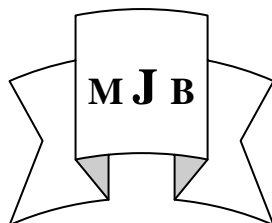


Physiological and Clinical Importance of Calcium Score and Risk Factors in Coronary Artery Disease

Saeed Hameed Lafta Saad Merza AL- Araji
Dep. of Medical Physiology, College of Medicine/ University of Babylon



Abstract

Objective: the calcium score is the best predictor for the coronary artery disease.

Patients: Fourty eight patients admitted to Al-Hussain General Teaching Hospital and to the Iraqi medical center in karbala, and 18 healthy controls were included in this study which lasted from November/2010 to September/2011. The patients included 34 males and 14 females, their ages ranged from 19-84 years, with a mean age of 58.63 years. Those patients were divided into male and female subgroups. As well as, the healthy controls were matched in age and sex with them.

The patients are classified in many groups according to the risk factors. The ages of these groups are divided as follows: the first group (30-50 years); the second group (≥ 51 years).

Results: This study demonstrated that The calcium score and the biochemical parameters (lipid profile & glucose level), have highly significant to the coronary artery disease ($p < 0.000$) and have also a significant correlation between calcium score and dyslipidemia ($p < 0.001$, $p < 0.002$) according to the risk factor taken, also shows significant increment in comparison with healthy controls ($p < 0.000$).

Calcium score have significant correlation with the age, weight & lipid elements $p < 0.000$ that is reflected the increasing incidence of the coronary artery disease with age and with the increasing the body weight specially the central obesity.

The distribution of the coronary artery calcification is more frequent in the male sex than in female ($p < 0.005$).

Regarding the diabetes mellitus which has important changes in the Ca^{++} score & the biochemical's results since there is strong correlation with Ca^{++} score & the dyslipidemia and then coronary artery disease ($p < 0.000$) while in non diabetic this is excluded.

In ex smoking have significant correlation between the Ca^{++} score and the coronary artery disease in addition to that there is more strong correlation if there is association between ex smoking & diabetes mellitus same thing apply to the lipid parameters in this group ($p < 0.007$).

Coronary computed tomography with +ve result show very high significance with Ca^{++} score in comparison to the normal coronary arteries which indicate the accuracy of the computed tomographic angiogram in prediction of the coronary calcification & in turn coronary artery disease ($p < 0.000$).

Conclusion: In view of the changes summarized, the presence or absence of the coronary calcification by computed tomographic angiogram and biochemical parameters changes may be attributed to prediction of the coronary artery disease due to atherosclerosis which arises mainly due to increase of accumulation of the risk factors.

الأهمية الفسلجية والسريرية لنتيجة الكالسيوم وعوامل الخطورة في مرض الشرايين التاجية.

الخلاصة

الهدف: إن نتيجة الكالسيوم هي الأفضل في تشخيص مرض الشرايين التاجية.
المرضى: الدراسة دامت من نوفمبر/تشرين الثاني / ٢٠١٠ إلى سبتمبر/أيلول / ٢٠١١. هناك ٤٨ مريض و ١٨ سيطرة صحية (قيمت سريريا من قبل الطبيب الاختصاصي) أخذت في هذه الدراسة. المرضى يُصنّفون في العديد من المجموعات طبقاً لعوامل الخطورة. تُحلّل أعمار هذه المجموعات مقسمة كالتالي: المجموعة الأولى (٣٠-٥٠ سنة)؛ المجموعة الثانية (≤ 51 سنة)؛ . أولئك المرضى يُدخلون إلى وحدة العناية التاجية في مستشفى الحسين التعليمي وهم يعانون من مرض الشرايين التاجية.

النتائج: إن نتيجة الكالسيوم والبارامترات الكيمياوية الحيوية (مستوى الدهون و مستوى السكر)، وجد أن نتيجة الكالسيوم هامة جداً عند مرضى الشرايين التاجية ($p < 0.000$) ولها أيضاً ارتباط معنوي مع عدم انتظام الدهون ($p < 0.002$, $p < 0.001$) طبقاً لعوامل الخطورة التي أخذت. أيضاً يلاحظ زيادة معنوية بالمقارنة بالسيطرة الصحية ($p < 0.000$).
 نتيجة الكالسيوم لها ارتباط معنوي بالعمر، الوزن وعناصر الدهون ($p < 0.000$) وهذا يعكس ازدياد الحوادث لمرضى الشرايين التاجية وارتباطها بالعمر وبتزايد وزن الجسم خصوصاً السمنة المركزية.
 إن توزيع تكلس الشرايين التاجية أكثر تكراراً في الجنس الذكري من الأنثى ($p < 0.005$).
 بخصوص داء السكري الذي له تغييرات مهمة في نتيجة الكالسيوم والنتائج الكيمياوية الحيوية حيث أن هناك ارتباط معنوي مع نتيجة الكالسيوم وعدم انتظام الدهون ومن ثم مرض الشرايين التاجية ($p < 0.000$) بينما في غير السكري هذا مستثنى.
 في التدخين المفرط له ارتباط معنوي مع نتيجة الكالسيوم ومرض الشرايين التاجية بالإضافة إلى أن هناك ارتباط أقوى وأكثر إذا كان هناك جمع بين التدخين المفرط و داء السكري والشئ نفسه يُقدّم إلى بارامترات الدهون في هذه المجموعة ($p < 0.007$).
 المفراس الخاص بالشرايين التاجية والمريض الذي معه نتيجة مؤكدة لوجود خلل في الشرايين يشير الى وجود مستوى عالي جداً بخصوص نتيجة الكالسيوم وهذا يبرهن بالمقارنة مع الشرايين التاجية الطبيعية التي تُشير إلى دقة هذا المفراس في حساب التكلس في الشرايين التاجية وبالتالي مرض هذه الشرايين التاجية ($p < 0.000$).
 الاستنتاج : نظراً للتغيرات الحاصلة، ان وجود أو غياب التكلس التاجي من قبل المفراس التاجي وتغيرات بارامترات الكيمياوية الحيوية قد تُنسب إلى تشخيص مرض الشرايين التاجية نتيجة تصلب الشرايين التي تُظهر بشكل رئيسي بسبب زيادة تراكم عوامل الخطر.

Introduction

Coronary artery disease is a major cause of mortality and ill-health. It presents in different ways, the underlying cause is a process called atherosclerosis, which leads to narrowing of the coronary arteries, restricting the blood flow to the heart muscle. Coronary heart disease prevalence is increasing all over the world including our community that is not only a need for better recognition of the warning signs of a heart attack, but also a tremendous need for more efforts targeting prevention[1].

