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ATHEROSCLEROSIS AND METABOLIC DISORDERS

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Abstract

Indians demonstrate high coronary cardiovascular disease mortality, for the most part unexplained by typical risk factors and unidentified by risk stratification tools. Developments in technology permit us to analyse coronary arteriosclerosis non-invasively, so offering the potential to spot presence of coronary arteriosclerosis before it manifests clinically. Arteria coronaria calcification is closely related with total plaque burden and provides an assessment of coronary plaque burden. Cardiac muscle perfusion scintigraphy provides an estimate of cardiac muscle blood flow and so, severity of artery malady. Enhanced artery calcification and silent cardiac muscle ischaemia predict future risk of coronary cardiovascular disease mortality, autonomous of standard factors.

Inflammation could be a key factor in initiation and development of arteriosclerosis. Excessive sensitivity C-reactive protein (CRP) is an important marker of energetic infection and is taken into thought an impartial predictor of future vessel activities. Therefore, markers of subclinical atherosclerosis and inflammation may offer us with a tool for early identification of Indians in danger of coronary events, unidentified by traditional means that. However, majority of the info for such markers is from North yank and European populations, with no information evaluating the role of artery calcification, cardiac muscle perfusion scintigraphy and C-reactive protein in assessing the coronary cardiovascular disease risk in Indians.

Key words — Atherosclerosis, cardiovascular, calcification, infection, coronary, CRP.

I. Introduction

Coronary heart disease (CHD) is the single largest contributor to global mortality, with more than 13% of the total deaths (7,000,000), attributed to it in 2002 [1]. There are, however, distinct ethnic disparities in the incidence and mortality due to CHD. Indians express a high CHD attributed mortality. Data from the WHO expressed that this cluster contributed a quarter of the global CHD deaths, about the same number of CHD deaths as all the developed countries from Europe and America combined [1]. Indians currently constitute 22% of the global population and as a result of a high growth rate are expected to increase this proportion to 28% by 2050 [2]. As a consequence of an increasing population with a high inherent CHD risk, Indians are expected to contribute a staggering 40% of the global CHD burden by 2050 [2].

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Among Indians there appears to be a gradation of CHD risk which correlates with the level of urbanization. A study using analysis of ECG Q waves expressed a 4-5 fold higher prevalence of CHD in urban India compared with rural India [3] and data from countries such as Fiji, Singapore, USA, Trinidad and UK have expressed higher CHD mortality among South Asian migrants compared with native populations [3] [4] [5] [6] [7] [8] [9] [10]. Thus, it appears that there is increasing CHD mortality with the level of urbanization; with the greatest risk amongst Indians living overseas.

In the United Kingdom, Indians shaped the largest ethnic minority cluster and make up 4% of the entire population. Improved healthcare and fitness focus during the last thirty years has notably decreased CHD associated mortality in the widespread population within the United Kingdom, with CHD mortality rates of 132/100,000 for the period from1993-2003. Indians in the United Kingdom, but, retain to expose a 2-fold higher CHD mortality charge (241 out of one hundred thousand) for the same duration [4]. Due to lack of prospective data regarding CHD risk and mortality in Indians, the reasons for this excess remain poorly understood.

A. Risk factors

Wider scale prospective studies together with the Framingham cohort have diagnosed vital threat elements for CHD such as hypertension, hyperlipidaemia, low HDL, smoking and growing age. One limitation of studies to this point is the predominantly Caucasian base populace. This probably limits their use in different ethnic populations. But, latest worldwide registries which include INTERHEART [5], done amongst multi ethnic populations, suggest a crucial position for conventional threat elements in CHD throughout different ethnic clusters.

Existing data for migrant Indians expresses that despite high CHD rates among Indians sub clusters; they do not consistently exhibit elevated levels of conventional risk factors [6] [7]. For example, among migrant Indians the level of serum cholesterol, hypertension, as well as cigarette smoking rates in some cases can be equivalent to, or lower than a comparable Caucasian population [8] [9] [10]. This risk factor prevalence is in contrast to the high CHD mortality, leading to the belief that conventional risk factors do not contribute to the high CHD mortality rates observed among Indians [9].

However, observational studies performed among Indians express that serum cholesterol, blood pressure, smoking rates, and body mass index are substantially higher in urban compared to rural Indians [11]. This is consistent with their higher CHD prevalence [3]. Similarly, overseas Indians express higher prevalence of conventional risk factors as well as a higher CHD prevalence compared with their non-migrant siblings [12]. Within the UK, Indians express higher mean blood pressure levels, compared with Europeans [9] [13]. Cigarette smoking is observed to be twice as common in Bangladeshis [6], and the prevalence of hypertension increased two-fold in Sikhs [11], compared with Europeans. Thus, it is clear that the conventional risk factors are relevant in pathogenesis of CHD among Indians. However, given the lack of consistency in prevalence of risk factors among various South Asian sub clusters, and indeed compared with Europeans, the question whether such risk factors explain the excess risk of CHD seen in this population remains unanswered.

The reduction in C-reactive protein levels was considerably associated with rates of progression of hardening of the arteries assessed by means of IVUS, with a coefficient of correlation of 0.11 for

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each total fatty tissue volume and % adipose tissue volume (p = 0.02 and 0.01, correspondingly). The association was somewhat feeble however still important in a statistical procedure. The reductions in LDL-c levels were additionally interrelated with hardening of the arteries progression. However, solely a feeble connection was establish among changes in LDL-c and C-reactive protein levels [15]

B. Diabetes Mellitus

Type 2 diabetes mellitus is a famous risk issue for CHD, with associated improved atherosclerotic disorder and higher rates of cardiovascular morbidity and mortality as compared with non diabetics [14]. The danger from diabetes is considered to be as high as that attributed to a history of preceding coronary event i.e. it's far considered a CAD 'threat equivalent" Indians express an excessive prevalence of non-insulin structured diabetes.

Reported figures suggest prevalence of 2-5% in rural, 5-10% in urban, and almost 20% in UK South Asian, compared to 4% prevalence of diabetes among European men [6] [16] [17] [18] [19] [20] [21]. Furthermore, Indians express a higher prevalence of insulin resistance and its related metabolic abnormalities (elevated glucose levels, central obesity, glucose intolerance, elevated plasma insulin, increased triglycerides, raised PAI-1, and reduced high-density lipoprotein cholesterol), compared with Europeans populations [6] [9] [11] [22]. The reasons for this higher prevalence in Indians are not clear, and there are several theories postulated:

C. Genetic susceptibility

Indians appear to have genetic predilection for diabetes [23] [24], as well as metabolic abnormalities such as high triglycerides [25], abdominal obesity and insulin resistance [26]. Furthermore, there appears to be positive correlation with the level of urbanization. While the prevalence of diabetes is approximately 2% in rural settings, it rises dramatically to as much as 5-10% in urban communities within India [16] [18] [27]. Exposed to a greater level of urbanization, such as that seen among South Asian immigrants to the Western world, this increase is even more apparent. In the United Kingdom, the prevalence of diabetes in Indians approaches 15% to 20%, markedly higher than the 4% diabetes prevalent among Europeans [6] [12] [20] [28].

Among Indians, urbanization and growing income has been seen to be associated with an excess calorific intake. This is in part due to excess sugar and fat consumption, coupled with decreased physical activity and sedentary way of life [28] [29], and leads to obesity. The increased prevalence of obesity can potentially explain to the greater blood pressure [30], increased prevalence of diabetes [21] [31] and the increase in serum insulin, insulin secretion and decreased insulin sensitivity [32].

D. Stumpy birth weight

There appears to be an increased prevalence of insulin resistance and obesity observed among low birth weight babies. This is hypothesized to be due to a poor maternal nourishment causing an adaptive state in the fetus for survival under such conditions, both ante and postnatal [33]. Such changes become harmful when the postnatal environment is different from that predicted antenatal, i.e. over abundant nutrients and consequent obesity. The risk of future disease is thus greatest amongst those that subsequently become obese during adult life [34] [35].

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Preceding research illustrates that infants of low delivery weight have advanced CHD mortality in later life [34] [36] [37]. Low birth weight has been connected with an stepped forward chance of high blood stress, diabetes, insulin resistance, dyslipidaemia, with expanded hsCRP and fibrinogen levels in later life [38] [39]. But, the main contributing factor to the hazard of CHD on this populace is deemed to be insulin resistance and the danger of diabetes.

South Asian babies are small compared to other populations with an average weight of a newborn native Indian at 2.7 kg, 3.1 kg in UK Indians, 3.4 kg in CaucIndians, and 3.7kg in North American Indians [40] [41] [42] [43]. Furthermore, previous studies have expressed higher insulin levels at birth for Indians babies, compared with Europeans, after adjusting for birth weight.

Observations that the prevalence of CHD is sort of four-fold higher among Indians with beginning-weight <2.5kg, compared a birth-weight >3.2 kg [37], support the idea of low birth weight and its sequelae contributing to excess CHD hazard among Indians. Hence, the genetic predilection attached with the swap over in life-style will enhance the probability for emergent an insulin resistant kingdom or the metabolic syndrome [44], with the connected excessive CHD chance amongst Indians ethnicity.

Whilst the prevalence of diabetes has been expressed to be better amongst Indians [45] [46], compared with Europeans; studies from the UK and Canada have expressed diabetics Indians have an nearly 2 fold higher hazard of cardiovascular activities compared with Europeans diabetic subjects even after adjusting for different cardiovascular chance factors [9] [47]. The cause of this excess is as yet absolutely elucidated and it consequently seems workable that chance elements other than the formerly taken into consideration ones play an important role in the excess CHD threat Indians.

E. Inflammation

Atherosclerosis has often been termed as a chronic inflammatory process [48]. Inflammation is one of the key factors in initiating atherosclerosis and is instrumental in pathogenesis of vulnerable plaques [49] [50].

Inflammation causes damage to the endothelial membrane, resulting in increased endothelial adhesiveness and permeability allowing increased LDL entry into arterial intima. Furthermore, the endothelial damage causes release of cytokines and growth factors whose chemotactic nature stimulates monocyte-derived macrophages and T lymphocytes accumulate at the site of injury. Inflammation is thought to play a critical role in predisposing to plaque rupture by destabilization of the fibrous cap tissue, triggering majority of the episodes of coronary thrombosis [48]. this is supported via research completed in animal fashions as well as those amongst human cases of unexpected death, demonstrating expanded macrophage hobby in plaques which underwent rupture and subsequent thrombosis [51]. Furthermore, recent research in human subjects has shown markedly expanded irritation within energetic atherosclerotic plaques in carotid arteries [52] [53].

Indians exhibit a high occurrence of metabolic syndrome, diabetes, abdominal obesity and hypertension, with reduction in levels of cholesterol in high density lipoprotein [54] [55] [56] [57]. Presence of those threat elements is related to more systemic infection [58] [59]. Further, Indians moreover have precise elevated degrees of C-reactive protein (CRP) [60]. This is regular with experimental research which recommend that stomach adipose tissue is a major source of cytokines, in conjunction with IL-6, an important determinant of hepatic CRP synthesis [61] [62].

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CRP is a crucial marker of irritation, with elevated levels of CRP strongly related to improved macrophage activation within plaques [63] [64], and is taken into consideration an autonomous predictor of forthcoming cardiovascular proceedings [51] [65]. Multiplied concentrations of CRP were shown in both medical and epidemiological research to be related to atherothrombotic events. Those observations advise a better stage of systemic infection, in addition to inflammatory hobby inside plaque, amongst South Asian compared with Europeans. Hence, it increases the possibility that inflammatory mechanisms make a contribution as a minimum in part, to the elevated threat of CHD among Indians.

