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RESEARCH ARTICLE

THE ROLE OF SOME DRUGS, GLYCEMIC CONTROL AND RENAL FUNCTION TEST IN PATIENT WITH CORONARY ARTERY CALCIFICATION

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ABSTRACT

Background: Coronary Computed Tomography Angiography (CCTA) is a rapidly growing, noninvasive imaging modality that developed quickly over the last decade, and its role for evaluation of Coronary Artery Disease (CAD) becomes of great promise with high diagnostic accuracy. The presence and extent of Coronary Artery Calcification (CAC) correlates with the overall magnitude of coronary atherosclerotic plaque burden and with the development of subsequent coronary events. Glycated hemoglobin (hemoglobin A1c, HbA1c, A1C, or Hb1c; sometimes also HbA1c or HGBA1C) is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. Glycated hemoglobin (hemoglobin A1c, HbA1c, A1C, or Hb1c; sometimes also HbA1c or HGBA1C) is a form of hemoglobin that is measured primarily to identify the average plasma glucose concentration over prolonged periods of time. This serves as a marker for average blood glucose levels over the previous 3 months prior to the measurement as this is the half life of red blood cells. It represents a reliable and moving average of blood glucose over preceding three months, Glycated haemoglobin has been the key measure of glycaemic control in diabetic patients for last two decades. It is considered to be the gold standard test, and most widely accepted test of glycaemia among clinicians and patients.

Subjects and Methods: This study was conducted at the Department of Biochemistry, College of Pharmacy, University of AL-Rasheed and at the Cardiologic Clinics of Ibn-Al-Bitar Hospital, Baghdad, Iraq, during the period from January 2015 to March 2015. The included 40 patients with ischemic heart disease were classified according to their obtained values of coronary artery Ca score into two groups: Group I (GII) involved 20 patients with coronary artery Ca score equal to 1- 399 (ASU), aged mean(54.95±1.764) with range (37-70 year), Group II (GI) included 20 subjects who have coronary artery Ca score=0.0 Agatston Score Unit (ASU), aged mean (45.80±2.163) range (31-65 year). These subjects were considered as control group. HbA1c, fasting serum glucose, lipid profile parameters and renal function test (Urea, Creatinine & uric Acid) were also measured by using spectrophotometric methods. All investigations were performed in patients of the two groups (GI and GII).

Results: The results of this study revealed significant increase in HbA1c significantly increased in GI compared with GII (P=0.019), with significant increased of (Urea, Creatinine & uric Acid) (P=0.001, p=0.004, p= 0.002) between groups. There was no significant differences in glucose & lipid profile between GI and GII in the these parameters. All patients of GII (with Ca Score =zero) taking statin & Aspirin as protective therapy compare to GI (13/20), (7/20) & which represent (65%) (35%) of this group, (p=0.004#, p=0.0001), these drugs play statically a significant role in treatment of Coronary Artery Calcification(CAC). There is non significant correlation between parameters of (lipid profile, glycemic control & renal function test) with ca- score in GI II(patients with mild to moderate degree of calcification).

Conclusion: (CAC) consider to be surrogate marker of atherosclerosis which has been associate with increase value of Hb A1c%, serum level of (Urea, Creatinine & uric Acid) in patients with mild to severe degree of calcification ,combine with high serum level of both glucose & VLDL. All these parameters may play important role in pathogenesis of atherosclerosis in patients with CAD, Statin, Aspirin have protective role in patients with CAD while B-blocker to increase of the survival in and improved QoL of these patients with mild to moderate degree of calcification in patients with Ca score =0.0 Agatston.

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INTRODUCTION

It is a non invasive tool for the detection and quantification of coronary artery calcium (CAC), a marker for atherosclerosis. The presence and extent of CAC correlates with the overall magnitude of coronary atherosclerotic plaque burden and with the development of subsequent coronary events, CAC occurs only in the setting of atherosclerosis, and is a better index of global atherosclerotic burden than stenosis severity (Budoff *et al*., 2009). Coronary calcium scans use a special X-ray test called computed tomography (CT) to check for the build up of calcium in plaque on the walls of the arteries of the heart (coronary arteries). This test is used to check for heart disease

