Correlation of impaired flow mediated dilatation in coronary artery disease patients with erectile dysfunction in north Indian population

Gaurav Kumar Chaudhary[*] MD,DM,V.S Narain[**]MD,DM ,SK DwivediDM,FSCAI [**],Rishi Sethi[**]DM,FACC,FESC Sharad Chandra[**]DM,FACC

[*] Assistant Professor
[**] Professor ,Department of Cardiology ,Department of Cardiology ,King George's Medical university ,Lucknow

Abstract- Endothelial dysfunction, an important antecedent event in atherosclerosisdevelopment, has been suggested as the common pathophysiologicalfactor between erectile dysfunction (ED) and coronary artery disease (CAD). Flow mediated dilatation (FMD) is frequently used, reliable non invasive marker for endothelial assessment. The present study, we set out to address the relationship of FMD with ED patients undergoing diagnostic coronary angiography. 243 male patients were enrolled in this study. Patients were evaluated by the erectile dysfunction domain of IIEF, a self validated 15 items. There was statistically significant value (P= .0001)between the severe ED patients and extent of CAD. Also the result shows that moderate and severe ED was more in patients with impaired FMD <5.5% as compared to those with normal, FMD > 5.5%. This association was statically significant, P value (<.001). Thus the study finally concludes that functional endothelial abnormality seems to contribute to generalized vascular atherosclerotic process.

Index Terms- Endothelial dysfunction, coronary artery disease, erectile dysfunction, and flow mediated dilatation.

I. INTRODUCTION

Endothelial dysfunction is observed in the early stages of atherosclerosis,and this abnormality can be assessed by measuringflow-mediated dilatation of the brachial artery (FMD)**(1-3)**. FMD is thought to be a marker of vascular damage and/ora predictor of future cardiovascular events in subjects withcardiovascular disease (CVD) risk factors**(1-3)**. Therelationship between ED and cardiovascular diseases (CVD) hasreceived considerable attention because they not only often coexistbut also share multiple risk factors including diabetes, hypertension,hyperlipidaemia, obesity and smoking. The presence of concomitantED is known to predict future coronary heart disease, stroke andincreased mortality in both low-risk and high-risk cardiovascularpatient populations, independent of conventional cardiovascular riskfactors**(4-6)**.

Flow-induced vasodilation is an endothelium-dependent process,and impaired response to reactive hyperaemia-induced shear stressis a sign of endothelial dysfunction. Ultrasonographic assessment ofbrachial artery flow-mediated vasodilatation (FMD) is a frequentlyused, reliable and reproducible non-invasive surrogate marker forendothelial function assessment**(7-**

8).Impaired brachial artery FMD in patients with ED has previouslybeen reported, usually in patients without associated CAD, thus demonstratingthe presence of endothelial dysfunction in these patients**(9-14)**.

There are no data regarding the endothelial function,FMD and ED in these patient populations with angiographicallydocumented CAD. The present study was conducted to examine the relationships between FMD and ED among patients undergoing coronary angiography for CAD.

II. METHOD

Design and Subjects:

The present study was conducted in the Department of Cardiology, King Georges Medical University, Lucknow. 243 Patients were enrolled in our study from November 2011 to October 2012 as per the inclusion criteria. Patients were evaluated by using IIEF questionnaire, and were divided into groups according to IIEF scores, angiographic involvement of coronary arteries, and presentation (acute and chronic). All the patients with ST elevation myocardial infarction, non ST elevation myocardial infarction or unstable angina having angiographically proven CAD,>50% lesion in at least one coronary artery, were included in this study. All patients went for the evaluation of erectile dysfunction at urology department. Patients with psychogenic and neurogenic cause of erectile dysfunction, chronic renal failure, cirrhosis, hypothyroidism,hyperthyroidism and also with pelvic, urethral,penile injury were excluded from the study. After the enrollment,patients were subjected to detailed history, physical examination, investigations including complete hemogram, lipid profile, blood sugar and renal function tests and treatment as per the protocol of the department. After taking the informed consent were obtained from all the patients they were divided into two groups based on the basis of presentation:

Group 1 -Acute Presentation (STEMI, NSTEMI, UA)
Group 2 - chronic (CSA)
Groups were divided according to coronary angiography findings –
Group A - minimal disease or single vessel disease
Group B – double vessel or triple vessel disease
Significant coronary artery disease was defined as   > 50 % luminal diameter stenosis

Evaluation of erectile function:

Erectile dysfunction was evaluated by the erectile function domain of the International Index of Erectile Function (IIEF-EFD) a validated 15-item self-administered questionnaire. IIEF questionnaire**(15)** was administered to patients after a mean time interval of 3 days since the admission to the hospital. Erectile function is specifically addressed by six questions that form the so called 'erectile function domain' of the questionnaire. Each question is scored 0 to 5.