F. Homocysteine and risk of CHD in Indians

Homocysteine is a sulphur-containing amino acid, increasingly diagnosed as an unbiased threat aspect for vascular disorder [66] [67]. The mechanisms aren't properly elucidated; but, studies suggest that they may be mediated via A movement at the endothelium. Studies in man show that multiplied plasma homocysteine concentrations are associated with impaired endothelium-based vasodilatation, an early manifestation of atherosclerosis [68]. Furthermore, in vitro research unique that prolonged exposure of cultured endothelial cells to homocysteine impairs nitric oxide mediated inhibition of platelet aggregation [69] [70] further to particular seasoned-inflammatory cytokines related to migration recruitment of leukocytes throughout the vascular endothelium [71].

Current research has expressed higher concentrations of plasma homocysteine amongst Indians compared with Europeans [9] [22] [72]. As a consequence it is concept that extended homocysteine may additionally make a contribution to expanded CHD mortality in Indians.

G. Endothelial dysfunction

The vascular endothelium is an essential part of the atherosclerotic cascade. A regular endothelium continues homeostasis via a ramification of mechanisms which encompass manipulate of vascular tone, clean muscle cellular proliferation and migration, together with consequences on thrombogenesis and fibrinolysis [73] [74]. Endothelial disorder is an early manifestation of atherosclerosis, previous plaque formation, and proof of angiographic ailment.

one of the crucial mediators for the endothelium is nitric oxide [75], which performs an critical role in preserving vascular integrity with the aid of modulating vascular tone, permitting endothelial restore [76], inhibiting thrombosis and leukocyte adhesion, and by influencing easy muscle cell proliferation [77]. Research have expressed that brachial artery float mediated dilatation is basically mediated via nitric oxide released with the aid of the endothelium [76], and is inhibited with the aid of L-NMMA [75].

While endothelial damage and resulting dysfunction normally occurs due to damage by free radicals generated by various toxic stimuli, endothelium dependent dilatation is impaired even among healthy UK Indians compared to Europeans [75] [78]. Several explanations for the impaired endothelial function among Indians have been postulated, including the elevated levels of homocysteine and early atherosclerosis; however, the exact mechanism remains unknown and the dysfunction is unexplained by conventional atherosclerotic risk factors [78]. Thus, endothelial dysfunction due to reduced activity of endothelial nitric oxide could be a significant contributor to vascular injury in Indians.

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H. Lipoprotein (α)

Lipoprotein (α), formed from the combination of the protein apolipoprotein (α), has been diagnosed as an impartial danger factor for vascular disorder, which include CHD [79] [80]. Though the precise mechanisms underlying this dating are uncertain, in vitro research proposes that lipoprotein (α) may also impact low density lipoprotein cholesterol uptake and inhibit fibrinolysis [79]. Serum lipoprotein (α) concentrations are being decided at beginning through variations in the LPA gene. Lipoprotein (α) concentrations are reported to be higher in Indians compared to Europeans, reflecting the high CHD risk in this racial cluster [12].

I. Psychosocial and economic factors

Stress has been considered an important risk factor for CAD. The two most recognized components of this are socio-economic and psychosocial stress. These encompass a variety of things including low income, poor education, poor job prospects, stress at work and home, overcrowding in household, racial discrimination and social support. Such factors have been shown to be associated with CAD, a role which has been further emphasized by the INTERHEART registry [5]. INTERHEART, which was a global registry, concluded that stress factors could be account for up-to 32.5% of the population attributable risk for MI.

This, to install context, become best barely much less than the populace attributable threat for lifetime smoking (35.7%), and extra than that for high blood pressure (17.9%) or weight problems (20.0%). Whilst INTERHEART end up a flow sectional observational, and the effect is however to be tested in a functionality cohort, although the take a look at highlights the feasible significance of such factors.

There are three doable methods wherein strain can affect health. First, pressure may additionally have an effect on health associated behaviors together with alcohol, smoking habit, bodily pastime and weight-reduction plan, which in flip may have an effect on the risk of coronary heart disease [81] [82] [83] [84] [85]. That is because of this via the usage of exposing to stated pathogens. Second, it may influence access to and content of medical care. This is more relevant in a healthcare system which is not state funded and there is no free access to healthcare [86] [87]. Third, stress may cause direct patho-physiological changes i.e. direct causal effect.

While the first two concepts are fairly self explanatory, a number of mechanisms have been proposed to explain the direct pathological effect of stress in CAD. those consist of activation of the sympathetic frightened gadget, endothelial dysfunction causing release of pro-inflammatory cytokines and prothrombotic responses which in turn sell atherogenesis and plaque rupture [88] [89] [90]. These factors may act independently or have a cumulative effect. Indians score poorly on measures of psychosocial stress i.e. higher levels of chronic stress, depression, lower levels of social support and expressed lower socioeconomic status [91]. Indians also are more likely to live in regions with increased social and economic deprivation [92]. Further, studies have additionally suggested variability in get admission to healthcare among UK Indians examine with the local European population. Even as it seems that Indians may are seeking in advance medical recommendation for signs suggestive of angina [93], nearby research propose that Indians can be much less in all likelihood to be referred for similarly investigation and referrals [94] [95] [96]. The poor access to healthcare, however, is not supported by contemporary studies, at least in the UK,

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which suggest comparable access to healthcare for Indians compared with Europeans [97] [98]. Thus within the UK, Indians appear to exhibit at least a few if not all of the stress components related to CAD.

Stress has been expressed to be correlated to measures of subclinical atherosclerosis such as CAC [99] and silent myocardial ischemia [100], as expressed by our cluster among others. Therefore, to be able to check the function of such elements in CHD amongst Indians, our analysis also conducted a complete psychosocial assessment on a share of the contributors. The psychosocial evaluation changed into divided into measures of chronic stress, protective factors within the social surroundings, mental factors and health behaviours. Univariate and multivariate regression evaluation had been performed to be expecting the presence and amount of calcification, the usage of those factors.

The effects from our analysis expressed that Asian and Europe clusters have marked differences in mental characteristics, with better hostility and despair rankings seen amongst Asian. In UK South Asian men, the only predictor for presence of CAC in univariate analysis was age of finishing education, however once behaviors were adjusted for, this was reduced to non-significance. In UK South Asian women, the indicators of socio-economic status, household consumables and social deprivation, were negatively associated with presence of CAC on univariate analysis. The association between consumables and CAC was no longer significant once social deprivation had been taken into account. Even after adjustment for health behaviours and adiposity, social deprivation was negatively related to presence of CAC.

In European men, social deprivation was positively associated with presence of CAC, independent of age and other risk factors. In European women, the work stress variables of labour demands, attempt-reward imbalance, and process stress had been positively related to presence of CAC, even after controlling for age, health behaviours, and adiposity. This advised that expanded tiers of work pressure in ecu women have been associated with an extended chance of coronary calcification and CHD.

Analysis for the extent of CAC expressed that job demands and effort were positively related to the extent of CAC in South Asian men, independent of age and other confounding variables. In European men, hostility emerged as having a strong association with the extent of CAC, and this effect was not attenuated by adjustment for health behaviours such as smoking, BMI and WHR.

Thus while psychosocial factors were related to CAC, the effect was variable among Europeans and South Asian participants and not necessarily in the direction expected. While stress appears to be associated with a higher incidence of acute coronary events [101] [102] [103] and coronary ischemia [104], and while Indians are more exposed to stress; measures of stress are not consistently related to CAC i.e. calcified plaque. This is due to a complex interplay of factors including systemic inflammation, plaque characteristics and neuro-endocrine activation which mediate the cascade of atherosclerosis. Thus the measures of plaque burden alone are poorly correlated with risk due to stress. Thus Indians have a combination of biological, psychosocial and lifestyle factors, the combination of which is likely to be responsible for their excess CHD.

II. Risk stratification

CHD is a complex sickness with a multi-factorial etiology. The impact of sum of chance factors is therefore not necessarily linear but frequently exponential i.e. the risk of CHD due to the presence of two risk factors is not twice that a single risk factor, but can be three, four times or higher. Thus,

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while it is important to assess and address individual risk factors, identification of the total burden of risk is extremely important. Risk assessment is often considered the key step in effective management of clinical risk and does so by differentiating low from high risk patients, and thereby identifying those that would benefit most from aggressive risk factor management. The rationale underlies the stability among treatment depth and patient hazard being the more gain of drug publicity while the affected person's chance is high.

In view of the high mortality and morbidity from CHD, and the importance of early identification of subjects at high risk of cardiovascular events, several risk stratification tools have been formulated to calculating risk of CHD incidence and mortality. These include Framingham, FINRISK and SCORE among others [105] [106]. Majority of these equations use conventional risk factors including age, gender, hypertension, smoking and hyperlipidaemia to calculate a medium to long term risk of CHD event. While the factors implicated in clinical coronary events as discussed in the previous section i.e. plaque burden, plaque morphology and systemic factors, are to an extent a downstream effect of the CHD risk factors, it is known that while calculating a risk proportion for the general population is a great variation of observed CHD risk within each stratum [107]. Thus, there is still a large amount of risk left unaccounted-for by such tools. Furthermore, while these equations have accurately predicted CHD risk in Caucasian populations, they fail to accurately estimate the risk in Indians [108] [109]. One important reason for inaccurate estimation in diverse ethnic clusters is that the baseline date used to create these risk stratification tools is from a predominantly Caucasian population. This has several crucial implications: first, risk equations take into account the baseline CHD risk in a population and then add the effect of each risk factor to formulate an overall risk score and therefore predictions. Since the baseline CHD risk differs among ethnic clusters any and any calculation which does not take this into account will be not providing accurate estimates. Second, as expressed by INTERHEART [5], the relative effect of risk factors differs among ethnic clusters, i.e. there is a large variation in the relative importance of risk factors. Thus the percentage risk attributed to an individual risk factor while formulating the equations is likely to differ. Furthermore, most risk stratification tools use a categorical representation of risk factors i.e. cut offs for risk factors such as hypertension, blood sugar levels etc. While these cut off points are in themselves chosen arbitrarily even for the Caucasian population, these might be poor in assessing the risk in an ethnic population.

Third, the risk factors which were seen as significant among the baseline population i.e. Cauc Indians, were incorporated. These might not reflect the risk among diverse ethnic populations. While impaired vascular endothelial function [78], raised C-reactive protein [60] [110], elevated homocysteine [22] and lipoprotein (α) [9] [12] [111] are known risk factors for CHD, and are more prevalent amongst Indians than Europeans, they are not accounted for in the assessment of CHD risk using these equations. In order to accurately identify the overall risk for CHD mortality, the pathophysiology of atherosclerotic coronary plaques, as well as the pertinent local and systemic factors must be taken into account in addition to the standard risk factors.

Numerous landmark trials have confirmed the advantages of lipid-lowering treatment in primary and secondary deterrence of CVD, and have shown a transparent correlation between reduced LDL-c levels and reduced risk of CVD. Statins are the foremost common pharmacological lipid-lowering therapies due to their established clinical result. Statins effectively scale back LDL-c levels, the first treatment target. The higher the reduction of LDL-c obtained with statins,

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the bigger the reduction in progression or perhaps regression of coronary-artery disease plaque formation. Over the past twenty years, QCA and then IMT and IVUS have shown that statins alter the usual record of the malady. The clinical advantage of statins in all probability results from modification of the coronary-artery disease plaque via diminution of macromolecule content and action on inflammatory parameters.

III. Pathophysiology of CHD

A. Initiation

The main pathological feature in coronary artery atherosclerosis is the atherosclerotic plaque, which develops following a complex interaction between inflammation, cell necrosis and deposition of lipid within the arterial wall [48] [112] [113] [114] [115].

Endothelial dysfunction secondary to damage by free radicals generated by factors such as smoking, diabetes, hypertension and elevated LDL is often considered as the initial step in formation of plaque [48]. This endothelial damage results in increased endothelial adhesiveness and permeability allowing increased LDL entry into arterial intima. In addition, the endothelial damage causes release of cytokines and growth factors whose chemotactic nature stimulates monocyte-derived macrophages and T lymphocytes accumulate at the site of injury. These macrophages engulf the LDL, and activate the hallmark foam cells of atherosclerosis.

