Erectile Dysfunction: a Marker for Myocardial Perfusion Impairment?

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Objective

To study the correlation between erectile dysfunction (ED) and myocardial perfusion impairment in men with suspected or diagnosed coronary artery disease (CAD).

Methods

In this prospective study a self-administered IIEF-5 questionnaire was answered by 287 patients that underwent myocardial perfusion imaging under both resting and stress condition with technetium-99m sestamibi, through gated SPECT nuclear scintigraphy technique, before and after physical or pharmacological stress.

Results

Some degree of erectile dysfunction (group ED+) was found in 137 (47.8%) patients and in these, age was significantly higher (60.60±9.84 vs 50.67±9.94 – $p<0.001$)) than in those without erectile dysfunction (group ED-). In the ED+ group, it was observed a higher prevalence of hypertension, diabetes, myocardial infarction (MI) and percutaneous coronary angioplasty (PCTA). Regardless of the age factor, ED+ patients also presented higher occurrence of myocardial perfusion impairment (necrosis and/or ischemia) and left ventricular systolic wall motion and thickening abnormalities.

Conclusion

Patients with ED have higher estimated probability of presenting segmental myocardial perfusion and functional contraction impairment and, therefore, CAD, independent of the aging factor. The authors conclude that ED may be considered not only a marker for CAD but also a condition related to the occurrence of major coronary events such as MI and PCTA.

Key words

erectile dysfunction, coronary artery disease, nuclear medicine, myocardial perfusion, risk factors, atherosclerosis

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Myocardial infarction (MI) is a major cardiovascular event related to coronary artery disease (CAD). Modern cardiology is still challenged by its high mortality rate, morbid consequences and social / economical repercussions. Since significant coronary atherosclerosis may occur without expressive clinical manifestation and MI may be its first morbid manifestation, a worldwide medical effort has been made in order to identify as precociously as possible, the presence of coronary arterys atherosclerosis.

Vascular disease of the penile arteries, including atherosclerosis, is the most common cause of erectile dysfunction (ED), accounting for up to 80% of the cases[1-4]. A significant relationship between ED and important non-transmissible chronic diseases, including diabetes, hypertension and CAD has been clearly established[1,2,5-12]. In fact, ED and ischemic heart disease share the same principal risk factors including diabetes and hypertension considered to induce vascular endothelial damage, resulting in arterial obstruction, plaque rupture and thrombosis. Thus, ED may be considered a symptom of damage of the vascular endothelium and be concomitant or, in certain conditions, even foregoing the existence of ischemic cardiovascular disease. In such conditions, ED would appear as a real marker of coronary atherosclerosis, and therefore, ischemic heart disease.

The aim of the present study is to investigate the relationship between ED and myocardial perfusion status in a population with suspected or established CAD diagnosis.

Methods

From August to October 2004, all consecutive male patients referred to myocardial perfusion evaluation in our Institution by their private physicians who agreed to participate in this study were enrolled. Studies were applied for CAD diagnosis or evaluation purposes. Among 300 patients prospectively enrolled in the study, thirteen (4.3%) were excluded due to the presence of iatrogenic ED related to radical prostatectomy in the past. Thus, the study sample consisted of 287 male patients that after a detailed clinical/cardiological interview were invited to answer the confidential self-administered International Index of Erectile Function (IIEF-5)[13] questionnaire in order to determine the presence or absence of ED.

Myocardial perfusion imaging was performed under both: a) resting and b) stress condition, either after treadmill exercise or dipyridamole myocardial induced hyperemia, using technetium-99m (Tc-99 sestamibi) through gated SPET nuclear scintigraphy technique.

In the resting condition, a required dose of TC-99 sestamibi was injected into a peripheral vein in order to evaluate the radionuclide distribution in proportion to myocardial regional blood flow. Hypoperfused segments indicating necrosis of the myocardium were, therefore, noticed.