With proper care, physicians face major challenges when it comes to figuring out just who is at risk of a major heart-related event.

This article will review the current status of coronary calcium scoring, how it improves risk stratification (particularly in intermediate-risk patients) and how, together with contrast-enhanced computed tomographic angiography (CTA), it will improve our understanding of the relationship between calcified plaque, soft plaque, and the risk of cardiovascular events. An association that has the potential to aid in the development of new diagnostic tests

and therapeutic interventions for the prevention of cardiovascular disease [2].

Some physicians have been questioning because they are concerned that patients with soft plaque (new atherosclerotic plaque which has not yet calcified) will be missed with electron beam tomogram. While the presence of a soft coronary plaque cannot be excluded by electron beam tomogram, numerous population studies have demonstrated that having a coronary calcium score of less than 11 is associated with an extremely low rate of cardiac events rate. From these studies we conclude that the clinical importance of soft plaques for the prediction of future events is very low and does not invalidate the use of this technology in everyday clinical practice. [3]

This study demonstrated that coronary calcium screening can further improve the identification of individuals who are at high risk for MI or cardiovascular death over the next 5 to 10 years [4]. When study participants were grouped according to an Agatston score above or below 300, those with an Agatston score ≥ 300 had significantly more cardiovascular events than did those with lower scores at every level of

risk (low, intermediate, and high), based on the traditional risk factors. This study found that the measurement of calcified coronary plaque prospectively provided significantly more information about the likelihood of myocardial infarction or cardiovascular death than traditional risk factors alone [5].

Aim of the study: This study aimed to provide insight to know the physiological changes that help in prediction and diagnosis of the coronary artery disease in our patient. The presence of calcium in the coronary arteries considered a strong predictor for the coronary artery disease by using the multi detector CT scan so can diagnosing the coronary artery disease more earlier and can surrogate the invasive coronary angiography. such information is of no doubt necessary as background for any programs devised in the future for studying the coronary artery disease and treating this disease.

And this ultimately leads to advance in design of drugs of choice in treatment and prevention of this disease then reduce the mortality and morbidity of the patient.

Patients and Methods

The study was conducted in Al-Hussain teaching hospital with the Iraqi medical center in Karbala city, from November 2010 to September 2011.

Forty-eight patients {34 male 70% with mean age ± SD (58.76±12.5) years and 14 female 29% with mean age ± SD (58.5±11.29) years} with ischemic heart disease (clinically assessed by specialist doctors), whom collected from Al-Hussain teaching hospital in Karbala city have been subjected to present study and these selected patients were divided into many groups according to the risk factors.

Table 1 Groups of the patients with CAD according to the risk factors

groups	No.	%
sex Male	34	70%
female	14	29%
Age (30-50)years	13	27%
≥51years	35	72%
Hypertensive patients	27	56%
Non hypertensive patients	21	43%
Diabetic patients	17	35%
Non diabetic patients	30	62.5%
Ex smoker	23	48.9%
Non smoker	24	51%
Treadmill +ve patients	11	23%
Treadmill -ve patients	7	2%
Echo study normal	15	36%
LV. dysfunction	12	29%
IHD	14	34%
ECG normal	13	27%
IHD	35	72%
Computerized Tomographic Angiogram		
Normal CTA	9	18%
Coronary art. defect	39	81%

Worthy to mention that those patients were suffering from many risk factors and rearranged in groups according to the risk factor taken.

All patients underwent a case history questionnaire and were sent for the biochemical investigations (lipid profile and blood glucose levels). Blood sample was drawn from both patients and

controls for the estimation of these investigations.

The glucose determination: The absorbance of standards and samples are measured against reagent blank at 546 nm (according to procedure recommended by the glucose kit from Human company, Germany) (fasting patient).

Determination of total cholesterol (TC) in human sera. Let the content stand for 5 minutes at 37°C or 10 minutes at room temperature Absorbance's at 500 nm was recorded against reagent blank(according to procedure recommended by the total cholesterol kit from BIOLABO SA, company, France) (fasting patient).

Determination of high-density lipoprotein cholesterol (HDL-C) in human sera: let the content stand for 10 minutes at room temperature, Absorbances was recorded at 500 nm against reagent blank(according to procedure recommended by the High density lipoprotein kit from BIOLABO SA, company, France) (fasting patient)..

Determination of serum Triglycerides (TGs) : The absorbance of the colored complex (quinoneimine), proportional to the amount of TGs in the serum, is measured at 500 nm(according to procedure recommended by the triglycerid kit from BIOLABO SA, company, France) (fasting patient).

Determination of serum LDL:

The LDL concentration is calculated as follows:

$$LDL = \text{Total cholesterol} - (HDL + TG/5)$$

Determination of serum VLDL:

The VLDL concentration is calculated as follows:

$$VLDL = TG/5$$

Determination of the Ca⁺⁺Score: this is done by GE 64 slices CT. Scan in a non-contrast enhanced CT The study takes <5 minutes and yields images of very high spatial resolution. It has very low radiation exposure and has been validated for cardiovascular disease risk prediction. The computer software sums the amount of calcification per lesion and per artery simply by adding up the pixel values and adjusting for the slice width . Pixel values are then converted to an Agatston score, plaque volume, or plaque mass. Each provides essentially the same information: The amount of calcified plaque in the coronary arteries.

Results

Age and sex distribution.

In our study the age of the subjects ranging between 33-84 years and the control group range from 19-67years as describe in table no. (2) the patients account 48 out of 66 subjects and 18 control ,the patients group contain 34 male (70%)and 14 female (29%), while the control group contain 12male(66.6%) and 6 female (33,3%) as shown in table below there is no significant difference in the mean and the standard deviation of the male and female.

Table 2 The age for the patient with CAD and control groups

Group	Patient			Control		
	NO.	%	Age (years) Mean ± SD	No.	%	Age(years) Mean ± SD
Male	34	70%	58.76±12.5	12	66.6%	45.0 ± 11.87
Female	14	29%	58.5±11.29	6	33.3%	55.16 ± 10.6
Total	48	72%	58.70±11.86	18	27%	48.44 ± 12.17

SD, Standard deviation

The age have highly significant correlation to the weight and Ca⁺⁺ score(p<0.000) in male group which

account 34 patients out of 48 patients (70%) as shown in table (3)

Table 3 the age in correlation to Ca⁺⁺ score & weight , for the male patient of the CAD group

		weight	Ca ⁺⁺ score
Age	Pearson corr.	-0.583**	0.631**
	Sign	0.000	0.000
	No.	34	34

** High Significant ,No. Number. Sign., Significant

The Weight: the mean of the weight for the male patients group 86.02 which is slightly differ from that of the female which is 74.20 table(4)

in male group, which account 34 patients, (p<0.005). this indicate good correlation between them, while in the female group which account 14 patients there is no significant correlation between the weight and the Ca⁺⁺ score (p<0.705).

