HIGH SENSITIVE C-REACTIVE PROTEIN (hs-CRP) AND ITS CORRELATION WITH CLINICAL PROFILE AND ANGIOGRAPHIC SEVERITY OF CORONARY ARTERY DISEASE

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CERTIFICATE

This is to certify that the dissertation entitled "**High Sensitive C-Reactive Protein (hs-CRP) and its Correlation with Clinical profile and Angiographic Severity of Coronary Artery Disease** " is the bonafide original work of **Dr.C.ELAMARAN** in partial fulfillment of the requirements for D.M. Branch-II (CARDIOLOGY) examination of THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY to be held in August 2011.The period of post-graduate study and training was from August 2008 to July 2011.

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DECLARATION

I Dr. C.ELAMARAN , solemnly declare that this dissertation entitled, "**High Sensitive C-Reactive Protein (hs-CRP) and its Correlation with Clinical profile and Angiographic Severity of Coronary Artery Disease**" is a bonafide work done by me at the department of Cardiology, Stanley Medical College and Government Stanley Hospital during the period 2008 – 2011 under the guidance and supervision of the Professor and Head of the department of Cardiology of Stanley Medical College and Government Stanley Hospital, **Prof. Dr.G. KARTHIKEYAN. M.D., D.M.** This dissertation is submitted to The Tamil Nadu Dr.M.G.R Medical University, towards partial fulfillment of requirement for the award of D.M. Degree (Branch-II) in Cardiology.

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INTRODUCTION

The importance of risk factors such as diabetes mellitus (DM), hypertension, smoking, family history of premature heart disease, dyslipidaemia, male gender and advanced age has been established in predicting the risk of cardiovascular disease (CVD) by numerous studies.

However, in half of those who develop CVD, the established risk factors are largely absent. Identification of additional factors is therefore necessary to identify more effectively those at risk of CVD.

Over the past decade, identification of novel risk factors and predictors for CVD has been an area of major interest in preventive cardiology. Serum high sensitivity C-reactive protein hs-CRP, a biomarker of inflammation, has been shown to effectively predict the risk of adverse cardiovascular (CV) events consistently. Despite its initial role as a marker of vascular inflammation, recent research has established the role of CRP in atherogenesis. It is involved throughout the evolvement of atheromatous lesions and is detectable even in the initial phases of plaque development.

The currently available highly sensitive assays may detect serum CRP levels below 0.3 mg per liter. These lower range hs-CRP levels, previously considered normal, have in fact got the predictive capabilities for adverse CV events. It has in fact been found to be the single best predictor of future CV events among the conventional and novel risk factor.Its role is an important

adjunct to conventional risk factors was established in 2003 according to guidelines from the Centers for Disease Control and Prevention (CDC) and the American Heart Association (AHA) Serum hs-CRP levels may aid in identifying patients at high risk for a first CV event who might otherwise be missed by screening for lipids and other conventional risk factors alone. The landmark "Justification for the Use of statins in Primary prevention: an Intervention Trial Evaluating Rosuvastatin" (JUPITER) trial stressed the benefits of treating individuals with raised hs-CRP levels (despite normal LDL levels) by showing a 44% reduction in cardiovascular (CV) events. This break-through led to the recent approval by United States Food and Drug Administration (FDA) for the primary preventive role of statins in such individuals who are at high risk for future CV events. The Gensini scoring system is a valuable aid to estimate the severity of CAD according to angiographicindings. The calculation is based on the evaluation of number of stenotic segments along with their respective degrees of luminal narrowing and localization within the coronary tree. Coronary atherosclerosis is the main substrate of adverse coronary events and serum hs-CRP levels may act as an indirect measure of its extent within the coronary vasculature. This may prove to be an inexpensive screening tool in CV risk assessment. Limited information is available regarding the correlation between serum hs-CRP levels and the extent and severity of CAD, as assessed by Gensini score in patients submitted to coronary angiography. We carried out a study to assess the correlation between plasma hs-CRP levels with severity of coronary atherosclerosis.

AIM OF THE STUDY

1. To correlate the levels of hs-C reactive protein with angiographic severity of coronary artery stenosis in patients with IHD admitted for CAG in Stanley Medical College.

2. To correlate the levels of hs-C reactive protein with vessel score.

3. To correlate the levels of hs C reactive protein with stenosis score.

REVIEW OF LITERATURE

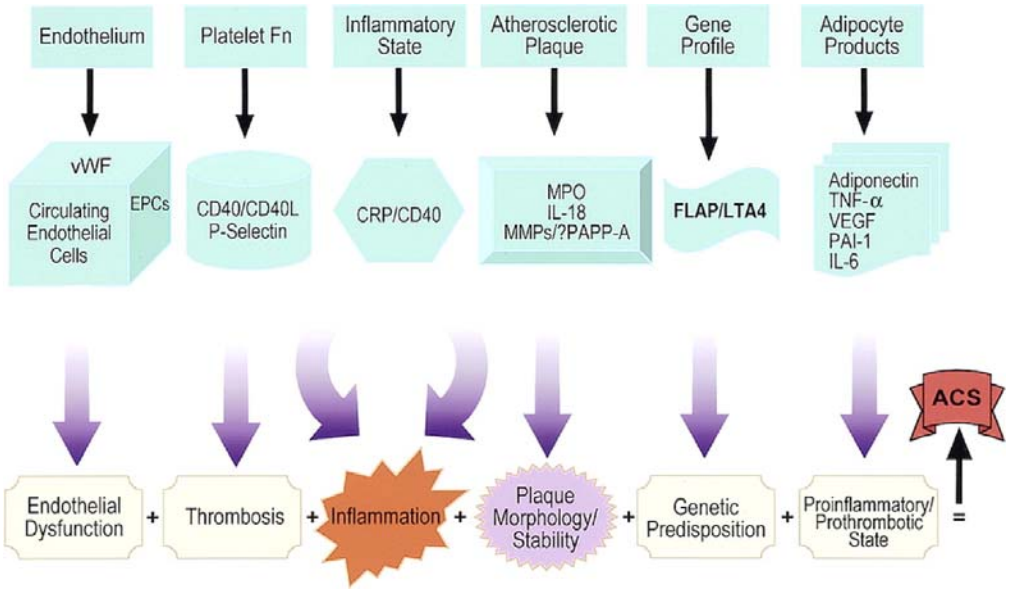
INTRODUCTION TO INFLAMMATION IN ATHEROGENESIS

A role for inflammation has become well established over the past decade or more in theories describing the atherosclerotic disease process.[1,2] From a pathological viewpoint, all stages, ie, initiation, growth, and complication of the atherosclerotic plaque, [3,4] might be considered to be an inflammatory response to injury.

The major injurious factors that promote atherogenesis - cigarette smoking, hypertension, atherogenic lipoproteins, and hyperglycemia are well established. These risk factors give rise to a variety of noxious stimuli that elicit secretion of both leukocyte soluble adhesion molecules, which facilitate the attachment of monocytes to endothelial cells, and chemotactic factors, which encourage the monocytes' migration into the subintimal space.

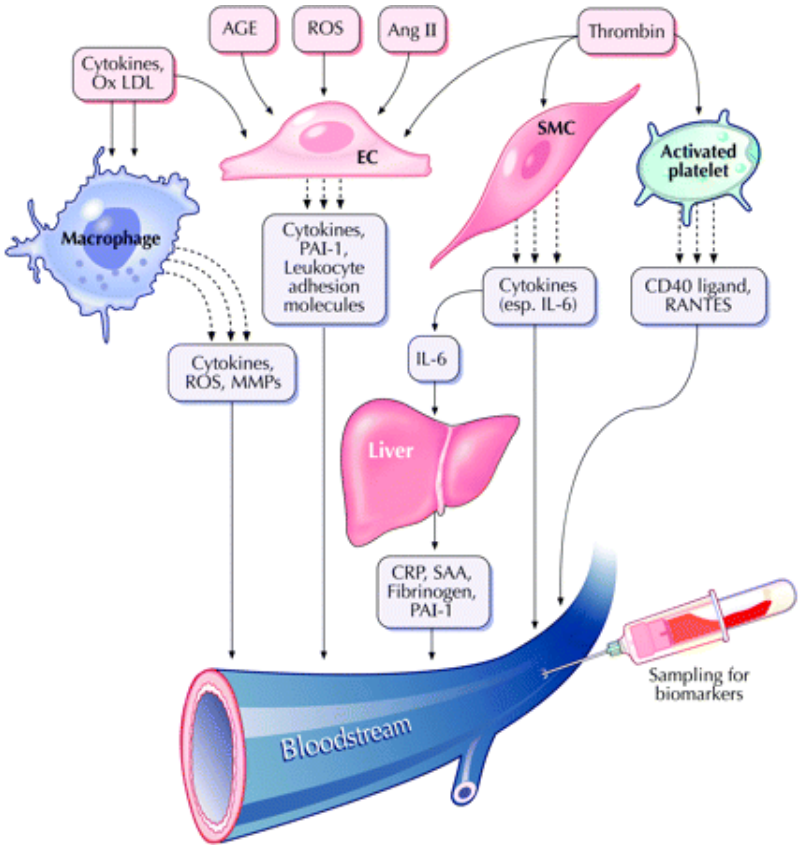
The transformation of monocytes into macrophages and the uptake of cholesterol lipoproteins are thought to initiate the fatty streak. Further injurious stimuli may continue the attraction and accumulation of macrophages, mast cells, and activated T cells within the growing atherosclerotic lesion. Oxidized low-density lipoproteins may be one of several factors that contribute to loss of smooth muscle cells through apoptosis in the atherosclerotic plaque cap, and secretion of metalloproteinases and other connective tissue enzymes by activated macrophages may break down collagen, weakening the cap and

making it prone to rupture. This disruption of the atherosclerotic plaque then exposes the atheronecrotic core to arterial blood, which induces thrombosis.



Thus, virtually every step in atherogenesis is believed to involve cytokines, other bioactive molecules, and cells that are characteristic of inflammation.

INFLAMMATORY MARKERS IN ATHEROGENESIS.



It should be pointed out that this inflammatory cascade may have sources other than an atherosclerotic coronary artery, including atherosclerosis in other arteries, as well as systemic inflammation (eg, connective tissue diseases) and local infections (eg, gingivitis, prostatitis, bronchitis, urinary tract infections, gastric inflammation). These systemic inflammations may result in elevated levels of inflammatory markers that may be incorrectly attributed to atherosclerotic CVD.

Nonetheless, increasing recognition of the inflammatory component of atherogenesis provides the biological plausibility for the *potential* use of inflammatory markers as indicators of atherogenesis or as predictors of atherosclerotic complications.

These pathophysiological insights provide potential targets for measurement as a means to identify and monitor the ongoing inflammatory process.

Potential targets for measurement include proinflammatory risk factors such as oxidized low-density lipoproteins, proinflammatory cytokines (eg, interleukin-1, tumor necrosis factor-α), adhesion molecules (eg, intercellular adhesion molecule-1, selectins), inflammatory stimuli with hepatic effects (eg, interleukin-6) or the products of the hepatic stimulation, such as SAA, C-reactive protein (CRP), and a host of other acute-phase reactants.