Once the endothelium is damaged, it activates a self sustaining cascade. Activated macrophages, T lymphocytes and oxidized LDL stimulate further release of inflammatory cytokines, chemokines, and boom factors which in flip stimulate migration and proliferation of smooth-muscle cells, in addition to hydrolytic enzymes. Such enzymes can set off similarly damage and focal necrosis, and cellular dying [116]. The end result of this cascade of events is accumulation of foam cells, migration and proliferation of smooth-muscle cells, and the ensuing formation of fibrous tissue over the necrotic lipid rich middle. This leads to formation of the characteristic atherosclerotic plaque.

Atherosclerotic plaques are further categorized into early and advanced lesions, divided according to their histological characteristics.

B. Early atherosclerosis

The density and distribution of the foam cells and the lipid particles is used to divide/separate early atherosclerosis into three stages:

1. 1. Type I lesion: This lesion composed of the first microscopically and chemically identifiable lipid deposits inside the intima and the cell reactions associated with such deposits. It characteristically consists of foam cells dispersed in small clusters within the arterial intima along with minimal amount of lipid deposits.

2. Type II lesion (fatty streak): It is the first grossly visible lesion in the development of atherosclerosis. The lesion characteristically consists of macrophage foam cells forming stratum, rather than isolated clusters. Also present in this stage are lipid-rich intimal smooth muscle cells, and a thin layer of extracellular lipid present in the intima. As it often appears as an irregular off white to yellow-white discoloration near the luminal surface of the artery, it is also called as the “fatty streak”.

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3. Type III lesion (pre-atheroma): This lesion is characterized by the presence of multiple extracellular lipid pools which lie below the layers of macrophages and macrophage foam cells. The lipid layer replaces intercellular matrix proteoglycans and fibres, and drive smooth muscle cells apart. As this stage lacks a well-delineated lipid core characteristic of an advanced atheroma, it is also named the "preatheroma"

C. Advanced atherosclerosis

Atherosclerotic lesions have been identified as advanced when accumulations of lipid, cells and matrix additives, occur in affiliation with intimal disorganization and thickening, deformity of the arterial wall. Such lesions are often related to complications including thrombosis, hematoma, and fissure. Such lesions are often associated with complications inclusive of thrombosis, hematoma, and fissure. Superior lesions may produce signs, however the lesions that precede them are clinically silent. Histologically, that is further divided into 3 levels:

4. Type IV lesion: This lesion is characterized by a presence of a thin intima and a large lipid core. It is considered to be the first atheroma or advanced atherosclerotic plaque and often forms the "thin cap fibro-atheroma". The plaque at this stage contains macrophage foam cells and isolated smooth muscle cells between the lipid core and the lesion surface, with none or minimal fibrous tissue. Such lesions are the most likely culprits in acute plaque rupture through disruptions of the lesion surface, haematoma or haemorrhage, and thrombotic deposits [51] [117].

5. Type V lesion: These lesions are formed after repeated subclinical rupture of plaque followed by healing and formation of fibrous tissue along with calcification. While the composition of the type V lesion can vary depending on the presence or absence of calcification and size of lipid core; type V lesions are generally more fibrosed and narrowed compared with type IV lesions with fibrous connective tissue in the intimal layer.

6. Type VI lesions are further subdivided according to the culprit pathology i.e. haemorrhage, fissures or thrombosis. While type VI lesions generally have the underlying morphology of type IV or V lesions, surface disruptions, haematoma, and thrombosis may be (although less often) superimposed on any other type of lesion and even on intima without an apparent lesion.

The lesions that constitute the histopathological classification are perceived as characteristic gradations or stages that span the transition from initial minimal changes to lesions associated with clinical manifestations. The resulting classification thus reflects the temporal history of the disease. In the early tiers of atherosclerosis the sequence is predictable, and uniform, however advanced lesions may also development in exceptional sequences, ensuing in numerous function lesion sorts and medical syndromes. This depends as much on plaque burden, as on plaque morphology and composition.

D. Plaque morphology

While a large coronary plaque burden portents obstructive coronary artery disease, studies now show suggest that lesion composition and morphology is a better predictor of clinical outcome than severity of stenosis [117] [118]. It has been observed that a high percentage of acute coronary events occur in vessels with angiographically moderately stenosis [119]. Furthermore, the recent studies using IVUS in subjects known to have < 50% stenosis of the coronary arteries by angiography, expressed bulk of new coronary events associated with lesions that were eccentric and contained relatively shallow but prominent echo lucent zones suggestive of large lipid collections

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[120]. They were similar in luminal obstruction to the plaques which remained stable, i.e. did not go on to have an acute event [121].

Histopathological and IVUS examination of atherosclerotic plaques associated with acute coronary events show two-thirds of acute events result from the rupture of the thin macrophage rich fibrous cap. The rupture of this thin inflamed fibrous cap exposes the necrotic core to the luminal blood and leads to thrombotic occlusion of the coronary vessel [51] [122]. These features support the concept that plaques that are prone to rupture express outward remodelling at the site of culprit lesions rather than luminal encroachment causing angiographically visible stenosis and have several important implications.

First, due to different remodeling patterns i.e. negative versus positive remodeling seen among coronary arteries with stable CAD versus acute coronary syndrome, angiography cannot necessarily risk stratify subjects well. Second, and extra importantly, the thrombogenic ability of a plaque relies upon to a massive degree on the composition of the underlying lesion or intima, as well as adjustments of shear and tensile forces to which the lesion or intima is uncovered, rather than presence of advanced stenosis.

E. Techniques for risk assessment

As discussed in previous sections, the risk of symptomatic clinical coronary events is an amalgamation of multiple risk factors. These include a) The degree of intra luminal coronary obstruction due to plaque burden, as well as plaque surface [123] [124], b) plaque characteristics/ morphology which can act as local thrombogenic agents [125], c) systemicrisk factors and thrombogenecity [126].

Plaque vulnerability can be quantified by the assessment of its morphological features such as thinning of the plaque cap, presence of a large lipid core, evidence of fissured plaque and a luminal stenosis >90%. While this has been traditionally through the assessment of the coronary arteries using invasive techniques such as intravascular ultrasound; the importance of assessment of atherosclerosis burden rather than individual plaque characteristics is also being recognized by means of non-invasive techniques [127] [128]. Modalities such as electron beam computed tomography allow detection of calcification within the coronary arteries, and thus quantify the atherosclerosis burden therein.

Arterial disease is rarely confined to one vascular bed, thus, ultrasonography of the carotid or an accessible peripheral artery, has been used to provide an insight into disease in the cerebral or coronary vasculature; a “pan arterial” assessment that represents subclinical peripheral, cerebral and coronary vascular disease. Moreover, assessments of plaque morphology undertaken in a peripheral artery are thought to be reflective of plaque characteristics coexisting in the coronary or cerebral vascular territories. The idea of plaque instability current simultaneously in more than one vascular beds has been described and echo lucent carotid plaques were proven to be strongly and independently associated with destiny coronary activities in patients with strong CHD [120].

While anatomical detection of atherosclerosis and quantifying plaque morphology is important, it's far equally crucial to evaluate blood thrombogenecity and systemic infection, identity of the “prone sufferers” [127], as opposed to just vulnerable plaque. Serum markers of atherosclerosis (ordinary lipoprotein profile), inflammation (excessive-sensitivity CRP), metabolic issues (homocysteine, triglycerides and blood glucose) and through coagulation issues (reduced anticoagulant factors,

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extended coagulation factors, component V Leiden, fibrinogen), are for that reason essential factors in assessing CHD danger.

However, in the absence of large scale population studies demonstrating the prognostic ability of many of the risk factors, they cannot be assimilated into population based risk stratification equations. As technology has advanced one possible improvement to such equations has been revealed in the form of ability to visualize coronary atherosclerosis and its functional significance, non-invasively before it becomes clinically manifest i.e. subclinical atherosclerosis.

F. Sub-clinical atherosclerosis

Traditional epidemiological studies have been instrumental in developing the concept of cardiovascular risk factors [180] and cardiovascular risk stratification. This is mainly through risk factors association with adverse outcomes such as death or myocardial infarction. However, there had been significant interest in shifting away from huge, final results based research to smaller research that use measures of subclinical atherosclerosis as their primary endpoint.

Studies based on such measures of atherosclerosis have several intrinsic advantages. It is much easier to examine the subclinical phase of atherosclerosis, when treatment or interventions have the most potential for altering the natural history of atherosclerotic disease. Treatment effects and behavioral changes are less likely to complicate interpretation of study results [188] [189].

Measurement of subclinical disease can enhance studies of CHD risk and prevention by allowing examination of its early stages, with other subclinical markers as well as associative factors. Eventually, when you consider that measures of subclinical atherosclerosis are typically quantitative, the strength to define threat institutions is a good deal advanced while as compared to outcome studies that use dichotomous end-factors, this is, presence or absence of disease. Thus, such studies have a potential to not only enhance the understanding of the disease process, but also risk assessments.

G. Imaging atherosclerosis

Imaging techniques can detect subclinical CHD by either directly visualizing the anatomical presence of arterial disease using markers such as coronary artery calcification imaging or by measuring the effects of disease processes through functional techniques such as myocardial perfusion imaging. Coronary artery calcification has been expressed to be an integral part of the atherosclerotic plaque by histo-pathological studies [129] and shows excellent correlation with total plaque burden [130]. Furthermore, numerous studies over the last decade have expressed the independent prognostic information provided by coronary artery calcium measurement in predicting CHD mortality, after adjustment for conventional risk factors. This thus identifies the actual “at risk” population and improve the predictive ability of risk stratification models i.e. subjects with high levels of coronary artery calcification have more events than those without even with the same prevalence of other CHD risk factors [131] [132] [133] [134] [135].

While coronary artery calcification imaging identifies presence of plaque and overall plaque burden, it does not allow quantification of obstructive coronary disease. Thus, while subjects at a higher risk of CHD are identified, the hemodynamic relevance and the resulting ischemic burden of the detected atherosclerotic lesions cannot be quantified. Myocardial perfusion imaging is a technique which has been validated for functional assessment of flow limiting lesions within coronary arteries. Myocardial ischemia as quantified by myocardial perfusion imaging has been

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shown to add prognostic benefit independent to known coronary anatomy in subjects with known coronary artery disease; as well as to risk assessed by traditional risk factors and risk factor equations among asymptomatic subjects [136] [137] [138] [139] [140].

At a population level, however, as the prevalence of silent myocardial ischemia varies according to the characteristics of the patient population screened, the prevalence of perfusion defects is understandably low in low risk asymptomatic populations with increasing prevalence as the risk of CHD increases. Thus, the importance of perfusion imaging is in delineating presence of flow limiting disease in subjects at a high risk of CHD. This risk could be quantified either through use of risk stratification equations or direct visualization of coronary plaque through calcium imaging.

Several studies have expressed the use of coronary artery calcium imaging as a screening test for presence of atherosclerotic plaque, with further quantification of flow limiting coronary disease through myocardial perfusion imaging [141] [142]. There appears to be an increase in prevalence and extent of ischemia with increasing coronary calcium.

Furthermore, these studies have expressed a greater mortality in subjects with higher levels of silent ischemia, with absence of inducible ischemia has been shown to identify subjects with very low (<1% per year) risk of coronary events [143] further supporting the rationale of such an approach. Thus a sequential imaging strategy using initial CAC imaging followed by selective MPI, combines the advantage of high sensitivity of CAC imaging with the specificity of MPI for predicting angiographic stenosis, thereby improving assessment of a high risk population for future CHD events [141].

IV. Coronary Artery Calcification

There were exceptional views concerning the mechanism of calcium deposition in the atherosclerotic plaques. while calcification became initially considered a passive system of adsorption or precipitation and simply a secondary impact of superior atherosclerotic degenerative methods; latest studies imply that atherosclerotic calcification is prearranged, degenerative processes that is mediated and regulated by using numerous organic elements [130] [144] inclusive of apoptosis of smooth muscle and foam cells, calcification-regulating proteins and lipoproteins

Apoptosis of smooth muscle cells and macrophages-derived foam cells is considered to be a critical trigger event in intimal vascular calcification [145], through formation of matrix vesicles [146]. Apoptotic bodies along with organelle-remnants from intimal vascular smooth muscle cells serve as nucleation sites for calcification. In vitro studies have expressed inhibition and stimulation of vascular calcification in cell cultures of human vascular smooth muscle cells [147], to be intrinsically affected by inhibition and stimulation of apoptosis. These observations further strengthening the argument for a role of apoptosis in calcification.

