A Study on the Impact of the Novel Biochemical Parameter—Calcium Score in Preventing the Progression of the Cardiovascular Diseases to Invasive Interventions

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Summary Cardiovascular diseases is increasing its pace day by day. Though the traditional biomarkers are made available the novel biomarkers are being incorporated to predict the risk of cardiovascular diseases for earlier detection. The present study aimed to investigate the impact of calcium score level the novel biochemical parameter in preventing the progression of the cardiovascular patients to PTCA (percutaneous transluminal coronary angioplasty) and CABG (coronary artery bypass grafting). Four hundred cardiovascular patients irrespective of sex were randomly selected from Visakhapatnam district Andhrapradesh. Information of subjects was collected using an interview schedule. Data collected were consolidated and tabulated. From this group a sub sample of 50 patients was selected and grouped as primordial, secondary and post PTCA. The subjects were then analyzed for their biochemical parameters before and after intervention. Statistical analysis was done and interpreted. An extensive evidence of calcium score was shown among 61.2% of the cardiovascular patients, a minimum evidence of 22.2% and moderate evidence of about 16.5%. The paired sample t-test is employed to observe any statistical significant difference between the before and after treatment effects. The analysis for the calcium score level was found to be significantly lower (mean difference = 424.0134; t = 13.297; df = 49; p = 0.01) in post intervention (mean = 88.3766 ± 88.40) than pre-intervention (512.39 ± 260.79812). The present study identified calcium score the novel biochemical parameter as a key preventive measure among the usual biochemical management conducted by the clinicians to diagnosis and confirm the progression of the disease.

Key Words cardiovascular patients, novel biochemical parameter, calcium score, prevention

Cardiovascular diseases (CVDs) have become the leading cause of mortality in India in the turn of the century (1). In comparison with the people of European ancestry, CVD affects Indians at least a decade earlier and in their most productive midlife years (2, 3). For example, in Western populations only 23% of CVD deaths occur before the age of 70 y; in India, this number is 52% (4). In addition, case fatality attributable to CVD in low-income countries, including India, appears to be much higher than in middle- and high-income countries (5, 6). The World Health Organization (WHO) has estimated that, with the current burden of CVD, India would lose $237 billion from the loss of productivity and spending on health care over a 10-year period (2005–2015) (7).

Adequate screening for identifying individuals at risk of developing cardiovascular disease (CVD) is important because vascular disorders are a preventable cause of morbidity and mortality worldwide. Furthermore, the lifetime risk of developing CVD is high (estimated at 66% for men and ≥50% for women), and often the first symptom of disease is a sudden death, thereby occurring without an opportunity for intervention (8–10).

The onset of CVD itself portends an adverse prognosis with greater risk of recurrent events, morbidity, and mortality. It is also increasingly clear that although clinical assessment is the keystone of patient management, such evaluation has its limitations. Clinicians have used additional tools to aid clinical assessment and to enhance their ability to identify the “vulnerable” patient at risk for CVD, as suggested by a recent National Institutes of Health (NIH) panel (11). Biomarkers are one such tool to better identify high-risk individuals, to diagnose disease conditions promptly and accurately, and to effectively prognosticate and treat patients with disease.

Vascular calcification is a life threatening complication of cardiovascular disease and an independent risk factor for high morbidity and mortality (12). It is an inevitable process particularly in the advanced stages of atherosclerosis which can cause the plaque rupture. Coronary artery calcification (CAC) is a surrogate marker for subclinical atherosclerosis and recently

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determined as strong predictor that comforts the prediction of future cardiovascular events particularly in intermediate risk subjects. It is determined by electron beam-computed tomography (EBCT). (13) Increased coronary artery calcium score (CACS) correlates with the risk of cardiovascular disease (14). Considering the necessity of novel biochemical parameters of ruling out cardiovascular diseases and their progression towards severity, the study was undertaken to assess the effectiveness of using calcium score as a biomarker for evaluating cardiovascular diseases.