As shown in the table no.(5)There is strong relation between weight and the Ca⁺⁺ deposition in the coronary arteries'

Table 4 the weight mean for the male &female patients group with CAD.

WT		No.	%	Mean ± SD
	male	34	70%	86.02 ± 18.63
	female	14	29%	74.20 ± 10.52

WT, weight. No., number. SD, standard deviation

Table 5 the correlation of the weight with Ca⁺⁺ score in the male & female of CAD patients group.

Male	WT	Ca ⁺⁺ score
	Pearson correlation	..475**
	Sign.	.005
	No.	34
Female	Pearson correlation	.111
	Sign.	.705
	No.	14

** high significant

WT , weight. Ca⁺⁺score , calcium score

Lipid profile: the next table show the correlation between lipid parameters ,weight and the Ca⁺⁺ score from this table we can extract that the Ca⁺⁺ score has strong correlation to the lipid parameters and weight since the relationship account (p<0.001) for the HDL which is the strongest correlation

in this group (male group) ,and also the Ca⁺⁺ score high significant correlation to the weight(p<0.005) in sequence the Ca⁺⁺ score also have a significant correlation to the total cholesterol and LDL (p<0.01) in addition to the inter relationship between the lipid

parameters themselves in male group as shown in table(6).

Table 6 the correlation between weight ,lipid element and Ca⁺⁺ score in male CAD patient.

	WT	TG	LDL	VLDL	Total cholesterol	HDL	Ca ⁺⁺ score
WT. Pearson correlation Sign.(2-tail) N.	1 .34	-.047 .795 34	.003 .988 34	.018 .919 34	-.148 .410 34	-.276 .120 34	-.475** .005 34
TG . Pearson correlation Sign.(2-tail) N.	-.047 .795 34	1 .34	.465** .006 34	.124 .491 34	.370* .034 34	.035 .846 34	.196 .274 34
LDL . Pearson correlation Sign.(2-tail) N.	.003 .988 34	.465** .006 34	1 .34	-.279 .116 34	.292 .099 34	.177 .325 34	.445* .010 34
VLDL Pearson correlation Sign.(2-tail) N.	.018 .919 34	.124 .491 34	-.279 .116 34	1 .34	-.047 .795 34	-.111 .540 34	-.313 .076 34
Total cholesterol Pearson correlation Sign.(2-tail) N.	-.148 .410 34	.370* .034 34	.292 .099 34	-.047 .795 34	1 .207 34	.226 .207 34	.438* .011 34
HDL . Pearson correlation Sign.(2-tail) N.	-.276 .120 34	.032 .846 34	.177 .325 34	-.111 .540 34	.226 .207 34	1 .34	.534** .001 34
Ca ⁺⁺ score. Pearson correlation Sign.(2-tail) N.	-.475** .005 34	.196 .274 34	.442* .010 34	-.313 .076 34	.438* .011 34	.534** .001 34	1 .34

**correlation is high significant at the level 0.01(2 tailed)

*Correlation is significant at the level 0.05(2 tailed)

Sex male. WT , weight .TG , triglyceride . LDL , low density lipoprotein . VLDL, very low density lipoprotein. HDL , high density lipoprotein. Ca⁺⁺score , calcium score.

The correlation mentioned above concern the male but the female result have no significant relationship with the factors mentioned above apart from the TG which have high significant correlation with Ca⁺⁺ score (p<0.01) while the other parameters have no

significant with the Ca⁺⁺ score like the total cholesterol (p>0.257) but the total cholesterol significantly correlated with the LDL (p<0.009) . In turn the CAD In men more frequent than that in the female due to the Ca⁺⁺ deposition in the coronary artery as in table (7) below

Table 7 correlation of lipid profile with Ca⁺⁺ score in female CAD patients group.

		LDL	Ca ⁺⁺ score
Total cholesterol	Pearson correlation	.666**	.325
	Sign.	.009	.257
	No.	14	14
TG	Pearson correlation	.161	.614*
	Sign.	.583	.019
	No.	14	14

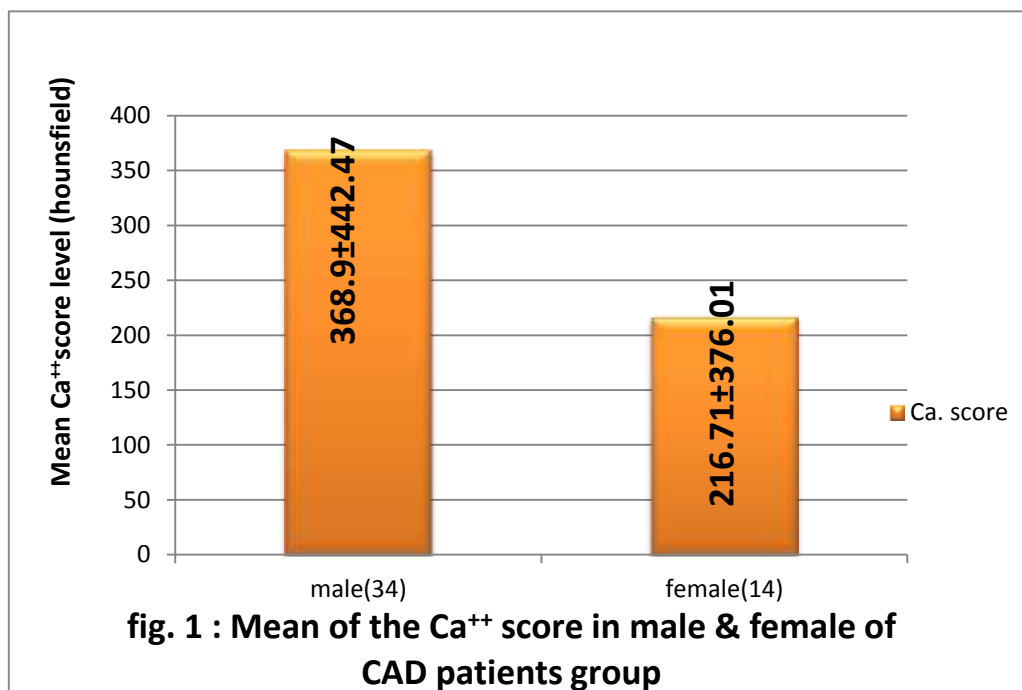
TG , triglyceride. . LDL , low density lipoprotein. Ca⁺⁺ score , calcium score

