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Association between Angiographic Severity of Coronary Artery Disease and Erectile Dysfunction due to Internal pudendal Artery Stenosis

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Abstract

Background: Erectile dysfunction (ED) is common in patients with coronary artery disease (CAD). As atherosclerosis is the common mechanism for vasculogenic ED and CAD, so there might be a correlation between these two.

Objective: To find out the association between angiographic severity of coronary artery disease and ED due to internal pudendal artery (IPA) stenosis.

Methods and Materials: This cross-sectional observational study was conducted at the Department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka among purposively sampled patients who had CAD on CAG & had ED on IIEF 5 questionnaire. A total 60 patient were divided in two groups depending on Gensini score being Gensini score < 20 in Group I and Gensini score ≥ 20 in Group II. Internal pudendal angiography was done in same settings following CAG. Correlation between Gensini score & significant IPA stenosis between two groups was done.

Results: The mean IIEF 5 score was 14.8 ± 3.83 being lower in group II (15.93 ± 3.14 vs 13.67 ± 4.17, p=0.021). Significant IPA stenosis (> 50%) was more common in group II (20% vs 43.3%, p=0.042). Spearman's rank correlation showed moderate negative correlation between Gensini score and IIEF 5 score (Spearman's ρ = -0.475, p=0.01). Spearman's rank correlation betwwen Gensini score & IPA atenosis showed moderate positive correlations (Spearman's ρ = 0.410, p=0.03). Multivariate logistic regression analysis revealed severe coronary artery stenosis (Gensini score more than ≥ 20) and DM were the risk factor for significant IPA stenosis with OR 9.13 and 4.75, respectively.

Conclusion: Angigraphic severity of coronary artery disease is positively correlated with ED due to IPA stenosis.

Keywords: Erectile Dysfunction; IPA Stenosis; IIEF 5 Score; Severe Coronary Artery Disease.

Introduction

Erectile dysfunction (ED) is defined as the consistent inability to reach and maintain an erection satisfactory for sexual activity [1]. About 52 % of adult American male of age between 40-70 years has been reported to suffering from some degree of ED (Feldman et al., 1994) & about 322 million men worldwide [2]. In Bangladesh prevalence of ED in diabetic patient is 53.98% [3] but exact prevalence of ED in general population or in patient of CAD is

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not known. Vasculogenic ED is a common cause of ED in patient with coronary artery disease. Prevalence of Internal pudendal Artery (IPA) stenosis in diabetic patient with ED with multi vessel CAD was 36.7% [4]. Penile erection is a neurovascular event modulated by psychological factors and hormonal status [1]. Erectile dysfunction can be classified as psychogenic, organic (neurogenic, hormonal, arterial, cavernosal, or drug-induced), or mixed psychogenic and organic [5]. Low testosterone levels have a pro-inflammatory and pro-apoptotic effect on endothelial cells [6]. Subclinical chronic inflammation might further impair endothelial function leading to a prothrombotic status [7]. The exact prevalence of coronary artery disease in Bangladesh is not known. More recent data indicates that coronary artery disease prevalence is 1.85% to 3.4% in rural population and 19.6% in an urban population [8]. According to WHO data, overall age standardized death rate for ischemic heart disease (IHD) in Bangladesh was 203.7 per 100,000 in 2008. In Bangladesh IHD was the most common cause of death among the estimated total deaths. Acute myocardial infarction (AMI) appeared as the top leading cause (3.7%) of deaths across 504 public hospitals in Bangladesh in 2012, as reported by the "health bulletin 2013" [9]. Coronary artery disease (CAD) & erectile dysfunction (ED) share similar pathological basis of etiology & progression [10]. Role of endothelial dysfunction & nitric oxide is well established in coronary artery disease (CAD) [11]. Normal erectile function is also a neurovascular event that relies heavily on vasodilation, which occurs largely due to endothelial derived nitric oxide (NO). In addition, it was seen that sexual symptoms occur a mean of 38.8 months prior to cardiac symptoms in patients suffering from both coronary artery disease & erectile dysfunction [12]. Artery size hypothesis explains the relative earlier presentation of erectile dysfunction than coronary artery disease (CAD) [12]. Systemic atherosclerosis affects the endothelium of all arteries similarly but symptoms rarely become clinically present in different arteries at the same time as larger arteries (coronary artery diameter larger than penile artery) can tolerate same amount of plaque than smaller arteries [5]. Significant internal pudendal artery disease was defined as 50% 0r more luminal obstruction seen in the projection that best delineates the take-off of the artery [4] ED is significantly predictive of cardiovascular death, myocardial infarction (MI), stroke and heart failure (HF) in men with cardiovascular disease (CVD). Erectile dysfunction severity also correlates with CAD severity [13]. Although ED is multifactorial in patient with CAD still vasculogenic ED is predominant & vasculogenic ED patient may get benefit from revascularization. This current study aims to evaluate the association of angiographic severity of coronary artery disease with IPA stenosis.