Calcification-regulating proteins consisting of osteopontin, matrix Gla protein phosphatase and bone sialoprotein seem to play an critical position of in the process of atherosclerotic calcification. They're expressed by using vascular smooth muscle cells, as well as by sure subsets of macrophages within plaque [148] [149] [150]. Subsistence of phosphorylated glycoprotein in atherosclerotic plaque and its nonexistence in ordinary arteries without atherosclerosis [151], at the facet of its co38 localization with web sites of early calcification within the plaque, provide aid for the feature of such reasons in vessel wall calcification.

Lipids and lipoproteins are considered important in the process of vascular calcification. Calcium

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and cholesterol crystals appear to co-localize within the lipid core [112], and oxidized lipids have been shown to induce osteoblastic differentiation and calcification of calcifying vascular cells [149]. This theory is further supported by studies which expressed spontaneous lipid accumulation within multicellular nodules prior to calcification, and stimulation of calcification in cultures of human vascular smooth muscle cells after addition of modified lipoproteins [150].

Calcification of the intima is thus the net result of a balance of these and many other factors, promoting and inhibiting calcification. Histopathological studies have expressed presence of calcified nodules containing calcium hydroxyapatite within atherosclerotic plaque in the form of microscopic deposits, as early as type III or IV wound, the "premature atherosclerotic injury". Calcification begins as small microscopic deposits within type III or IV lesions which coalesce to form large macroscopically detectable deposits as disease advances [152].

A. Repercussion of plaque

While the initiation and development of coronary artery calcification is multi-factorial, it is essentially connected with the technique of atherosclerosis, research have expressed that it exists simplest in arteries with an active atherosclerosis method and is absent in ordinary arteries [153]. There is but lack of consensus concerning the role of calcium in the atherosclerotic plaque as to whether or not it denotes a plaque as stable or prone to rupture.

Studies which have used fluoroscopy to assess segments of the coronary tree with known plaques morphology, have indicated a wide range of histological plaque types present at segments, showing a specific pattern of calcification [154]. While plaque ruptures were seen frequently in areas with speckled calcification, fragmented calcification, there was no evidence of rupture seen in segments without calcification. Healed or old ruptures were seen in areas of calcification, majority of the times associated with diffusely calcified areas [154].

As a consequence there are two interpretations of coronary artery calcification: First, at the personage lesion level, calcification will increase with progression of the plaque, frequently at later ranges i.e. IV or V. At some stage in these preliminary stages of calcification there is probably expanded pressure near the junction of the cap and the adjacent intima. It is right here, on the interface between an excessive and stumpy density tissue i.e. calcified and non-calcified atherosclerotic section, that plaque rupture often takes place. As a result throughout early ranges of plaque disease, with mild (specked, fragmented) calcification, it would make the plaque more vulnerable to rupture, given that the plaque itself is susceptible.

As the level of calcification will increase, the quantity of interfaces between rigid and distensible plaque initially might increase until the factor at which the rigid plaques combine. Calcification past this point can be related to decreasing hazard of plaque rupture, whereas the early or intermediate stages of calcification may without a doubt decorate plaque vulnerability, by creating more junctions.

A second interpretation could be at the level of the entire coronary tree i.e. for the patient rather than a single lesion. Thus, a heavily/ diffusely calcified plaque itself might not be prone to rupture, as supported by the stiffness and resistance to rupture expressed by plaques with extensively calcified plaques, compared with cellular lesions or normal vessel walls [155]. However, as it is a late feature in the cascade of atherosclerotic plaque formation, its presence implies the presence of early lesions elsewhere in the coronary tree.

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The capability lipid-wealthy and possibly risky plaques "the thin cap fibro-atheromas", with lower amounts of detectable calcification. for this reason at the same time as the position of calcification in the plaque is not but absolutely understood, in the absence of available technology that allows easy visualization of the vulnerable plaque thus limiting ability to assess the risk of rupture at the level of an individual lesion, coronary artery calcium scores are useful for detection of individuals at "high risk" of CHD [130] [156].

V. Calcification imaging

Coronary artery calcification can be detected by various modalities including fluoroscopy, CT, Xray, IVUS among others. Conventional fluoroscopy was the first technique for imaging coronary artery calcification [129], followed by digital subtraction fluoroscopy. Due to the poor spatial resolution, this technique was unable to detect small plaques and was taken over by high resolution EBCT, with its superior temporal and spatial resolution [157].

The guiding principle of CT scanners is the differential attenuation of X-rays passing through various tissues of the body. EBCT scanners do not have the disadvantage of having a mechanically rotating gantry, unlike conventional CT scanners. An electron gun shoots the electrons that are then guided electro-magnetically to Tungsten target rings. The X-rays thus produced then pass through the patient and are detected on two parallel rings housed within the gantry of the scanner. It takes 100 milli-seconds for one sweep of the target rings.

Considering that it requires 30-40 slices for an average 3 mm (range 1.5 – 6 mm) thickness to image the entire coronary tree, the entire heart can be imaged in 30 – 40 seconds. The radiation burden and motion artifacts are reduced by prospective gating, whereby the image acquisition is triggered at 60% - 80% of the RR interval on the ECG, corresponding to the end of diastole. The total radiation distributed during an analysis is roughly 0.8 – 1.3mSv.

The main disadvantage of using conventional CT i.e. multi-slice CT, rather than EBCT scanners was the use of a mechanically rotating gantry, and thus problems with movement and acceleration, necessitating much longer radiation exposure and poor temporal resolution. The gantry speed has improved through successive scanner generations and the current state of the art scanners can complete one rotation in 330 milli- seconds. However, they are still limited and any further improvement is unlikely due to problems in handling the huge gravitational force generated by the rapid movement of a relatively heavy gantry.

A few studies have compared the information variability between these two imaging modalities (EBCT and MSCT scanners) and they show good correlation between the scanners in terms of accuracy and reproducibility. Knez et al showed an excellent correlation between MSCT and EBCT for quantification of coronary calcium in 99 patients ($r = 0.994$, $p = 0.01$) [158]. Becker et al compared the two modalities in 100 patients and found a good correlation between the two types of scanners [159]. However, for the purpose of this study an EBCT scanner as used by Agatston et al, was used for all patients.

A. Computing Coronary Calcium

The calcium scoring system was first described by Agatston et al [157]. They described a scoring algorithm, which takes into consideration the area and density of the calcified plaque. Calcified foci within the outline of epicardial coronary arteries with a threshold area of 1 mm^2 and a threshold

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attenuation value of 130 Hounsfield units are scored.
CAC score is calculated as Maximal Computed Tomographic Number (MCTN) multiplied by area of calcification in mm^2. The MCTN is obtained from the maximal Hounsfield intensity within the area of interest**.** For example, if the peak X-ray density of a calcified lesion is 400 Hounsfield Units and the total area occupied is 10 mm^2, then the CAC score using this method is: 4x10 = 40 Agatston units (Au). The score for each lesion in a given patient is measured as shown above and all the scores are added to give the total CAC score for the patient.
While several other methods of calculating calcium mass such as volume based calcium quantification was proposed by Callister et al [160] and calculation of total calcium mass of as a product of lesion volume, average CT density of the lesion in Hounsfield units and a calibration factor [161]. However, there is no standardized reference database for the mass and volume scores as yet. Further, majority of the existing studies have used the Agatston score in relation to coronary artery calcification. Thus, it continues to be the clinical standard used in majority of the centres.

B. Predictive value of calcification

Coronary artery calcification provides us a non- invasive anatomic assessment of the coronary tree. Presence of calcium within coronary arteries is pathognomic of plaque [153] and portents extensive atherosclerotic disease with the amount/extent of calcification closely related to total atherosclerotic plaque burden [144] [153], and severity of coronary disease. It is a strong predictor of coronary events and all-cause mortality in subjects with and without known coronary disease.
The risk of coronary event and mortality rises with the presence of calcification (> 0 Au); with worsening prognosis as the amount of calcification increases, i.e. with increasing burden of calcification (>100 Agatston units and > 400 Agatston units) [134] [162].
Coronary artery calcification adds independent prognostic value to that offered by conventional risk factors alone [134] [163] [164], supporting its role as an important risk stratification tool. More recently, a report regarding the risk assessment for CHD in asymptomatic adults has also supported the independent prognostic ability of coronary artery calcification for CHD outcomes, beyond traditional risk factors [165].
Several large scale studies in the last few years have evaluated the role of coronary artery calcification in different ethnic populations [134] [166]. While the prevalence of coronary calcification is significantly higher in subjects with traditional cardiovascular risk factors such as hypertension, diabetes, obesity, infrequent exercise, previous smoking, and hypercholesterolemia [148] [166] [167] [168] [169], the presence and burden of calcification differs among different clusters [166] [170] [171]. This difference is most striking among African, American participants, who have been shown to express lower levels of calcification, despite demonstrating worse cardiovascular risk profiles, compared with North American Caucasian populations [166] [170] [172]. However, recent prospective studies suggest similar mortality among different ethnic clusters, for a given level of calcification [134] [164] supporting its role as a risk stratification tool.
When compared to the vast amount of information evaluating coronary calcification among CaucIndians, there may be little statistics concerning prevalence and quantity of coronary artery calcification in Indians. Till date, only two studies have evaluated the prevalence of coronary artery calcification among Indians. They both involved a small number of subjects, and expressed conflicting results. The first study was by Hatwalkar et al [173] with a cohort of 156 South Asian

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subjects. They expressed a similar prevalence of coronary artery calcification between younger Indians and North American Caucasian, but a higher prevalence and extent of calcification when compared to Hispanics, African Americans and Indians. Furthermore, the higher prevalence of expressed a higher prevalence of coronary artery calcification in Indians in the older age clusters. Apparently, this study had decrease charge of smoking among CaucIndians, with decrease rates of hypertension and diabetes amongst Indians than seen in maximum other research.

The exaggerated levels of total sterol, triglycerides, LDL, and low levels of high-density lipoprotein associated with fatness showing higher rate of risk of cardiovascular diseases in fatness. With many complications associated fatness, especially the macromolecular (lipid) abnormalities that are most appropriate reason for morbidity, and mortality, it's of importance, that the prevalence of fatness must be reduced. Early detection and deterrence of fatness and abnormal macromolecular (lipid) profile will facilitate to diminish morbidity, and mortality through rising public awareness concerning healthy life-style and food habit [174].

VI. Results

The research is being carried out assessments including coronary artery calcium, myocardial perfusion imaging and assessment of high sensitivity C-reactive protein for a cohort of asymptomatic Indians and Europeans men and women, aged 35 to 75 years. We found that: 1) 3 Coronary artery calcification rankings were carefully associated with age, blood pressure, gender, low density lipoprotein cholesterol, smoking habit, hypertension, and diabetes [188] [189]. 2) There have been no variations in both coronary artery calcification prevalence or suggest degrees of coronary artery calcification among Indians and Europeans, after adjustment for the measured cardiovascular threat elements. 3) Presence of diabetes and growing coronary artery calcification were impartial predictors for silent myocardial ischemia.4) South Asian ethnicity did not influence the prevalence or the extent of silent myocardial ischemia, after adjustment for conventional risk factors. 5) C-reactive protein levels did not correlate with measures of plaque burden. 5) South Asian ethnicity was an independent predictor of inflammation as seen by levels of high sensitivity C-reactive protein.

This effect become unbiased of, and remained full-size after adjusting for traditional cardiovascular hazard factors and novel elements connected to infection together with diabetes and indices of stomach obesity [174].