In the stress condition the patient was referred to the treadmill test under conventional protocols (physical stress) or pharmacological assay using dipyridamole protocol aiming to induce myocardial ischemia (pharmacological protocol). Around 45 minutes after the end of the treadmill test or dipyridamole injection, stress condition images were obtained.

Two properly trained physicians performed radionuclide cardiac imaging analysis. A positive tomogram for necrosis was defined by a segmental perfusion defect in the resting condition and ischemia as a new segmental perfusion abnormality, identified only in the stress condition. The two independent observers compared the resting and stress images without the knowledge of the clinical/cardiological interview and IIF-5 questionnaire results. In case of divergence between the two observers, the definitive result was given by consensus. No situation required a third observer opinion.

Studied variables are found in Table I.

Table I - Studied Variables

Clinical Variables	Nuclear Medicine Variables
Age	Resting myocardial perfusion
Erectile function:	Stress myocardial perfusion
Presence of erectile dysfunction (ED+)	Systolic myocardial thikening
Absence of erectile dysfunction (ED-)	Systolic myocardial movement
Personal past medical record:	Left ventricular ejection fraction
Diabetes	
Arterial hypertension	
Stroke	
Myocardial inferction	
Coronary by pass surgery	
Percutaneous transluminal coronary angioplasty	
Habits:	
Smoking	
Alcohol	
Family medical record:	
Myocardial infarction	
Stroke	

Table II - Age in patients with (ED+) and without (ED-) erectile dysfunction

Group	Patients (n)	Age Minimal	Age Maximal	Age Mean ± SD	p
DE-	150	24	76	50.67 ± 9.94	<0.001
DE+	137	39	83	60.60 ± 9.84	
Total	287				

Table III - Clinical variables in patients with (ED+) and without (ED-) erectile dysfunction

	ED+ n	ED+ %	ED- n	ED- %	p
Hypertension	79	57.7	56	37.3	0.001
Diabetes	33	24.1	16	10.7	0.003
Stroke	2	1.5	1	0.7	0.607(1)
Myocardial infarction	40	29.2	25	16.7	0.011
Coronary bypass surgery	26	19.0	18	12.0	0.101
Percutaneous transluminal coronarioplasty	36	26.3	21	14.0	0.009
Smoking	11	8.0	19	12.7	0.200
Alcohol	14	10.2	14	9.3	0.801
Family record of cardiovascular disease	85	62.0	92	61.3	0.902

p= probability calculated by qui-square except in (1) when Fisher's test was used

Previous exams such as blood cholesterol level and coronary angiography as well as patient medication were not considered in the analysis.

Based in the past occurrence of major cardiological events (MI and/or myocardial surgical or percutaneous revascularization) and also the results of the myocardial perfusion studies the patients were grouped into three final diagnostic possibilities concerning the presence or absence of CAD: a) CAD + ; b) CAD – ; c) CAD undefined.

Categorical data was analyzed using Fisher's exact or Chi-square, when applicable. Comparison between groups regarding continuous variables was performed using Student's t-test or Bonferroni test. Logistic regression analysis was used in order to predict the probability of CAD according to the erectile function condition. Odds ratio and age-adjusted Odds ratio were calculated for all myocardial perfusion and performance variables proved to be different in the comparison of patients with and without ED. All tests were two-sided and conducted at a 0.05 significance level.

Results

Erectile Dysfunction and age – 150 patients (52.3%) presented normal erectile function (ED- group) while in 137 (47.8%), some degree of erectile dysfunction was found (ED+ group). In the entire sample age ranged from 24 and 83 y/o with a mean value of 55.41 ± 11.05 years and was significantly higher in the ED+ group (Table II).

Clinical variables (Tables III and IV) - In the entire sample, arterial hypertension was found in 135 patients (47%) and diabetes in 49 (17.1%), both, with higher occurrence in the ED+ group. However, we found no significant correlation between these diseases and myocardial perfusion impairment, either in the resting or stress conditions. Personal history of MI occurred in 65 (22.6%) patients and PCTA in 57 (19.9%). Also, these major events were prevalent in the ED+ group but only MI had significant correlation with myocardial perfusion abnormalities. No statistical difference between ED- and ED+ groups was found concerning the remaining studied variables.