Understanding of the inflammatory cascade allows the consideration of a number of inflammatory markers as potentially useful predictors of prevalent or incident CVD. Such markers, however, may not be useful in the clinical arena unless they possess additional characteristics. These include: (1) the ability to standardize the assay and to control the variability of the measurement; (2) independence from established risk factors; (3) association with CVD clinical end points in observational studies and clinical trials; (4) the presence of population norms to guide interpretation of results; (5) ability to improve the

overall prediction beyond that of traditional risk factors; (6) generalization of results to various population groups; and (7) acceptable cost of the assays. The use of the marker is also affected by the type of relationship with CVD (eg, linear, nonlinear, dichotomous). These characteristics then can be examined in the inflammatory markers currently under consideration.

Table 1. Assays of Inflammatory Markers for Potential Clinical Use*

Analyte	Stability	Assay Availability	World Health Organization Standards Available?	Inter Assay Precision
Soluble adhesion molecules (eg, E-selectin, P-selectin, intracellular adhesion molecule-1, vascular cell adhesion molecule-1)	Unstable (unless frozen)	Limited	No	CV<15%
Cytokines (eg,interleukin-1ß, 6, 8, and -10 and tumor necrosis factor - α)	Unstable (unless frozen)	Few	Yes (Reference)	CV<15%
Acute-phase reactants				
Fibrinogen	Unstable (unless frozen)	Many	Yes (Reference)	CV<8%
SAA	Stable	One	Yes (Reference)	CV<9%
hs-CRP	Stable	Many	Yes (Reference)	CV<10%
WBC count	Stable	Many	Yes	CV<3%

A sizable number of studies have examined the inflammation–CVD association through measurement of a variety of analytes. Only some of these assays, however, are currently employable in clinical settings, after

consideration of the stability of the analyte, the commercial availability of assays, the standardization of those assays to allow comparison of results, and the precision of the assays as measured by the coefficient of variation. Table 1 summarizes the currently available assays for inflammatory markers. Several markers are only stable when frozen, which limits their use to research settings. Likewise, only the acute-phase reactants (fibrinogen and CRP) and WBC count have widely available assays. CRP has a proficiency-testing program from the College of American Pathologists. A program to standardize CRP testing is underway at the Centers for Disease Control and Prevention. Most of the acute-phase reactant assays have acceptable coefficients of variation.

These comparisons of the various inflammatory markers favor CRP from the clinical chemistry perspective. It needs to be emphasized that the assays considered in Table 1 were for hs-CRP with acceptable precisions down to or below 0.3 mg/L. It is within these lower, previously "normal" ranges that the hs-CRP levels seem to have predictive abilities for CVD events. Although new assays of other inflammatory markers, with precision, standardization, and other characteristics that are superior to those of the current assays, may become available, the hs-CRP assay represents the best candidate at this time.

CRP AS AN INFLAMMATORY MARKER

C-reactive protein is the prototypic marker of inflammation in humans and a member of a highly conserved family of proteins called the pentraxins. It comprises 5 noncovalently associated protomers arranged symmetrically

around a central pore and has a molecular weight of 118 000 Da[5]. It is a nonglycosylated protein in humans, and its gene has been mapped to chromosome 1. To date, in phagocytes, it has been shown to bind Fcγ receptor (FcγR) I and II, and its function appears to clear apoptotic and necrotic cells (opsonophagocytosis).

CRP is predominantly synthesized in hepatocytes as an acute-phase reactant and is transcriptionally driven by IL-6, with synergistic enhancement by IL-1. Some recent data challenge the dogma that CRP is exclusively produced by the liver, however, and suggest that it is produced in the atherosclerotic lesion (especially by smooth muscle cells and macrophages), the kidney, neurons, and alveolar macrophages[11,12,13,14.] mRNA and protein for CRP is expressed in arterial plaque tissue, and both CRP mRNA and protein levels are 10-fold higher in plaque compared with the normal artery[13.] Also, it is shown that human aortic endothelial cells (HAECs) synthesize and secrete CRP.[15]

The most potent agonist for CRP production from HAECs is the combination of IL-1 and IL-6. Thus, synthesis and secretion of CRP by cells in the atherosclerotic lesion by paracrine/autocrine loops could result in local concentrations of CRP far in excess of plasma concentrations and could contribute to proinflammatory, proatherogenic effects. Ouchi et al.[16] have demonstrated CRP mRNA in human adipose tissue. Adiponectin, an adipocytokine, significantly decreases CRP mRNA and protein levels, whereas leptin has been shown to enhance CRP synthesis in endothelial cells incubated with IL-1 and IL-6[17].

Sources of Variability of Inflammatory Markers

Generally, the precision and reproducibility of inflammatory marker assays such as the acute-phase reactants have been acceptable (Table1). For example, the coefficient of variation of hs-CRP assays is generally <10% from the 0.3- to 10-mg/L range. 17 Considerable within-individual variability exists, however, for both hs-CRP and fibrinogen. In general, although CRP is an acute-phase reactant and as such has higher within-subject variability than an established risk factor such as serum cholesterol, it also has a broader distribution in the population. The final result is that, in a manner similar to cholesterol, two separate measurements of hs-CRP are adequate to classify a person's risk level and to account for the increased within-individual variablility. The distribution of the logarithm of hs-CRP level is a normal distribution, and the nontransformed values are skewed toward the higher values, with most populations showing >95% of subjects with hs-CRP values of <10 mg/L. There seems to be population-to-population consistency in this, though as previously stated, data for racial and ethnic populations are limited (eg, NHANES III).

Sources of variation of inflammatory markers have been studied to varying degrees. There seems to be little seasonal or diurnal variation with hs-CRP. Several factors have been identified as being associated with increased or decreased levels of hs-CRP this list is likely incomplete. For example, body weight and the metabolic syndrome are consistently associated with elevated

hs-CRP, and weight loss is associated with reduction in hs-CRP levels, with some authors suggesting that hs-CRP is merely a marker for obesity and insulin resistance. This association of hs-CRP with these conditions is poorly defined from a mechanism standpoint, and is possibly due to coassociation with prevalent vascular disease. Individuals with evidence of active infection, systemic inflammatory processes, or trauma should not be tested until these conditions have abated. An hs-CRP level of >10 mg/L, for example, should be discarded and repeated in 2 weeks to allow acute inflammations to subside before retesting.

Studies of Use of Inflammatory Markers in Clinical Practice

Despite the ability of some inflammatory markers to predict incident or recurring events, various analyte characteristics and within-individual variation seem to limit the analytes to hs-CRP and possibly fibrinogen. The specific clinical settings in which hs-CRP or other factors would be most useful, however, need to be defined by careful clinical investigations, including clinical trials. Inflammatory markers may have greater potential as a means to augment risk assessment in the identification of persons who should be considered for lipid-lowering, antiplatelet, or other cardioprotective drug therapies, as well as for increased emphasis on therapeutic lifestyle changes. If the patient is already targeted for these treatments according to current guidelines (eg, secondary prevention), then a level of inflammatory marker is less useful. A better potential use may be in those patients at baseline risk for whom an additional

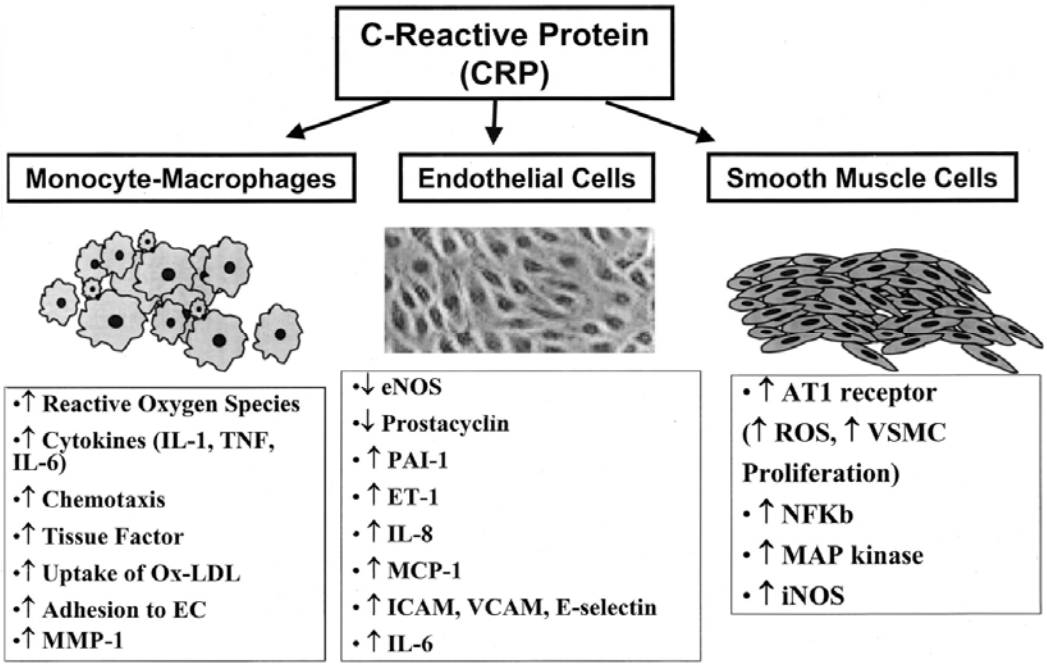
risk predictor may provide support for or against additional lifestyle or drug therapies. Post hoc analyses from two randomized controlled trials (AFCAPS/TexCAPS [Air Force/Texas Coronary Atherosclerosis Prevention Study] trial of lovastatin versus placebo[18] and the Physicians' Health Study of aspirin versus placebo) both suggest that persons with elevated hs-CRP levels have a larger absolute risk reduction in the intervention groups, which supports the potential utility of hs-CRP to target patients for primary preventive interventions.

One potential use for markers that might be considered is that of monitoring of the effects of therapy, such as an HMG-CoA reductase inhibitor. For example, if the marker does not fall, treatment might be intensified. HMG-CoA reductase inhibitors do seem to reduce hs-CRP levels, but the response is very heterogeneous, with many nonresponders and a few hyper-responders contributing to the reduction in mean hs-CRP level. Unfortunately, it is not known if the responders with lowered hs-CRP levels have a greater reduction in risk than the nonresponders. Conversely, despite recent indications of possible increased risk with the use of estrogen in hormone replacement therapy (HRT)and the finding that hs-CRP is increased with estrogen use, it is not yet possible to conclude that an increased hs-CRP brought about by estrogen use is an indicator of increased CVD risk. Thus, a role of these markers in the monitoring of therapy has not been established.

CRP AND ENDOTHELIAL CELLS

Several studies have shown an inverse relationship between CRP levels and endothelial function[19,20,21]. CRP induces increased expression of ICAM, VCAM, E-selectin, and the chemokine MCP-1, resulting in increased adhesion of U937 cells (monocytic cell line) to human umbilical vein endothelial cells. A critical enzyme in endothelial cells is endothelial nitric oxide synthase (eNOS).

CRP uncouples eNOS, resulting in increased superoxide production, decreased NO production, and altered eNOS phosphorylation. These effects appear to be mediated via the Fcγ receptors CD32 and CD64. These data further support a role for CRP in mediating endothelial dysfunction.



By virtue of inhibiting eNOS expression and NO release, CRP blocks NO-dependent processes.

Furthermore, several groups have shown that CRP in vivo impairs endothelial vasoreactivity[22,23] Bisoendial et al.[24] also demonstrated that CRP infusion in patients with hypercholesterolemia resulted in marked deterioration of endothelial vasoreactivity.