Methods

Study Design: Cross-sectional study.

Place of study: Department of Cardiology, National Institute of Cardiovascular Diseases, Dhaka, Bangladesh.

Study period: Study was conducted from January 2020 to December 2020.

Target population: Patient of coronary artery disease having erectile dysfunction.

Study Population:

Group 1: 30 patients having Gensini score < 20

Group 2: 30 patients having Gensini score ≥ 20

Sampling Technique:

Purposive type sampling.

Sample size: Considering the time constraints 30 patient was taken as a sample in each group.

Group 1: 30 patient having Gensini score < 20

Group 2: 30 patient having Gensini score ≥ 20

Enrolment of subjects

A) Inclusion Criteria:

1. Male patient age between 40-70years have CAD on CAG.
2. Patient have ED i.e. IIEF-5 score < 22.

Exclusion Criteria:

3. Patients with previous percutaneous or surgical myocardial revascularization procedures.
4. Primary PCI, Pharmacoinvasive PCI.
5. Aorto-iliac disease on angiography.

4. Patients with diseases that could alter sexual activity, such as

   - liver cirrhosis,
   - renal failure,
   - thyroid disease (hypo- and hyperthyroidism on replacement treatment),
   - major depression (DSM IV criteria)
   - Patient on antidepressant /antipsychotic)
   - Neurological causes like PD, spinal cord injuries,
   - Previous pelvic, penile, urethral, or prostate trauma or surgery, pelvic radiation.

5. Patients with primary erectile dysfunction (including primary hypogonadism, psychogenic erectile dysfunction due to troubled marriage or relationship, psychiatric disorders) were excluded.

Data collection Procedure:

- With considering inclusion & exclusion criteria patient admitted in NICVD for CAG to confirm CAD was selected.

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- Informed written consent was taken from each patient before enrollment.
- Meticulous history was taken and detailed clinical examination was done and recorded in predesigned structured questionnaire.
- Following risk factors profile was noted:

• Age, BMI (obese/ non obese), Smoking, Hypertension, Diabetes Mellitus, Dyslipidemia, Drugs might be responsible for ED.

- Baseline laboratory investigations RBS, serum creatinine, serum electrolytes, blood lipids profiles, blood grouping and screening blood tests was carried out.
- Patients planned for CAG will be assessed for ED using IIEF- 5 questionnaire.
- Classification of ED was done into one of five possible categories: severe (5-7 points), moderate (8-11), mild to moderate (12-16), mild (17-21), and absence of ED (22-25).
- CAG was carried out following standard protocol.
- Patient having CAD on CAG & ED (IIEF- 5 score <22) was carried out IPA angiogram at the same settings.
- IPA angiogram was done using pigtail catheter placed at bifurcation of abdominal aorta into common iliac arteries. Low osmolar dye was injected using power injector. AP view was taken as default view; further LAO, RAO view was taken if necessary. Minimum view was taken to reduce gonadal radiation.
- CAD severity was assessed by Gensini score.
- IPA stenosis ≥ 50% was considered as significant.
- Angiogram reporting was done by a qualified interventional cardiologist.

Statistical Methods:

• Nature of the data was explored.

• Quantitative (continuous) data such as age was expressed as mean and standard deviation and comparison was done by "student t" test.

• Qualitative (categorical) data such as BMI, DM, HTN and smoking was expressed as frequency and percentage and comparison was done by Chi-square ($\chi 2$) Test.

• Spearman's rank correlation was done to see the association between independent & dependent variables.

• Multivariate regression analysis was done.

• A p value <0.05 was considered as statistically significant.

• Analysis was conducted by SPSS 23.0 for windows software.

Results

Total 60 patients were studied dividing into 2 groups being 30 in each group. Group 1 was non severe CAD (Gensini score < 20) & Group 2 was severe CAD (Gensini score ≥ 20). Clinical characteristics, biochemical tests, severity of coronary artery, ED severity and internal pudendal artery stenosis were studied.

Group I- Gensini score <20, Group II - Gensini score ≥20, Independent sample t test, s -significant

Table-1 showed comparison of study group according to age distribution. Highest frequency was 51-60 years age, 15 and 12 in group I and group II, respectively. Mean age of group I and group II was 52.33 ± 6.95 years and 56.10 ± 9.4 years, but this difference was not statistically significant (p=0.083).