VII. Discussion

The idea for myocardial perfusion imaging is the visualization of myocardial blood flow. In regular coronary circulate, the blood go with the flow through coronary epicardial arteries is auto regulated via the arterial bed with a purpose to maintain tissue perfusion. Whilst a stenosis develops, the pressure throughout the lesion drops and consequently, the arteriolar bed progressively dilates to hold ordinary blood drift to the myocardium. But, this compensatory dilatation fails to deal with growing severity of stenosis, beyond a certain point. Those auto-regulatory and vasodilatory reserves are notion to reach a maximum when a stenosis past ninety percentage of the coronary artery diameter is present [175]. As the severity increases past this point the artery can no longer dilate to keep regular perfusion flow and pressure, ensuing in decreased myocardial blood flow at

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some point of relaxation.
However, for the duration of strain or hyperaemia, this disparity of blood float among a normal and a stenosed artery is apparent at a much decrease grade of coronary artery stenosis, beginning at approximately forty five percentage diameter stenosis and step by step worsening with growing severity of stenosis [176]. Accordingly a regular artery will dilate to a far more extent than a stenose done, causing accelerated blood flows. The ensuing differential uptake, between regions supplied by everyday and stenosed epicardial arteries forms the basis for myocardial perfusion imaging [177].
The stress may be carried out thru physiological approach or pharmacological means i.e. throughout exercise using a tread-mill or bicycle or through or pharmacological way i.e. the usage of either vasodilators along with adenosine or dipyridamole or inotropes such as dobutamine.
The myocardial blood flow is visualized through use of radioactive tracers such as Thallium -201, 99m Technetium Sestamibi or 99m Technetium Tetrofosmin which are extracted up by the myocardium and the resulting gamma rays captured by the gamma camera. The resulting differential uptake of radioactive tracer secondary to regional myocardial flow disparities, downstream of coronary arteries with significant obstructive coronary artery ailment at some point of strain produces myocardial perfusion defects.

A. Perfusion imaging

The usage of the approach of solitary photon emission computed tomography (SPECT) myocardial perfusion imaging is achieved. The affected person is injected with a radioactive isotope during stress, accompanied with the aid of picture acquisition; and then one by one undergoes photo acquisition and “redistribution” injection or “rest”. The isotope enters feasible myocardial cells and emits gamma or X-rays. A gamma digital camera on a moving gantry rotates across the patient, and detects light created while the gamma rays collide with the sodium iodide crystals in front of the digicam. The device software is programmed to know where camera head is in space and consequently can orient the coronary heart in area. The pix are then consolidated to produce a three-dimensional model of the source of activity by using either filtered lower back projection or iterative strategies. This version can then be viewed from any perspective, or sliced in any aircraft for ease of interpretation.
Myocardial perfusion scans constitute worldwide LV perfusion; consequently the dimensions, severity and reversibility of the perfusion defect suggest the total ischemic burden. Similarly a calculation of the range of segments concerned on a multi slice tomographic assessment of the SPECT study can be used to calculate each the quantity and severity of the ischemic myocardium. Small axis slices are used to assess the uptake in 4 massive quadrants (inferior, lateral, septal, and anterior). The LV is similarly divided into apical, mid and basal segments; the apex is classed with the vertical prolonged axis slice. The slices are divided into 17-20 segments. The uptake is scored in 5 grades (4, apparent absence of tracer uptake; three, extreme bargain of radioisotope uptake; 2, moderate; 1, equivocal; and 0, normal).
A representative approach of scoring the whole ischemic burden [178] is using summed stress, relaxation, and difference ratings (SSS, SRS, and SDS). SSS and SRS decided by the sum of scores of each phase from the pressure and relaxation pix, respectively at the same time as summed distinction scores (SDS) are decided through the sum of the difference among the SSS and the SRS. The SDS can then be converted to percent myocardium ischemia with the aid of dividing the SDS

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by 68—the maximum potential score (4 X 17)—and multiplying by means of one hundred [179]. While as SSS> 4 is considered suggestive of presence of myocardial ischemia (one hundred eighty), the share myocardium indicates severity of ischemia [181].

B. Clinical relationship

The Myocardial perfusion imaging is a properly verified method for the non-invasive diagnosis of coronary artery disease [90] [91]. Presence of ischemia on myocardial perfusion scintigraphy is strongly associated with destructive cardiovascular activities even inside the absence of ischemic signs and symptoms, whilst absence of ischemia on perfusion imaging predicts a low risk of cardiovascular occasions [182]. Numerous studies using this technique have been performed among subjects with known coronary disease, and have expressed independent prognostic value of total ischemic burden in predicting adverse clinical outcome independent of severity of coronary disease and concomitant risk factors [136] [137] [138].

More recently, the importance of flow limiting coronary disease as quantified by myocardial perfusion imaging have been assessed among asymptomatic populations including asymptomatic diabetics [139] [183], those with intermediate Framingham risk scores [139], as well in subjects with high coronary artery calcium scores [141] [142]. These studies have expressed a greater mortality in subjects with higher levels of silent ischemia, with absence of inducible ischemia has been shown to identify subjects with very low (<1% per year) risk of coronary events [143].

Previous studies have also expressed an increasing prevalence of stress-induced ischemia detected by MPS with increase in CAC, among patients suspected to have CHD [179] [184] as well as asymptomatic healthy subjects [140] [185]. However, while a high prevalence of silent myocardial ischemia is observed amongst subjects with CAC scores of more than 100 Agatston units, a negligible ischemia is expressed among subjects with low/ absent coronary calcium as expressed by our cluster and others [140] [179] [184] [186].

For that reason, MPS is frequently used at the side of CAC imaging; with CAC imparting a screening take a look at for detecting presence of atherosclerotic coronary artery disorder and MPS supplying a functional assessment of flow difficulty due to enormous obstructive coronary artery disorder.

Though there are ethnic differences in atherosclerotic burden as quantified via coronary artery calcification and related mortality, there's little statistics assessing ethnic difference in myocardial perfusion. Shaw et al [187], in an analysis carried out among African-American and North American caucasian populations, expressed a higher occurrence of slight to extreme myocardial perfusion defects amongst African-American compared with North American Caucasian. However, follow up from the study recognized a greater threat of events among African- individuals for all grades of perfusion abnormalities as compared with North American Caucasian, each before and after adjustment for cardiovascular hazard elements. However, there appears to be no information regarding prevalence of myocardial ischemia in relation to coronary artery calcification among Indians.

VIII. Conclusions

The Indians have a higher prevalence of CHD and a higher mortality attributable to CHD. The reasons for this excess are not fully known. The currently known risk factors and risk stratification

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equations do not accurately assess the CHD risk in this population. Thus, we have an ethnic population which forms a quarter of the global population, with one of the highest CHD rates globally, both increasing at an exponential rate [2]. Despite the need for aggressive risk assessment and management in Indians [188], there is a lack of accurate and robust risk stratification tools.

Coronary artery calcification imaging and myocardial perfusion scintigraphy are well validated techniques for the non-invasive diagnosis of coronary artery disease. While coronary calcium scores correlate strongly with the total atherosclerotic plaque burden and elevated coronary artery calcification portents advanced atherosclerotic plaque, MPS detects presence of a hemodynamically significant flow-limiting coronary stenosis. The combination of these two tests thus provides a comprehensive assessment of the coronary arterial system.

It is especially useful when studying the early stages of atherosclerotic disease i.e. before it becomes clinically manifest. Along with this there is a growing body of evidence to substantiate the role of inflammation in atherosclerosis initiation and progression. This has been measured through a variety of modality from intravascular imaging, plaque imaging to assessment of systemic inflammation using molecules such as CRP. However, majority of the studies using such techniques have been performed in predominantly European populations with little information available for Indians.

While traditional danger factor correlate nicely with markers of atherosclerosis, the better coronary heart disorder danger and mortality found in Indians isn't diagnosed through markers of atherosclerotic burden together with coronary artery calcification and myocardial perfusion scintigraphy. Indians have extended stages of infection as seen by using excessive sensitivity C-reactive protein tiers. C-reactive protein levels aren't correlated with coronary artery calcium. These findings endorse a position of factors together with systemic and plaque irritation, unrelated to and unmeasured with the aid of plaque burden assessment inside the better coronary heart disease mortality determined amongst Indians. The look at therefore indicates a position of potential risk stratification equipment reflecting the multisystem nature of CHD. Those will be a combination of clinical risk factors contributing in the direction of CHD, imaging of atherosclerotic plaque and assessment of plaque or systemic infection.

REFERENCES

[1] World Health Organization. World Health Report 2004: changing history.2004.
[2] United Nations, Department of Economic and Social Affairs, Population Division (2007). World Population Prospects: The 2006 Revision, Highlights, Working Paper No. ESA/P/WP.202. 2006.
[3] Chadha SL, Gopinath N, Shekhawat S. Urban-rural differences in theprevalence of coronary heart disease and its risk factors in Delhi. Bull WorldHealth Organ 1997;75:31-8.
[4] Harding S, Rosato M, Teyhan A. Trends for coronary heart disease and strokemortality among migrants in England and Wales, 1979-2003: slow declines notable for some clusters. Heart 2008;94:463-470.
[5] Yusuf S, Hawken S, Ounpuu S, et al. Effect of potentially modifiable riskfactors associated with myocardial infarction in 52 countries (theINTERHEART study): case-control study. Lancet 2004;364:937-52.
[6] Bhopal R, Unwin N, White M, et al. Heterogeneity of coronary heart disease risk factors in Indian, Pakistani, Bangladeshi, and European originpopulations: cross sectional study. BMJ

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

1999;319:215-20.
[7] Ye J, Rust G, Baltrus P, Daniels E. Cardiovascular Risk Factors among AsianAmericans: Results from a National Health Survey. Annals of Epidemiology2009;19:718-723.
[8] Forouhi NG, Sattar N, Tillin T, McKeigue PM, Chaturvedi N. Do known riskfactors explain the higher coronary heart disease mortality in South Asiancompared with European men? Prospective follow-up of the Southall andBrent studies, UK. Diabetologia 2006;49:2580-8.
[9] Anand SS, Yusuf S, Vuksan V, et al. Differences in risk factors, atherosclerosis, and cardiovascular disease between ethnic clusters in Canada: the Study of Health Assessment and Risk in Ethnic clusters (SHARE). Lancet 2000;356:279-84.
[10] Vallapuri S, Gupta D, Talwar KK, et al. Comparison of atherosclerotic riskfactors in Asian Indian and American Caucasian patients with angiographiccoronary artery disease. Am J Cardiol2002;90:1147-50.
[11] McKeigue PM, Shah B, Marmot MG. Relation of central obesity and insulinresistance with high diabetes prevalence and cardiovascular risk in Indians. Lancet 1991;337:382-6.
[12] Bhatnagar D, Anand IS, Durrington PN, et al. Coronary risk factors in peoplefrom the Indian subcontinent living in west London and their siblings in India.Lancet 1995;345:405-9.
[13] Whitty CJ, Brunner EJ, Shipley MJ, Hemingway H, Marmot MG. Differences in biological risk factors for cardiovascular disease between three ethnicclusters in the Whitehall II study. Atherosclerosis 1999;142:279-86.
[14] Beckman JA, Creager MA, Libby P. Diabetes and Atherosclerosis. JAMA:The Journal of the American Medical Association 2002;287:2570-2581.
[15] Syed Ibrahim MS. Alteration of Atherosclerotic Plague by Statin Therapy. International Journal of Core Engineering and Management, 2015: 2,(9): 1-13.
https://www.researchgate.net/publication/289378931_ALTERATION_OF_ATHEROSCLEROTIC_PLAQUE_BY_STATIN_THERAPY
[16] Ramachandran A, Snehalatha C, Latha E, Manoharan M, Vijay V. Impacts of urbanisation on the lifestyle and on the prevalence of diabetes in native Asian Indian population. Diabetes Res Clin Pract 1999;44:207-13.
[17] Ramachandran A, Snehalatha C, Shyamala P, Vijay V, Viswanathan M. Highprevalence of NIDDM and IGT in an elderly south Indian population with low rates of obesity. Diabetes Care 1994;17:1190-2.
[18] Wander GS, Khurana SB, Gulati R, et al. Epidemiology of coronary heart disease in a rural Punjab population--prevalence and correlation with various risk factors. Indian Heart J 1994;46:319-23.
[19] Singh RB, Beegom R, Mehta AS, et al. Prevalence and risk factors of hypertension and age-specific blood pressures in five cities: a study of Indian women. NKP Salve Institute of Medical Sciences, Nagpur, India.Five City Study Cluster. Int J Cardiol 1998;63:165-73.
[20] Mather HM, Keen H. The Southall Diabetes Survey: prevalence of known diabetes in Indians and Europeans. Br Med J (Clin Res Ed) 1985;291:1081-4.
[21] Huffman MD, Prabhakaran D, Osmond C, et al. Incidence of Cardiovascular Risk Factors in an Indian Urban Cohort: Results From the New Delhi Birth Cohort. Journal of the American College of Cardiology 2011;57:1765-1774.
[22] Chambers JC, Obeid OA, Refsum H, et al. Plasma homocysteine concentrations and risk of

