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Assessment of Coronary Microvascular Diastolic Transit Time (CMDTT) and its Correlation with Myocardial Dysfunction

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Abstract: ***Aim: We assessed the CMDTT in patients with coronary atherosclerosis risk factors such as Diabetes Mellitus, Hypertension and smoking to those without risk factors and correlated with insipient LV myocardial dysfunction. Methods: 104 patients (54 females, 50 males) were included. 52 patients in each risk factor group such as DM, HTN, smoking and 52 were in control group without any risk factors. Results: The mean age of the subjects was 53.8 +/- 11.04 years. Mean CMDTT in subjects without any risk factor was 2.31±0.25 seconds, 2.51±0.59 seconds in subjects with risk factors (p<0.05). Conclusion: Presence of increased CMDTT in patients with risk factors for endothelial dysfunction of main vessels and is predictor of onset of left ventricular dysfunction well before any non invasive testing modality for assessment of left ventricular muscle dysfunction.***

Keywords: Coronary microcirculation, Coronary microvascular dysfunction, Diabetes mellitus, Hypertension, Left ventricular dysfunction

1. Introduction

Historically, the only practical methods available for the assessment of coronary microvascular dysfunction (CMD) have been invasive, such as intracoronary (IC) Doppler flow wire or thermodilution. This has likely impaired the objective evaluation of CMD in patients presenting with chest pain without obstructive CAD. Thus, the treatment of CMD has often been studied within imprecise clinical entities such as cardiac syndrome X [1].

There are multiple diagnoses that may cause chest pain without obstructive CAD. These diagnoses include microvascular angina, gastroesophageal reflux disease, musculoskeletal chest pain, cardiac syndrome X, cardiac syndrome Y (slow coronary flow), coronary spasm, and no reflow phenomena, among others. These entities derive from multiple different pathophysiological processes. These various pathophysiological causes can be described as causing noncardiac pain, cardiac ischemic pain, and cardiac nonischemic pain [2].

Coronary microcirculation is dependent on central aortic pressure, epicardial coronary vessel stenosis and autonomic influences and local paracrine endothelial dysfunction in R_2 and R_3 vessels. Hence, CMDTT is affected by these in a steady state. CMDTT is a good parameter to predict onset of insipient LV myocardial dysfunction and can be correlated with the magnitude of myocardial dysfunction as well.

Aim: We aimed to calculate CMDTT in health and disease state viz HTN, DM and smokers and to correlate it with magnitude of LV myocardial dysfunction.

Inclusion criteria: Patients with positive exercise stress test and normal CAG. Some authors accept a diagnosis of microvascular angina in patients with non-flow limiting stenosis (that is, less than 50%). However, since data from intravascular ultrasound studies suggest that the degree of stenosis might be underestimated angiographically, [3] we have selected only those patients with entirely normal arteriograms. Patients were asked about history for risk factors for coronary artery disease such as Diabetes, hypertension, smoking. [4-7]

Exclusion criteria: patients with obstructive coronary artery disease, S. creatinine > 1.2mg/dl, coronary arteries with slow flow phenomenon, significant valvular heart disease, cardiomyopathy, previous revascularization, arrhythmias, heart blocks.

2. Method

Levophase of the coronary angiogram has been neglected in literature. Cardiac contrast transit has 3 components. Arterial component is time taken to travel from coronary ostium to the tip of epicardial artery. Myocardial component starts at the end of arterial component and ends with myocardial blushing. Venous component is the time taken from the appearance of contrast at the venules to exit at coronary sinus ostium. Arterial component is affected by plaque, thrombus, myocardial bridge, LVEDP and spasm. Obstruction at R2/ R3 levels affects the myocardial component. Venous component is affected by rare causes such as venous spasm and foreign bodies (e.g. LV endocardial pacing lead). Cardiac syndrome x is defined as angina and other signs associated with decreased myocardial blood flow in a patient with normal coronary angiogram. Slow flow of blood into microvasculature may cause angina even if epicardial coronaries are normal. We are interested in the myocardial component as the reason for cardiac syndrome X. Also, coronary arterial blood flow, its forward flow into microvasculature occurs in diastole and R3 component is eliminated in diastole. This is extensively validated in instantaneous wave free ratio (IFR) studies. So, CMDTT can detect abnormal microvasculature.