In our study samples, business men were most prevalent (n=38, 64%) followed by retired person (n=14). There was no

Table 1: Comparison of the study groups according to their age.

Age (in years)	Total (n=60)		Group-I (n=30)		Group-II (n=30)		*p value*
	n	%	n	%	n	%	
41-50	17	28.3	10	33.3	7	23.3	
51-60	27	45	15	50	12	40	
61-70	16	26.7	6	16.7	10	33.3	
Mean ± SD	54.22 ± 8.4		52.33 ± 6.95		56.10 ± 9.4		*0.083*^{ns}

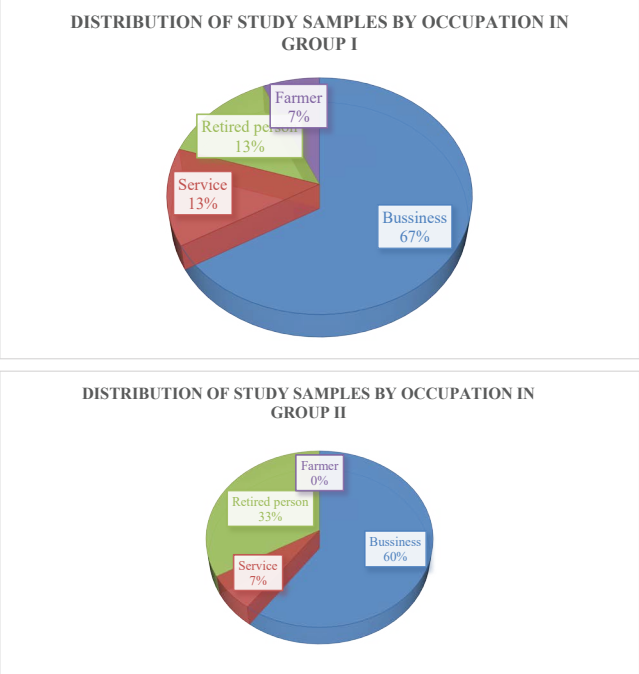

Figure 1: Distribution of study samples by occupation in group I and group II.

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difference in distribution of occupation among both groups (p=0.148) (Figure 1).

Figure 2 showed indications of coronary angiography among study samples. Most of the patients underwent CAG for STEMI (n=33, 55%). 20 (66.6%) patients in group I had STEMI and 13 in group II. CCS was the least frequent indications for CAG in our study groups. There was no difference in indications for CAG between these two groups (p=0.189).

Among 22 hypertensive patients in our study sample, 12 (40%) patients were hypertensive in group I, whereas 10 (33.3%) patients in group II and this difference was not statistically significant (p=0.352). No difference (p=1.00) existed in between two groups regarding prevalence of DM. Overall, there was no significant difference present in traditional cardiovascular risk factors between these two groups (Table 2).

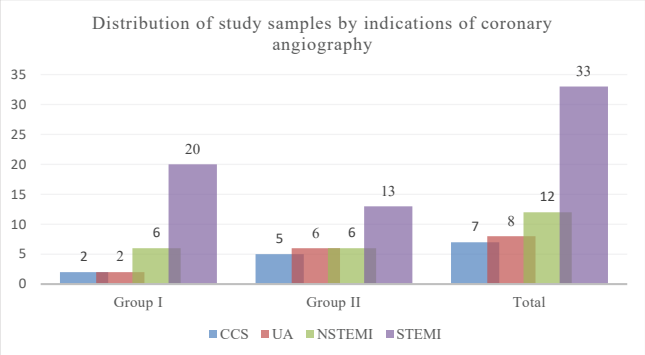

Figure 2: Distribution of study samples by indications of coronary angiography.

Table 2: Comparison of the study group according to risk factors.

ED/CAD risk factor profiles	Group-I (n=30)		Group-II (n=30)		*p* value
	n	%	n	%	
Hypertension	12	40	10	33.3	0.592^{ns}
Diabetes mellitus	10	33.3	10	33.3	1.00 ^{ns}
Dyslipidemia	14	46.7	10	33.3	0.292^{ns}
Smoking	18	60.0	20	66.7	0.592 ^{ns}
Obesity	4	13.3	4	13.3	1.00 ^{ns}
Drug	16	53.3	22	73.3	0.108^{ns}

Table 3 showed mean Gensini score in group was 11.67 ± 5.46 and group 2 was51.13 ± 17.69. There was lower mean IIEF-5 score in group 2 (13.67 ± 4.17) compared to group 1 (15.93 ± 3.14) which was statistically significant (p=0.021).