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International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

coronary heart disease in UK Indian Asian and European men. Lancet 2000;355:523-7.
[23] Kooner JS, Baliga RR, Wilding J, et al. Abdominal obesity, impaired nonesterified fatty acid suppression, and insulin-mediated glucose disposal are early metabolic abnormalities in families with premature myocardial infarction. Arterioscler Thromb Vasc Biol 1998;18:1021-6.
[24] Zabaneh D, Chambers J, Elliott P, Scott J, Balding D, Kooner J. Heritability and genetic correlations of insulin resistance and component phenotypes in Asian Indian families using a multivariate analysis. Diabetologia 2009;52:2585-2589.
[25] Kooner JS, Chambers JC, Aguilar-Salinas CA, et al. Genome-wide scan identifies variation in MLXIPL associated with plasma triglycerides. Nat Genet 2008;40:149-151.
[26] Chambers JC, Elliott P, Zabaneh D, et al. Common genetic variation near MC4R is associated with waist circumference and insulin resistance. Nat Genet 2008;40:716-718.
[27] Singh RB, Bajaj S, Niaz MA, Rastogi SS, Moshiri M. Prevalence of type 2 diabetes mellitus and risk of hypertension and coronary artery disease in rural and urban population with low rates of obesity. Int J Cardiol 1998;66:65-72.
[28] Patel JV, Vyas A, Cruickshank JK, et al. Impact of migration on coronary heart disease risk factors: Comparison of Gujaratis in Britain and their contemporaries in villages of origin in India. Atherosclerosis 2006;185:297- 306.
[29] Mohan V, Shanthirani S, Deepa R, Premalatha G, Sastry NG, Saroja R. Intraurban differences in the prevalence of the metabolic syndrome in southern India -- the Chennai Urban Population Study (CUPS No. 4). Diabet Med 2001;18:280-7.
[30] Kannel WB, Brand N, Skinner 1 JJ, Jr., Dawber TR, McNamara PM. The relation of adiposity to blood pressure and development of hypertension.The Framingham study. Ann Intern Med 1967;67:48-59.
[31] Harris MI, Flegal KM, Cowie CC, et al. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. Diabetes Care 1998;21:518-24.
[32] Perley M, Kipnis DM. Plasma insulin responses to glucose and tolbutamide of normal weight and obese diabetic and nondiabetic subjects. Diabetes 1966;15:867-74.
[33] Hales CN, Barker DJP. The thrifty phenotype hypothesis: Type 2 diabetes. Br Med Bull 2001;60:5-20.
[34] Barker DJ, Osmond C, Forsen TJ, Kajantie E, Eriksson JG. Trajectories of growth among children who have coronary events as adults. N Engl J Med 2005;353:1802-9.
[35] Eriksson JG, Forsen T, Tuomilehto J, Winter PD, Osmond C, Barker DJ. Catch-up growth in childhood and death from coronary heart disease: longitudinal study. BMJ 1999;318:427-31.
[36] Godfrey KM, Barker DJ. Fetal nutrition and adult disease. Am J Clin Nutr 2000;71:1344S-52S.
[37] Stein CE, Fall CH, Kumaran K, Osmond C, Cox V, Barker DJ. Fetal growth and coronary heart disease in south India. Lancet 1996;348:1269-73.
[38] Lakshmy R, Fall CHD, Sachdev HS, et al. Childhood body mass index and adult pro-inflammatory and pro-thrombotic risk factors: data from the New Delhi birth cohort. International Journal of Epidemiology 2011;40:102-111.
[39] Barker DJ. The developmental origins of insulin resistance. Horm Res 2005;64 Suppl 3:2-7.
[40] Peabody JW, Gertler PJ, Leibowitz A. The policy implications of better structure and process on birth outcomes in Jamaica. Health Policy 1998;43:1- 13.

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

[41] Wen SW, Kramer MS, Usher RH. Comparison of birth weight distributions between Chinese and Caucasian infants. Am J Epidemiol 1995;141:1177-87.
[42] Steer P, Alam MA, Wadsworth J, Welch A. Relation between maternal haemoglobin concentration and birth weight in different ethnic clusters. BMJ 1995;310:489-91.
[43] Caulfield LE, Harris SB, Whalen EA, Sugamori ME. Maternal nutritional status, diabetes and risk of macrosomia among Native Canadian women. Early Hum Dev 1998;50:293-303.
[44] Jain P, Lahiri A. Metabolic syndrome: an evolving threat in the genesis of coronary artery disease. J Cardiometab Syndr 2007;2:190-7.
[45] Health Survey for England 2004- Office of National Statistics. 2004.
[46] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998;21:1414-1431.
[47] Mather HM, Chaturvedi N, Fuller JH. Mortality and morbidity from diabetes in Indians and Europeans: 11-year follow-up of the Southall Diabetes Survey, London, UK. Diabetic Medicine 1998;15:53-59.
[48] Ross R. Atherosclerosis--1 an inflammatory disease. N Engl J Med 1999;340:115-26.
[49] Davies MJ. A macro and micro view of coronary vascular insult in ischemic heart disease. Circulation 1990;82:II38-46.
50] Muller JE, Tawakol A, Kathiresan S, Narula J. New Opportunities for Identification and Reduction of Coronary Risk: Treatment of Vulnerable Patients, Arteries, and Plaques. Journal of the American College of Cardiology 2006;47:C2-C6.
[51] Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable0 plaque. J Am Coll Cardiol 2006;47:C13-8.
[52] Rudd JHF, Warburton EA, Fryer TD, et al. Imaging Atherosclerotic Plaque Inflammation With [18F]-Fluorodeoxyglucose Positron Emission Tomography. Circulation 2002;105:2708-2711.
[53] Davies JR, Rudd JH, Weissberg PL, Narula J. Radionuclide imaging for the detection of inflammation in vulnerable plaques. J Am Coll Cardiol 2006;47:C57-68]
[54] Tillin T, Forouhi NG, McKeigue PM, Chaturvedi N. The role of diabetes and components of the metabolic syndrome in stroke and coronary heart disease mortality in U.K. white and African-Caribbean populations. Diabetes Care\ 2006;29:2127-9.
[55] Deepa M, Farooq S, Datta M, Deepa R, Mohan V. Prevalence of metabolic syndrome using WHO, ATPIII and IDF definitions in Asian Indians: the Chennai Urban Rural Epidemiology Study (CURES-34). Diabetes Metab Res Rev 2007;23:127-34.
[56] Miller GJ, Beckles GLA, Maude GH, et al. Ethnicity and Other Characteristics Predictive of Coronary Heart Disease in a Developing Community: Principal Results of the St James Survey, Trinidad. Int. J. Epidemiol. 1989;18:808-817.
[57] Whincup PH, Nightingale CM, Owen CG, et al. Early emergence of ethnic differences in type 2 diabetes precursors in the UK: the Child Heart and Health Study in England (CHASE Study). PLoS Med 2010;7:e1000263.
[58] Rosito GA, Massaro JM, Hoffmann U, et al. Pericardial Fat, Visceral Abdominal Fat, Cardiovascular Disease Risk Factors, and Vascular Calcification in a Community-Based Sample: The Framingham Heart Study. Circulation 2008;117:605-613.
[59] Grundy SM, Brewer HB, Jr., Cleeman JI, Smith SC, Jr., Lenfant C. Definition of metabolic syndrome: Report of the National Heart, Lung, and Blood Institute/American Heart Association

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

conference on scientific issues related to definition. Circulation 2004;109:433-8.
[60] Chambers JC, Eda S, Bassett P, et al. C-reactive protein, insulin resistance, central obesity, and coronary heart disease risk in Indian Indians from the United Kingdom compared with European whites. Circulation 2001;104:145- 50.
[61] Yudkin JS, Stehouwer CD, Emeis JJ, Coppack SW. C-reactive protein in healthy subjects: associations with obesity, insulin resistance, and endothelial dysfunction: a potential role for cytokines originating from adipose tissue? Arterioscler Thromb Vasc Biol 1999;19:972-8.
[62] Mohamed-Ali V, Goodrick S, 1 Rawesh A, et al. Subcutaneous adipose tissue releases interleukin-6, but not tumor necrosis factor-alpha, in vivo. J Clin Endocrinol Metab 1997;82:4196-200.
[63] Aziz K, Berger K, Claycombe K, Huan R, Patel R, Abela GS. Noninvasive Detection and Localization of Vulnerable Plaque and Arterial thrombosis With Computed Tomography Angiography/ Positron Emission Tomography. Circulation 2008;117.
[64] Otake H, Shite J, Shinke T, et al. Relation Between Plasma Adiponectin, High-Sensitivity C-Reactive Protein, and Coronary Plaque Components in Patients With Acute Coronary Syndrome. The American Journal of Cardiology 2008;101:1-7.
[65] Ridker PM, Buring JE, Cook NR, Rifai N. C-Reactive Protein, the Metabolic Syndrome, and Risk of Incident Cardiovascular Events: An 8-Year Follow-Up of 14 719 Initially Healthy American Women. Circulation 2003;107.
[66] Clarke R, Daly L, Robinson K, et al. Hyperhomocysteinemia: an independent risk factor for vascular disease. N Engl J Med 1991;324:1149-55.
[67] Nygard O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE. Plasma homocysteine levels and mortality in patients with coronary artery disease. N Engl J Med 1997;337:230-6.
[68] Chambers JC, McGregor A, Jean-Marie J, Obeid OA, Kooner JS. Demonstration of rapid onset vascular endothelial dysfunction after hyperhomocysteinemia: an effect reversible with vitamin C therapy.Circulation 1999;99:1156-60.
[69] Stamler JS, Osborne JA, Jaraki O, et al. Adverse vascular effects of homocysteine are modulated by endothelium-derived relaxing factor and related oxides of nitrogen. J Clin Invest 1993;91:308-18.
[70] Blundell G, Jones BG, Rose FA, Tudball N. Homocysteine mediated endothelial cell toxicity and its amelioration. Atherosclerosis 1996;122:163- 72.
[71] Poddar R, Sivasubramanian N, DiBello PM, Robinson K, Jacobsen DW. Homocysteine Induces Expression and Secretion of Monocyte Chemoattractant Protein-1 and Interleukin-8 in Human Aortic Endothelial Cells : Implications for Vascular Disease. Circulation 2001;103:2717-2723.
[72] Chambers JC, Kooner JS. Homocysteine: a novel risk factor for coronary heart disease in UK Indian Indians. Heart 2001;86:121-2.
[73] Davignon J, Ganz P. Role of endothelial dysfunction in atherosclerosis. Circulation 2004;109:III27-32.
[74] Gonzalez MA, Selwyn AP. Endothelial function, inflammation, and prognosis in cardiovascular disease. Am J Med 2003;115 Suppl 8A:99S-106S.
[75] Joannides R, Haefeli WE, Linder L, et al. Nitric oxide is responsible for flow41