Nuclear medicine variables and final CAD diagnosis (Tables V and VI) - Myocardial perfusion impairment was detected in 65 (22.6%) patients in resting condition and in 72 (25%) in the stress condition and both had higher prevalence in the DE+ group in relation to the ED- one, independent of the aging factor, according to the logistic regression analysis (Graphic I).

In 75 patients (26.1%) nuclear medicine detected impairment of systolic thickening in at least one segment of the left ventricular wall and in 73 (25.4%) an abnormal systolic movement of the myocardial segment was found. Ocurrence of both abnormalities was prevalent in the ED+ group, independent of the aging factor ($p<0.036$ and $p<0.43$ respectively).

Decrease a left ventricular ejection fraction was observed in 74 patients (25.78%) and its occurrence was higher in the ED+ in comparison to the ED- one.

Final diagnosis of coronary disease (CAD+) was established in 120 patients (41.8%). DE+ group had a significantly higher prevalence of CAD+ in comparison to the ED- one. Regression analyses confirmed that such prevalence occurred independently of the aging factor (Table VI – Graphic II).

Discussion

Despite the fact that the present sample had a very high prevalence of CAD, occurrence of ED closely reached 50%, a comparable prevalence found in the major epidemiologic studies [14-15].

Table IV - Presence (ED+) or absence (ED-) of erectile dysfunction, clinical variables and Odds Ratio

	Resting				Stress			
	OR	IL	SL	p	OR	IL	SL	p
ED-	1.00	-	-		1.00	-	-	
ED+	2.35	1.07	5.19	0.034	2.29	1.09	4.79	0.028
MI	10.16	4.77	21.65	<0.001	9.83	4.74	20.38	<0.001
AH	1.33	0.66	2.70	0.424	1.31	0.67	2.54	0.429
DM	1.51	0.66	3.43	0.326	1.15	0.51	2.58	0.736
PCTA	1.47	0.67	3.22	0.333	1.43	0.67	3.04	0.355
Idade	1.07	1.03	1.12	0.004	1.06	1.02	1.10	0.002

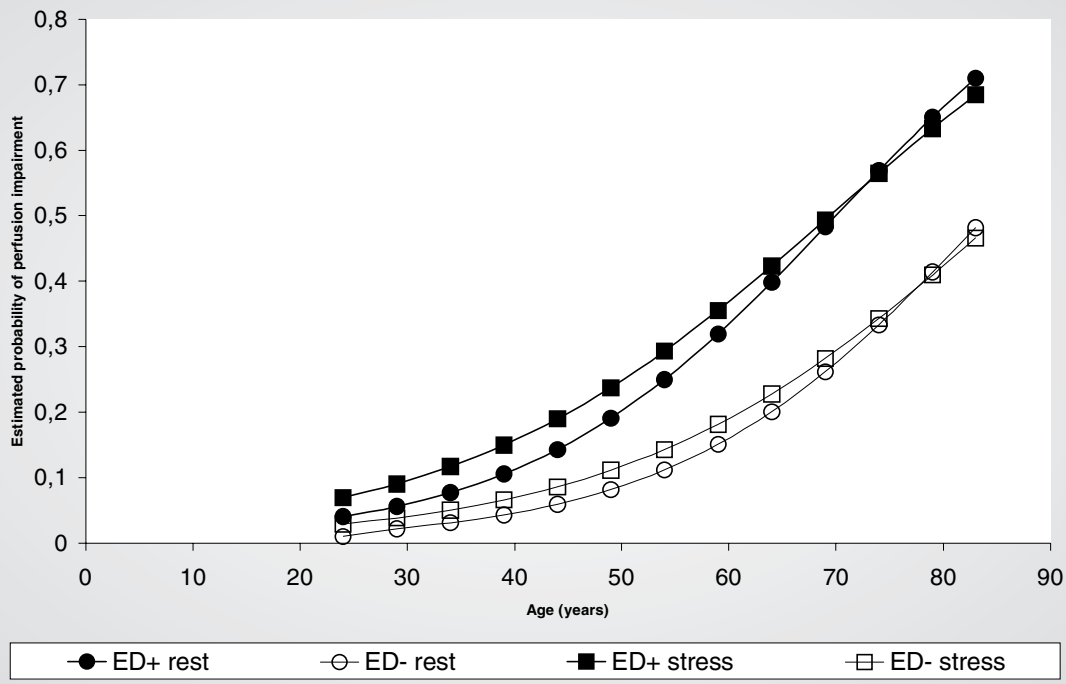
AH= Arterial hypertension; DM= Diabetes Melitus; IL= Inferior limit; MI = Myocardial infarction; OR= Odds Ratio; PCTA= Percutaneous transluminal coronary angioplasty; SL= Superior limit