CRP-induced PAI-1 appears to occur via activation of Rho kinase and the nuclear factor (NF)-κB pathway[25]. CRP inhibits tissue plasminogen activator (tPA) activity via generation of proinflammatory cytokines [IL-1β and tumor necrosis factor-α (TNF-α)][26]. These studies provide additional evidence that CRP may be a procoagulant, which has implications for atherothrombosis.

An important chemokine is IL-8, a powerful trigger of adhesion of monocytes to endothelium. CRP induces IL-8 expression in human coronary artery endothelial cells (HCAECs) via activation of NF-κB[27]. This was confirmed by Wang et al.[28], who showed that IL-8 release was induced by CRP via upregulation of MEK (mitogen-activated protein kinase or extracellular signal-regulated kinase) and extracellular signal-regulated kinase (ERK) 1/2. Also, the CD40–CD40 ligand (CD40L) pathway plays an important role in plaque stability, and CRP has been shown to upregulate surface expression of CD40 and CD40L.

The Du Clos laboratory and others have shown that CRP binds mainly to FcγR2 (CD32) on leukocytes[29]. CRP binds to both CD32 and CD64 on HAECs but not CD16, and that CRP mediates its biological effects in EC via these 2 receptors. Studies have also shown that CRP binds to LOX-1 and may exert proatherogenic effects by binding to the receptors for advanced glycation end products.

CRP AND ENDOTHELIAL DYSFUNCTION.

There is tremendous interest in a special subtype of progenitor cells isolated from peripheral blood and bone marrow of adults, endothelial progenitor cells (EPCs), which have the capacity to circulate, proliferate, and differentiate into mature endothelial cells. Importantly, the measurement of circulating EPCs is a surrogate marker of endothelial dysfunction and future cardiovascular events. Clinical studies suggest that traditional risk factors for coronary atherosclerosis are associated with lower levels of circulating EPCs[30,31]. Importantly, a negative correlation between systemic CRP levels and circulating EPC number has been reported in patients with unstable angina. Also, low levels of EPCs are associated with adverse cardiovascular events. A recent article suggests that in mature ECs, CRP appears to stimulate angiogenesis and may be a mediator of neovessel formation in the intima of vulnerable plaques, thus suggesting different biological effects on EPCs and mature ECs[32]. EPC-induced angiogenesis was dependent on the presence of NO, and CRP treatment caused a decrease in eNOS mRNA expression by

EPCs. Also, subsequently, CRP was demonstrated to increase oxidative stress and induce apoptosis in these EPCs. Thus, CRP may negatively affect EPCs by quenching antioxidant defenses and promoting telomerase inactivation.

Thus, a large body of evidence from in vitro studies points to a proatherogenic, prothrombotic role for CRP in ECs. These effects of CRP may result in endothelial dysfunction and impairment of EPC survival and differentiation.

It is clear that CRP is proatherogenic in monocyte-macrophages since it increases tissue factor expression, promotes monocyte chemotaxis and adhesion to ECs, reactive oxygen species release, MMP-1, CCR2, cytokines, and M-CSF, and promotes OxLDL uptake, thus leading to increased foam cell formation. Furthermore, CRP is present in foam cells in the atherosclerotic lesion and activates complement.

CRP exerts direct proatherosclerotic effects at the level of VSMCs. Also, in VSMCs, CRP has been shown to upregulate inducible NO synthase (iNOS) and certain cell signal transduction pathways including MAPK pathway and NF-κB. CRP promotes apoptosis of VSMCs and thus may contribute to plaque instability.

CRP AS A MARKER OF ENDOTHELIAL DYSFUNCTION

However, there have been few studies to compare the relationship of various inflammatory biomarkers with vascular inflammation assessed by 18F-FDG PET. Recently, Rudd et al.[33] demonstrated that arterial 18F-FDG uptake showed the trends of positive correlation with levels of several circulating inflammatory biomarkers including hsCRP. According to Hye Jin Yoo et al,[34] Compared with individuals with low hsCRP and high LDL-C levels (hsCRP < 2 mg/L and LDL-C ≥130 mg/dL) or low hsCRP and low LDL-C levels (hsCRP < 2 mg/L and LDL-C < 130 mg/dL), healthy subjects with high hsCRP and low LDL-C levels (hsCRP ≥2 mg/L and LDL-C < 130 mg/dL) had increased vascular inflammation, measured using ^{18}F-FDG PET. However, no significant differences in IMT were observed. TBR levels measured using 18F-FDG PET are independently associated with hsCRP levels and diastolic blood pressure, whereas IMT values are related to age, diastolic blood pressure, and LDL-C levels. Further studies are needed to determine the clinical roles of ^{18}F-FDG PET and hsCRP in prognostic and therapeutic implications for cardiovascular events.

CRP AND CLINICAL PROFILE OF CAD

A meta-analysis of prospective population-based studies has compared persons in the lower tertile of hs-CRP with those in the upper tertile.[35,36] With a good consistency between studies, a relative odds of 2.0 (95% CI 1.6–2.5) for

major coronary events was observed for the upper tertile with the lowest tertile used as a reference. These prospective studies include men,[37,38] women,[39,40] and the elderly.[41-43] Large population-based studies such as the study from the MONICA (Monitoring trends and determinants in Cardiovascular disease) Augsberg Center in Germany, the Atherosclerosis Risk in Communities Study,[44] the Women's Health Study, the Honolulu Heart Study, and the NHANES (National Health And Nutrition Examination Survey) studies (cross-sectional[44-46] are also represented. In general, most studies show a dose-response relationship between the level of hs-CRP and risk of incident coronary disease. It should be noted that studies of other, newer inflammatory markers such as interleukin-6 and SAA show similar results A notable characteristic of all these studies is their limitation to white North American or European populations, with the exception of Japanese-American men in the Honolulu Heart Study [47] Data are limited for persons of African, South Asian, or Native American descent, who may be at particularly high risk for CVD, and for other racial/ethnic groups. Race and ethnicity did not appear to be an effect modifier of the hs-CRP–stroke association in one study.

The ability of hs-CRP to add to the predictive capacity of other, established risk factors has been examined in several studies. Through stratification or multivariable statistical adjustment, hs-CRP retains an independent association with incident coronary events after adjusting for age, total cholesterol, HDL cholesterol, smoking, body mass index, diabetes, history

of hypertension, exercise level, and family history of coronary disease. In some studies, the magnitude of the relative risk in the upper percentiles of hs-CRP is attenuated after this adjustment, including loss of statistical significance. Recent studies demonstrate the capability of elevated hs-CRP to predict coronary events in women after adjusting for risk factors used in the Framingham risk score, and in the elderly with extensive adjustment for CVD risk factors and measures of subclinical atherosclerosis. Relatively few studies have adjusted for body mass index or for measures of diabetes or glucose metabolism.

A growing number of studies have examined inflammatory markers as predictors of recurrent CVD and death in different settings, including the short-term risk, long-term risk, and risk after revascularization procedures such as percutaneous coronary intervention (PCI), including the risk of restenosis. Although several markers have been studied, the strongest association with prognosis has been with fibrinogen and hs-CRP. hs-CRP consistently predicts new coronary events in patients with unstable angina and acute myocardial infarction.[48-56] Most of these studies have been long term, but some in-hospital survivorship studies [57-60] have also shown an association.

For patients with acute coronary syndromes, cutpoints for elevated hs-CRP different than those for prediction in asymptomatic patients may be useful. For example, a level of >10 mg/L in acute coronary syndromes may have better

predictive qualities, whereas a level of >3 mg/L may be more useful in patients with stable coronary disease.

Many analyses have adjusted for other prognostic factors, demonstrating continued predictive capacity with hs-CRP. In acute coronary syndromes, hs-CRP predicts recurrent myocardial infarction independent of troponins, which suggests it is not merely a marker for the extent of myocardial damage. Recent data also suggest that hs-CRP may be a marker for risk of restenosis after PCIs,[61,62] but all studies are not in agreement with these results. Elevated hs-CRP levels also seem to predict prognosis and recurrent events in patients with stroke and peripheral arterial disease. These data suggest that hs-CRP may have a role in risk stratification of patients with established CVD, although more data are needed that compare the prognostic value of elevated levels of hs-CRP with other prognostic measures currently in use.

The factors that make up the Framingham risk score (age, sex, blood pressure, serum total cholesterol or low-density lipoprotein cholesterol level, high-density lipoprotein cholesterol level, cigarette smoking, and diabetes) account for most of the excess risk for incident coronary heart disease (CHD). However, these factors do not explain all of the excess risk, and approximately 40% of CHD deaths occur in persons with cholesterol levels that are lower than the population average. Several lines of evidence have implicated chronic inflammation in CHD, and inflammatory markers have received much attention

as new or emerging risk factors that could account for some of the unexplained variability in CHD risk.

In the Framingham risk scoring system, intermediate-risk persons are those with a 10% to 20% risk for coronary death or nonfatal myocardial infarction ("hard CHD events") over 10 years. Further stratification by using new markers might reclassify some intermediate-risk persons as low-risk (10-year risk <10%) and others as high-risk (10-year risk >20%). This would permit more aggressive risk reduction therapy in persons reclassified as high-risk and may consequently reduce incident CHD events. Several previous meta-analyses [63-65] have assessed the possible independent predictive ability of CRP level for incident CHD risk. In 1998, a meta-analysis of 5 long-term, population-based prospective cohort studies and 2 cohorts of patients with pre-existing CHD calculated a risk ratio for coronary events of 1.7 (95% CI, 1.4 to 2.1) for CRP levels in the top tertile versus the bottom tertile.

Although the underlying pathobiology remains under study, the overall epidemiological data supporting the association between CRP and adverse cardiovascular outcomes are clear. To that end, the CDC and the AHA have now recognized the prognostic utility of hs-CRP in a joint statement.[66]

Marc S. Sabatin et al showed the population which included both patients with stable and patients with unstable angina, there were only 75 coronary events during the 2 years of follow-up, and excess risk was

demonstrated only when hs-CRP levels were in the top quintile (>3.6 mg/L), with no evidence for a gradient of risk across the lower quintiles.[9]

In contrast, using a large cohort of patients with stable CAD, it was able to prospectively apply the CDC/AHA hs-CRP cut points and demonstrate that an elevated level of hs-CRP, even >1 mg/L, was associated with an increased risk of cardiovascular death, MI, or stroke.

The risk was consistent across all the elements of the composite end point and remained significant even after adjustment for elements of the Framingham Risk Score and other clinical and laboratory parameters. These data suggest that among patients with CAD, hs-CRP levels can be used to gain fundamental insight into which patients are, despite being asymptomatic at a given time and hence deemed clinically stable, in fact pathobiologically unstable and at higher risk for adverse cardiovascular events. However, an elevated hs-CRP does not appear to identify patients with stable CAD and preserved ejection fraction who derive particular benefit from ACE inhibition.

From a clinical perspective, the most meaningful measure of CRP's value as a marker is its effect on rates of reclassification from intermediate-risk to other risk categories. Recent articles have proposed methods of assessing clinical risk reclassification when the goal of analysis is risk prediction.

Five studies [67,68,69,70,71] included an analysis that compared predictive models that used all Framingham risk factors, with and without CRP level,

specifically among participants whose 10-year Framingham risk score categorized them as intermediate-risk.