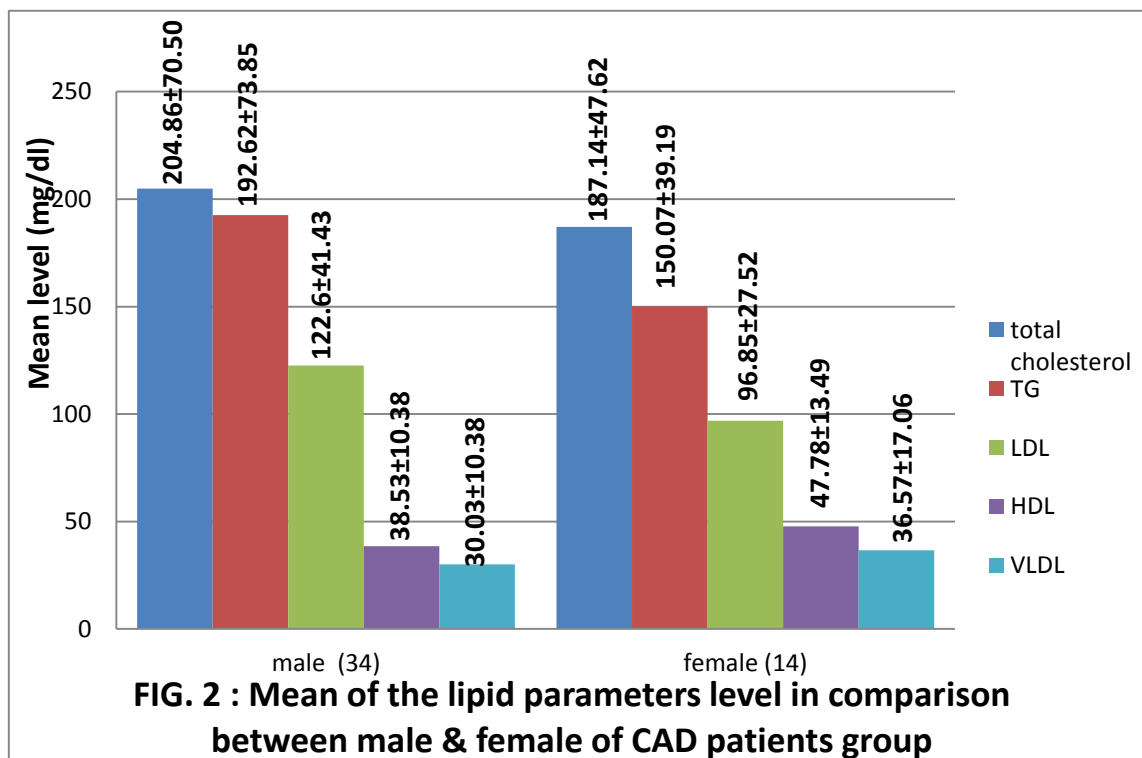
** high significant

* significant

In the figure(1)below it is obvious that the distribution of the Ca⁺⁺ Score in comprise between male and female notice there is highly significant in male group than that of the female group, in sequence significant difference in TG

mean level between the two groups while the other lipid parameters have no significant difference between the male and the female groups as shown in figure (2).





Diabetes mellitus: seventeen patient out of 48, which is 35% of the total, are diabetic patient most of them are type 2 diabetes mellitus so from the table below we can see the strong correlation between the Ca^{++} score & the age in diabetic patient ($p<.000$) also the Ca^{++} score with the total cholesterol & the LDL, HDL, VLDL ($p<0.004, p<0.02, P<0.0, P<0.05, P<0.05$) respectively. in other word the rest of the risk factors like weight, age, lipid profile have

strong correlation with each other as show in table (8) like HDL have strong correlation to the LDL, total cholesterol ($p<0.000, p<0.001$) respectively while the LDL in addition to the relation above with Ca^{++} score it has high significant correlation with total cholesterol ($p<0.000$) respectively. in turn the Ca^{++} score have strong correlation for the age and all lipid elements except the TG as shows in the table below.

Table 8 the correlation between the age, weight , lipid elements, Ca⁺⁺ score in diabetic patient group.

		Age	WT	TG	HDL	LDL	VLDL	Total cholesterol	Ca ⁺⁺ score
Age	Pearson correlation	1	-	.614**	.282	.393	-.448	.490*	.793**
	Sig.	.	.767**	.009	.274	.120	.071	.048	.000
	N	17	.000	17	17	17	17	17	17
WT	Pearson correlation	-.767**	1	-	.060	-.096	.555**	-.109	-.391
	Sig.	.000	.	.606**	.820	.714	.021	.678	.121
	N	17	17	.010	17	17	17	18	17
TG	Pearson correlation	.614**	-	1	.377	.570*	-.164	.553*	.457
	Sig.	.009	.606**	.	.136	.017	.028	.028	.065
	N	17	.010	17	17	17	17	17	17
HDL	Pearson correlation	.282	.060	.377	1	.855**	-.004	.716**	.475
	Sig.	.274	.820	.136	.	.000	.988	.001	.054
	N	17	17	17	17	17	17	17	17
LDL	Pearson correlation	.392	-.096	.570*	.855**	1	-.093	.913**	.530*
	Sig.	.192	.714	.017	.000	.	.723	.000	.029
	N	17	17	17	17	17	17	17	17
VLDL	Pearson correlation	-.448	.555*	-.164	-.004	-.093	1	-.175	-.468
	Sig.	.071	.021	.529	.988	.723	.	.501	.058
	N	17	17	17	17	17	17	17	17
Total Cholesterol	Pearson correlation	.490*	-.109	.533*	.716**	.913**	-.175	1	.665**
	Sig.	.046	.678	.028	.001	.000	.501	.	.004
	N	17	17	17	17	17	17	17	17
Ca ⁺⁺ score	Pearson correlation	.793**	-.391	.457	.475	.530*	-.468	.665**	1
	Sig.	.000	.121	.065	.054	.029	.058	.004	.
	N	17	17	17	17	17	17	17	17

**correlation is significant at the 0.01 level (2 tailed) *correlation is significant at 0.05 level (2 tailed) Diabetic group patient. WT , weight .TG , triglyceride .LDL , low density lipoprotein .VLDL, very low density lipoprotein .HDL , high density lipoprotein .Ca⁺⁺ score , calcium score.

While in non diabetic patient group which account 30 patient out of 48(62.5%) there is significant difference in relationship of the Ca⁺⁺ score between the two group which have high significant relation in the diabetic

patient more than that in the non diabetic patient .