Majority of patients (53.4%) in group I had mild ED whereas majority in group II had moderate ED and this difference was statistically significant (p=0.016) (Table 4).

There was moderate negative correlation between Gensini score and IIEF 5 score in our study samples (Spearman's ρ = -0.475, p=0.01) (Figure 3).

In group II, 13 (43.3%) patients had significant (>50%) internal pudendal artery stenosis but in group I only 6 (20%) had stenosis and this difference was statistically significant (p=0.042).

There was moderate positive correlation between Gensini score and IPA stenosis (Spearman's ρ= 0.410, p=0.003)

There was very good negative correlation between IIEF-5 score (Spearman's ρ= -0.637, p=0.0001).

Multivariate logistic regression analysis of risk factor for internal pudendal artery stenosis showed severe coronary artery stenosis was significantly associated with IPA stenosis (OR= 9.13, 95% CI = 1.37-60.99). Moreover, diabetes mellitus was also found to be risk factors for IPA stenosis, OR 4.75 (Table 5).

Table 2: Comparison of the study group according to risk factors.

ED/CAD risk factor profiles	Group-I (n=30)		Group-II (n=30)		*p* value
	n	%	n	%	
Hypertension	12	40	10	33.3	0.592^{ns}
Diabetes mellitus	10	33.3	10	33.3	1.00 ^{ns}
Dyslipidemia	14	46.7	10	33.3	0.292^{ns}
Smoking	18	60.0	20	66.7	0.592 ^{ns}
Obesity	4	13.3	4	13.3	1.00 ^{ns}
Drug	16	53.3	22	73.3	0.108^{ns}

Table 3: Comparison of Gensini score and IIEF 5 score between study groups.

	Total (n=60) Mean ± SD	Group I (n=30) Mean ± SD	Group II (n=30) Mean ± SD	p-value
Gensini score	31.4 ± 23.76	11.67 ± 5.46	51.13 ± 17.69	
IIEF 5 score	14.8 ± 3.83	15.93 ± 3.14	13.67 ± 4.17	**0.021^{s}**

Table 4: Comparison of severity of erectile dysfunction between the study groups.

Erectile dysfunction	Group-I (n=30) n (%)	Group-II (n=30) n (%)	p-value
Severe	0(0)	1(3.3)	**0.016^{s}**
Moderate	4(13.3)	12(40.1)	
Mild to moderate	10(33.3)	10(33.3)	
Mild	16(53.4)	7(23.3)	
Total	30(100)	30(100)	

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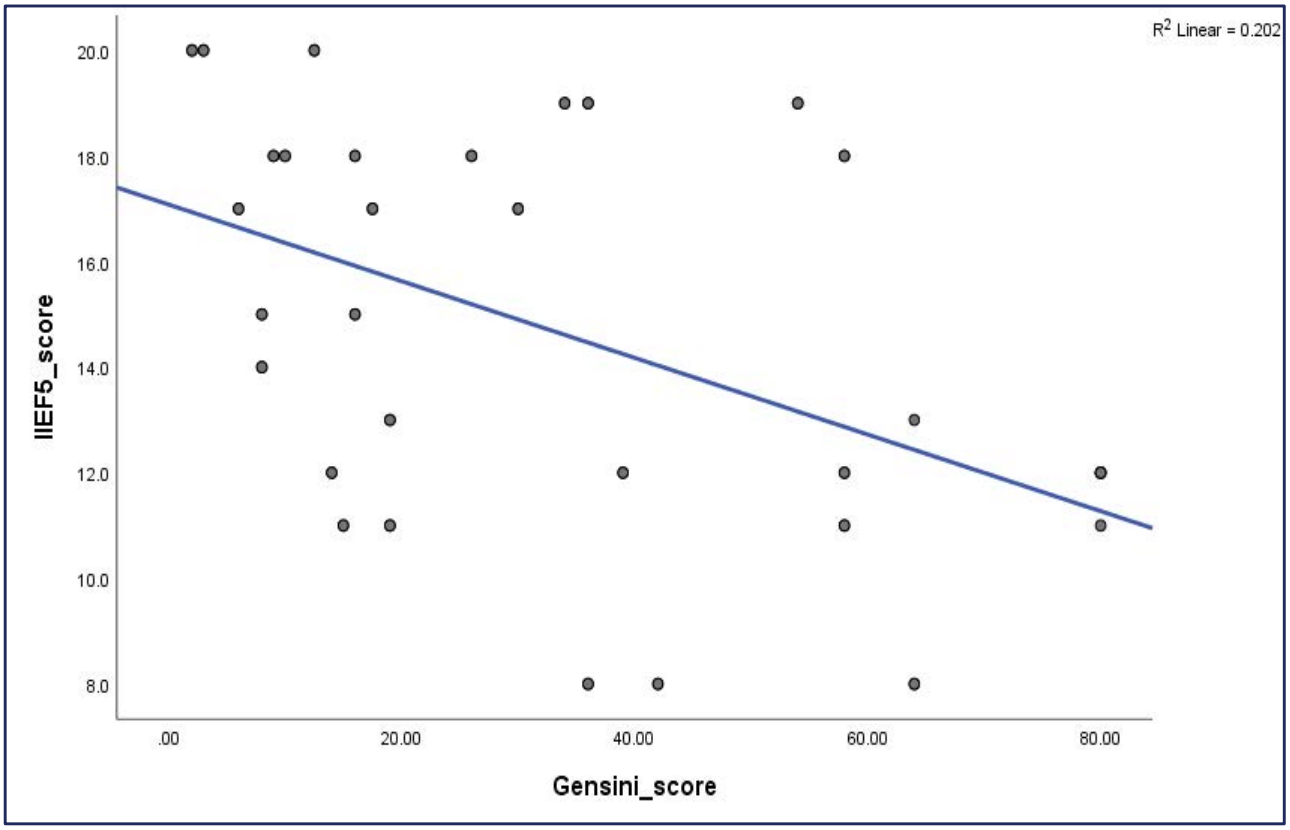