Table V - Nuclear medicine variables and final diagnosis of CAD in patients with (ED+) and without (ED-) erectile dysfunction

	ED + N	ED + %	ED - n	ED - %	p
Abnormal resting myocardial perfusion	49	35.8	16	10.7	0.001
Abnormal stress myocardial perfusion	52	38.2	20	13.3	0.001
Abnormal myocardial systolic thikening	53	38.7	22	14.7	0.001
Abnormal myocardial systolic motion	51	37.2	22	14.7	0.001
Decreased left ventricular ejection fraction	53	38.7	21	14.0	0.001
CAD	79	64.8	41	29.7	0.001

p= probability by qui-square

***Graphic I** - Erectile dysfunction (ED) - Estimated probability of resting and stress myocardial perfusion impairment according to age*



Besides hypertension and diabetes, known CAD and ED risk factors, patients with abnormal erectile function also presented higher prevalence of major coronary events in the past, such as MI and PCTA. This observation suggests that ED should be detected as precociously as possible since it may represent not only a CAD marker but also been probably related to coronary disease severity.

Others risk factors such as smoking and alcohol. We hypothesized a possible relationship between ED and impairment of myocardial perfusion and our main approach was to evaluate oxygen demand heart muscle induced disorders guided by the existence, and degrees, of erectile function abnormalities.

As expected, ED prevalence in the present sample was

around 50%, comparable to most of the epidemiological studies, despite the fact that we had worked with a high CAD prevalent population. Such peculiarity may be the explanation for the unusually high occurrence of severe ED.

Besides hypertension and diabetes, known CAD and ED risk factors, patients with abnormal erectile function have had significant higher prevalence of major coronary events in their past medical history, such as MI, CS and PCTA. The present data point out the importance of detecting ED, as precociously as possible, since not only a marker for CAD will be recognized but also a condition related with its severity as well.

Additional risk factors such as smoking and alcohol abuse were no different regarding the presence or absence of ED. A possible explanation for this was the very the low percentage of smokers and alcohol addicts in the sample. Family history of stroke or MI it is recognized as related to CAD but, in the present sample, we found no correlation between ED and such family parameters. Further investigation based on more specific epidemiological study design for better understanding of such relationship is required.

Considering the high influence of age in the prevalence of ED as much as in the occurrence of CAD and, additionally, the fact that, in the present sample, age has been proved to be significantly higher in the ED + group compared with the ED – one, the authors have tested, through the age-adjusted Odds ratio, the real relationship between clinical and myocardial perfusion parameters and ED.

Myocardial perfusion, left ventricular systolic wall motion and thickening abnormalities were highly prevalent in patients with ED, regardless of age. Furthermore, these ischemic induced functional alterations prevalence rise increasingly with the severity of ED. Thus, patients with ED have higher estimated probability of presenting segmental myocardial perfusion and functional contraction impairment and, therefore, CAD, independent of the aging factor.