*Assessment of the Flow-Mediated Dilation of Brachial Artery***:**

Subgroup analysis was also done by doing flow mediated dilation in patients endothelial function in the form of flow-mediated brachial artery vasodilatation (FMD) was measured using high-frequency 7.5 MHz ultrasound probe at our department. FMD of the brachial artery was assessed from the subject's left arm once it was comfortably immobilized in the extended position. The diameter of the brachialartery is measured by a 7.5 MHz ultrasound probe , positioned 5 cm above the elbow, at rest and during reactive hyperemia induced by 5-min occlusionof the brachial artery by an inflated cuff positioned on the forearmFMD (%) was defined as maximum vessel diameter change after cuff deflation/average control diameter. Flow mediated dilatation of <5.5% was taken impairment, based on available literature**(16).** Vasoactive medications, such as nitrates, calcium antagonists, angiotensin-converting enzyme inhibitors, and beta blockers were withheld 24 to 48 h before the study. Caffeinated beverages and smoking were not allowed on the day of the study.

Statistical analysis:

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean±SD. The ANOVA test was used to compare the within group and between group variances amongst the study groups *i.e.* the three different sealers. Analysis of variance of these three sealers at a particular time interval revealed the differences amongst them. ANOVA provided "F" ratio, where a higher "F" value depicted a higher inter-group difference.

III.   RESULTS

During the one year period of study, a total of 243 patients with CAD (acute and chronic), undergoing coronary angiography in the Cardiology Department of King George's Medical University, were enrolled.The baseline characteristics of the patients (only male patients enrolled) were similar in both groups shown in **Table 1**. Mean age of patients in group A was 56 +- 8.43 yrs,and in group B patients was 58+- 8.53 yrs.The average systolic blood pressure was 143.48±14.17 mm Hg and diastolic 82.54±8.82 mm Hg at presentation in hospital during this study. In group A,57.3 % Patients were hypertensive where as group B,54.7 % Patient were hypertensive. Hypertension was defined as systolic BP greater than 140 mm of Hg and diastolic greater than 90 mm of Hg.Smoking and tobacco usage percentages in group A and B were 35.4% and 31.7% respectively .Patients in both groups had comparable proportion of diabetic patients ,41.5 %and 42.33% in group A and B respectively.The mean BMI of

patients ingroup A and group B was 24.75 and25.32 respectively. Patients having BMI above 25 indicates obesity(BMI >25 according to Indian standards).Low ejection fraction was seen (LVEF <50%) in 135 patients(55.55%) out of total 243 patients.In our study majority of patients had acute presentation, 171patients (70.3 %) presented as ACS (STEMI,NSTEMI, UA) where as patients with chronic stable angina comprised smaller fraction of 72 patients (29.6%), **Table-1**. The CVD risk factors were defined as follows: obesity:BMI≥25; smoking: current smoker; hypertension: bloodpressure levels at the time of measurement of FMD≥140/90mmHg; hypercholesterolemia: TC≥6.22 mmol/L; diabetesmellitus: FPG 6.99>mmol/L.

In this study patients with progressive lower IIEF score (severe ED), more frequently had triple or double vessel CAD on coronary angiography. Group B (double vessel ds or more) patients had more prevalence of severe ED as compared to Group A (single vessel or minimal ds) This finding was statistically significant (P=.0001). The correlation between severe ED and extent of CAD is demonstrated in **Table-2 and Figure-1**

Table-3 shows that moderate and severe ED was more in patients with impaired FMD <5.5% as compared to those with normal, FMD > 5.5%. This association was statically significant, P value (<.001).Thus functional endothelial abnormality seems to contribute to generalized vascular atherosclerotic process**Figure-2**.

IV.   DISCUSSION

There is rapidly growing interest in the association between ED and risk of CAD. A recent Meta-analysis by **jia–yi-dong et al(17)**, of 12 prospective cohort studies, provides evidence that ED is significantly and independently associated with an increased risk of CVD, CHD, stroke, and all-cause mortality. Men with ED, compared with the reference group, experienced a significantly increased risk of 48% for CVD, 46% for CHD, 35% for stroke, and 19% for all-cause mortality. ED may be considered an independent risk factor of CAD.