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in an early stage and to determine how severe it is, .Also the Coronary calcium scans are also called cardiac calcium scoring (Maury and Brichard 2010). The presence of calcium in coronary arteries is known to be a strong indicator for coronary artery disease (CAD), It has been shown that quantification of coronary calcium enables the assessment of cardiac event risk stratification Dijkstra *et al*, described a method which determines the amount of coronary calcium from tomographic images : In order to use Ca-scoring as a useful diagnostic test, it must be demonstrated as accurate, clinically relevant and reproducible (Dijkstra *et al*., 2010). The recent study summarized that the CT coronary calcium score (CTCS) is used in both the diagnosis of coronary artery disease (CAD) and the prediction of cardiovascular events. Although substantial evidence is available on the incremental value of CTCS in predicting future cardiovascular events and mortality in asymptomatic individuals, but the diagnostic value in symptomatic patients is less clear (Genders *et al*., 2010). Coronary artery disease (CAD, is still a leading cause of morbidity and mortality in the world. There has been much interest in developing screening methods to identify those at risk of having a primary cardiac event. The presence of calcium in coronary arteries is almost always indicative of atherosclerotic plaque (but bears no relationship to plaque stability or instability (Grayburn, 2012).

HbA1C is the metabolic product of a stable connection of glucose to the N-terminal valise of the beta-chain of hemoglobin. It defines the average blood glucose level of the preceding 3 months and shows the result of diabetes treatment. Normally the average HbA1C level varies between 4% and 6.4%. Higher values are a sign of insufficient blood glucose control and poor metabolic control. An HbA1C target of 7.0% for the treatment of diabetes is generally accepted to lower the risk of long-term micro or macrovascular diabetes complications (Laakso *et al*., 2012). Hemoglobin A1C provides an average of blood sugar control over a six to 12 week period. When diabetes is not controlled, sugar builds up in blood and combines with haemoglobin, becoming "glycated. Studies suggest that the lower the haemoglobin A1C level, the lower the incidence of diabetic complications (eye, kidney, heart, blood vessel, and nerve disease). The American Diabetes Association (ADA) recommends keeping the haemoglobin A1C less than 7%. (Raval, Shah *et al*., 2011).

The main concern arising from some studies is that tight glycaemic control in individuals with or at high risk of CVD, increases the risk of death. When considered together with the other trials above, there remains a clear benefit of maintaining an HbA1c ≤7.0% for the majority of patients. Tight glycaemic control early in the diabetes disease process is desirable, and is likely to yield the greatest benefit for the prevention of micro- and macrovascular complications, as well as overall mortality. There is no evidence that maintenance of tight glycaemic control (e.g. HbA1c <6.0-6.5%) in a patient with long-standing well-controlled type 2 diabetes increases mortality risk. Attaining tight glycaemic control in advanced disease yields little, if any, benefit for macrovascular disease but this is still effective in retarding the development and progression of microvascular disease (Wright, Cull *et al*. 2006).

MATERIALS AND MATHODS

This study was conducted at the Department of Biochemistry, College of AL-Rasheed, and at the Cardiologic Clinics of Ibn-Al-Bitar Hospital, Baghdad, Iraq, during the period from January 2015 to March 2015. A total of 70 subjects with suspected Corenary Artery Disese (CAD) were encountered, 40 of them were included in this study. Those patients were investigated firstly for coronary artery calcium score and the percent of coronary artery stenosis (< 50 % as non obstrusctive lesion well and>50 % obstructive lesion) using Multi-Slice Computed Tomography Scanner (Brilliance 64, Philips Medical Systems). The included 40 patients with ischemic heart disease were classified according to their obtained values of coronary artery Ca score into two groups:

Group I (GII) involved 20 patients with coronary artery Ca score equal to 1- 399 (ASU), aged mean (54.95±1.764) with range (37-70) year.

Group II (GI) included 20 subjects who have coronary artery Ca score =0.0 Agatston Score Unit (ASU), aged mean (45.80±2.163) range (31-65 year). These subjects were considered as control group.

Careful Clinical examination, electrocardiographic (ECG), and a detailed history about other complicated diseases including diabetes mellitus (D M), hypertension, primary dyslipidemia, presence of previous heart events, family history were investigated and reported by aiding of Consultant Cardiologist. Inclusion criteria for CT. Angiography in patients with suspected CAD :atypical chest pain, ECG normal, Troponin test (-). Exclusion criteria included those patients with documanted CAD, and who were on statin derivatives treatment, atrial fibrillation, thyroid dysfunction (thyrotoxicosis) and/or abnormal serum TSH and Bronchial Asthma.