**MATERIALS AND METHOD**

**Study design and participants.**

This study was conducted on randomly selected 400 subjects with cardiovascular disease \((n=400)\) aged 30–65 y from hospitals in and around Visakhapatnam district. All the selected subjects were screened for their biochemical parameters. The subjects were grouped into 3 groups, each with 50 subjects namely primordial group (on diet and medicine), secondary group (advised PTCA), and post PTCA (advised CABG). The inclusion criteria were subjects who were not screened for any cardiac profiles (total cholesterol >220 mg/dL and/or serum triglyceride >140 mg/dL, ECG-ischemic elevations positive) as primordial group. Subjects who have undergone PTCA and the subjects who are referred for CABG (CAG lesions >90%). The exclusion criteria were pregnant women, subjects who were affected with complete cardiac failure, subjects who were having triple vessel diseases and subjects undergone CABG.

Approvals from the head of the hospital authorities were taken. Informed consent of medical superintendent, relatives and accent of patients was taken before the study commenced. The cardiovascular patients were oriented about the questionnaire to be administered in advance and were informed about their right to withdraw from the study anytime.

**Study dimensions.**

**Socio-economic profile.** The socioeconomic status has been reported also as a determinant of CVD and its risk factors. Questions related with their ethnicity, type of family, age and gender were also included in the questionnaire.

**Interview proforma development.** The interview method of collecting data involves presentation of oral-verbal stimuli and reply in terms of oral-verbal responses. A structured personal interview was used for the collection of information from the subjects. This type of interviews involves the use of a set of predetermined questions and of highly standardized techniques of recording and the interviewer follows a rigid procedure laid down, asking questions in a form and order prescribe. The objective was to administer a short interview schedule covering various aspects following the nutritional status of the patient.

**Content validation.** The content validation of the questionnaire was assessed by the cardiac panel, a physician (General Medicine) and a nutritionist. A pool of

| Table 1. Background details of the selected subjects. \((N=400)\) |
|---------------------------------------------------------------|
| **Particulars** | **Number** | **Per cent** |
| Age Category | | |
| 30–40 | 208 | 52 |
| 40–50 | 67 | 16.8 |
| 50–60 | 90 | 22.5 |
| 60–70 | 35 | 8.8 |
| Family history | | |
| None | 290 | 72.5 |
| First Degree Relatives | 62 | 15.5 |
| Second Degree Relatives | 48 | 12.0 |
| Religion | | |
| Hindu | 65 | 16.2 |
| Christian | 80 | 20.0 |
| Muslim | 255 | 63.8 |
| Education | | |
| Below High School | 235 | 58.8 |
| High School | 136 | 34.0 |
| Above High School | 29 | 7.2 |

| Table 2. Biochemical indices of the selected subjects. \((N=400)\) |
|---------------------------------------------------------------|
| **Particulars** | **Number** | **Per cent** |
| C-reactive Protein | | |
| Mild Evidence | 16 | 4.0 |
| Moderate Evidence | 148 | 37.0 |
| Extensive Evidence | 236 | 59.0 |
| Serum Albumin | | |
| Lower than normal | 200 | 50.0 |
| Normal | 192 | 48.0 |
| Greater than normal | 8 | 2.0 |
| Homocysteine levels | | |
| Lower than normal | 14 | 3.5 |
| Normal | 22 | 5.5 |
| (15–30 micromoles/L) | 172 | 43.0 |
| Greater than normal | 192 | 48.0 |
| (100 micromoles/L) | | |
| Intermediate | 245 | 61.2 |
| Calcium Score Levels | | |
| Mild Evidence | 89 | 22.2 |
| Moderate Evidence | 66 | 16.5 |
| Extensive Evidence | 245 | 61.2 |

![Fig. 1. Treatment advised to selected cardiovascular patients.](image-url)
fifty questions was generated. Content validity was checked by rating the questions as most relevant, relevant and least relevant. The most relevant forty-two questions out of fifty questions based on the economic background, anthropometric measurements, diet history, life style habit and medical history of the subjects were administered by the researchers in a short period of time were included. The questionnaire was pretested on cardiovascular patients (males) and then finally administered to the cardiovascular subjects as a whole.