Figure 3 shows the distribution of the calcium mean value in diabetic non diabetic patient of the coronary artery disease.

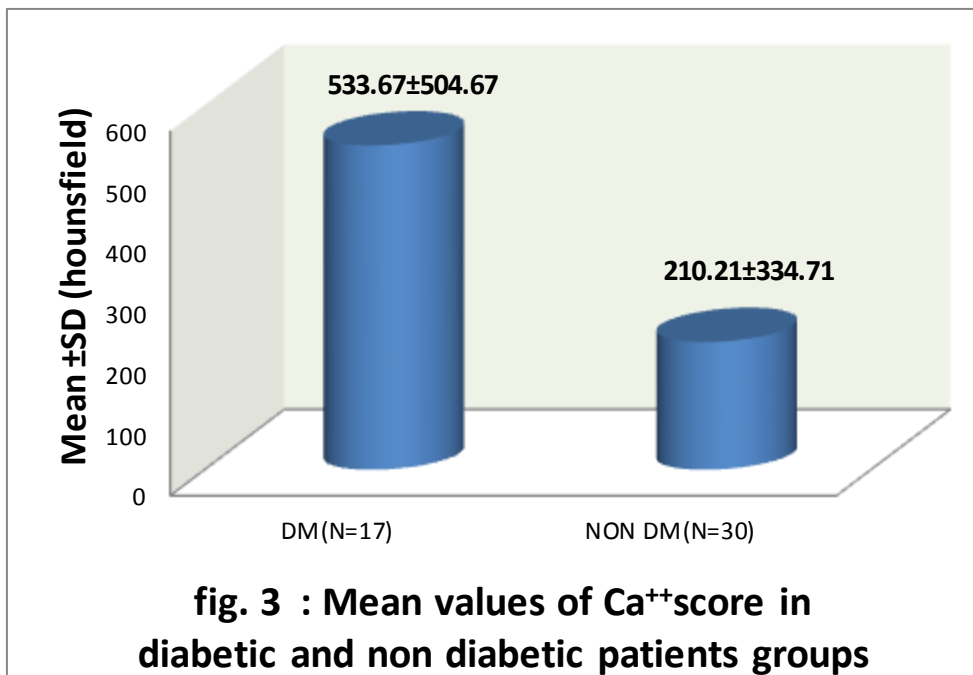
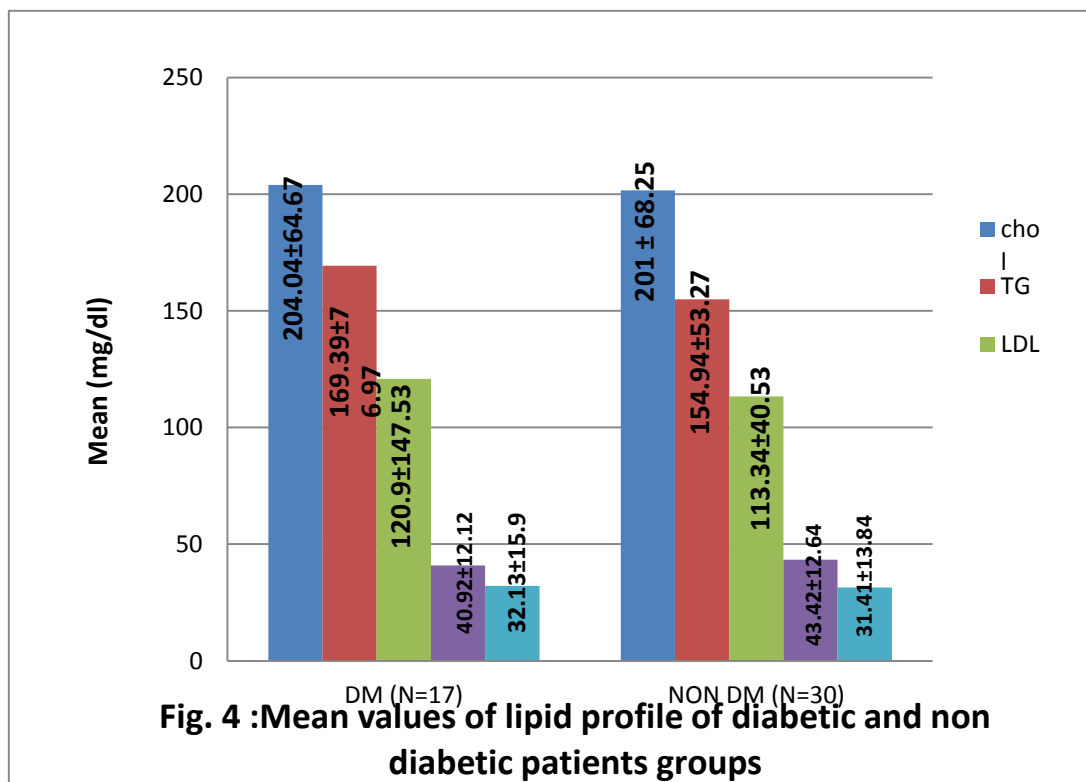


Figure 4 shows the means level of the lipid parameters in diabetic and non

diabetic of the coronary artery disease patients.



Smoking: the table below show the risk factors which include lipid elements and Ca⁺⁺score in smoker group patients by T. test method for the patients ex. smoker which include 23 patients out of

47 patients (48.9%) and 24 patient non smoker out of 47 patients (51%), this table show the high significant in VLDL, Ca⁺⁺ score which is (p<0.005 and p<0.007) respectively.