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

dependent dilatation of human peripheral conduit arteries in vivo. Circulation 1995;91:1314-9.
[76] Cubbon RM, Murgatroyd SR, Ferguson C, et al. Human Exercise-Induced Circulating Progenitor Cell Mobilization Is Nitric Oxide-Dependent and Is Blunted in South Asian Men. Arterioscler Thromb Vasc Biol 2010;30:878- 884.
[77] Drexler H. Nitric oxide and coronary endothelial dysfunction in humans. Cardiovasc Res 1999;43:572-9.
[78] Chambers JC, McGregor A, Jean-1 Marie J, Kooner JS. Abnormalities of vascular endothelial function may contribute to increased coronary heart disease risk in UK Indian Indians. Heart 1999;81:501-4.
[79] Scanu AM. The role of lipoprotein(a) in the pathogenesis of atherosclerotic cardiovascular disease and its utility as predictor of coronary heart disease events. Curr Cardiol Rep 2001;3:385-90.
[80] Shlipak MG, Simon JA, Vittinghoff E, et al. Estrogen and progestin, lipoprotein(a), and the risk of recurrent coronary heart disease events after menopause. JAMA 2000;283:1845-52.
[81] Deverts DJ, Cohen S, Kalra P, Matthews KA. The prospective association of socioeconomic status with C-reactive protein levels in the CARDIA study. Brain, Behavior, and Immunity 2012;26:1128-1135.
[82] A. Nandi MG, S. Subramanian. Association Among Socioeconomic Status, Health Behaviors, and All-Cause Mortality in the United States. Epidemiology 2014;25.
[83] Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. Annals of the New York Academy of Sciences 2012;1248:107-123.
[84] Judith B, Martin W, Joe K, Judith R, Raj B. Understanding influences on smoking in Bangladeshi and Pakistani adults: community based, qualitative study. BMJ 2003;326:962.
[85] Jacqui W. UK survey confirms link between deprivation and smoking. BMJ 2014;348.
[86] Statistics NCfH. National Center for Health Statistics Health 2012.
[87] Doty MM, Holmgren AL. Unequal Access: Insurance Instability Among Low-Income Workers and Minorities. TASK FORCE ON THE FUTURE OF HEALTH INSURANCE 2004.
[88] Girod JP, Brotman DJ. Does altered glucocorticoid homeostasis increase cardiovascular risk? Cardiovascular Research 2004;64:217-226.
[89] Burg MM, Martens EJ, Collins D, Soufer R. Depression predicts elevated endothelin-1 in patients with coronary artery disease. Psychosom Med 2010;73:2-6.
[90] Burg MM, Soufer A, Lampert R, Collins D, Soufer R. Autonomic contribution to endothelin-1 increase during laboratory anger-recall stress in patients with coronary artery disease. Mol Med 2011;17:495-501.
[91] Williams ED, Steptoe A, Chambers JC, Kooner JS. Psychosocial risk factors for coronary heart disease in UK South Asian men and women. J Epidemiol Community Health 2009:jech.2008.084186.
[92] Barakat K, Stevenson S, Wilkinson P, Suliman A, Ranjadayalan K, Timmis AD. Socioeconomic differentials in recurrent ischaemia and mortality after acute myocardial infarction. Heart 2001;85:390-4.
[93] Chaturvedi N, Rai H, Ben-Shlomo Y. Lay diagnosis and health-care-seeking behaviour for chest pain in Indians and Europeans. Lancet 1997;350:1578-83.
[94] Lear JT, Lawrence IG, Burden AC, Pohl JE.A comparison of stress test referral rates and

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

outcome between Indians and Europeans. J R Soc Med 1994;87:661-2.
[95] Lear JT, Lawrence IG, Pohl JE, 1 Burden AC. Myocardial infarction and thrombolysis: a comparison of the Indian and European populations on a coronary care unit. J R Coll Physicians Lond 1994;28:143-7.
[96] Kendall H, Marley A, Patel JV, et al. Hospital delay in South Asian patients with acute ST-elevation myocardial infarction in the UK. Eur J Prev Cardiol 2012.
[97] Black N, Langham S, Petticrew M. Coronary revascularisation: why do rates vary geographically in the UK? Journal of Epidemiology and Community Health 1995;49:408-412.
[98] Gene F, Angela MC, Patrick M, Shrilla B, Adam DT, Harry H. Ethnic differences in invasive management of coronary disease: prospective cohort study of patients undergoing angiography. BMJ 2002;324:511-516.
[99] Hamer M, O'Donnell K, Lahiri A, Steptoe A. Salivary cortisol responses to mental stress are associated with coronary artery calcification in healthy men and women. European Heart Journal 2010;31:424-429.
[100] Deanfield JE, Shea M, Kensett M, et al. Silent myocardial ischaemia due to mental stress. Lancet 1984;2:1001-5.
[101] Tofler GH, Muller JE. Triggering of Acute Cardiovascular Disease and Potential Preventive Strategies. Circulation 2006;114:1863-1872.
[102] Muller JE, Tofler GH, Edelman E. Probable triggers of onset of acute myocardial infarction. Clin Cardiol 1989;12:473-5.
[103] Moller J, Theorell T, de Faire U, Ahlbom A, Hallqvist J. Work related stressful life events and the risk of myocardial infarction. Case-control and case-crossover analyses within the Stockholm heart epidemiology programme (SHEEP). Journal of Epidemiology and Community Health 2005;59:23-30.
[104] Jiang W, Samad Z, Boyle S, et al. Prevalence and Clinical Characteristics of Mental Stress Induced Myocardial Ischemia in Patients With Coronary Heart Disease. Journal of the American College of Cardiology 2012;61:714-722.
[105] Conroy RM, Pyorala K, Fitzgerald AP, et al. Estimation of ten-year risk of fatal cardiovascular disease in Europe: the SCORE project. European Heart Journal 2003;24:987-1003.
[106] Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. Am Heart J 1991;121:293-8.
[107] Kannel WB, McGee DL. Composite scoring--methods and predictive validity: insights from the Framingham Study. Health Serv Res 1987;22:499-535.
[108] Bhopal R, Fischbacher C, Vartiainen E, Unwin N, White M, Alberti G. Predicted and observed cardiovascular disease in Indians: application of FINRISK, Framingham and SCORE models to Newcastle Heart Project data. J Public Health (Oxf) 2005;27:93-100.
[109] Kooner J, Chambers J. Conceptualising the causes of coronary heart disease in Indians In: Patel KC, Bhopal RS, eds.The epidemic of coronary heart disease in South Asian populations: causes and consequences. South Asian Health Foundation 2004.
[110] Chandalia M, Cabo-Chan AV, Jr., Devaraj S, Jialal I, Grundy SM, Abate N. Elevated Plasma High-Sensitivity C-Reactive Protein Concentrations in Asian Indians Living in the United States. J Clin Endocrinol Metab 2003;88:3773-3776.
[111] Anand SS, Enas EA, Pogue J, 1 Haffner S, Pearson T, Yusuf S. Elevated lipoprotein(a) levels

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

in Indians in North America. Metabolism 1998;47:182-4.
[112] Hirsch D, Azoury R, Sarig S, Kruth HS. Colocalization of cholesterol and hydroxyapatite in human atherosclerotic lesions. Calcif Tissue Int 1993;52:94- 8.
[113] Watson KE, Demer LL.The atherosclerosis-calcification link? Curr Opin Lipidol 1996;7:101-4.
[114] Tanimura A, McGregor DH, Anderson HC. Calcification in atherosclerosis. II. Animal studies. J Exp Pathol 1986;2:275-97.
[115] Tanimura A, McGregor DH, Anderson HC. Calcification in atherosclerosis. I. Human studies. J Exp Pathol 1986;2:261-73.
[116] Libby P. Inflammation in atherosclerosis. Nature 2002;420:868-874.
[117] Falk E, Shah PK, Fuster V. Coronary plaque disruption. Circulation1995;92:657-71.
[118] Johnson JM, Kennelly MM, Decesare D, Morgan S, Sparrow A. Natural history of asymptomatic carotid plaque. Arch Surg 1985;120:1010-2.
[119] Ambrose JA, Tannenbaum MA, Alexopoulos D, et al. Angiographicprogression of coronary artery disease and the development of myocardial infarction. J Am Coll Cardiol 1988;12:56-62.
[120] Honda O, Sugiyama S, Kugiyama K, et al. Echolucent carotid plaques predict future coronary events in patients with coronary artery disease. J Am Coll Cardiol 2004;43:1177-84.
[121] Yamagishi M, Terashima M, Awano K, et al. Morphology of vulnerable coronary plaque: insights from follow-up of patients examined by intravascular ultrasound before an acute coronary syndrome. J Am Coll Cardiol 2000;35:106-11.
[122] Hong MK, Mintz GS, Lee CW, et al. Comparison of coronary plaque rupture between stable angina and acute myocardial infarction: a three-vessel intravascular ultrasound study in 235 patients. Circulation 2004;110:928-33.
[123] Ellis S, Alderman E, Cain K, Fisher L, Sanders W, Bourassa M. Prediction of risk of anterior myocardial infarction by lesion severity and measurement method of stenoses in the left anterior descending coronary distribution: a CASS Registry Study. J Am Coll Cardiol 1988;11:908-16.
[124] Merino A, Cohen M, Badimon JJ, Fuster V, Badimon L. Synergistic action of severe wall injury and shear forces on thrombus formation in arterial stenosis: definition of a thrombotic shear rate threshold. J Am Coll Cardiol 1994;24:1091-7.
[125] van Zanten GH, de Graaf S, Slootweg PJ, et al. Increased platelet deposition on atherosclerotic coronary arteries. J Clin Invest 1994;93:615-32.
[126] Prins MH, Hirsh J. A critical review of the relationship between impaired fibrinolysis and myocardial infarction. Am Heart J 1991;122:545-51.
[127] Naghavi M, Libby P, Falk E, et al. From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: Part II. Circulation 2003;108:1772-8.
[128] Naghavi M, Libby P, Falk E, et al. From vulnerable plaque to vulnerable patient: a call for new definitions and risk assessment strategies: Part I. Circulation 2003;108:1664-72.
[129] Lieber A, Jorgens J. Cinefluorography of 1 coronary artery calcification. Correlation with clinical arteriosclerotic heart disease and autopsy findings. Am J Roentgenol Radium Ther Nucl Med 1961;86:1063-72.
[130] Sangiorgi G, Rumberger JA, Severson A, et al. Arterial calcification and not lumen stenosis is highly correlated with atherosclerotic plaque burden inhumans: a histologic study of 723 coronary artery segments usingnondecalcifying methodology. J Am Coll Cardiol 1998;31:126-33.