Figure 3: Correlation between Gensini score and IIEF 5 score in study samples.

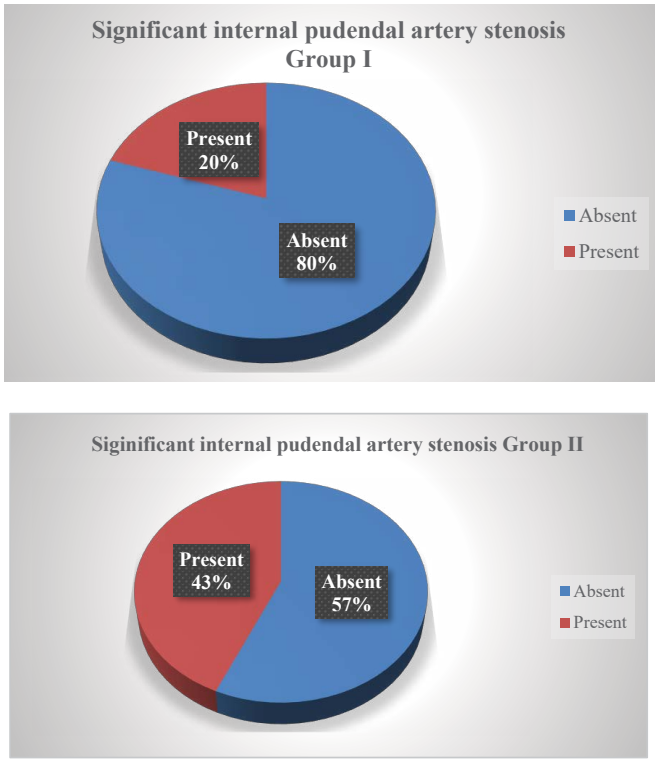

Figure 4: Comparison of significant internal pudendal artery stenosis between study groups.

Discussion

This hospital-based cross-sectional study was conducted to find out association between angiographic severity of coronary artery disease and erectile dysfunction due to internal pudendal artery (IPA) stenosis. The study was conducted at the Department of Cardiology at National Institute of Cardiovascular Diseases (NICVD), Dhaka, Bangladesh from January 2020 to December 2020. Total 60 patients with coronary artery disease on CAG & had ED were divided into two groups, patients with Gensini score<20 (group I) and those with Gensini score≥ 20 (group II). All patients were interviewed with IIEF5 questionnaire to detect erectile dysfunction and also underwent pudendal artery angiography to detect internal pudendal artery stenosis. During this study, age distribution of the samples showed highest frequency (45%) was seen in 51-60 years age group 45% followed by 41-50 years group. The mean age was 54.22 ± 8.4 years and that of group I and group II was 52.33 ± 6.95 years and 56.10 ± 9.4 years, respectively. Our findings were similar to age distribution of a study among Bangladeshi population, where 37.5% patients belonged to 51-60 years and 32.5% to 41-50 years [14]. In Brazil, mean age of patients with CAD was reported to 57.2± 11.1 years, higher than our report [15]. Discrepancy of mean age between our results compared to this proves the concept of earlier incidence of coronary artery