Using data from the Women's Health Study, Cook and colleagues demonstrated that although measures of discrimination did not substantially differ between models with and without CRP level, a model that included CRP level had better fit, as measured by the Hosmer–Lemeshow calibration statistic. In that analysis, 14% of participants originally classified as intermediate-risk (10% to 20%) were reclassified as low-risk (<10%) and 5% were reclassified as high-risk (>20%). The actual 10-year risk was 19.9% for those reclassified as high-risk and 11.5% for those who remained intermediate-risk.

The other 4 studies used less rigorous analyses to assess the effect of CRP level on risk classification and did not measure calibration, with mixed results. Three studies [67,68,70] found that assessing CRP improved risk stratification specifically among intermediate-risk participants.

In the Monitoring of Trends and Determinants in Cardiovascular Disease study [67], assessing CRP level in addition to the Framingham risk factors resulted in improved risk classification among participants with an initial 10-year risk of 11% to 19%. Among participants with a CRP level greater than 3.0 mg/L, some with an initial 10-year risk of 15% to 19% were reclassified as high-risk, whereas no participants with an initial 10-year risk of 11% to 14% were reclassified as high-risk.

In an analysis of data from the Women's Health Study, [68] CRP level was clearly predictive of incident cardiovascular disease among participants with 10-year Framingham risk scores between 10% and 20%. The risk for cardiovascular events was twice as high for those with CRP levels between 1.0 and 3.0 mg/L or between 3.0 and 10.0 mg/L than for those with levels less than 1.0 mg/L, although CIs were not reported. Similarly, in an analysis from the Cardiovascular Health Study, CRP level added to risk prediction among men at intermediate risk[70]. Among men with a 10-year Framingham risk score between 10% and 20%, the observed 10-year incidence of CHD was 32% for those with CRP levels greater than 3.0 mg/L, compared with between 15% and 16% for those with CRP levels between 1.0 and 3.0 mg/L or less than 1.0 mg/L[70]. In that cohort, however, CRP level did not add to risk prediction among intermediate-risk women.

The negative study[69], an analysis from the Framingham cohort, estimated the 10-year risk for incident cardiovascular disease by tertile of CRP level among participants previously stratified as having a 10-year Framingham risk score between 10% and 20%. Tertile cut-points were 0.81 mg/L and 3.78 mg/L. The estimated 10-year risk did not significantly differ among the 3 CRP tertiles, and all 3 subgroups based on CRP level had an estimated 10-year risk in the intermediate range.

The body of evidence that CRP level is independently associated with incident CHD is strong, with a risk ratio of 1.58 (CI, 1.37 to 1.83).

The strength of evidence from studies that attempted to measure the effect of using CRP level to improve risk classification among persons initially classified as intermediate-risk is moderate. Among intermediate-risk persons, subgroups with high CRP levels generally had a higher risk for coronary events than did those with average or low CRP levels.

Recently, these researchers reported a good-quality analysis of Framingham data[71] in which they calculated the risk reclassification of individual study participants when CRP level was added to traditional risk factors; including CRP level improved risk assessment by appropriately reclassifying a statistically significant percentage of incident CHD cases and noncases into higher or lower risk categories.

Although the types of analyses differed, 4 large, good-quality cohort studies are consistent in finding that assessing CRP level improves CHD risk stratification [43,67,68,70] These consistent findings provide moderately strong evidence that adding CRP level to risk models in intermediate-risk patients improves the identification of those at higher risk for incident CHD.

However, additional research is needed to assess the effect of CRP level on risk reclassification of initially intermediate-risk persons and to statistically evaluate the calibration of prediction models to observed risk .

Establishing the independent predictive ability of a new risk factor is necessary but not sufficient for assessing its potential usefulness in screening

for CHD risk. Other criteria must be considered, such as the prevalence of the factor in the target population, the reliability and cost of the test, potential harms of testing, and the effect that treatment for the risk factor has on modifying risk. C-reactive protein level favorably satisfies most of these criteria.

National survey data suggest a prevalence of high CRP level of at least 20% to 25% among intermediate-risk persons[66,72]. Inexpensive, precise, high-sensitivity CRP serum assays are available. Although considerable within-patient variation among CRP measurements has been reported, the reliability of 2 or 3 serial measurements is similar to that of a total cholesterol assay.

Weight loss, exercise, and smoking cessation can reduce serum CRP levels, and lowering CRP levels with statin therapy in patients with acute coronary syndrome can lower their risk for recurrent myocardial infarction or coronary death.

The viability of CRP as a new factor in global risk assessment for incident CHD is limited by sparse evidence that directly links therapeutic changes in CRP level to primary prevention of CHD events.

JUPITER (Justification for the Use of Statins in Prevention: an Intervention Trial Evaluating Rosuvastatin), a good-quality randomized, controlled trial of rosuvastatin for primary prevention of cardiovascular events in 17 802 men and women with elevated (>2 mg/L) CRP levels, low-density

lipoprotein cholesterol levels less than 3.4 mmol/L (<130 mg/dL) (median, 2.8 mmol/L [108 mg/dL]), and no other indication (such as diabetes) for statin therapy [73].

Current guidelines recommend aggressive therapy only for high-risk patients, such as those with a Framingham risk score greater than 20%, diabetes, or known cardiovascular disease. Because approximately half of the patients in JUPITER had a Framingham risk score greater than 10%, these results provide evidence that 1 form of intensive risk reduction - aggressive lipid-lowering therapy - produces benefit for a population that includes intermediate-risk persons.

JUPITER did not evaluate whether intermediate-risk patients who are reclassified as high-risk by using CRP level would benefit from treatment compared with intermediate-risk patients who are not reclassified.

For example, the risk reduction from rosuvastatin therapy may have been as great in intermediate-risk participants who had CRP levels closer to the population average. The study also did not directly test whether lowering CRP levels reduced cardiac risk.

Finally, JUPITER did not report rates of coronary events separately for low-risk and intermediate-risk persons.

Other issues may influence guideline recommendations and merit discussion. Cross-sectional studies have found correlations between CRP level and traditional CHD risk factors, but the implications for the use of CRP in global risk assessment are not clear.

The findings have been interpreted to mean that CRP level may represent a different aspect of risk, with complex interrelationships among CRP level, traditional risk factors, and CHD. Others conclude that elevated CRP level is largely attributable to traditional risk factors, and CRP level "may have limited clinical utility as a screening tool" [66].

Correlation of CRP level with traditional risk factors does not preclude its potential association with CHD. The findings of many studies suggest that the degree of correlation between CRP level and traditional risk factors is not so great that CRP loses its independent effect.

Although this statistical independence does not establish causality, it does support the potential use of CRP level as an adjunct in global risk assessment, particularly for targeted groups-such as intermediate-risk persons.

CRP AND ANGIOGRAPHIC CORRELATION

High sensitivity C-reactive protein (CRP) ,a marker of systemic inflammation, has been evaluated as a risk predictor in subjects without known coronary artery disease (CAD) ,in those at risk of CAD and in patients with

stable angina ,unstable angina or acute myocardial infarction(MI). Even small elevations of CRP, within or just beyond the "normal" range (determined by high sensitivity CRP assay) have been found to strongly predict future cardiovascular events in almost all studies. However, these studies have not adjusted for plaque burden as assessed by coronary angiography .When adjustments for CAD have been made, they generally have been limited to adjustment for one -,two-or three-vessel disease previous studies have shown a correlation between CRP and the presence of atherosclerosis.

Tataru MC et al [74] showed correlation hs CRP and the severity of atherosclerosis in myocardial infarction patients with stable angina pectoris.

Zebrack et al, [75] showed hs CRP correlates with extent of coronary artery disease, Nyandak et al,[76] also showed correlation of hs CRP with extent of coronary artery disease. And hs CRP levels have a correlation with the disease burden in coronary artery disease patients.

Peppes et al, [77] study showed correlation between myocardial enzyme serum levels and markers of inflammation with severity of coronary artery disease and Gensini score .

Monterio et al, Liu Haihang et al [78] Katrisis et al [79] showed correlation of hs CRP with severity of coronary artery disease

Study characteristics and adjusted estimates of CHD risk Associated with CRP

Study	Participants n	Follow up y	Men%	Out comes	Framingham Risk factors at	Other Adjusted covariates	CRP quantile analysed	Effects size (95%CI)
COHORT STUDIES								
Kflenig et al., 2005	3971	10	54.3	Major CHD events	7	5	>3.0 vs <1.0 mg/L 1.3-3.0 vs. <1.0 mg/L	1.45 1.08
Koenig et al., 2004	3435	6.6	100	Major CHD events	7	0	>3.0 vs <1.0 mg/L 1.0-3.0 vs. <1.0 mg/L	2.21 1.44
St. Pierre et al., 2005	1982	13	100	Major CHD events	7	3	Highest vs Lowest Quartile	0.98
Wilson et al., 2005	4446	8	43.8	Major CHD events	6	0	>3.0 vs <1.0 mg/L 1.0-3.0 vs. <1.0 mg/L	1.22 1.38
Park et al, 2002	967	6.4	90.5	Major CHD events	5	3	1 Unit increase in log scale	1.49
Lowe et al., 2004	3065	7.5	100	Major CHD events	5	1	Highest vs Lowest Quartile	1.72
Lawlor et al., 2005	2723	3.5	0	CHD events	6	6	Doubling Of CRP Level	1.03
Mora et al., 2006	27742	9.9	0	CVD events	7	2	Increasing quantiles	1.22 1.24 1.40 1.68
Tzoulaki et al, 2007	923	17	67.1	CVD events	6	3	Highest Vc lowest tertile	1.62

Nested Case - Control Studies								
Boekholdt et al., 2006	3272	6	64.1/ 63.4	Major CHD events	7	1	Increasing quartiles	0.87 1.28 1.66
Luc et al., 2003	772	5	100	Major CHD events	7	1	Increasing tertiles	0.81 2.16
Danesh et al., 2004	5933	19.4	72/69	Major CHD events	6	3	Highest Vc lowest tertile	1.37
Danish et al., 2000	1149	9.5	100	Major CHD events	6	2	Highest Vc lowest tertile	2.61
Ridker et al., 1997	492	8	100	Major CHD events	5	3	Increasing Quartiles	1.5 2.4 2.6
Case - Cohort studies								
Pischon et al ., 2007	979	6	75.2/39.5	Major CHD events	7	0	>3.0 vs <1.0 mg/L 1.3-3.0 vs. <1.0 mg/L	2.56 1.88
Koenig et al., 2006	1058	11	0	Major CHD events	7	4	Highest Vc lowest tertile	1.35

A prespecified analysis of the Pravastatin or Atorvastatin Evaluation and Infection Therapy-Thrombolysis in Myocardial Infarction 22 (PROVE-IT TIMI 22) trial[82] revealed similar associations between CRP reduction and risk of recurrent coronary events among patients w The Reversal of Atherosclerosis with Aggressive Lipid Lowering (REVERSAL) trial[83] demonstrated that lowering CRP concentrations in patients with coronary disease with intensive statin therapy results in reduced atherosclerotic lesion progression with acute coronary syndromes Previously, Cholesterol and Recurrent Events trial, which had enrolled patients with an MI in the preceding 3 to 20 months, examined the association between hs-CRP and coronary events.[84] Again, however, an increased risk of coronary events became apparent only with hs-CRP levels in the top quintile (in this case, >6.6 mg/L), with no evidence for a gradient of risk across the lower quintiles. Moreover, the association between CRP levels and coronary events was greatly attenuated and no longer significant in patients randomized to statin therapy. An association between hs-CRP and cardiovascular outcomes has been seen in 2 cohorts of patients with angiographically proven coronary artery disease.[85] However, both studies included a mix of patients with stable and unstable angina, and the latter group is known to have acutely elevated levels of CRP and a worse prognosis Moreover in one of the studies, only CRP in the top quartile (>12.7 mg/L) was a significant predictor of cardiovascular events, and this association was no longer apparent in patients taking a statin.