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

[131] Mohlenkamp S, Lehmann N, Greenland P, et al. Coronary artery calciumscore improves cardiovascular risk prediction in persons without indicationfor statin therapy. Atherosclerosis 2011;215:229-236.
[132] Erbel R, Mohlenkamp S, Moebus S, et al. Coronary risk stratification,discrimination, and reclassification improvement based on quantification ofsubclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. J Am Coll Cardiol 2010;56:1397-406.
[133] Polonsky TS, McClelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. JAMA2010;303:1610-6.
[134] Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor ofcoronary events in four racial or ethnic clusters. N Engl J Med 2008;358:1336-45.
[135] Greenland P, LaBree L, Azen SP, Doherty TM, Detrano RC. Coronary Artery Calcium Score Combined With Framingham Score for Risk Prediction inAsymptomatic Individuals. JAMA 2004;291:210-215.
[136] Iskandrian AS, Chae SC, Heo J, Stanberry CD, Wasserleben V, Cave V.Independent and incremental prognostic value of exercise single-photonemission computed tomographic (SPECT) thallium imaging in coronary arterydisease. Journal of the American College of Cardiology 1993;22:665-670.
[137] Marie P-Y, Danchin N, Durand JF, et al. Long-term prediction of majorischemic events by exercise thallium-201 single-photon emission computedtomography: Incremental prognostic value compared with clinical, exercisetesting, catheterization and radionuclide angiographic data. Journal of theAmerican College of Cardiology 1995;26:879-886.
[138] Shaw LJ, Hendel RC, Heller GV, Borges-Neto S, Cerqueira M, Berman DS.Prognostic estimation of coronary artery disease risk with resting perfusionabnormalities and stress ischemia on myocardial perfusion SPECT. Journal ofNuclear Cardiology 2008;15:762-773.
[139] Khandaker MH, Miller TD, Chareonthaitawee P, Askew JW, Hodge DO,Gibbons RJ. Stress single photon emission computed tomography fordetection of coronary artery disease and risk stratification of asymptomaticpatients at moderate risk. J Nucl Cardiol 2009;16:516-23.
[140] Anand DV, Lim E, Hopkins D, et al. Risk stratification in uncomplicated type2 diabetes: prospective evaluation of the combined use of coronary arterycalcium imaging and selective myocardial perfusion scintigraphy. Eur Heart J2006;27:713-21.
[141] Perrone-Filardi P, Achenbach S, MÃ¶hlenkamp S, et al. Cardiac computedtomography and myocardial perfusion scintigraphy for risk stratification inasymptomatic individuals without known cardiovascular disease: a positionstatement of the Working Cluster on Nuclear 1 Cardiology and Cardiac CT ofthe European Society of Cardiology. European Heart Journal 2010.
[142] Anand DV, Lim E, Raval U, Lipkin D, Lahiri A. Prevalence of silentmyocardial ischemia in asymptomatic individuals with subclinicalatherosclerosis detected by electron beam tomography. J Nucl Cardiol2004;11:450-7.
[143] Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusionSPECT. J Nucl Cardiol 2004;11:171-85.
[144] Rumberger JA, Simons DB, Fitzpatrick LA, Sheedy PF, Schwartz RS.Coronary Artery Calcium Area by Electron-Beam Computed Tomographyand Coronary Atherosclerotic Plaque Area : A Histopathologic CorrelativeStudy. Circulation 1995;92:2157-2162.
[145] Proudfoot D, Skepper JN, Hegyi L, Farzaneh-Far A, Shanahan CM,Weissberg PL. The role of

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

apoptosis in the initiation of vascular calcification.Z Kardiol 2001;90 Suppl 3:43-6.
[146] Kockx MM, De Meyer GR, Muhring J, Jacob W, Bult H, Herman AG.Apoptosis and related proteins in different stages of human atherosclerotic plaques. Circulation 1998;97:2307-15.
[147] Pati U, Pati N. Lipoprotein(a), atherosclerosis, and apolipoprotein(a) genepolymorphism. Mol Genet Metab 2000;71:87-92.
[148] Anand DV, Lahiri A, Lim E, Hopkins D, Corder R. The relationship betweenplasma osteoprotegerin levels and coronary artery calcification inuncomplicated type 2 diabetic subjects. J Am Coll Cardiol 2006;47:1850-7.
[149] Proudfoot D, Skepper JN, Hegyi L, Bennett MR, Shanahan CM, WeissbergPL. Apoptosis regulates human vascular calcification in vitro: evidence forinitiation of vascular calcification by apoptotic bodies. Circ Res2000;87:1055-62.
[150] Shanahan CM, Proudfoot D, Farzaneh-Far A, Weissberg PL. The role of Glaproteins in vascular calcification. Crit Rev Eukaryot Gene Expr 1998;8:357-75.
[151] Steinberg D, Witztum JL. Lipoproteins and atherogenesis.Current concepts.JAMA 1990;264:3047-52.
[152] Stary HC. The development of calcium deposits in atherosclerotic lesions andtheir persistence after lipid regression. The American Journal of Cardiology2001;88:16-19.
[153] Simons DB, Schwartz RS, Edwards WD, Sheedy PF, Breen JF, Rumberger JA. Noninvasive definition of anatomic coronary artery disease by ultrafastcomputed tomographic scanning: a quantitative pathologic comparison study.J Am Coll Cardiol 1992;20:1118-26.
[154] Burke AP, Weber DK, Kolodgie FD, Farb A, Taylor AJ, Virmani R.Pathophysiology of calcium deposition in coronary arteries. Herz2001;26:239-44.
[155] Richardson PD, Davies MJ, Born GV. Influence of plaque configuration andstress distribution on fissuring of coronary atherosclerotic plaques. Lancetn 1989;2:941-4]
[156] Fallavollita JA, Brody AS, Bunnell IL, Kumar K, Canty JM, Jr. Fastcomputed tomography detection of coronary calcification in the diagnosis ofcoronary artery disease. Comparison with 1 angiography in patients < 50 yearsold. Circulation 1994;89:285-90.
[157] Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M, Jr.,Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 1990;15:827-32.
[158] Knez A, Becker C, Becker A, et al. Determination of coronary calcium with multi-slice spiral computed tomography: a comparative study with electronbeam CT. Int J Cardiovasc Imaging 2002;18:295-303.
[159] Becker CR, Kleffel T, Crispin A, et al. Coronary artery calcium measurement:agreement of multirow detector and electron beam CT. AJR Am J Roentgenol2001;176:1295-8.
[160] Callister TQ, Cooil B, Raya SP, Lippolis NJ, Russo DJ, Raggi P. Coronary artery disease: improved reproducibility of calcium scoring with an electronbeam CT volumetric method. Radiology 1998;208:807-14.
[161] Hong C, Becker CR, Schoepf UJ, Ohnesorge B, Bruening R, Reiser MF. Coronary artery calcium: absolute quantification in nonenhanced and contrast enhanced multi-detector row CT studies. Radiology 2002;223:474-80.
[162] Vliegenthart R, Oudkerk M, Hofman A, et al. Coronary calcification improvescardiovascular risk prediction in the elderly. Circulation 2005;112:572-7.

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

[163] Arad Y, Spadaro LA, Goodman K, Newstein D, Guerci AD. Prediction of coronary events with electron beam computed tomography. J Am Coll Cardiol2000;36:1253-60.
[164] Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated withcoronary calcification: observations from a registry of 25,253 patients. J AmColl Cardiol 2007;49:1860-70.
[165] ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain. Circulation2007;115:402-426.
[166] Bild DE, Detrano R, Peterson D, et al. Ethnic differences in coronary calcification: the Multi-Ethnic Study of Atherosclerosis (MESA). Circulation2005;111:1313-20.
[167] Wong ND, Kouwabunpat D, Vo AN, et al. Coronary calcium and atherosclerosis by ultrafast computed tomography in asymptomatic men and women: relation to age and risk factors. Am Heart J 1994;127:422-30.
[168] 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 Cardiol1993;72:247-54.
[169] Goel M, Wong ND, Eisenberg H, Hagar J, Kelly K, Tobis JM. Risk factor correlates of coronary calcium as evaluated by ultrafast computed tomography. The American Journal of Cardiology 1992;70:977-980.
[170] Budoff MJ, Yang TP, Shavelle RM, Lamont DH, Brundage BH.Ethnic differences in coronary atherosclerosis. J Am Coll Cardiol 2002;39:408-12.
[171] Tang W, Detrano RC, Brezden OS, et al. Racial differences in coronary calcium prevalence among high-risk adults. The American Journal of Cardiology 1995;75:1088-1091.
[172] Doherty TM, Tang W, Detrano RC. Racial 1 differences in the significance ofcoronary calcium in asymptomatic black and white subjects with coronary risk factors. J Am Coll Cardiol 1999;34:787-94.
[173] Hatwalkar A, Agrawal N, Reiss DS, Budoff MJ. Comparison of prevalence and severity of coronary calcium determined by electron beam tomography among various ethnic clusters. Am J Cardiol 2003;91:1225-7.
[174] Syed Ibrahim MS. Atherosclerosis and Macromolecular Lipoproteins. International Journal of Emerging Research in Management &Technology, 2015: 4,(11): 95-97. https://www.researchgate.net/publication/285720789_Athrosclerosis_and_Macromolecular_Lipoproteins
[175] Wilson RF, Marcus ML, White CW. Prediction of the physiologic significance of coronary arterial lesions by quantitative lesion geometry in patients with limited coronary artery disease. Circulation 1987;75:723-32.
[176] Uren NG, Melin JA, De Bruyne B, Wijns W, Baudhuin T, Camici PG. Relation between myocardial blood flow and the severity of coronary-artery stenosis. N Engl J Med 1994;330:1782-8.
[177] Iskandrian AE, Heo J. Myocardial perfusion imaging during adenosine induced coronary hyperemia. Am J Cardiol 1997;79:20-4.
[178] Berman D, Hachamovitch R, Lewin H, Friedman J, Shaw L, Germano G. Riskstratification in coronary artery disease: implications for stabilization and prevention. Am J Cardiol 1997;79:10-6.
[179] Berman DS, Wong ND, Gransar H, et al. Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol

ISSN: 2348 9510
International Journal Of Core Engineering & Management (IJCEM)
Volume 2, Issue 10, January 2016

2004;44:923-30.
[180] Syed Ibrahim MS., Bajaj MM. and Singh VR., Physiological Quantum Chaos, *Proceedings of the SERC Schools on Chemical and Biological Applications of Lasers and Accelerators*, University of Poona, Jan. 3-15, 1994.
https://www.researchgate.net/publication/294090889_Physiological_Quantum_Chaos.
[181] Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation 2003;107:2900-7.
[182] Rozanski A, Gransar H, Wong ND, et al. Clinical outcomes after both coronary calcium scanning and exercise myocardial perfusion scintigraphy. J Am Coll Cardiol 2007;49:1352-61.
[183] Yamasaki Y, Nakajima K, Kusuoka H, et al. Prognostic Value of Gated Myocardial Perfusion Imaging for Asymptomatic Patients With Type 2 Diabetes. Diabetes Care 2010;33:2320-2326.
[184] He Z-X, Hedrick TD, Pratt CM, et al. Severity of Coronary Artery Calcification by Electron Beam Computed Tomography Predicts Silent Myocardial Ischemia. Circulation 2000;101:244-251.
[185] Wang L, Jerosch-Herold M, Jacob DR, Jr., Shahar E, Detrano R, Folsom AR. Coronary Artery Calcification and Myocardial Perfusion in Asymptomatic Adults: The MESA (Multi-Ethnic Study of Atherosclerosis) J Am Coll Cardiol 2006;48.
[186] Esteves FP, Sanyal R, Santana CA, Shaw L, Raggi P. Potential impact of noncontrast computed tomography as gatekeeper for myocardial perfusion positron emission tomography in patients admitted to the chest pain unit. Am J Cardiol 2008;101:149-52.
[187] Shaw LJ, Hendel RC, Cerquiera M, et al. Ethnic 1 differences in the prognosticvalue of stress technetium-99m tetrofosmin gated single-photon emission computed tomography myocardial perfusion imaging. J Am Coll Cardiol2005;45:1494-504.
[188] Bajaj M.M. and Ibrahim M.S.M., Impact of Body Pollutants on the Signal Transduction Conducted by G Proteins, *XXVII Annual Convention of the Indian College of Allergy and Applied Immunology* (AICON-94) April 2-5, 1994, p.33.
https://www.researchgate.net/publication/294090795_Impact_of_Body_Pollutants_on_the_Signal_Transduction_Conducted_by_G-Proteins
[189] Bajaj M.M. and Ibrahim M.S.M., Molecular and Cellular Chaos in Alcoholic Addiction and its Relationship with the Rossler Attractor: Collapse of Physiological Self-Organization, M.M.., International Conference on "The Criteria for Self - Organization in Physical, Chemical and Biological Systems" 11-17 June 1995, Souzdal (Russia). https://www.researchgate.net/publication/294090985_Molecular_and_Cellular_Chaos_in_Alcoholic_Addiction_and_its_Relationship_with_the_Rossler_Attractor_Collapse_of_Physiological_Self-Organization