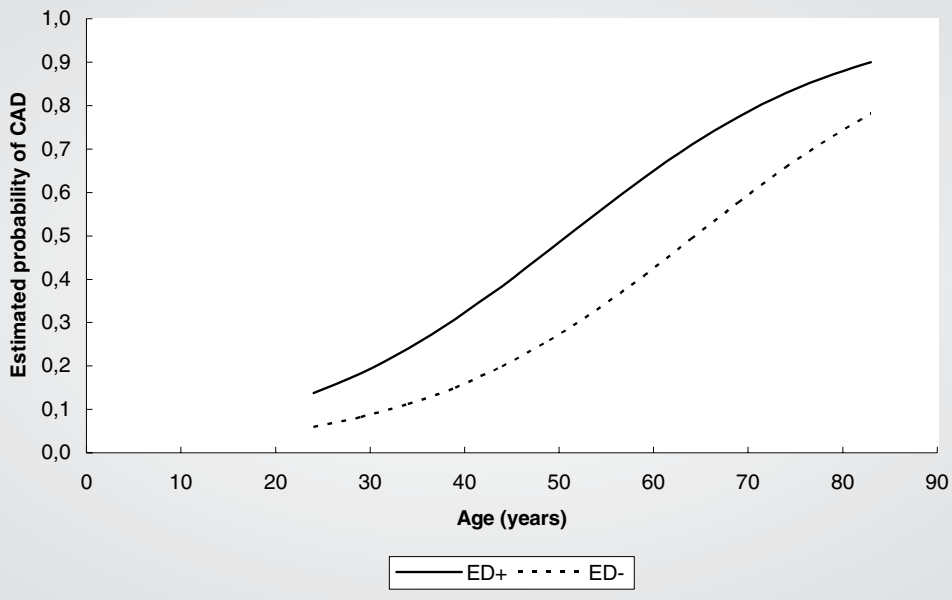
Studies have shown a high prevalence of ED in patients with cardiovascular disease including hypertension and CAD. The present study, however, demonstrated a significant age-adjusted correlation between the presence of ED and functional repercussions of ischemic heart disease, not only compromising myocardial perfusion but also left ventricular performance as well.

In the present sample, patients with ED had 2.35 times higher risk of presenting abnormal resting myocardial perfusion impairment and 2.29 times during stress than those with normal erectile function. These

Table VI - Perfusion, myocardial performance and CAD

	Age non adjusted Odds Ratio			*Age adjusted Odds Ratio*			p
	OR	Inferior limit	Superior limit	OR	Inferior limit	Superior limit	
Abnormal resting myocardial perfusion	4.66	2.50	8.71	2.63	1.33	5.20	0.005
Abnormal stress myocardial perfusion	4.02	2.24	7.22	2.48	1.31	4.70	0.005
Abnormal systolic myocardial thikening	3.67	2.08	6.48	2.00	1.06	3.76	0.032
Abnormal systolic myocardial motion	3.45	1.95	6.10	1.92	1.02	3.62	0.043
CAD	4.35	2.58	7.32	2.52	1.42	4.47	0.002

Graphic II *- Erectile dysfunction (ED) - Estimated probability of CAD according to age*



numbers, strongly suggest that ED is a real marker of perfusional and functional myocardial abnormalities induced by ischemic heart disease. Proved CAD was significantly higher prevalent in the ED + group regardless of the aging factor.

In this study, despite the fact that hypertension and diabetes being prevalent in patients with ED, we found no significant correlation of any of these conditions, themselves, with an increased probability of occurrence of myocardial perfusion impairment. This may distinguish a risk factor from a real CAD marker.

Conclusion

The authors conclude that ED is highly related to CAD and its detection may suggest an increased risk for the existence of perfusional and functional abnormalities of the heart muscle, typical of the CAD.

ED may be considered not only a marker for CAD but also a condition related to the occurrence of coronary major events such as MI, and PCTA. Based in these findings the authors suggest the inclusion of erectile function questionnaires in daily clinical practice.

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