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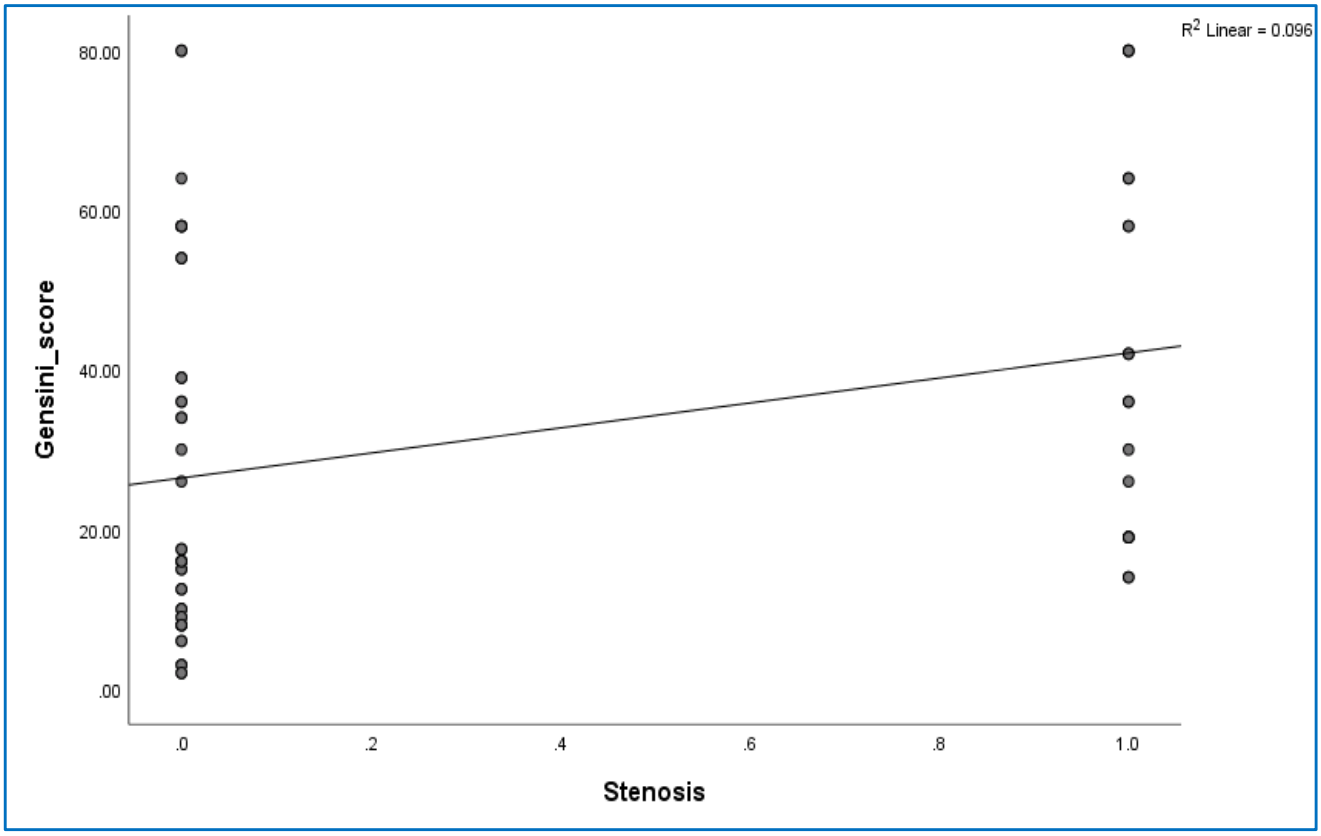

Figure 5: Correlation between Gensini score and IPA stenosis.