At present, the association between ED and CAD is not fully understood. It is well accepted that CAD is a risk factor of ED. It is also recognized that ED is a marker of further vascular diseases. However, whether ED is independently associated with incidence of CVD remains controversial. Results from sensitivity analysis restricted to studies with control for conventional cardiovascular risk factors, including age, body mass index, blood pressure, diabetes, cholesterol, and smoking, suggest that ED is probably an independent risk factor of CVD. Moreover, if ED was merely an early marker, it would be more likely to occur near the time of onset of cardiovascular events. In fact, the mean length of follow-up in primary studies ranged from 4 to 16 years. Such a large interval between the 2 diseases further supports the hypothesis that ED is an independent risk factor.

In our study majority of patients had acute presentation ,171 patients (70.3 %)presented as ACS (STEMI ,NSTEMI,UA) where as patients with chronics stable angina comprised smaller fraction of 72 patients (29.6%), ED was seen more in patients with ACS (65.50%)compared to stable angina(51.38) but no statistical significant association seen between presentation of CAD and prevalence of ED. This finding was different from

study by PieroMontorsi et al**(18)**which showed more prevalence of ED in patients of stable angina.

Another explanation is endothelial function is a systemic phenomenon, and it hasbeen proposed that FMD might provide indirect but relevant informationon clinically more valuable vascular beds. Flow-mediateddilation is strongly influenced by the presence of risk factors andtheir interaction**(19)**. However, it remains to be clarified whetherthe assessment of endothelial function provides information thatis additive to, or whether it simply recapitulates, that of traditionalrisk factors. Findings concerning the existence of a correlation between FMD and the extent of CAD patients with erectile dysfunction are somewhat controversial.

In this study **42.7 %** of total patients had impaired FMD ,out of these moderate and severe ED was more**(31.73%)** in patients with impaired   FMD <5.5% as compared to those with normal , FMD > 5.5% i.e**(10.07 %).** This association was stastically   significant,   P   value   (<.001).Thus   functional endothelial abnormality   seems to contribute to generalized vascular atherosclerotic process .Thus this suggest that patients with CAD have impaired endothelial function prior to development of actual anatomical obstruction ,as in our study **42.7 %** had impaired FMD,**one third** of these cases also had severe ED suggesting generalized involvement of endothelium in systemic vasculature involving penile arteries also.Only **8.65%** of patients had normal penile erections those having impaired FMD, whereas only **10.07**% with normal FMD had abnormal penile   erections.Large   percentage   **(42.7%)**in   our   study population had abnormal FMD suggesting importance of endothelial dysfunction in development of CAD,ED may alarm about ongoing endothelial dysfunction,which may involve coronary bed in future .

In our study, we showed a relationship between FMD values and IIEF scores in a patient population with ED and CAD. This correlation of FMD in brachial artery suggests that the endothelial dysfunction in ED is not confined to the cavernosal circulation, but is probably a part of a generalized vasomotor Endothelial dysfunction is the key feature in the early phase of ED, whereas it is one of many factors accounting for sexual dysfunction in the late phase of the disease. Evidence is accumulating in favor of ED as an independent predictor of future cardiovascular events in patients without overt heart disease.

V.   CONCLUSION

From this study it has shown that erectile dysfunction is a common in north Indian patients with angiographically documented CAD, with most patients have modest or severe erectile dysfunction. It has been also shown that impaired FMD is significantly correlate with erectile dysfunction patients. Resultimplicating that endothelial dysfunction as animportant underlying pathophysiological factor in CAD patients.

CONFLICT OF INTEREST-None

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AUTHORS

First Author – Dr Gaurav Kumar Chaudhary, MD,DM Assistant Professor , Department of Cardiology , King George's Medical University ,Lucknow , Pincode 226003 ,U.P ,India Email :gauravchaudharydr@gmail.com, Phone : 919936062507
Second Author – V.S Narain**MD,DM ,SK, Professor ,Department of Cardiology ,Department of Cardiology ,King George's Medical university ,Lucknow

Third Author – DwivediDM,FSCAI, Professor ,Department of Cardiology ,Department of Cardiology ,King George's Medical university ,Lucknow
Fourth Author – Rishi Sethi**DM,FACC,FESC,Professor ,Department of Cardiology ,Department of Cardiology ,King George's Medical university ,Lucknow
Fifth Author - Sharad Chandra**DM,FACC, Professor ,Department of Cardiology ,Department of Cardiology ,King George's Medical university ,Lucknow

