recruited 5,209 men and women between the ages of 30 and 62 from the town of Framingham, Massachusetts, and began the first round of extensive physical examinations and lifestyle interviews that they would later

analyze for common patterns related to CVD development. Since 1948, the subjects have continued to return to the study every two years for a detailed medical history, physical examination, and laboratory tests, and in 1971, the Study enrolled a second generation - 5,124 of the original participants' adult children and their spouses - to participate in similar examinations. In April 2002 the Study entered a new phase, the enrollment of a third generation of participants, the grandchildren of the Original Cohort.

Over the years, careful monitoring of the Framingham Study population has led to the identification of the major CVD risk factors - high blood pressure, high blood cholesterol, smoking, obesity, diabetes, and physical inactivity - as well as a great deal of valuable information on the effects of related factors such as blood triglyceride and HDL cholesterol levels, age, gender, and psychosocial issues. Although the Framingham cohort is primarily Caucasian, the importance of the major CVD risk factors identified in this group have been shown in other studies to apply almost universally among racial and ethnic groups, even though the patterns of distribution may vary from group to group. In the past half century, the Study has produced approximately 1,200 articles in leading medical journals. The concept of CVD risk factors has become an integral part of the modern medical curriculum and has led to the development of effective treatment and preventive strategies in clinical practice.

The Framingham Heart Study continues to make important scientific contributions by enhancing its research capabilities and capitalizing on its inherent resources. New diagnostic technologies, such as echocardiography, carotid artery ultrasound, magnetic resonance imaging of the heart and brain, CT scans of the heart and its vessels and bone densitometry (for monitoring osteoporosis), have been integrated into past and ongoing protocols.

While pursuing the Study's established research goals, the NHLBI and the Framingham investigators are expanding their research into other areas such as the role of genetic factors in CVD. Framingham investigators also collaborate with leading researchers from around the country and throughout the world on projects in stroke and dementia, osteoporosis and arthritis, nutrition, diabetes, eye diseases, hearing disorders, lung diseases, and genetic patterns of common diseases.

Application:

Because risk scores such as the Framingham Risk Score give an indication of the likely benefits of prevention, they are useful for both the individual patient and for the clinician in helping decide whether lifestyle modification and preventive medical treatment, and for patient education, by identifying men and women at increased risk for future cardiovascular events.

Coronary heart disease (CHD) risk at 10 years in percent can be calculated with the help of the Framingham Risk Score. Individuals with low risk have 10% or less CHD risk at 10 years, with intermediate risk 10-20%, and with high risk 20% or more.

Framingham Risk Score not only estimate the cardiovascular risk but also guide for prevention of cardiovascular disease. Prevention can be achieved by modification of lifestyle and initiating the preventive drug therapy. It is important to be able to decide when to initiate lifestyle modification and preventive drug therapy.

Usually individuals with low to intermediate risk are recommended for lifestyle modification. Lifestyle modification including avoid cigarette smoking, perform regular exercise (minimum of 20 minutes, three times per week), intake healthy diet that contains less amount of saturated fat and rich in fresh fruits and vegetables, maintain an ideal body weight, and reduce alcohol consumption. Individuals with intermediate risk should monitor their risk profile every 6–12 months.

High risk individuals are recommended for both lifestyle modification and preventive drug therapy. Preventive drug therapy including statin intake to control cholesterol level, low dose aspirin to prevent thromboembolic manifestations, treatment for diabetes and treatment for high blood pressure (blood pressure should be treated to a target of 140/85 mmHg

or lower in non-diabetic persons and 130/80 mmHg or lower in diabetic persons). High risk individuals should monitor their risk profile every 3–6 months.

Current version of the Framingham Risk Score:

The current version of the Framingham Risk Score was published in 2002. The publishing body is the ATP III, i.e. the «Adult Treatment Panel III», an expert panel of the National Heart, Lung, and Blood Institute, which is part of the National Institutes of Health (NIH), USA.

The first Framingham Risk Score included age, gender, LDL cholesterol, HDL cholesterol, blood pressure (and also whether the patient is treated or not for his/her hypertension), diabetes, and smoking. It estimated the 10-year risk for coronary heart disease (CHD). It performed well, and correctly predicted 10-year risk for CHD in American men and women of European and African descent.