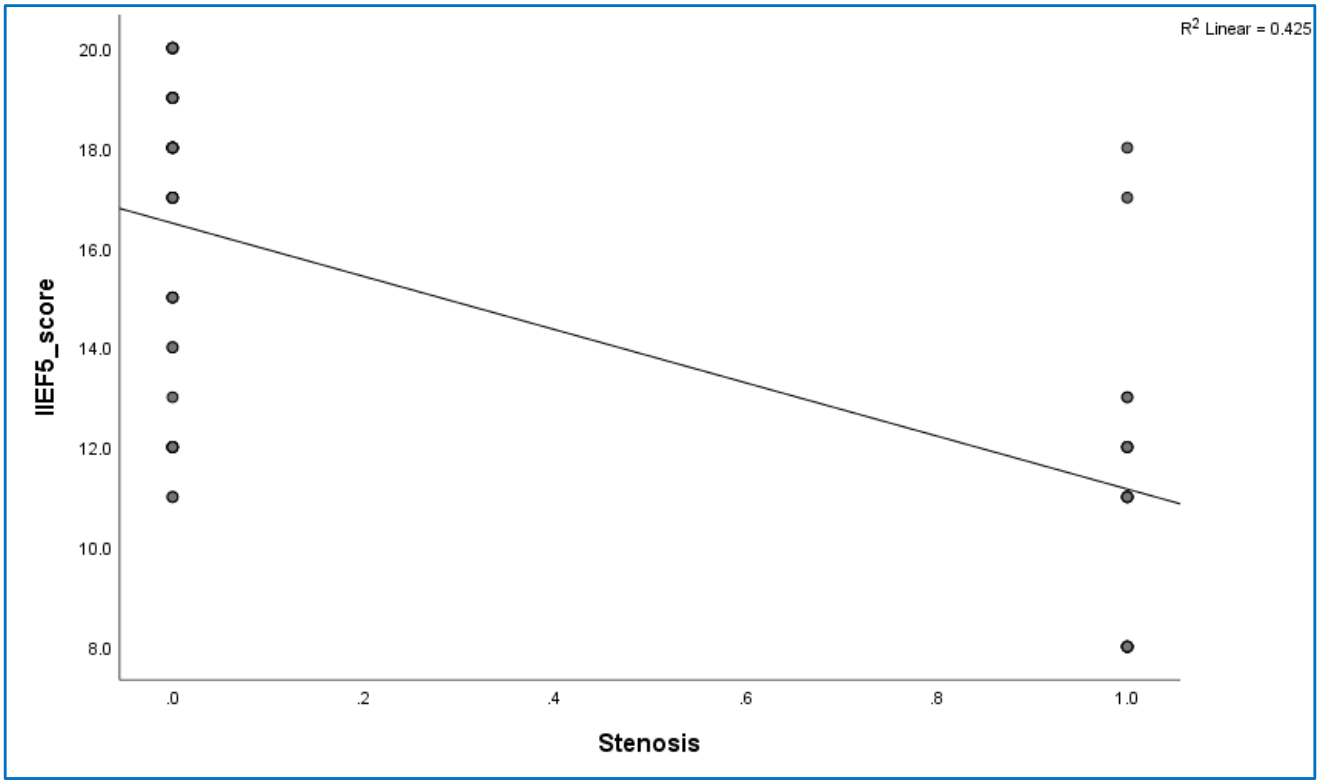

Figure 6: Correlation between IIEF-5 score & IPA stenosis.

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Table 5: Multivariate logistic regression analysis of risk factors for significant internal pudendal artery stenosis.

Risk factor for significant IPA stenosis	β	Std. Err	OR	95% CI for OR		p-value
				Lower Bound	Upper Bound	
Severe coronary stenosis (Gensini ≥20)	2.21	.97	9.13	1.37	60.99	**0.022**[s]
Obese	0.66	1.03	1.94	0.25	14.67	0.517[ns]
Smoking	0.98	0.76	0.37	0.08	1.68	0.200[ns]
HTN	1.16	0.83	3.22	0.45	23.31	0.247[ns]
DM	3.24	0.91	4.75	1.29	46.33	**0.017**[s]
Dyslipidemia	0.75	0.82	2.11	0.41	10.74	0.365[ns]
Age	0.005	0.03	1.01	0.94	1.07	0.89[ns]
Drug (1 or more)	1.08	0.65	2.94	0.83	10.39	0.095[ns]