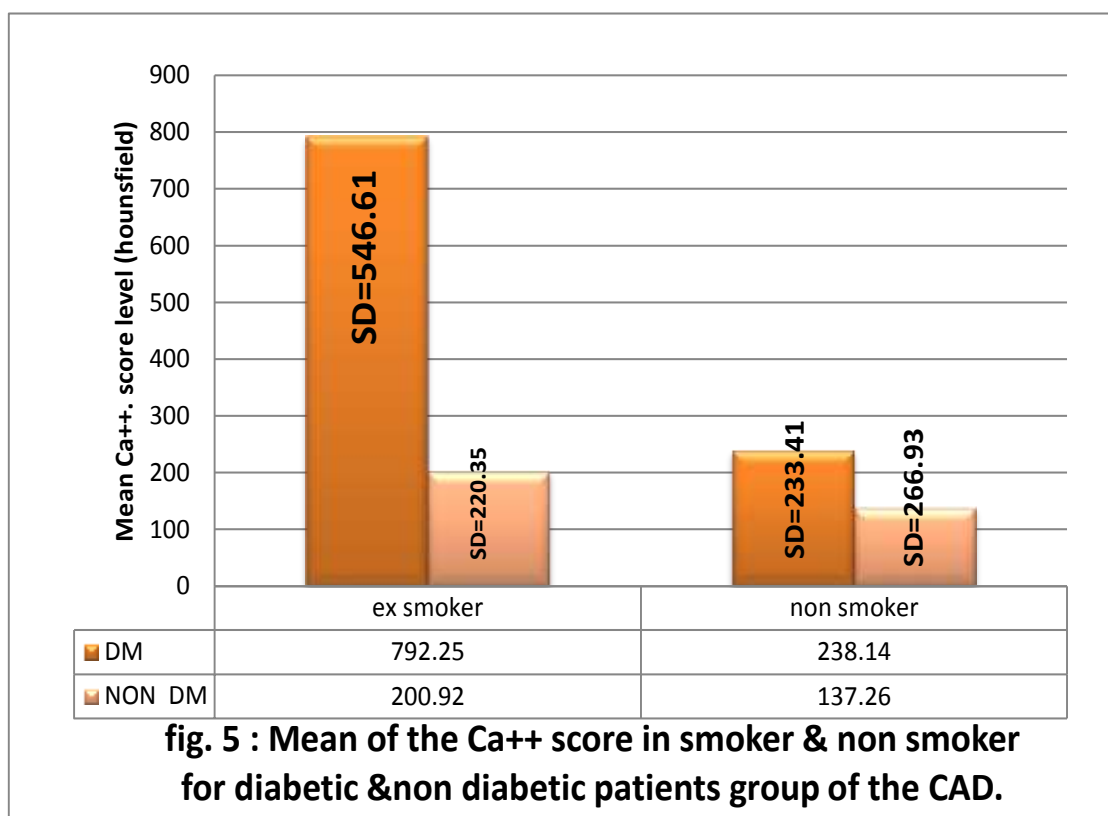
Table 9 the correlation of the ex smoker & non smoker with the lipid elements and Ca⁺⁺ score in the CAD patients.

Smoking	Number&%	Mean ±Sd.	Sign.(2tailed)	
TG	ex smoker Non smoker	23 48.9% 24 51%	181.18±60.92 179.29±76.51	0.901
LDL	ex smoker Non smoker	23 48.9% 24 51%	124.08±46.54 108.91±34.04	0.211
VLDL	ex smoker Non smoker	23 48.9% 24 51%	36.31±11.77 45.95±10.54	0.005
Total cholesterol	ex smoker Non smoker	23 48.9% 24 51%	223.00±77.96 200.00±57.40	0.258
HDL	ex smoker Non smoker	23 48.9% 24 51%	32.95±11.60 32.03±15.09	0.825
Ca ⁺⁺ score	ex smoker Non smoker	23 48.9% 24 51%	515.30±536.16 163.83±245.04	0.007

TG , triglyceride .LDL , low density lipoprotein .VLDL, very low density lipoprotein .HDL , high density lipoprotein .Ca⁺⁺ score , calcium score.SD, standard deviation . sign, significant

Smoking with diabetes: depending on the result of this study to see if there is association between smoking and diabetes risk factors in prediction of Calcium in the coronary arteries, there is significant increment in the mean of the

Ca⁺⁺ score in ex smoker and diabetic patient rather than ex smoker but non diabetic also in comprise to non smoker , diabetic and non diabetic as in figure (5) below. the highly increasing in the mean Ca⁺⁺ score in diabetic and ex smoker in comprise to non smoker whether diabetic or not indication the strong correlation between the smoking & diabetes mellitus in the process of the atherosclerosis.



Coronary computed tomography:

The table below show the relation of the CT. angiography whether normal or there is coronary arteries defect like stenosis , the normal CT angiography account 9 out of 48 patients (18%) while those have coronary arteries' defect

account 39 patient out of 48 (81%) by T. test , it show that there is significant difference in comparison between normal and +ve CT angiography in relation to the Ca⁺⁺ score which is (p<0.000). Also the VLDL, (p<0.03) as shown in table (10) .

Table 10 The relation of the CT angiography to the Ca⁺⁺ score & the lipid elements by T .test

	C.T . angio.	Number & %	Mean± SD	Sign.
Total cholesterol	normal	9 18%	194.44±25.60	.237
	Coron. Art. Defect	39 81%	212.30±76.09	
TG	normal	9 18%	152.21±39.33	.113
	Coron. Art. Defect	39 81%	183.02±84.35	
LDL	normal	9 18%	106.33±32.44	.336
	Coron. Art. Defect	39 81%	119.00±42.18	
VLDL	normal	9 18%	49.11±11.06	.033
	Coron. Art. Defect	39 81%	39.18±11.57	
HDL	normal	9 18%	32,00±10.27	.921
	Coron. Art. Defect	39 81%	32.41±13.99	
Ca ⁺⁺ score	normal	9 18%	47.77±113.45	.000
	Coron. Art. Defect	39 81%	430.20±490.52	

TG, triglyceride. LDL, low density lipoprotein. VLDL, very low density lipoprotein. HDL, high density lipoprotein. SD, standard deviation. CT. angio, computed tomographic angiogram. coron. Art., coronary artery. the Control: the control group account 18 subjects in comparison to the patients group which account 48 patients. The

comparison in the table below for the Ca⁺⁺ score and lipid elements between patients group and control group which show very high significant in the Ca⁺⁺ score & HDL (P<0.000) for both of them while the age, LDL, VLDL. p< 0.002, (p<0.006 , p< 0.004) respectively, and have no significant with total cholesterol and TG.

Table 11 Ca⁺⁺ score, lipid profile, age & weight comparison between patients group and control group by T. test

subjects	No.	Mean ± SD	Sign.
Age	48	59.79 ± 12.32	.002
patient control	18	48.44 ± 12.17	
Weight	48	82.16 ± 17.72	.731
patient control	18	80.50 ± 17.22	
Total cholesterol	48	208.95 ± 69.59	.369
patient control	18	195.77 ± 44.64	
TG	48	177.24 ± 78.50	.113
patient control	18	145.88 ± 66.39	
LDL	48	116.62 ± 40.53	.006
patient control	18	90.61 ± 28.81	
VLDL	48	41.04 ± 12.01	.004
patient control	18	29.55 ± 13.62	
HDL	48	32.33 ± 13.27	.000
patient control	18	43.66 ± 8.13	
Ca ⁺⁺ score	48	358.50 ± 468.49	.000
patient control	18	.000 ± .000	

TG, triglyceride. LDL, low density lipoprotein. VLDL, very low density lipoprotein. HDL, high density lipoprotein. SD, standard deviation. Ca⁺⁺ score, Calcium score. No., number. sign., significant

Discussion

Age mean, age distribution and sex:

The coronary calcium score is a strong predictor of mortality in the elderly that is independent of other cardiovascular risk factors but it is important to put their score into the context of normal for their age. The thinking is that plaque that occurs prematurely in younger individuals is more aggressive and hence more unstable than plaque that develops slowly with age. Although it is associated with aging, arterial calcification is NOT due to a

degenerative process and is NOT related to the aging process itself [6]

Women develop coronary atherosclerosis 10 years later than men, on average, and the occurrence of coronary calcification tracks with this later onset of CAD. These differences start to diminish at about age 60 [7].