Coronary Artery Calcification Scoring (CACS)

It has as its primary goal of the early detection of Coronary Artery Disease (CAD). CAD is the most ommon cause of death. Calcification within the coronary artery wall can be anindicator of the presence of coronary artery disease. CACS can detect calcium in many people with CAD at an early stage, before the symptoms of heart disease – such as angina, heart attack or sudden death occur. The first symptom of CAD in up to 25% of people is sudden death. A high calcium score increases the probability that a person may have a clinically significant coronary narrowing in a least one vessel. In some people, additional investigations such as stress testing may be warranted.

CT Imaging

1 ECG: is monitored before and through the scan
2 Contrast: Uniform distribution of contrast media throughout study.
3 Beta-Blockers: Sometimes required to lower heart rate (< 60 beat per minute).

CT techniques

The protocol for coronary (CTA) includes 0.067 mm slice thickness cuts obtained at 0.64 – millimeter mm interval with a tracing marker placed upon the ascending thoracic aorta. Usually, 100 ml of nonionic contrast media is injected at 6ml/s through a large –bore intravenous access in the antecubital fossa. Reconstruction of the raw data was performed using the Philips work stations. Serial axial images, as well as the reconstructed multi planar and maximum intensity projections, were used primarily for diagnostic purposes. Three dimensional volume rendering was also used to help diagnose patients. The calculator of radiation dose (3-12) megahertz (Msir) (Shaw *et al.,* 2003). Three-five millilitre (ml) of blood was aspirated from peripheral vein of each subject before and after statin treatment course (GI and GII) after an overnight fasting state (10 -12 hour). The blood was divided into two parts, 2.5 ml was transferred into EDTA anti-coagulant tube with immediate mixing for HbA1c measurement, the second part was left to clot for 30 minute, and then the serum was obtained by centrifugation at 2500 X g for 15 minutes and stored at 20º C till the time of estimation. Glycated Hemoglobin (HbA1c) was measured by spectrophotometric method by using the kit provided from (Human Gesellschaftfùr Biochemical and DiagnosticambH Max-Planck-Ring 21.62505 Wiesbaden. Germany). Measurements of fasting serum glucose, total cholesterol, TG, HDL-cholesterol concentrations and the estimated levels of LDL-cholesterol, non-HDL-cholesterol and atherogenic index (AI) were performed using the methods reported by (Onat *et al.*, 2010).

Statistical Analysis of data was carried out using the available statistical package of SPSS-22 (Statistical Packages for Social Sciences- version 22). Data were presented in simple measures of mean and standard deviation (SD) values. The significance of difference of different means (quantitative data) were tested using Paired-t-test for difference of paired observations. Pearson correlation was calculated for the correlation between two quantitative variables with its t-test for testing the significance of correlation. Statistical significance was considered whenever the P-value was less than 0.05.

RESULTS

The mean of Ca score of patients of GI equal to (70.65±17.018) with range between (2-341) ASU, these patient had mild to moderate degree of calsification. Table1 reveals the clinical characteristics of patients. The mean age of GI was (54.95±1.764 year) with range (37-70 year) compared to (45.80±2.163 year) with range (31-65year) GII, respectively. The mean value of age of patients of GI was significantly higher than that of GII (P=0.002). All patients of GII taking statin & Asprin as protective theray compare to GI (13/20), (7/20) & which represent (65%) (35%) of this group, (p=0.004#, p=0.0001), these drugs play statically a significant role in treatment of Coronary Artery Calcification (CAC).

Table 2 reveals the mean (±SD) values of HbA1c, serum levels of glucose and lipid profile parameters. Serum levels of glucose and HbA1c % were measured as glycemic index of

Table 1. Clinical Characteristics & some important drugs used in treatment of CAC in patient of GI (with mild to moderate degree of calcification) & GII

		Group I	GII Normal	P value
		Mean+SEM (Range) No(%)	Mean+SEM(Range) No(%)	
Age (years)		54.95±1.764 (37-70)	45.80±2.163 (31-65)	0.002*
Gender (Male)		13(65%)	10(50%)	0.337 NS
Ca-score		70.65±17.018 (2-341)	Zero	-
Statin		13(65%)	20(100%)	0.004#
Statin type	Atrovastatin	1(5%)	-	
	Rosuvastatin	1(5%)	-	
Aspirin		7(35%)	20(100%)	0.0001#
BMI (Kg/m2)		34.00±3.524 (22.0-98.0)	30.75±1.233 (16.0-41.0)	0.389 NS

*Significant using Student-t-test for two independent means at 0.05 level
#Significant using Pearson Chi-square test at 0.05 level

*Significant difference between proportions using Pearson Chi-square test between GI and GII for the: Age (p=0.0002). #Significant using Pearson Chi-square test is statically signifigant between GI and GII for the using of the following treatment : Statin, p=0.004# and A sprin, p= 0.0001#
NS; not statically significant difference between GI, GII.