The updated version was modified to include dyslipidemia, age range, hypertension treatment, smoking, and total cholesterol, and it excluded diabetes, because Type 2 diabetes meanwhile was considered to be a CHD Risk Equivalent, having the same 10-year risk as individuals with prior CHD.

Estimate of 10-Year Risk for Men:

Table (1): Framingham Point Scores by Age Group

Age	Points
20-34	-9
35-39	-4
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	11
70-74	12
75-79	13

Table (2): Framingham Point Scores by Age Group and Total Cholesterol

Total Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	0
200-239	7	5	3	1	0
240-279	9	6	4	2	1
280+	11	8	5	3	1

Table (3): Framingham Point Scores by Age and Smoking Status

	Age 20-39	**Age 40-49**	**Age 50-59**	**Age 60-69**	**Age 70-79**
Nonsmoker	0	0	0	0	0
Smoker	8	5	3	1	1

Table (4): Framingham Point Scores by HDL Level

HDL	**Points**
60+	-1
50-59	0
40-49	1
<40	2

Table (5): Framingham Point Scores by Systolic Blood Pressure and Treatment Status

Systolic BP	**If Untreated**	**If Treated**
<120	0	0
120-129	0	1
130-139	1	2
140-159	1	2
160+	2	3

Table (6): 10-Year Risk by Total Framingham Point Scores

Point Total	10-Year Risk
< 0	< 1%
0	1%
1	1%
2	1%
3	1%
4	1%
5	2%
6	2%
7	3%
8	4%
9	5%
10	6%
11	8%
12	10%
13	12%
14	16%
15	20%
16	25%
17 or more	≥30%

Estimate of 10-Year Risk for Women

Table (7): Framingham Point Scores by Age Group

Age	Points
20-34	-7
35-39	-3
40-44	0
45-49	3
50-54	6
55-59	8
60-64	10
65-69	12
70-74	14
75-79	16

Table (8): Framingham Point Scores by Age Group and Total Cholesterol

Total Cholesterol	Age 20-39	Age 40-49	Age 50-59	Age 60-69	Age 70-79
<160	0	0	0	0	0
160-199	4	3	2	1	1
200-239	8	6	4	2	1
240-279	11	8	5	3	2
280+	13	10	7	4	2

Table (9): Framingham Point Scores by Age and Smoking Status

	Age 20-39	**Age 40-49**	**Age 50-59**	**Age 60-69**	**Age 70-79**
Nonsmoker	0	0	0	0	0
Smoker	9	7	4	2	1

Table (10): Framingham Point Scores by HDL Level

HDL	**Points**
60+	-1
50-59	0
40-49	1
<40	2

Table (11): Framingham Point Scores by Systolic Blood Pressure and Treatment Status

Systolic BP	**If Untreated**	**If Treated**
<120	0	0
120-129	1	3
130-139	2	4
140-159	3	5
160+	4	6

Table (12): 10-Year Risk by Total Framingham Point Scores

Point Total	10-Year Risk
< 9	< 1%
9	1%
10	1%
11	1%
12	1%
13	2%
14	2%
15	3%
16	4%
17	5%
18	6%
19	8%
20	11%
21	14%
22	17%
23	22%
24	27%
25 or more	≥30%

Analysis using the Framingham/ATP III criteria:

According to Framingham risk score, Individuals with low risk have 10% or less CHD risk at 10 years, with intermediate risk10-20%, and with high risk 20% or more.

CHAPTER (2)

METHODS FOR VISUALIZATION OF CORONARY ARTERY DISEASE

Coronary artery disease can result in obstruction of the coronary lumen, leading to ischemia and even infarction of the myocardium.[201] From a classical point of view, the obstruction is thought to gradually aggravate. Accordingly, non-obstructive coronary artery stenosis does not yet lead to inadequate blood flow and symptoms. In case of a more severe obstruction and/or a higher myocardial oxygen demand, the myocardium supplied by the affected coronary artery can become ischemic.[202, 203] As a result, patients can experience symptoms of chest pain during exercise. These symptoms are known as stable chest pain, as they are refractory after cessation of exercise. Eventually, an aggravating coronary obstruction will also produce symptoms during rest. Subsequently, the myocardium becomes ischemic or even infarcted, which causes irreversible damage to the heart and can result in arrhythmias and death.

The majority of coronary events are caused by rupture of a non obstructive plaque, [204] leading to acute thrombus formation and obstruction of the coronary artery. [205] Pathology studies have suggested that certain plaques are more vulnerable