These gender differences in occurrence of coronary calcium support the association of CAC with coronary atherosclerosis and underline the importance of age- and gender-specific reference points for CAC scoring [8].

The Weight: The weight have strong relation to the Ca⁺⁺ score as show in

table (4.4), in our study there is a link between calcium score and obesity or over weight that is agree with the study of Marsh, J.(2003). In our study the high significance correlation was in the male group but female side have no significance & that may be due to late presenting of the female patients and this agree with the study which said ,female presented with CAD 10 years later than male [7]. Regional body fat distribution has an important influence on metabolic and cardiovascular risk factors. Many prospective studies have shown that increased abdominal (visceral) fat accumulation is an independent risk factor for CAD, hypertension, stroke, and type 2 diabetes (DM2) [9].

Lipid profile: From our study we can conclude that correlation between lipid parameters ,weight and Ca^{++} score for the male patients group strongly significant correlation. The calcium score correlation to lipid parameters account ($p<0.001$) for the HDL which is the strongest correlation in this group (male group) this relation agree with the mean & SD which reached to 30.57 ± 11.20 .

That is consider the most important step for forming the atherosclerosis that predisposing for CAD .this fact in our study was improved and agree with study done by the journal of the clinical endocrinology and metabolism through Molly C. Carr and John D. Brunzell they said that, The changes in lipid metabolism seen with abdominal fat accumulation have been well characterized and include hypertriglyceridemia , reduced HDL cholesterol, and increased numbers of small, dense LDL particles.

Other features of the dyslipidemia of abdominal adiposity include elevated very low density lipoproteins (VLDL), and reduced HDL2, which are the large buoyant antiatherogenic subspecies of total HDL [5].

The risk associated with the levels of HDL-C and LDL-C was dependent on the level of triglycerides, and vice versa [10].

Individuals with the metabolic syndrome typically have normal LDL cholesterol levels, but their LDL particles are small and dense, and current lipid-lowering guidelines may underestimate their coronary artery disease (CAD) risk [9].

In turn the CAD In men more frequent than that in the female and the Ca^{++} deposition in the coronary artery is more than that of the female . In general, studies of the use of coronary calcium as a component of the CHD risk assessment include fewer women than men. Studies also vary according to the analysis of women as a separate subgroup. Because many of the existing studies have included women and men of similar age (typically between ages 50 and 60), the reported 10-year event rates for women have been predictably lower than in men.

Diabetes mellitus: In this group there are 17 patient out of 48 that is mean 35% are diabetic patient most of them are type 2 diabetes mellitus so we conclude that there is strong correlation between Ca^{++} Score & the age in diabetic patient ($p<.000$) also Ca^{++} Score with the total cholesterol , the LDL,HDL & VLDL ($p<0.004,p<0.02, P<0.05 , P<0.05$) respectively.

Numerous cross-sectional studies have documented that patients with diabetes have a higher prevalence and extent of coronary calcium than non-diabetic patients [11].

Recent study suggested that CAC scoring may be superior to established cardiovascular risk factors for predicting silent myocardial ischemia and short-term cardiovascular outcomes among stable, uncomplicated type 2 diabetic patients [3].

Patients with diabetes are considered to be in the highest risk category

according to the Adult Treatment Panel III guidelines [12,13].

Therefore, there is a clear clinical need to detect CAD at an early stage in DM patients who are at risk of both fatal and non fatal cardiac events before the onset of symptoms [14].

Smoking: the data obtained from smoker patients group which account 23 for ex. Smoker (48.9%) and non smoker about 24 patients out of 47 patients (51%). this data show the strong correlation of the VLDL, and Ca^{++} score ($p < 0.005$, $p < 0.007$) respectively ,that is explain how the smoking have strong influence on the CAD by playing important role in deposition of the Ca^{++} in the coronary arteries and through strong correlation with VLDL, our results agree with study done in CHEST journal / 131 / 5 / MAY, 2007 which said that ,Endothelial dysfunction is mainly caused by diminished production or availability of NO. It has been demonstrated that the serum concentration of nitrate and nitrite, metabolic end-products of NO, is significantly decreased in smokers relative to that in nonsmokers.

Although most of smoking-induced changes are reversible after quitting, some inflammatory mediators like CRP are still significantly raised in ex-smokers up to 10 to 20 years after quitting, suggesting ongoing low-grade inflammatory response persisting in former smokers [15].

Our study also reveal important results that explain the strong correlation between the diabetes and the smoking since there is significant increase in the lipid parameters level and Ca^{++} score in diabetic and ex smoker patients more than those who are non smoking but non diabetic, That is agree with study done in CHEST / 131 / 5 / MAY, 2007 Besides inflammation, proposed potential mechanisms by which smoking increases the risk of cardiovascular

pathology include several other pathways: vascular endothelial dysfunction, systemic haemostatic and coagulation disturbances, and lipid abnormalities [15].

Coronary computed tomographic angiogram: our study a prove there is high significant difference in between the two group(normal & coronary artery defect) in relation to the CAD the strong relation between the presence of the Ca^{++} in the coronary artery and presence of the CAD ($p < 0.000$) , this highly significant indicate the prediction of the CAD. that is agree with many studies which improve that purpose one of these studies is [3] which said that the Electron-beam computed tomography (EBCT) and multi-detector computed tomography (MDCT) are the primary fast CT methods for CAC measurement at this time.

Control: the control group account 18 (27%) out of 66 subjects in comparison to the patients group which account 48 (72%) patients out of 66 subjects. the significant difference between the patients group and the control group in the Ca^{++} score & HDL ($P < 0.000$) for both of them while the age, LDL, VLDL. $p < 0.002$, ($p < 0.006$, $p < 0.004$) respectively , and have no significant with total cholesterol and TG that is indicate the important role of the dyslipidemia & the Ca^{++} score in the process of the atherosclerosis then CAD.