CRP AS A SCREENING TEST. GUIDELINES AND RECOMMENDATIONS.

"**How should hs-CRP be measured?"** The hs-CRP assay, to reduce within-individual variability, should be performed in a metabolically stable person without obvious inflammatory or infectious conditions. Results for hs-CRP should be expressed as mg/L only. Two assays, averaged, fasting or nonfasting, and optimally 2 weeks apart, provide a more stable estimate of level of this marker. If a level of >10 mg/L is identified, there should be a search initiated for an obvious source of infection or inflammation, which could obscure any prediction of coronary risk that might be attributed to the elevated level. That result of >10 mg/L should then be discarded and the hs-CRP measured again in 2 weeks.

The cutpoints of low risk (<1.0 mg/L), average risk (1.0 to 3.0 mg/L), and high risk (>3.0 mg/L) correspond to approximate tertiles of hs-CRP in the adult population. The high-risk tertile has an ≈2-fold increase in relative risk compared with the low-risk tertile. These tertiles are based on distributions of hs-CRP samples from >15 populations involving >40 000 persons gathered for the purpose of this workshop, allowing adequate definition of the population distribution. In general, the high-risk category includes the skewed tail of the distribution.

CRP AND FUTURE RESEARCH.

Despite the statistically significant results of these studies, larger cohorts are required in local settings to assess the relationship of hs-CRP levels with the severity of coronary atherosclerosis in local settings. The coronary angiographic assessment is based upon luminal assessment and lacks plaque visualization. Intravascular ultrasound (IVUS) based assessment of coronary atherosclerotic burden in correlation with hs-CRP levels may be an area of interest for future investigation

Finally, the entire adult population should not be screened for hs-CRP for purposes of cardiovascular risk assessment. Little evidence supports a recommendation for widespread screening for hs-CRP as a public health measure (Class III, Level of Evidence C). Such a recommendation would have to be based on additional evidence from studies of potential benefits and harm for such a screening initiative.[81]

MATERIALS AND METHODS

This study included 80 patients undergoing diagnostic coronary angiography at the Cardiology Department of Stanley medical college and Hospital. CAG was done in the cath lab of the Department of Cardiology, Stanley medical college and Hospital.

Inclusion criteria

All patients of IHD admitted for CAG in department of cardiology SMCH

Exclusion criteria

1. Patient with past CABG
2. Patient with PTCA
3. Patient with valvular heart disease.
4. Patient with hepatic dysfunction.
5. Patient with a major non-cardiovasculardisease.
6. Patient with collagen vascular disease.
7. Any systemic infection.
8. Patients with history of coronary angiography in the recent past
9. Unwilling to give consent .

The selected cases were those who had suffered recent Acute Coronary Syndrome and those with Chronic CAD .

Recent myocardial infarction is defined as an acute episode of infarction < 1 months from the time of the investigation.

80 cases were selected for inclusion in the study based on clinical assessment and laboratory screening. An informed consent was obtained from each patient before inclusion in the study. Patient age , gender ,smoking history body mass index, hypertension (systolic and diastolic blood pressures), heart rate, and medication history were recorded. Serum concentrations of total cholesterol, triglyceride, low-density lipoprotein cholesterol, high-density lipoprotein (HDL) cholesterol, glucose and creatinine using standard laboratory procedures

Hypertension was defined as systolic pressure more than140mmHg or diastolic pressure more than 90 mmHg after multiple measurements in a sitting position at rest, or patients already on antihypertensive medication. Diabetes mellitus was defined as fasting blood sugar more than 126 mg/d L on two occasions, or as patients already on oral hypoglycemic agents or insulin shots. Hypercholesterolemia was defined as total cholesterol more than 200 mg/ dL or LDL-C more than 130 mg/dL, or as patients already on statin (3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor) treatment.

Blood samples of the participants were sent for analysis of serum hs-CRP levels.

Determination of CRP

C-reactive protein was quantified by the particle enhanced immuno-turbidimetric assay.

Human CRP agglutinates with latex particles coated with monoclonal anti CRP antibodies. The precipitate is determined turbidimetrically, Measuring range is between 0.15-20.0 g/dl

Patients were divided into three risk groups according to hs-CRP levels (< 1 mg/L - low risk , 1-3 mg/L - average risk and >3 mg/L- high risk).

ECHOCARDIOGRAPHIC DATA

Two dimensional and M-mode measurements were obtained with patients in left lateral position using an Aloka SSD 4000 phased array system equipped with Tissue doppler and Harmonic imaging technology with Doppler frequency of 2.5 to 3.8 MHz. With measurement of LV end diastolic dimension in diastole and LV end systolic dimension in systole, LV Ejection fraction was measured.

CORONARY ANGIOGRAPHIC DATA

Coronary angiogram was done in the Siemens mobile unit cath lab in our hospital. Coronary angiography was performed by the Radial approach or by femoral approach.

Coronary angiograms were done through radial or right femoral approach using modified seldinger technique after getting patient's and patient's relative consent and included at least 4 views of the left coronary artery and 2 views of the right coronary artery Low osmolar non ionic contrast agent (Omnipaque) was used. Coronary artery stenosis was evaluated by use of multiple projection quantitative analysis was done with a medical imaging system CMS analysis software.

Determination of CAD severity

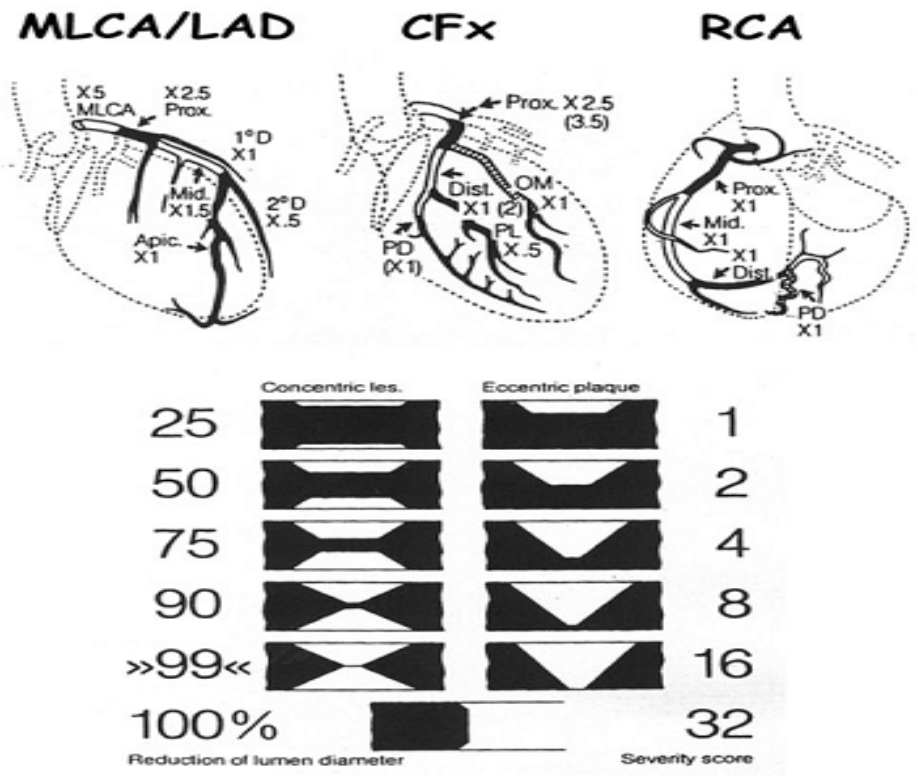
Following coronary angiogram, the extent and severity of CAD were assessed using Gensini score (86,87). The degree of narrowing was assessed by taking into account the maximum narrowing of each stenotic lesion in at least two orthogonal views.

The severity of CAD was evaluated by the 0 to 3 vessel disease score and the Gensini score . In the clinical 0 to 3 vessel disease scoring system ,arteries were as being involved if more than 50 % luminal diameter narrowing

occurred, and the patients were defined as having 0-,1-,2-,3-vessel disease according to the number of involved vessels.

The Gensini scoring system is a valuable aid to estimate the severity of CAD according to angiographic findings . The calculation is based on the evaluation of number of stenotic segments along with their respective degrees of luminal narrowing and localization within the coronary tree.

The Gensini score system yields a qualitative evaluation of coronary angiogram , which grades the narrowing of the coronary artery lumen as 1 for 1 to 25 % narrowing, 2 for 26% to 50% narrowing, 4 for 51% to 75% narrowing, 8 for 76% to 90% narrowing, 16 for 91% to 99% narrowing, and 32 for total occlusion. This score is then multiplied by a factor that takes into account the importance of the lesion position in the coronary arterial tree, e.g., 5 for the left main coronary artery , 2.5 for the proximal portion left anterior descending branch or proximal circumflex artery, 1.5 for the mid LAD region,1 for the distal left anterior descending branch, and 1 for the mid-distal region of the circumflex artery or the right coronary artery, 0.5 points for second diagonal branch or LCX posterolateral branch.



Schematic drawing of the GENSINI score. The method assigns a different severity score depending on the degree of stenosis, its location (proximal, middle or distal) along the target vessel and the type of coronary vessel involved (LAD, LCX or RCA). MLCA, main left coronary artery; LAD, Left anterior descending; LCx, Left circumflex; RCA, Rignt coronary artery.

STATISTICAL ANALYSIS

Data was analysed using Statistical Package for the Social Science (SPSS) Version 11.5 for Windows. Descriptive (frequencies, Percentages, Mean and Standard Deviation) and inferential Statistics were used to analyze the data. The inferential statistics used included Chi square, analysis of Variance, correlation coefficient.

Continues variables were presented as mean ± (SD). Continuous variables were compared through ANOVA test, Categorical variables by chi-square test and correlation Coefficient was done where applicable. For all statistical tests $P < 0.05$ was considered as statistically significant.

RESULTS AND DATA ANALYSIS

The data were collected from a sample of 80 patients. In this chapter deals with the analysis and interpretation of data collected. A total of 80 patients were include in the study. Patients were divided into three groups according to their level of CRP. The level of CRP < 1.0 mg/L was consider as group I, 1.0 mg/L to 3.0 mg /L group II and > 3.0 mg /L group III. Out of 80 study subjects, 19 subjects were in Group I, 30 in Group II and 31 subjects were in group III,.

Table-1

High Sensitive C-reactive Protein (hs-CRP) distribution of the study Patients

hs-CRP	**Number of Patients**	**Percentage**
GROUP-I (< 1.0 mg / L)	19	23.75
GROUP –II (1.0 – 3.0 mg / L)	30	37.50
GROUP-III (> 3.0 mg / L)	31	38.75
TOTAL	**80**	**100**

The above shows that distribution of the hs-CPR level among the study patients. A total of 80 patients were included in the study. Patients were divided into three groups according to their level of hs-CRP. Out of 80 patients 19 (23.8) belongs to Group I, 30 (37.50 %) was group II and rest 31 (38.75) was group III.