**Interview schedule administration.** The purpose of the interview schedule administration was explained to cardiovascular subjects once their assent was obtained. They were informed about the participation in study was voluntary and they were free to withdraw at any stage. The interview schedule was administered during the period of stay of the patient in the hospital or at home when the patient is registered under outpatient department. The bystander or the immediate relative of the cardiovascular subjects were called individually for filling the questionnaire and the data was self-reported by the patient or his immediate relative after each and every question was read and explained to them.

**Nutritional assessment.** A vertical tape settled perpendicular to the ground on the wall was utilized as the scale to gauge the height of the respondents. Height was read to the nearest of 0.5 cm. An average of three measurements was taken as the final measurement.

Weight of the subjects was measured using a bathroom balance. Checks on the scale were made routinely before recording the weight of each sample and the pointer was adjusted to zero using the screw provided. The weight was recorded to the nearest 0.25 kg. Each
Subjects’ weight was taken thrice and the average was taken as the final measurement.

The biochemical parameters were studied among a sample size of 400 subjects. The subjects were analyzed for fasting blood sugar, lipid profile, homocysteine, serum albumin, calcium score etc. Apart from this, the invasive cardiac parameter, calcium score level was recognized to be a novel parameter and considered one of the major characteristic for diagnosis of the disease.

Dietary counselling as an intervention was given to the selected 150 subjects. The counselling was given for six months to each group. The improvement in the biochemical values showed the effectiveness of the intervention.

After the intervention (Dietary counselling) the biochemical indices were evaluated by comparing the pre and post intervention values. As the randomly selected cardiovascular patients were grouped into three, the biochemical indices were even compared among the group.

Statistical analysis.

Data analysis was conducted using SPSS version 16. Quantitative variables are expressed in mean±SD. For testing the effect of intervention paired t test was applied. For comparing the three groups, one way ANOVA was done with Games Howell post-hoc test.

To know whether there is any significant difference among the three groups one way ANOVA was done by taking the difference between final and baseline values. Since homogenity of variance assumption is violated Welch’s F statistic was used.

RESULTS

It was observed that among the 400 cardiovascular patients, majority (52%) belonged to middle age group of 30–40 y. The distribution of family history of the respondents in the occurrence of the cardiovascular diseases showed that the highest percentage (72.5%) of the subjects had no family history of cardiovascular diseases. About 15.5% of the patients had first degree relative with cardiovascular diseases. The religious distribution of respondents was that nearly 63.8% of the subjects were Muslims, whereas Christians and Hindus constituted 20 per cent and 16.2 per cent respectively. It is remarkable that 58.8% of the cardiovascular patients had education below high school. Among them, 41.8% of the subjects had passed higher secondary levels and only 7.2% were above high school level and possessed professional qualifications.

The C-reactive protein levels were found to be intermediate or severe in about 96% of the cases. C-reactive protein (CRP) is the best studied of the inflammatory biomarkers in CAD. About 50% of patients had albumin levels lower than normal levels. Presence of homocysteine observed was intermediate or severe in about 90% of the cases.
From the heat-map representation it can be observed that a very prominent difference in the level of cholesterol, systolic blood pressure and triglyceride was observed among the individual subjects of the pre and post dietary intervention group. Although the level of cholesterol, systolic blood pressure and triglyceride deceased to only 0.93, 0.96 and 0.82 fold in the post dietary intervention group but it helped in lowering these values to the normal level. Calcium scoring levels in the post dietary intervention group was found to decrease to a significant 0.74 fold in comparison to pre dietary group but even then the level was found to be above the normal levels in most of the individual subjects. The calcium score levels after the intervention (Nutritional counseling) are found to be significantly less. The analysis for the calcium score level was found to be significantly lower (mean difference=424.0134; t=13.297; df=49; p=0.01) in post intervention (mean=88.3766±88.40) than pre-intervention (512.39±260.79812).