Conclusions

1. The physiological study for CAD patients shows a significant increase of Ca^{++} score which is predicted by non contrast CTA & then confirmed this strong correlation by contrast CTA that shows the luminal arterial defects .
2. It shows a significant decrease or zero Ca^{++} score for normal individuals .
3. The study shows the significant association of the Ca^{++} score and the risk factors like smoking, hypertension,

diabetes mellitus, dyslipidemia, obesity or physical inactivity.

4. The biochemical study for CAD patients shows a significant increase of lipid parameters (total cholesterol , TG ,LDL ,VLDL) but HDL significantly decrease .

5. Lipid profile shows significant correlation with the Ca⁺⁺ score in CAD patients also strong correlation with each other that explains the mechanism of the atherosclerosis process.

6. Lipid profile shows a significant correlation with diabetes mellitus.

Recommendation

1.Measurement of coronary artery calcification is useful & sensitive mean to the early diagnosis of the CAD , although it does not reflects the degree of the artery stenosis but it predicts the CAD even in asymptomatic individuals.

It changes in the risk score of those who were regarded in the previous studies as low or intermediate to a high risk score according to Ca⁺⁺score, which give high degree of accuracy .

It can be used in early diagnosis of CAD and asses its severity so it decreased the morbidity & mortality of the patients but of more benefits in low or intermediate risk group or those presented with atypical presentation of the ischemic heart disease or in asymptomatic patients in addition to that it can be used in screening test.

2. The monitoring of the lipid profile is of great importance during the evaluation and care of CAD patients. Whenever abnormal level detected , all measures to restore the normal level should be started immediately, including the administration of antilipid drugs and diet restriction.

3. Early management of CAD especially those with dyslipidemia or atherosclerosis will provide optimal reduction of the morbidity & mortality rate. Maintaining treatment & life style modification within the normal range,

and enhanced their physical activity it gives good response.

References

1 -Agatston AS, Janowitz WR, Hildner FJ, et al. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;15:827–32 .

2-Steven M. Haffner, M.D., Seppo L Ehto ,M.D., Tapani Ronnema , M.D., Kalevi Pyorala ,M.D., And M Arkku L Aakso , M.D. mortality from coronary heart disease in subjects with and without type 2 diabetes. Volume 339 Number 4, The New England Journal of Medicine,201117-Steven M. Haffner, M.D., Seppo L Ehto ,M.D., Tapani Ronnema , M.D., Kalevi Pyorala ,M.D., And M Arkku L Aakso , M.D. mortality from coronary heart disease in subjects with and without type 2 diabetes. Volume 339 Number 4, The New England Journal of Medicine,2011

3-Philip Greenland, Robert O. Bonow, Bruce H. Brundage, Matthew J. Budoff, Mark J. Eisenberg, Scott M. Grundy, Michael S. Lauer, Wendy S. Post, Paolo Raggi, Rita F. Redberg, George P. Rodgers, Leslee J. Shaw, Allen J. Taylor, William S. Weintraub, Robert A. Harrington, Jonathan Abrams, Jeffrey L. Anderson, Eric R. Bates, Mark J. Eisenberg, Cindy L. Grines, Mark A. Hlatky, Robert C. Lichtenberg, Jonathan R. Lindner, Gerald M. Pohost, Richard S. Schofield, Samuel J. Shubrooks, Jr, James H. Stein, Cynthia M. Tracy, Robert A. Vogel, and Deborah J. Wesley *J. Am. Coll. Cardiol.* 2007;49:378-402.

4-Budoff, MJ. ; Raggi, P. (2001).Coronary artery disease progression assessed by electron –beam computed tomography . *AM.J.cardiol.*; jul 19:88(2-A):46E-50E.

20-Budoff, MJ.(2003).progress in cardiovascular disease. *Advanced*

- BodyScan of Newport; 46#2 (September /October):135-145.
- 5- Achenbach S, Ropers D, Hoffmann U, et al. Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. *J Am Coll Cardiol.* 2004;43:842-847.
- 6- Rumberger JA: progress in cardiovascular disease 2003: 46#2 (September/ October): 123-134
- 7- Janowitz WR, Agatston AS, Kaplan G, Viamonte M Jr. Differences in prevalence and extent of coronary artery calcium detected by ultrafast computed tomography in asymptomatic men and women. *Am J Cardiol* 1993;72:247-54.
- 8- Hoff JA, Chomka EV, Krainik AJ, et al. Age and gender distributions of coronary artery calcium detected by electron beam tomography in 35,246 adults. *Am J Cardiol* 2001;87:1335-9.
- 9- Molly C. Carr and John D. Brunzell, *J. Clin. Endocrinol. Metab.* 2004 89: 2601-2607, doi: 10.1210/jc.2004-0432
- 10- Vesa Manninen, MD; Leena Tenkanen, MSci; Pekka Koskinen, MD; Jussi K. Huttunen, MD; Matti Manttari, MD; Olli P. Heinonen, MD, DSci; and M. Heikki Frick, MD. Joint Effects of Serum Triglyceride and LDL Cholesterol and HDL Cholesterol Concentrations on Coronary Heart Disease Risk in the Helsinki Heart Study Implications for Treatment *Circulation* Vol 85, No 1 January 1992.
- 11- Raggi P, Shaw LJ, Berman DS, Callister TQ. Gender-based differences in the prognostic value of coronary calcification. *J Womens Health (Larchmt)* 2004;13:273- 83.
- 12- Raggi P, Shaw LJ, Berman DS, Callister TQ: Prognostic value of coronary artery calcium screening in subjects with and without diabetes. *J Am Coll Cardiol* 2004, 43:1663-1669.
- 13- Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). *JAMA.* 2001;285:2486-2497.
- 14- Daniele Andreini¹, Gianluca Pontone¹, Antonio L Bartorelli¹, Piergiuseppe Agostoni¹, Saima Mushtaq¹, Laura Antonioli¹, Sarah Cortinovi¹, Mauro Canestrari², Andrea Annoni¹, Giovanni Ballerini¹, Cesare Fiorentini¹, Mauro Pepi , Comparison of the diagnostic performance of 64-slice computed tomography coronary angiography in diabetic and non-diabetic patients with suspected coronary artery disease Andreini et al. *Cardiovascular Diabetology* 2010, 9:80,
- 15- Dilyara G. Yanbaeva, PhD; Mieke A. Dentener, PhD; Eva C. Creutzberg, PhD; Geertjan Wesseling, MD, PhD; and Emiel F. M. Wouters, MD, PhD, FCCP Systemic Effects of Smoking *CHEST* 2007; 131:1557-1566.