Table-2

The distribution of Demographical characteristics of study sample

Variables		**GROUP-I (N=19)**		**GROUP-II (N=30)**		**GROUP-III (N=31)**		**TOTAL**	
		N	%	N	%	N	%	N	%
Sex	Male	16	84.20	25	83.30	25	80.60	66	82.50
	Female	3	15.80	5	16.70	6	19.40	14	17.50
Age Mean ±(SD)		48.74 ±10.84		49.77 ±7.63		55.48 ±7.93		51.74 ± 9.01	

From the above table, a total sample of 80 was used for analysis. Males comprised 66 (82.50%) and female 14 (17.50%) of the total, Majority of them were males. The mean age of the whole group was 51.74 ± 9.01. Males had a lower mean age (51.41± 9.20) when compared to females (53.29 ± 8.21). The age group ranged from 28 to 73 years.

Table - 3

Major risk factors status of the study patients

Variables	GROUP-I (N=19)		GROUP-II (N=30)		GROUP-III (N=31)		Chi-square	
	N	%	N	%	N	%	P-value	Sign.
Hypertensive	12	63.2	13	56.7	14	45.2	1.94	0.38 *
Normotensive	07	36.8	17	43.3	17	54.8		
Diabetics	06	31.6	13	43.3	13	41.9	0.749	0.69 *
Non Diabetics	13	68.4	17	56.7	18	58.1		
Dyslipidemia	05	26.3	10	33.3	12	38.7	0.813	0.67 *
Non Dyslipidemia	14	73.7	20	66.7	19	61.3		
Smoker	05	26.3	07	23.3	09	29.0	0.256	0.88*
Non Smoker	14	73.7	23	76.7	22	71.0		

The above table shows distribution of major risk factors among the study patients.

Hypertension was found in 12 (63.2 %) in group I, 13 (26.7 %) in group II and 14 (14.52 %) in group III. The difference is not significant ($p > 0.05$) among the three groups in chi square test. Hypertensive is higher in all the groups then the Normotensive.

Diabetes mellitus was found 6 (31.6 %) in group I, 13 (43.3 %) in group II and 13 (41.9 %) in group III. No significant ($p > 0.05$) difference was found among the three in Chi squre test. Diabetics are less than the Non Diabetics in all the groups.

Dyslipidemia was found in 5 (26.3 %) in group I, 7 (23.3 %) in group II and 09 (29.0 %) in group III. No significant ($P > 0.05$) difference was found among three groups in Chi square test. The table stated that Dyslipidemia is less than Non Dyslipidemia in all the groups. Non smokers are high in all the groups.

Smoking status it was found in 5 (26.3%) in group I, 07 (23.3%) in group II and 09 (29.00%) in group III. The difference is not significant ($p> 0.05$) among the three groups in chi square test

Table-4

Base line Clinical Characteristics of the Study Patients

Variables	GROUP-I (N=19)	GROUP-II (N=30)	GROUP-III (N=31)	ANOVA	
				F-value	Sign.
Hs-CRP(mg /L) Mean ±(SD)	0.76 ± 0..13	2.51±0.41	6.67±1.46	268.21	P < 0.0001
TC Mean ±(SD)	167.42 ± 30.34	169.80±33.20	180.74±36.97	1.071	0.34 *
TG Mean ±(SD)	134.63±44.57	155.03±49.86	146.23±36.20	1.087	0.07 *
HDL Mean ±(SD)	43.11±7.39	40.97±7.65	42.68±7.05	0.627	0.54 *
LDL Mean ±(SD)	98.74±29.79	99.57±33.17	108.81±33.52	0.823	0.44 *
BMI Mean ±(SD)	24.58±4.25	23.98±2.90	23.60±3.02	0.516	0.60 *

* Not Significant

The above table shows base line clinical characteristics of the sample.

Hs-CRP mean level was found in 0.76 ± 0.13 in group I, 2.51 ± 0.41 in group II and 6.67 ± 1.46 in group III. The difference is significant ($p< 0.0001$) among the three groups in ANOVA test. hs-CRP is higher in group III.

TC mean level was found 167.42 ± 30.34 in group I, 169.80±33.20 in group II and 180.74 ± 36.97 in group III. The difference is not significant ($p > 0.05$) among the three groups in ANOVA test.

TG mean level was found 134.63 ± 44.57 in group I, 155.03 ± 49.86 in group II and 146.23 ± 36.20 in group III. The difference is not significant ($p > 0.05$) among the three groups in ANOVA test.

HDL mean level was found 43.11 ± 7.39 in group I, 40.97 ± 7.65 in group II and 42.68 ± 7.05 in group III. The difference is Not significant ($p > 0.05$) among the three groups in ANOVA test.

LDL mean level was found 98.74 ± 29.79 in group I, 99.57 ± 33.17 in group II and 108.81 ± 33.52 in group III. The difference is not significant ($p > 0.05$) among the three groups in ANOVA test.

BMI mean level was found 24.58 ± 4.25 in group I, 23.98 ± 2.90 in group II and 23.60 ± 3.02 in group III. The difference is not significant ($p > 0.05$) among the three groups in ANOVA test.

Table - 5

SEX VERSUS MEAN CRP LEVEL

Hs-CRP	**MALE (N=66)**	**FEMALE (N=14)**
Mean	3.65	3.97
S Deviation	2.59	2.97
t-value	0.40	
Significant	0.68 (Not Significant)	

This table shows mean hs CRP levels between male and female. Mean hs CRP level is slightly higher in female patients than in male patients. but the difference is statistically not significant.

Table-6

Distribution of mean vessel and stenosis score

Variables	Group-I (N=19)	Group-II (N=30)	Group-III (N=31)	Significant ANOVA	
				F-value	Sign.
Vessel Score Mean ±(SD)	0.37 ± 0.83	1.40 ± 0.81	2.45± 0.85	37.84	P < 0.001
Stenosis Score Mean ±(SD)	4.00 ± 6.74	17.67 ± 11.40	45.13 ± 23.33	42.47	P < 0.001

The above table showing the distribution of mean vessel and Stenosis Score between the three hs CRP groups of patients. The mean vessel score was 0.37 ± 0.83, 1.40 ± 0.81 and 2.45 ± 0.85 in group I, group II and group III respectively. F-Values reveals that mean score difference were statistically significant (P<0.05) among the three groups in ANOVA Test.

The mean Stenosis score was 4.00 ± 6.74 , 17.67 ± 11.40 and 45.13 ± 23.33 in group I, group II and group III respectively. The score difference were statistically significant (P <0.05) among the three groups in ANOVA Test.

Table-7

Correlation between hs-CRP score with Stenosis score and Vessel score

Variables	Stenosis Score	Vessel Score
hs-CRP level	0.760 **	0.697**

****** Correlation is significant at $P < 0.01$

Significant correlation were found between hs-CRP and vessel Score. The scatter diagram shows that correlation coefficient was 0.760 which is highly significant ($P < 0.01$). Therefore there was linear positive correlation between hs-CRP and stenosis Score.

Significant correlation were found between hs-CRP and vessel Score. The scatter diagram shows that correlation coefficient was 0.697 which is highly significant ($P < 0.01$). Therefore there was linear positive correlation between hs-CRP and vessel Score .

Table-8

Distribution of patients by Vessel Scores

Vessel Score	**Group-I (N=19)**		**Group-II (N=30)**		**Group-III (N=31)**		**Total (N=80)**	
	N	%	N	%	N	%	N	%
0	15	78.9	3	10.0	1	3.2	19	23.8
1	2	10.5	15	50.0	4	12.9	21	26.3
2	1	5.3	9	30.0	6	19.4	16	20.0
3	1	5.3	3	10	20	64.5	24	30.0
Total	19	100	30	100	31	100	80	100

This table shows distribution of patients by vessel score in CRP groups. In group I, 15 patients (78.9%) had 0 vessel score, 2 patients (10.5 %) had 1 vessel score,1 patient each with vessel score of 2 and 3 (5.3 %). In group II, 3 patients had 0 vessel score (10 %), 15 patients had 1 vessel involvement (50%), 9 patients had 2 vessel involvement (30%), 3 patients had 3 vessel involvement (10 %). In group III, 1 patient had 1 vessel involvement (3.2 %), 4 patients had 1 vessel involvement (12.9%), 6 patients had 2 vessel involvement (19.4 %), and 20 patients had 3 vessel involvement (64.5 %). Increased hs CRP level associated with increased vessel score .

Table-9

hs-CRP Group with Diagnosis

	Group-I (N=19)		**Group-II (N=30)**		**Group-III (N=31)**		**Total (N=80)**	
	N	%	N	%	N	%	N	%
MI	9	47.4	18	60.0	17	54.8	44	55.0
UA/NSTEMI	4	21.1	4	13.3	4	12.9	12	15.0
CSA	6	25.0	8	26.7	10	32.3	24	30.0

This table shows patient population in CRP groups. In group I, 9 patients had myocardial infarction. 4 patients had UA/NSTEMI. 6 patients had CSA. In group II 18 patients had myocardial infarction,4 patients had UA/NSTEMI, 8 patients had CSA. In group III, 17 patients had myocardial infarction, 4 patients had UA/NSTEMI, 10 patients had CSA. Myocardial infarction patients were common in all the three groups.

Table-10

hs-CRP Group with vessel involvement.

Variables	Group-I (N=19)		Group-II (N=30)		Group-III (N=31)		Total (N=80)	
	N	%	N	%	N	%	N	%
Left Main	-	-	-	-	5	16.13	05	06.25
LAD	3	15.79	21	70.00	29	93.55	53	66.25
LCX	3	15.79	12	40.00	20	64.52	35	43.75
RCA	1	05.26	11	36.67	22	70.97	34	42.50

This table shows the distribution of vessel involvement in three Hs CRP groups. left main involvement was seen in 5 patients .All 5 patients were in group III. Left anterior descending artery is the most commonly involved vessel in all three groups. Followed by circumflex and Right coronary artery.

Table-11

Hs-CRP levels with Diagnosis

Variables	MI	UA/NSTEMI	CSA	Significant ANOVA	
				F-value	Sign.
Mean	3.99	3.62	3.24	0.631	0.54*
Sd	2.75	2.96	2.64		

* Not Significant

This table shows mean hs CRP levels in three groups of patients. Mean hs CRP of 3.99 was seen in patients with previous myocardial infarction, 3.62 in patients who had UA/NSTEMI and in patients with chronic stable angina.

Table12

Mean EF with diagnosis.

Variables	MI (N=44)	UA/NSTEMI (N=12)	CSA (N=24)	Significant ANOVA	
				F-value	Sign.
E-F	44.48 ± 3.78	57.42 ± 2.87	58.04± 3.22	144.35	P < 0.001

This table shows mean Ejection fraction in different diagnostic groups of patients. Mean ejection fraction was lower in previous myocardial infarction

Table-13

Correlation between hs-CRP score with EF

Variables	E F
hs-CRP Score	-0.043

The poor inverse correlation between hs-CRP level and E-F where found in our study.

DISCUSSION

Several population based studies have revealed that high sensitive C-reactive protein (hs-CRP) is an exquisitely sensitive systemic marker of inflammation and a powerful predictive marker of future cardiovascular risk, Ample data supports that CRP levels are elevated in patients with clinical CAD identified by angiography.