Table 2. Lipid Profile, Glycemic Control and Renal Function Test in patients with CAC

	Group I	Normal	P value
	Mean+SEM (Range) No(%)	Mean+SEM (Range) No(%)	
Glucose (mmol/L)	8.63±1.212 (5.2-28.64)	6.15±0.316 (3.6-9.2)	0.055 NS
HbA1C%	6.95±0.337 (4.1-9.0)	5.78±0.339 (2.4-8.1)	0.019*
Cholesterol (mmol/L)	4.35±0.214 (3.0-6.44)	4.78±0.215 (3.5-6.5)	0.170 NS
Triglycerides (mmol/L)	2.61±0.275 (0.7-4.7)	2.05±0.255 (0.9-5.08)	0.141 NS
HDL (mmol/L)	1.04±0.045 (0.7-1.3)	1.19±0.077 (0.6-1.8)	0.112 NS
LDL (mmol/L)	2.74±0.183 (1.50-4.5)	3.18±0.188 (1.9-4.84)	0.100 NS
VLDL (mmol/L)	0.52±0.056 (0.14-0.94)	0.41±0.051 (0.18-1.01)	0.161 NS
Atherogenic Index	0.43±0.074 (0.03-1.6)	0.46±0.035 (0.12-0.74)	0.684 NS
Blood urea (mmol/L)	6.89±0.417 (3.5-10.1)	5.10±0.270 (3.5-8.73)	0.001*
Serum creatinine	115.5±10.09 (45.7-186)	81.61±4.837 (43-120)	0.004*
Serum uric acid (mmol/L)	385.27±24.168 (204-578)	279.00±19.711 (104-410)	0.002*

*Significant using Student-t-test for two independent means at 0.05 level
#Significant using Pearson Chi-square test at 0.05 level

*Significant difference between proportions using Pearson Chi-square test between GI and GII for the: HbA1c% (p=0.019), urea (p= 0.001), creatinie (p=0.004) and uric acid (p=0.002.
NS; not statically significant difference between GI, GII.

patients enrolled in this study and found to be (8.63±1.212 mmol/l as mean±SD, 6.95±0.337 %) for GI, (6.15±0.316 mmol/l, 5.78 ± 0.339 %) for GII, respectively. The mean of serum glucose levels did not differ significantly among the studied groups (p=0.055, while the mean value of HbA1c was found to be significantly increased in GI compared with GII (P=0.019). The mean value of serum total cholesterol of patients of GI (4.35±0.214 mmol/l), GII (4.78±0.215 mmol/l) with no significant differences (p =0.170), The serum level of TG was non significantly increased in GI (2.61±0.275 mmol/l) in comparison to that of GII (2.05±0.255 mmol/l), (p=0.141). The mean value of serum HDL-C levels of GI was non significantly decreased in comparison with that of GII (1.04±0.045 mmol/l, 1.19±0.077 mmol/l, respectively; (P=0.112). Serum mean values of LDL-C levels were non signifigant decrease in GI compare to GII (2.74±0.183 mmol/l, 3.18±0.188 mmol/l, respectively).The serum level of VLDL-C was non significantly increase in GI (0.52±0.056 mmol/l) in compassion to GII (0.41±0.051 mmol/l), P=0.161). The mean value of atherogenic index of GI (0.43±0.074) was not significantly different in compare to GII (P=0.684). With respect to the values of renal function aasesment, This study show significantdifferance in serum level of the following : (urea, creatinine & uric acid) 6.89±0.417mmol/l, 115.5±10.09 mmol/l, 385.27±24.168 mmol/l) respectively, which significant increase in GI compare to GII (5.10±0.270 mmol/l, 81.61±4.837 mmol/l, 279.00±19.711 mmol/l), (P=0.001,p=0.004, p= 0.002*).

Finally This study demonstrated non sigmficant correlation between parameters of (lipid profile, glycemic control & renal function test) with ca- score in GI II(patients with mild to moderate degree of calcification**,**Also it show that the most of patients of GI were used (Concor10/20 (50%), Metaprolol 7/20(35%)and Plavex6/20 (30%)) for management of CAC through theire effect on degree of calcification .