Table 1: Base line characteristics in two groups (Group A and Group B)

	Group A (Single Vessel) (n=82) Mean±SD	Group B (Double vessel or more) (n=161) Mean±SD	p value
Age (Years)	56.83±8.43	58.08±8.53	0.25 NS
Diabetes Mellitus	34 (41.5%)	68 42.33%)	1.0
Hypertension	47 (57.3%)	88 (54.7%)	0.56
Smoking	29 (35.4%)	51 (31.7%)	0.78
Mean Hb (gm%)	11.59±1.25	11.52±1.78	0.46NS
Serum Creatinine (mg/dl)	1.28±1.07	1.14±0.3	0.12 NS
LVEF %	52.45±8.85	48.92±11.15	0.08 NS
BMI kg/m^2)	24.75±2.90	25.32±2.93	0.15 NS
Beta blocker	22%	38%	0.056%
Statins	21%	32%	0.062%

Table 2: Correlation of severity of ED and CAD in two groups (Group A and Group B)

	Group A Single vessel ds (n=82)	GroupB Double vessel ds. or more (n=161)	OR CI	P value
No ED	51 (62.2)	33 (20.5)	-	-
Mild ED	8 (9.8)	22 (13.66)	4.25 (1.69-10.66)	0.001
Mild-Mod ED	11 (13.41)	24 (14.90)	3.37(1.45-7.79)	0.0047
Mod ED	10 (12.2)	44 (27.32)	6.80(3.01-15.36)	0.0001
Severe ED	2 (2.44)	38(23.60)	29.36(6.63-130.05)	0.0001

Table 3: Correlation of FMD and ED with CAD

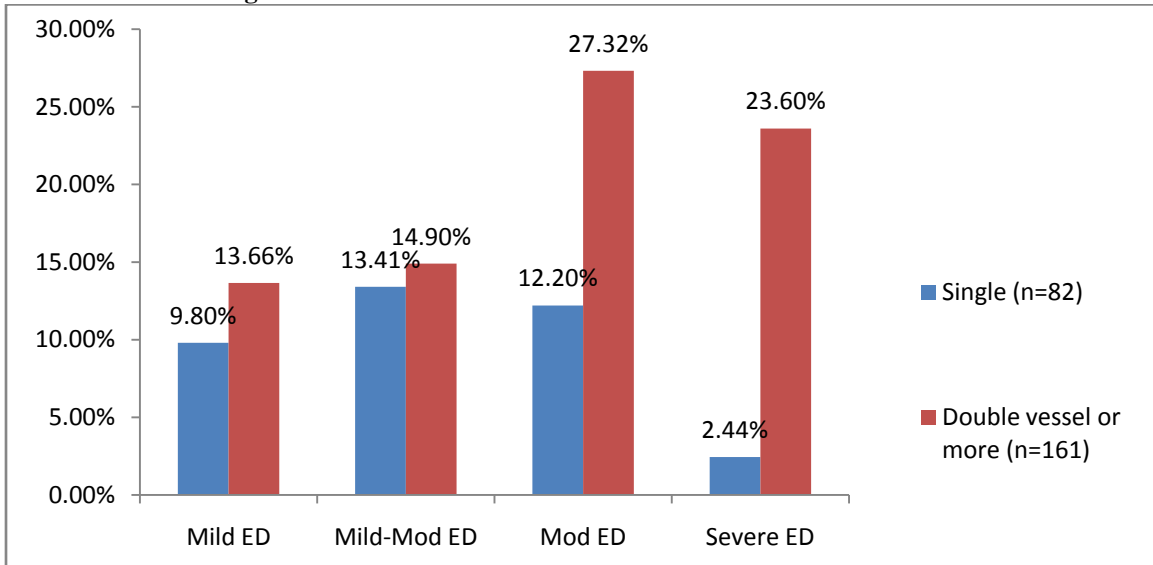|	>5.5 % (n=139)	<5.5% (n=104)	OR CI	P value
No ED	65 (46.76)	9 (8.65)	-	-
Mild ED	17 (12.233	9(8.65)	1.47 (0.63-3.44)	0.40
Mild moderate	23 (16.54)	15 (14.42)	1.17 (0.58-2.38)	0.72
Mod ED	20 (14.38)	38 (36.5)	3.42(1.84-6.36)	<0.001
Severe ED	14 (10.07)	33 (31.73)	4.15 (2.08-8.27)	<0.001

Figure 1-The correlation between severe ED and extent of CAD

Figure 2: Association of FMD and ED with CAD