The mechanisms responsible for the association between CRP and cardiovascular disease are not clear. CRP may be only a marker of inflammation and thrombotic risk, without any specific role in the degree of atherosclerosis[8,9] or it may have a direct effect. The following observations suggest that there may be a direct effect: i) CRP has been found in atherosclerotic lesions, ii) CRP binds to low density lipoprotein (LDL), allowing LDL to be taken up by macrophages without the need for modification,[7] and iii) Administration of CRP promotes inflammation in humans and atherosclerosis in an animal model.[10,11]

Various studies have found that CRP is a determining factor in plaque rupture,[12-13] prognosis after non-ST elevation MI,[56] recurrent in-hospital cardiac event, long term mortality after MI,[58] and recurrent ischemic event after coronary artery bypass grafting.[52] Also, among patients with known stable coronary disease, a strong positive correlation between CRP measured at

baseline and future acute coronary events has been demonstrated in most studies.[35-37]

A statement from the Centers for Disease Control and Prevention and the American Heart Association (CDC/AHA) reached the following conclusions for the use of serum hs-CRP to estimate cardiovascular risk:[30] i) The average of two assays, fasting or non-fasting, and optimally obtained two weeks apart provide a more stable estimate than a single measurement, ii) For the determination of cardiovascular risk, low, average, and high risk values were defined as <1, 1 to 3, and >3 mg/L; these values correspond to approximate tertiles in the general population. It was suggested that a value above 10 mg/L should initiate a search for a source of infection or inflammation. The measurement of hs-CRP should be repeated in two weeks and iii) Among patients with known coronary heart disease (CHD), it was suggested that a value >3 mg/L is appropriate for predicting outcomes in patients with stable CHD.

In a large study using the above recommendations from the CDC/AHA, 3771 patients with stable coronary artery disease in the PEACE trial were evaluated.[31] Patients had hs-CRP measured at baseline and were followed for outcomes of cardiovascular death, MI or stroke over a mean follow-up of 4.8 years. The following findings were noted: i) Across all measured subgroups, including men and women, patients on or off statin therapy, and patients with or without prior coronary revascularization, higher baseline hs-CRP levels were

associated with significantly a higher rate of cardiovascular events compared to those with hs-CRP <1 mg/L (hs-CRP 1 to 3 mg/L: adjusted hazard ratio [HR] 1.39, 95% CI 1.06-1.81; hs-CRP >3 mg/L: adjusted HR 1.52; 95% CI 1.15-2.02) and ii) An elevated hs-CRP was predictive of the development of heart failure and new diabetes. In addition, serum CRP may predict coronary disease progression and coronary disease with inducible ischemia on stress testing.

Despite abundant studies, there is still a debate in scientific societies whether inflammation is a chronic process leading to atherosclerosis or it is an acute response to plaque rupture, the main pathogenic event in acute coronary syndrome. In this context this present study was designed to evaluate the role of CRP in prediction of degree of coronary stenosis in patients with chronic stable angina and acute coronary syndromes, compared CRP to other established CHD risk factors to see whether it has an independent role after adjustment for other risk factors.

In our study we also observed that CRP levels did not vary much with history of smoking, though many studies revealed smoking increases CRP levels, we could not either confirm this or disprove this, based on our data.

In this study, it is revealed that CRP levels >1 mg is an independent predictor of stenotic lesions after adjustment for other risk factors.

Zebrak et al[57] also found c reactive protein corrrelates with extent of coronary artery disease. Accordingly, our study revealed majority of our

patients with multi vessel disease had higher CRP levels added to that, only few patients with single disease had higher CRP levels.

Besides the degree of stenosis, the Gensini scoring system gives ample weightage to the proximity of lesions within the coronary tree, the lesions in left main coronary artery getting the maximum score. The overall score thus reflects not only the product of number of lesions with their respective degrees of stenosis, but also the functional significance of lesions in terms of the area of myocardium at stake.

This study also showed reasonable variation in mean hs-CRP levels according to the severity of Coronary atherosclerosis as assessed by the Gensini score angiographic stenosis score was found to be higher in patients with higher hs-CRP levels (Table 6). This shows that hs-CRP level also has correlation with the disease burden apart from being a well known indicator of presence of Acute coronary syndrome.

Nyandak et al,[76] observed in their studies correlation between hs CRP levels and angiographic severity and also studies by **Hansat et al**[89] observed correlation between extent of coronary artery disease and hs-CRP levels which are consistent with our present study.

It therefore suggests that inflammation is not only an important trigger mechanism of acute coronary syndrome related to plaque rupture, but also a

promoter of chronic atherosclerosis, as proposed that CRP might play an atherogenic role through an interaction with low density lipoproteins.

Elevated CRP levels were correlated with the complexity of coronary artery lesions by **Moukarbel** et al[90] who found elevated CRP levels in 56%, 84% and 93% of cases with low, intermediate and highly complex coronary lesion groups respectively. In our study elevated CRP levels (> 1mg) were observed in patients with more stenosis scores. Moreover patients with CRP levels < 1 mg only rarely had higher stenosis score.

There have also been attempts to link serum hs-CRP levels to the vulnerability of coronary plaques in terms of plaque ulceration and inflammation.

Espligureal R et al[91] reported significantly higher hs-CRP levels in patients with acute coronary syndrome compared to chronic stable angina. Evidences like this emphasize the importance of plaque morphologies in addition to the extent of coronary atherosclerosis.

The issue was addressed recently in the study by **Peppes** et al[77] in which significant positive correlations were found between angiographic findings, extent of myocardial damage and serum levels of myocardial enzyme and inflammatory biomarkers.

Higher hs-CRP levels were associated with higher stenosis score in CAD patients, which are consistent with the present study results. Hence, hs-CRP is a single cardiovascular risk factor and increases in CRP concentration within reference limit are associated with future cardiovascular events. Furthermore elevated level of C reactive protein can predict the coronary atherosclerotic disease burden.

Limitations: Despite the statistically significant results of this study, larger cohorts are required in local settings to assess the relationship of hs-CRP levels with the severity of coronary atherosclerosis in local settings.

The coronary angiographic assessment is based upon luminal assessment and lacks plaque visualization. Intravascular ultrasound (IVUS) based assessment of coronary atherosclerotic burden in correlation with hs-CRP levels may be an area of interest for future investigation.

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CONCLUSION

- CRP levels were elevated in our study group irrespective of other traditional risk factors in Acute coronary syndromes.
- Gensini scoring of CAD angiographic severity is in linear correlation to mean CRP levels.
- CRP Levels is correlating well with angiographic stenosis severity.
- Low CRP (<1 mg) is associated with less severe stenotic lesions.
- High CRP (>3 mg)is associated with severe stenotic lesions.
- Number of vessels involved in CAD patients correlates directly with CRP level groupings.
- Higher the CRP levels, more vessels involved.
- Those with Low CRP (<1 mg), had single vessel disease.
- Those with left main disease and its equivalents, triple vessel disease had very high mean CRP levels.
- It appears that ejection fraction did not predict CRP elevation.

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PROFORMA

Name : **IP NO :**

Age : **D.O.A. :**

Sex : **D.O.D. :**

Address :

Admission Diagnosis : UA / NSTEMI

STEMI – AW / IW

Thrombolysis : Given / Not (Time interval –

Killip Class on admission :

Presenting complaints and duration :

Chest Pain :

Dyspnea :

Palpitations :

Other Symptoms :

Past History :

Diabetes mellitus / Systemic Hypertension / CKD / PVD / Stroke / Prior MI

Personal History :

Smoking / alcoholic

Clinical examination :

Height : Weight : BMI :

Vitals :- Pulse : BP :

CVS Examination :

RS Examination :

Other systems examination :

INVESTIGATIONS

1. Hb, TC, DC, ESR, PLATELET COUNT

2. BLOOD SUGAR - F / PP / R –

   BLOOD UREA

3. SERUM CREATININE

4. SERUM ELECTROLYTES

5. CARDIAC ENZYMES

5. LIPID PROFILE –

6 . hs-CRP

6. ECG

7. ECHO

8. CAG

NAME : Age: MRD No:

D.O.P: CD No :

Cath No :

Angio No:

Unit: DONE BY:

Pre cath Diagnosis:

CAG Procedure : Hemodynamic Parameters

Artery Used : Aortic Systolic:

Technique : Diastolic:

Catheters used:

Dye Used :

PROCEDURE:

REPORT:

LMCA :

LAD :

LCX :

RCA :

IMPRESSION :

ADVICE :

GLOSSARY

CAD	:	Coronary Artery disease
hs CRP	:	High sensitive C Reactive protein
DM	:	Diabetes Mellitus
BMI	:	Body mass index
ECG	:	Electro cardio Gram
LMS	:	Left Main Stenosis
MI	:	Myocardial Infarction
CVD	:	Cardio Vascular Disease
LDL	:	Low Density Lipoprotein
HDL	:	High density lipoprotein
LVEF	:	Left Ventricular Ejection Fraction
LVEDV	:	Left Ventricular End Diastolic Volume
LVESV	:	Left Ventricular End Systolic Volume
LVEDD	:	Left Ventricular End Diastolic Dimension
LVESD	:	Left Ventricular End Systolic Dimension
LMCA	:	Left Main Coronary Artery
LAD	:	Left Anterior Descending Artery
LCX	:	Left Circumflex Artery
RCA	:	Right Coronary Artery