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It was observed that the dietary counselling which was given before and after intervention among the primordial, secondary and post PTCA group had significant effect on the various physical and biochemical parameters under consideration for the study. Among all the parameters significant difference was observed among the pre and post dietary intervention groups in calcium score level of which was prominently seen in the majority of cases. Mild and moderate evidence was seen in lesser number of cases (39%). The standard values of the calcium score levels, as the score difference was seen in lesser number of cases (39%).

## DISCUSSION

Biomarkers can indicate a variety of health or disease characteristics, including the level or type of exposure to an environmental factor, genetic susceptibility, genetic responses to exposures, markers of subclinical or clinical disease, or indicators of response to therapy. Thus, a simplistic way to think of biomarkers is as indicators of disease trait (risk factor or risk marker), disease state (preclinical or clinical), or disease rate (progression) (15). Estimation of the CAC score is, therefore, currently considered a valuable supplement to the Framingham Risk Score for the assessment of CVD risk in individuals with a familial history of premature vascular disease (16, 17) and among patients classified as having an intermediate 10-year risk of CHD based on the Framingham Risk Score (18, 19).

Calcium evidence was seen to be a sure bio-marker in the case of heart diseases. Extensive evidence was seen in the majority of cases. Mild and moderate evidence was seen in lesser number of cases (39%). The standard values of the calcium score levels, as the score 1–112 indicates average risk, 100–400 for moderate

### Table 3. The difference in the levels of various physiological and biochemical parameters among the pre and post dietary intervention group in the primordial, secondary and post PTCA group.

| Group             | Mean ± SD  | Mean Fold difference | p valuea |
|-------------------|------------|---------------------|----------|
| **Primordial**    |            |                     |          |
| Blood glucose     | Pre 150.9±40.13 | 1 | <0.01** |
|                   | Post 128.2±9.9 | 0.85 |        |
| Cholesterol       | Pre 254.4±31.3 | 1 | <0.01** |
|                   | Post 236.7±17.6 | 0.93 |        |
| SBP               | Pre 135.6±17.28 | 1 | <0.05* |
|                   | Post 131.2±12.16 | 0.96 |        |
| DBP               | Pre 84.6±5.54 | 1 | 0.43 |
|                   | Post 83.5±4.3 | 0.98 |        |
| Plasma HDL        | Pre 64.58±6.2 | 1 | 0.14 |
|                   | Post 63.4±6.72 | 0.98 |        |
| Triglyceride      | Pre 211.5±63.43 | 1 | <0.01** |
|                   | Post 172.2±31.3 | 0.82 |        |
| Plasma LDL        | Pre 147.5±26.55 | 1 | <0.01** |
|                   | Post 138.1±16.1 | 0.94 |        |
| Serum albumin     | Pre 3.3±0.51 | 1 | <0.05* |
|                   | Post 3.5±0.24 | 1.06 |        |
| Homocysteine      | Pre 27.18±9.88 | 1 | <0.05* |
|                   | Post 25.7±9.14 | 0.94 |        |
| Calcium score     | Pre 91.55±78.76 | 1 | <0.01** |
|                   | Post 68.5±74.06 | 0.74 |        |
| CRP               | Pre 1.02±0.44 | 1 | <0.01** |
|                   | Post 0.83±0.22 | 0.81 |        |