104 patients (54 females, 50 males) were included. The LAO cranial view for the left coronary system was used. Once the left coronary system was identified as normal, cine

exposure was continued till exit of the contrast from coronary sinus. Image acquisition was done at 15 frames/sec. Time was calculated by number of frames from the point dye reaches the pitch forked end of the LAD till it exits the coronary sinus. CMDTT was calculated by E.C.G. based discrimination from the total transit time. Diastolic transit time was calculated as summation of the duration of diastole (time from end of T wave to starting of QRS complex on ECG) for each cardiac cycle during the microvascular transit time.

3. Discussion

Primary stable MVA is characterised by angina episodes that are exclusively or predominantly triggered by effort or other conditions that increase myocardial oxygen demand. The ECG taken during effort usually shows typical ST-segment depression in most patients, and reversible stress-induced myocardial perfusion defects are usually detectable in over 50 % of patients.[9] In MVA patients exercise- and/or stress-induced angina, tends to be longer lasting with a slower resolution (>10–15 min) of chest pain after stopping exercise, and/or following the administration of short-acting nitrates, compared with anginal episodes in CAD patients.[9–11]

Several studies have demonstrated CMD in patients with stable angina who have normal or near normal epicardial coronary arteries.[12–16] Structural abnormalities of the small coronary arteries have been described in several studies, including vascular smooth muscle hypertrophy, capillary rarefaction or vascular wall fibrosis.[12,13] Functional changes of the coronary microcirculation appear to be more frequently found to be the mechanism for MVA and include both a reduction of the vasodilator response and increased vasoconstrictor activity, i.e. microvascular spasm.[14–16] Initial studies showed an impaired increase of coronary blood flow in response to dilator stimuli such as dipyridamole and atrial pacing using the invasive xenon wash-out and thermodilution methods, respectively.[12–17] Impaired CFR was subsequently confirmed in many studies using various other methods. PET and CMR studies showed abnormal CBF responses and myocardial perfusion abnormalities involving mainly the subendocardium in patients without obstructive CAD, suggesting an involvement of the coronary microcirculation.[18] All these are expensive and time comsuming tests, CMDTT provides this information with a coronary angiogram without any extra cost.

Larger studies, however, have recently challenged the view that MVA carries a good long-term prognosis.[19] These studies, however, included more heterogenous groups of patients, with potential markers of worse outcome, including subcritical coronary atherosclerosis, impaired LV function and arrhythmias. So, CMDTT also provides prognostic information by predicting microvascular dysfunction and resulting left ventricular functional impairment.

4. Conclusion

CMDTT can be easily calculated using the LAO cranial view and in patients with normal CAG and classic angina can predict microvascular dysfunction and the resulting left ventricular dysfunction.

5. Limitations

Despite the normalization process that serves to standardize each experiment, CMDTT does not fully replicate physiological conditions in vivo.

Although we have achieved statistical significance, Small sample size and Single centre data are potential pitfalls of our study. But we have laid down the groundwork for future studies with long term follow up to evaluate prognostic significance of CMDTT.

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Table 1: Patient characteristics

Risk Factor	Risk factor	No risk factor
n	52	52
Age, in years *	52.6±8.9(p>0.05)	53.1±9.4
Females, No.	26 (p>0.05)	28
Males, No.	26 (p>0.05)	24
Heart Rate *	85.2±12.4 (p>0.05)	82.4±10.9
CMDTT, in seconds*	2.51±0.59 (P=0.003)	2.31±0.25
BMI	22.8 (p>0.05)	22.1
Family history of IHD	33 (p>0.05)	29
Family history of CVD	21 (p>0.05)	20

* Plus–minus values are means ±SD. There were no significant differences between the groups (p value>0.05) except CMDTT (p value >0.05), with values not adjusted for multiple testing. Percentages may not total 100 because of rounding. p values are for comparison between the respective risk factor group and the no risk factor group.