S.No	Age	Sex	CD.No	Diaganosis	HT	DM	DYSL.	SM	TC	TG	HDL	LDL		WT	BMI	EF	CRP	LM	LAD	LCX	RCA	VESSEL	STENOSIS
1	59	M	208773	MI	Yes	NO	Yes	NO	210	137	33	146	167	65	23.30	48	5.80	0	P80	P80	D30,PDA90	3	50
2	58	F	206304	MI	NO	NO	NO	NO	170	134	48	82	151	55	24.10	52	8.37	0	p99	p70	0	2	50
3	55	M	209303	MI	NO	NO	NO	NO	113	73	44	54	150	48	21.30	46	0.76	0	0	0	0	0	0
4	72	F	208813	MI	Yes	Yes	NO	NO	140	180	36	80	171	69	23.60	42	9.08	D30	p80	m99	p60,m99	3	66
5	46	F	208776	UA /NSTEM	NO	NO	NO	NO	162	134	48	91	148	55	25.10	55	0.74	0	0	0	0	0	0
6	54	M	208797	MI	NO	Yes	NO	NO	184	150	47	103	166	50	18.00	42	7.20	0	p90	p40	0	1	27
7	38	M	208813	MI	NO	NO	NO	NO	182	137	40	98	166	50	18.10	48	0.63	0	p50	p50	0	2	10
8	49	F	208798	UA /NSTEM	Yes	NO	NO	NO	138	202	39	62	150	48	21.00	58	2.68	0	p70	0	0	1	18
9	55	M	208820	CSA	Yes	NO	NO	NO	181	135	44	113	151	65	28.50	58	4.80	0	0	0	0	0	0
10	73	M	211085	CSA	Yes	Yes	NO	NO	180	146	42	90	156	65	26.70	55	0.79	0	0	p70,d70	0	1	14
11	50	F	211121	CSA	Yes	Yes	Yes	NO	224	148	59	150	164	69	25.70	55	2.70	0	m70	m70	p99	3	26
12	54	F	211282	CSA	Yes	Yes	Yes	NO	170	212	38	82	172	74	25.00	55	2.50	0	p70	0	m70	2	18
13	65	M	126280	MI	NO	NO	Yes	NO	202	213	40	136	156	65	26.70	44	7.84	0	p90	d99	m99,d30	3	60
14	45	M	211294	MI	NO	NO	NO	Yes	180	146	42	90	156	65	26.70	46	2.84	0	p70,m70	0	m99	2	32
15	62	M	211206	CSA	Yes	Yes	Yes	NO	194	137	33	146	166	50	18.10	60	5.20	0	p70	m70	d99	3	30
16	41	M	209826	UA /NSTEM	NO	NO	NO	Yes	194	137	40	126	166	50	18.00	60	6.32	0	m99	0	0	1	24
17	55	F	122851	CSA	Yes	NO	NO	NO	150	148	45	76	153	80	34.20	60	0.63	0	0	0	0	0	0
18	40	M	208806	MI	NO	NO	NO	Yes	166	123	50	91	170	72	24.90	42	0.82	0	0	0	m20	0	1
19	47	M	208816	MI	NO	Yes	NO	NO	105	130	39	46	156	65	26.70	46	2.56	0	p30	0	m60.m70	1	14
20	43	M	208805	MI	NO	Yes	NO	NO	123	105	40	62	171	69	23.60	37	2.80	0	p30	0	0	0	5
21	28	M	208823	MI	NO	NO	NO	NO	140	94	44	75	164	69	25.70	50	0.93	0	0	0	p20,m40	0	3
22	61	M	211463	CSA	Yes	NO	NO	NO	127	73	40	75	164	69	25.70	56	2.20	0	m70	om1 40	0	1	8
23	50	M	211534	CSA	NO	NO	Yes	NO	184	82	33	135	160	65	25.40	55	0.94	0	0	0	0	0	0
24	48	M	211732	CSA	NO	NO	NO	NO	140	180	25	80	171	69	23.60	65	2.60	0	0	m90	m70,d99	2	28
25	46	M	211508	MI	NO	NO	NO	NO	180	146	42	90	156	65	26.70	50	8.82	0	m100	om1-90	p100	3	88
26	58	M	208834	MI	Yes	NO	NO	Yes	124	105	40	63	164	69	25.70	50	5.83	0	m50,d1-70	m30	p40	2	12
27	48	M	208837	MI	NO	NO	NO	Yes	115	79	41	59	164	69	25.70	50	6.12	0	m70	p99	p70,m50	3	52
28	64	M	208836	MI	NO	NO	NO	NO	150	148	45	76	167	66	23.70	38	5.43	0	M70,	D70	0	2	10
29	48	F	199367	CSA	Yes	Yes	Yes	NO	240	134	48	168	151	55	24.10	60	3.96	0	M90,D1 90,D299	OM1 70,M90	M70,D99	3	28
30	51	M	208848	MI	NO	Yes	NO	NO	170	148	38	82	172	74	25.00	47	3.00	0	0	D90	M90,D99	2	32
31	48	M	208824	MI	NO	Yes	Yes	NO	249	264	49	147	166	50	18.10	44	2.76	0	P30	M50,OM1 70	P30,D50	2	15
32	46	M	208838	MI	Yes	NO	Yes	Yes	213	118	39	150	156	65	26.70	47	2.40	0	0	0	D50,70	1	4
33	58	M	212334	UA /NSTEM	Yes	Yes	NO	NO	138	123	35	81	170	72	24.90	55	7.20	0	M40,70	P30,OM1 50	P40,M95	3	31
34	61	M	212077	UA /NSTEM	NO	NO	NO	Yes	151	147	42	88	153	71	30.70	55	2.76	0	P70	P70,M70,D50	P70	3	28
35	63	M	208873	CSA	Yes	NO	Yes	Yes	246	258	30	165	178	63	19.90	60	1.50	0	M 90	OM2 99	0	2	28

S.No	Age	Sex	CD.No	Diaganosis	HT	DM	DYSL.	SM	TC	TG	HDL	LDL		WT	BMI	EF	CRP	LM	LAD	LCX	RCA	VESSEL	STENOSIS
36	65	M	212066	CSA	Yes	NO	Yes	NO	194	137	33	146	168	60	21.30	55	6.24	D30	M 40	OM1 30	P 99,M99D99	3	47
37	66	M	208847	MI	NO	NO	NO	NO	161	148	48	83	165	58	21.30	42	0.92	0	m30	0	0	0	3
38	60	M	208857	MI	NO	Yes	NO	NO	194	137	33	146	172	70	23.70	48	2.35	0	M 50,D 30	0	0	1	5
39	65	M	212795	CSA	NO	NO	NO	NO	164	148	41	93	170	68	23.50	60	3.95	0	M90,D70	M99	P99,M100	3	64
40	61	M	208864	MI	NO	NO	NO	Yes	173	128	42	105	176	66	21.30	44	9.00	D50	P 50,M 70	0	P50,M100	3	55
41	54	M	211581	CSA	Yes	Yes	NO	NO	155	115	43	99	156	68	27.90	55	0.50	0	0	0	0	0	0
42	53	F	208867	UA /NSTEM	Yes	NO	NO	NO	182	139	42	112	150	48	21.30	55	7.95	D30	P50	P 90	M99	3	51
43	39	M	208878	MI	NO	NO	Yes	Yes	278	87	42	118	184	67	19.70	40	5.62	0	100% MID	0	0	1	48
44	62	M	208886	MI	NO	NO	NO	NO	188	130	48	107	172	74	25.00	43	2.38	0	95 ,70 D	0	0	1	28
45	48	M	208880	UA /NSTEM	NO	NO	NO	NO	161	148	40	91	168	56	19.80	57	0.86	0	0	0	P 30	0	2
46	57	M	213083	CSA	NO	NO	NO	NO	152	79	54	82	153	71	30.70	55	5.80	D50	90P,99M	P50,D90	M90	3	70
47	50	M	177807	MI	NO	NO	NO	NO	142	130	36	101	167	53	19.00	42	2.38	0	M70	P90,	0	2	26
48	38	M	94221	CSA	NO	NO	NO	NO	180	146	42	90	174	72	23.80	55	1.72	0	M99	0	M50	2	26
49	40	M	208933	MI	Yes	NO	Yes	Yes	205	182	32	137	164	69	25.70	43	0.71	0	M70	0	0	1	6
50	38	M	208933	MI	NO	NO	NO	Yes	140	180	41	80	171	69	23.60	47	1.80	0	0	0	0	0	0
51	43	M	208897	MI	NO	Yes	NO	NO	124	105	40	63	164	69	25.70	47	2.65	0	M 50	P30	0	1	8
52	40	M	213476	MI	Yes	Yes	Yes	Yes	170	212	38	82	166	82	29.80	47	3.00	0	P99	0	0	1	24
53	41	F	208896	MI	Yes	Yes	Yes	NO	222	164	36	153	153	80	34.20	40	0.94	0	0	P30	0	0	5
54	40	M	208916	MI	NO	NO	NO	NO	145	56	64	70	158	64	25.60	43	0.61	0	M30	0	0	0	3
55	55	M	212667	MI	Yes	Yes	NO	Yes	177	143	48	103	176	70	22.60	44	9.02	0	M60	M100	M60,D90	3	50
56	53	M	212912	UA /NSTEM	Yes	Yes	Yes	NO	194	137	36	144	168	72	25.50	55	2.40	0	M70	M90%	M90	3	29
57	51	M	213612	MI	NO	NO	Yes	Yes	201	109	46	143	174	60	19.80	38	2.90	0	M70	0	0	1	6
58	47	M	213486	MI	Yes	NO	Yes	Yes	202	67	39	150	160	52	20.30	48	7.03	0	M100,D1 100	OM1 70	P50,D80	3	94
59	48	M	123125	UA /NSTEM	Yes	Yes	Yes	NO	211	177	53	123	165	64	23.50	55	8.24	0	P70	P90,	D 99	3	38
60	47	M	208907	UA /NSTEM	Yes	NO	NO	NO	127	156	40	61	167	65	23.30	60	0.80	0	0	0	0	0	0
61	37	M	213475	MI	NO	NO	NO	NO	150	148	45	76	167	66	23.70	40	2.28	0	P90	0	0	1	20
62	60	M	214219	CSA	Yes	Yes	Yes	Yes	245	131	39	196	162	69	26.30	55	5.97	0	P100	0	P70	2	84
63	60	M	210402	CSA	Yes	Yes	NO	NO	140	180	25	80	152	47	20.30	58	6.43	0	P90	0	M70	2	24
64	42	M	213860	MI	Yes	Yes	Yes	NO	140	180	25	80	168	72	25.50	44	2.77	0	P 70	0	0	1	10
65	45	M	213857	MI	NO	NO	NO	NO	185	122	49	112	164	62	23.10	50	2.75	0	0	M50	L	1	2
66	46	M	213430	UA /NSTEM	Yes	NO	Yes	NO	201	256	55	95	158	58	23.20	62	2.85	0	D140	D 90	0	1	10
67	58	F	212984	CSA	Yes	Yes	NO	NO	137	180	48	105	150	48	21.30	58	1.60	0	0	0	0	0	0
68	49	M	213867	MI	NO	Yes	NO	NO	195	138	35	125	164	68	25.30	40	3.00	0	P70	0	0	1	10
69	56	M	214213	MI	NO	NO	NO	NO	141	102	40	87	165	58	21.30	38	0.75	0	0	0	0	0	0
70	60	F	213284	MI	NO	NO	NO	NO	195	148	42	111	147	45	20.80	42	2.83	0	P 99%	0	0	1	40

S.No	Age	Sex	CD.No	Diaganosis	HT	DM	DYSL.	SM	TC	TG	HDL	LDL		WT	BMI	EF	CRP	LM	LAD	LCX	RCA	VESSEL	STENOSIS
71	50	M	213120	CSA	Yes	Yes	Yes	Yes	214	151	52	132	173	62	20.70	58	0.85	0	0	M30	0	0	2
72	55	M	213708	CSA	Yes	NO	NO	NO	122	62	50	48	160	57	22.30	62	2.30	0	P 90	P70,OM170	P 30	2	30
73	55	M	211859	CSA	Yes	Yes	NO	NO	154	148	48	91	164	69	25.70	62	6.25	0	M90,D70	M99	P99,M100	3	64
74	60	M	213894	UA /NSTEM	Yes	Yes	Yes	NO	214	258	36	155	158	57	22.80	62	0.66	0	P50,M70D90	D70,OM3 70	M50	3	27
75	63	M	211647	CSA	Yes	Yes	Yes	NO	201	256	55	95	169	67	23.50	65	7.66	0	P70,M70	OM370	M99	3	34
76	52	M	213900	MI	NO	NO	Yes	Yes	211	234	49	156	164	69	25.70	43	7.64	0	P90	M100	M70	3	56
77	50	M	213885	MI	NO	NO	NO	NO	124	105	40	63	164	69	25.70	46	6.52	0	P99	OM3 50	0	2	41
78	60	F	213853	MI	Yes	Yes	NO	NO	172	165	46	96	170	72	24.90	46	7.10	0	M50	M50	M 100	3	41
79	42	F	213902	MI	NO	Yes	Yes	NO	201	256	55	95	151	55	24.20	43	4.50	0	P 70	0	0	1	10
80	39	M	213933	CSA	NO	Yes	NO	Yes	159	141	42	98	172	68	23.00	56	0.57	0	0	0	0	0	0