DISCUSSION

The results this study demonstrated the evident effect of DM in progression of CAD as indicated by significant occurrence of DM in patients with high score of CAC. Raggi *et al*. documented that patients with diabetes have a higher prevalence and extent of coronary calcium than non-diabetic patients. These authors also found that coronary calcium predicted all-cause mortality in diabetics referred for fast coronary CT scanning; patients with diabetes have a greater increase in risk for mortality associated with a given degree of calcium than the non-diabetic patients (Raggi *et al*., 2004). Consistent with the observation that diabetics have a high burden of atherosclerosis, asymptomatic diabetic patients without known CAD have a similar prevalence of CAC as non-diabetic patients with obstructive CAD. Diabetic patients without any evidence of coronary calcification have a survival rate similar to non-diabetic patients with a zero calcium score during 5 years of follow-up (Greenland *et al*., 2007). CAD in patients with DM is often more advanced at the time of diagnosis compared with patients without DM. (Petcherski *et al*., 2013). Krul *et al*. study showed that many patients with DM already developed serious CAD at the time of examination. One explanation could be that DM had existed long before it was diagnosed, due to lack of typical symptoms of the disease, and cardiovascular damage could have developed meanwhile (Krul *et al*., 2014). The mean of serum glucose levels non significantly increase in GI compare to GII, However the mean value of HbA1c was found to be significantly increased in patients with mild to moderate degree of calcification GI compared with GII , These finding pointed to the significant link of HbA1c and the severity of CAC. hyperglycaemia is the main metabolic abnormality of diabetes. Hyperglycaemia with other metabolic abnormalities of diabetes e.g. Insulin resistance and dyslipidaemia (characterized by elevated triglycerides and low HDL) plays a role in inhibition of nitric acid (NO) production and excess production of reactive oxygen species in endothelium and vascular smooth muscles. This phenomenon is called oxidative stress when cellular production of reactive oxygen species (ROS) exceeds the ability to neutralise them by antioxidant mechanisms. This may be regarded as first step in production of atherosclerosis. ROS reduces nitric oxide level, causing endothelial dysfunction, it also increases expression of various intracellular adhesion molecules (Kaneto *et al*., 2010). In addition, they evaluated CAD patients and they suggest that HbA1c has a high sensitivity and specificity for predicting severe CAD (Ayhan, Tosun *et al*., 2012). Also, the HbA1c levels can predict the severity of coronary atherosclerosis in patients younger than 40 years. In this respect, the findings demonstrated the importance of maintaining an optimal HbA1c level for increased cardiovascular atherosclerosis, not only in diabetics, but also in non-diabetics (Ayhan, Tosun *et al*., 2012). With respect to the values of renal function amassment. This study show significant increase in serum level of the following : (urea, creatinine) in GI compare to GII these finding highlight the important role of urea & creatinine which play important role in progression of calcification reflect by increase the value of Ca score which explain degree of severity.

Recent study counter numerous therapeutic interventions have been tested in everyday healthcare, mostly targeting classical risk factors, such as uremia consider to appears to be pro-atherogenic. Given that the state of uremia involves the accumulation of a whole array of proteins Christian *et al*., 2011, While other study found that low creatinine was associated with higher risk of incident CAC, although creatinine was not associated with progression of existing CAC (Richard *et al*., 2007). Finally other study, observed a modest U-shaped relationship of creatinine with the risk of incident CAC. Specifically, those with creatinine levels of 1 mg/dL had the lowest risk, those with creatinine <1 mg/dL had significantly higher risk, and those with creatinine >1 mg/dL had higher risk, but not significantly so. Renal dysfunction has been associated with a greater amount and progression of coronary calcium (Bursztyn *et al*., 2003). There is demonstrated significant increase in serum level of uric acid in GI compare to GII, this finding support the important role of uric acid as early predictor of calcification. Recentally, Several studies have demonstrated a relationship between serum UA levels and CAC score, (Rodrigues *et al*., 2010) but other studies do not support these findings (Neogi *et al*., 2011). However, the principal mechanism that contributes to biological effects of serum uric acid in patients with

asymptomatic coronary artery disease without reducing left ventricular pump function is still to be understood. It has been postulated that serum uric acid plays a pivotal role in the pathogenesis of cardiovascular diseases affecting xanthine oxidase pathway that contributes to the production of active oxygen species generation with deterioration of cells membranes Reactive oxygen species contribute to vascular oxidative stress and endothelial dysfunction, which are associated with the risk of atherosclerosis, damages of both cardiomyocytes and vascular endothelium inducing disturbances of myocardial contractility and vasoconstriction also (Puddu *et al*., 2011). Other study disagree with finding of this study , which suggest that uric acid did not seem to be an independent risk factor for coronary artery calcium, although the prevalence and extent of coronary artery calcium increased along with the increasing trend of uric acid (Hui *et al*., 2013). Most recent study support a hypothesis that serum uric acid can contribute to influence of inflammatory activation, metabolic disorders, and calcium deposition in plaques and in vasculature. The evidence of microinflammation as an independent risk factor for the progression of CAC in HD patients (Demircan *et al*., 2014).