disease in Bangladeshi people [8]. In our study, prevalence of hypertension, diabetes mellitus, dyslipidemia, smoking and obesity was present in 36.7%, 33.3%, 40%, 63.3% and 13.3% respectively. Our findings were close to that described by Ahmed et al [16] except they reported higher frequency of obesity (43%) in their study samples. In our study, DM was associated with significant internal pudendal artery stenosis (OR 4.75, 95% CI 1.29- 46.33). Mahbub, et al., showed increasing age was associated with increasing prevalence of ED in diabetic patient, 5.5% in 28-39 years of age and 77.4% in 60-69 years of age [17]. Drugs & duration of diabetes was also associated with severe ED, 100% patient whose duration was more than 20 years developed ED. Improvement of glycemic control was suggested as a good measure to reduce severity of ED [17]. Selim, et al. [3] showed 53.98% prevalence of ED in diabetic men although smoking and obesity was not associated with ED which was similar to our finding. An Egyptian study concluded that hypertension (OR = 5.2), diabetes mellitus (OR = 5.4) and smoking (OR = 3.1) were significant risk factors for erectile dysfunction [18]. We did not find relation between smoking and hypertension with significant internal pudendal artery stenosis. There are other mechanisms like endothelial dysfunction may cause erectile dysfunction which explains our findings. In our study, IIEF 5 score was significantly lower (15.93 ± 3.14 vs 13.67 ± 4.17) in those with Gensini score ≥20 and there was moderate negative correlation exist between Gensini score and IIEF 5 score. We also found that majority (16 out of 30) of group I patients had mild ED whereas 13 patients in group II had moderate to severe ED. Our findings was similar to Foroutan and Rajabi [18] which reported that prevalence of ED was high (>50%) in patients with CAD and IIEF 5 score was negatively associated with number of stenotic vessel involved. However, El-Sakka et al [20] reported severity of ED was associated with higher degree of coronary artery disease in Saudi population. In another study, 65% of angiographically proven CAD patients had erectile dysfunction and IIEF 5 score was correlated with atherosclerotic burden measured by Gensini score [21,22]. Al-Daydamony et al [23] grouped 85 ACS patients into mild or no ED group (IIEF score ≥ 17) and moderate to severe ED group. They found that Gensini score was significantly higher in moderate to severe ED group compare to mild or no ED group (23.5 ± 10.8 versus 34.1 ±12.7, p = 0.0001). There was negative correlation between IIEF score and Gensini score (r = -0.383, p = 0.0003) similar to our study. In COBRA trial, investigators compared ED prevalence among ACS patients who have single vessel disease versus multi-vessel disease and found that ED prevalence was significantly higher in those with multi-vessel disease (55% vs 22%). Similar to our study, IIEF score was lower in multi-vessel disease group & showed inverse correlation between Gensini score and IIEF score. An Indian study also reported inverse relation of IIEF score and Gensini score close to our study [15]. This study also reported usual onset of ED symptoms preceded the occurrence of CAD symptoms by 2-3 years [18]. As a result men with overt CAD frequently complains of ED symptoms, although patients with only ED symptoms may not have significant CAD. This phenomenon can be explained by "artery size" hypothesis. This is based on a conceptual model that exposure of common risk factors across all vascular beds lead to endothelial dysfunction, intima-media thickening and lastly, vascular obstruction and flow-limiting stenoses. As the coronary arteries are larger than the penile arteries, it can better tolerate larger amount of plaque burden compared to smaller penile arteries [24]. We have found that among 60 patients, 19 (31.7%) patients had internal pudendal artery stenosis and that was significantly higher with patients who had Gensini score ≥ 20 compared to those who had not (43.3% vs 20%). This findings also reflected the artery size hypothesis, as severe CAD patients had more atherosclerotic plaque burden in all vascular bed including pudendal artery [24]. El-Sakka and Morsi [20] showed 30.5% of IHD patients had arteriogenic ED in Saudi population, very close to our study. Sanad et al [25] reported that severity of CAD including left main disease was significantly associated with aorto-ilio-pudendal disease. They also concluded that ED correlates with vascular lesions. We have also found that Gensini score

were positively (moderate) correlated with significant IPA stenosis. However, Park and his colleagues failed to correlate the extent of IPA stenosis with severity of ED [26]. IPA is the main source of blood flow to the corpora of the penis and appears to have a crucial role in erectile function. Not only the reduced blood supply but also vascular endothelial dysfunction may cause vasculogenic ED. Thats may be a reason for the discrepancy between severity of ED & severity of IPA stenosis [26].

Limitations of the study

1. Time and resources were limited.
2. Sample size was not adequate to generalize the finding.
3. COVID-19 situation adversely affected admission of patients in hospital.
4. This is single center study that does not represent the situation of whole country.

Conclusion

Internal pudendal stenosis is an important cause of erectile dysfunction (ED) in patient with coronary artery disease (CAD). Coronary artery disease severity (Gensini score) is negatively correlated with IIEF-5 score of erectile dysfunctions. Coronary artery disease severity also positively correlated with internal pudendal artery stenosis.

Recommendation

1. Every cardiologist should use IIEF - questionnaire to identify ED in CAD patient.
2. Vasculogenic erectile dysfunction is a common association of coronary artery disease. Internal pudendal artery stenosis can be sought as part of diagnostic evaluation of erectile dysfunction in CAD patient which may have an impact on management plan of erectile dysfunction.

A larger multicenter randomized study is recommended to find out the relationship between angiographic severity of coronary artery disease and ED due to internal pudendal artery stenosis.

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