| **Secondary**     |            |                     |          |
| Blood glucose     | Pre 126±19.4 | 1 | 0.38 |
|                   | Post 143±14.9 | 0.98 |        |
| Cholesterol       | Pre 303±44.5 | 1 | <0.01** |
|                   | Post 211±23.4 | 0.7 |        |
| SBP               | Pre 137.2±18.41 | 1 | <0.01** |
|                   | Post 126.6±7.17 | 0.92 |        |
| DBP               | Pre 84±11.95 | 1 | 1 |
|                   | Post 84±5.7 | 1 |        |
| Plasma HDL        | Pre 39.3±11.85 | 1 | <0.01** |
|                   | Post 68.38±8.09 | 1.73 |        |
| Triglyceride      | Pre 641±204 | 1 | <0.01** |
|                   | Post 166.7±71.02 | 0.26 |        |
| Plasma LDL        | Pre 134.88±31.77 | 1 | <0.01** |
|                   | Post 108.96±20.14 | 0.8 |        |
| Serum albumin     | Pre 2.71±0.54 | 1 | <0.01** |
|                   | Post 3.0±0.51 | 1.13 |        |
| Homocysteine      | Pre 117.01±30.83 | 1 | <0.01** |
|                   | Post 30.1±27.62 | 0.25 |        |
| Calcium score     | Pre 512.39±260.79 | 1 | <0.01** |
|                   | Post 88.37±88.40 | 0.17 |        |
| CRP               | Pre 4.32±2.47 | 1 | <0.01** |
|                   | Post 1±0.36 | 0.23 |        |

| **Post-PTCA**     |            |                     |          |
| Blood glucose     | Pre 238±93.67 | 1 | <0.01** |
|                   | Post 207.5±75.81 | 0.87 |        |
| Cholesterol       | Pre 262.4±44.96 | 1 | <0.01** |
|                   | Post 225.8±28.97 | 0.86 |        |
| SBP               | Pre 149.8±15.84 | 1 | <0.01** |
|                   | Post 139.8±12.37 | 0.93 |        |
| DBP               | Pre 88.6±15.65 | 1 | 0.68 |
|                   | Post 87.8±5.81 | 0.99 |        |
| Plasma HDL        | Pre 44.14±10.74 | 1 | <0.01** |
|                   | Post 55.36±10.77 | 1.25 |        |
| Triglyceride      | Pre 376.2±196.28 | 1 | <0.01** |
|                   | Post 204.32±47.23 | 0.54 |        |
| Plasma LDL        | Pre 142.94±29.35 | 1 | <0.01** |
|                   | Post 129.54±23.84 | 0.9 |        |
| Serum albumin     | Pre 2.24±0.6 | 1 | <0.01** |
|                   | Post 2.85±0.43 | 1.27 |        |
| Homocysteine      | Pre 59.05±17.9 | 1 | <0.01** |
|                   | Post 40.54±12.52 | 0.68 |        |
| Calcium score     | Pre 250.39±180.46 | 1 | <0.01** |
|                   | Post 105.5±72.02 | 0.42 |        |
| CRP               | Pre 4.32±1.62 | 1 | <0.01** |
|                   | Post 3.18±1.25 | 0.73 |        |

*p<0.05, **p<0.01 a- t-test.

Among the 400 cardiovascular patients 48.25% of them were treated with PTCA. 28.25% were advised CABG and 23.25% were on medical management.

260.79812).
risk. 400–999 high risk and 100 and above as very high risk (20).

Detection of coronary calcium score by a helical computed tomography scanner is a useful tool for predicting the presence of significant coronary artery disease in intermediate-to-high risk patients. On the other extreme, score >400 is highly predictive of the presence of coronary artery disease, and virtually confirms the presence of significant coronary artery disease in intermediate-to-high risk patients (21).

Biomarkers, defined as alterations in the constituents of tissues or body fluids, provide a powerful approach to understanding the spectrum of CVD with applications in at least 5 areas: screening, diagnosis, prognostication, prediction of disease recurrence, and therapeutic monitoring.

To improve the efficiency of diagnosis of the progression of the cardiovascular diseases novel biochemical parameters can add on to the protocol even though this cannot be relied on as a major biochemical tool for the evaluation of the disease.

Disclosure of state of COI

No conflicts of interest to be declared.

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