Most patients of GI were used Plavex for management of CAC through theire effect on degree of calcification .Some study suggest that, Atherosclerosis progresses by the pathologic sequence of subclinical plaque rupture, thrombosis, and healing. In this setting, increased platelet reactivity may lead to more extensive arterial thrombosis at the time of plaque rupture, leading to a more rapid progression of the disease. Alternatively, abnormal vessel wall biology with advanced atherosclerosis is known to enhance platelet reactivity. Therefore, it is possible that by either mechanism, increased platelet reactivity may be associated with greater atherosclerotic burden. Increased platelet reactivity on clopidogrel treatment, is associated with greater coronary artery atherosclerotic disease burden and plaque calcification (Chirumamilla *et al*., 2012). Despite aspirin's established role in the treatment of atherosclerotic vascular disease, considerable uncertainty exists regarding its most effective dosing strategy. More frequent adverse side effects occur with escalating aspirin dose however, it is not clear whether the relation between aspirin and efficacy is also dose-dependent, These are the first data to suggest that higher aspirindoses are associated with less frequent fatal ischemic events in patients with clinically manifest atherosclerotic vascular atherosclerosis At the time of that publication, we suspected that geographic region of enrollment confounded the association between lower aspirin dose and higher mortality (Herbert *et al*., 2008). The finding of this study improved that β-blockers are a particularly useful group of drugs in the treatment of patients with coronary artery disease and the appropriate use has led to increased survival and improved QoL of these patients. Some study explain the important of Beta-blockers in mangment of CAD, one of them suggested that Beta-blockers are a multiform group of drugs with multiple applications in the treatment of patients with cardiovascular disease. Disease, but especially in acute myocardial infarction and acute coronary syndromes. The administration to patients with coronary artery disease resulted in increased survival and improved QoL o these patients and therefore they are a key group of drugs for their management (Boudonas *et al*., 2010). Though, their actions differ, depending on their influence on these receptor and particularly they can present: a) blockade of both β1 and β2 receptors (non selective), b) selective blockade of β1 versus β2 receptors (in different degrees), c) blockade of β1 with concomitant stimulation of β2 receptors, partial agonist activity of the receptors (intrinsic sympathomimetic activity, ISA) and e) simultaneous blockade of all receptors (α, β1 and β2). The newer β-blockers have vasodilative action via either α-blockade (carvedilol) or nitric oxide (NO) production (nebivolol). Also, some of them are hydrophilic and some are lipophilic, which penetrate the blood-brain barrier causing nightmares (Boudonas *et al*., 2010).

Conclusion

The value of HbA1c% and serum level of (urea, Cr & uric acid) may be increase in patients with CAD who have mild to severe degree of calcification may reflect the cardio metabolic role of these parameters in development of vascular calcification. The present study that elevated serum UA levels are associated with presence of CAC, Serum Uric Acid as a Marker of Coronary Calcification in Patients with Asymptomatic Coronary Artery Disease, this study presumed that the dual paradoxical action of UA in CAC, therefore the relation is still unknown whether high serum uric acid is causally an independent risk factor, a consequence, or merely a marker for CAD through its association with the presence and severity of CAD. This study suggests relationship between UA and plaque characteristics, and further studies are required. UA is a general antioxidant in the body, and a high UA level is suggestive of oxidative stress, endothelial dysfunction, and slow coronary artery flow UA promotes vascular smooth muscle proliferation, and upregulates the expression of monocyte chemoattractantprotein-1 and platelet-derived growth factor Endothelial dysfunction is an important step in the development of atherosclerosis One of the goals of the pharmacological therapy in this study is to management patient with CAD, through increase their survival. This is achieved with the thrombolytic therapy, aspirin and β-blockers administration. Beta-blockers were the first group of drugs that led to increase of the survival in these patients. Also the present study indicate that it can be used to guide aspirin therapy regardless of whether patients "qualify" for primary prevention is recommended only for patients at elevated risk for a cardiovascular event.

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