

# ASSOCIATION BETWEEN ERECTILE DYSFUNCTION AND SEVERITY OF CORONARY ARTERY DISEASE

By

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## ABSTRACT

**Background:** Erectile dysfunction (ED) is the most common sexual problem in men and defined as inability to attain or maintain a penile erection sufficient for successful vaginal intercourse. Erectile dysfunction is considered a primarily vascular disease in the majority of the cases. Numerous risk factors that contribute to the development and onset of ED are principal for the development of coronary artery disease (CAD).

**Objective:** Documentation of the relation between erectile dysfunction and severity of coronary artery disease in patients presented with acute coronary syndrome focusing on the relation between onset of erectile dysfunction and onset of acute coronary ischemia.

**Patients and methods:** This study included Egyptian patients admitted with acute coronary syndrome (ACS) with history of erectile dysfunction (ED), and underwent coronary angiography. They were subdivided into 3 groups: Group1 (control group G1, n= 30) which have a normal coronary angiography or non-atherosclerotic coronary artery disease, group 2 (G2, n= 36) which have a single coronary artery disease, group 3 (G3, n= 34) which have more than one coronary artery disease. Comparative study was done between three groups according to risk factors, comorbidities and severity of atherosclerotic coronary artery lesions according Gensini score, degree of erectile dysfunction which was assessed by international index of erectile function (IIEF) and penile artery duplex.

**Results:** The total number of patients admitted with acute coronary syndrome (ACS) and diagnosed as erectile dysfunction patients according international index of erectile function (IIEF) was 36. The total number was 6 (20.0%) in the control group, 10 (27.8%) in the second group, 20 (58.8%) in the third group with a significant difference between groups. Comparison between results of penile artery duplex in our study groups was classified according to response to papaverine injection into either no erection, tumescence and rigidity not sufficient for intercourse, tumescence and rigidity sufficient for intercourse or full erection. There was no significant difference between groups.

**Conclusion:** The recognition of ED was a warning sign of silent vascular disease. It has led to the concept that a man with ED and no cardiac symptoms is a cardiac (or vascular) patient until proven otherwise.

**Key words:** Acute Coronary Syndrome, Coronary Artery Disease, Erectile Dysfunction, Gensini score, IIEF.

## INTRODUCTION

Erectile dysfunction is a common disorder. The prevalence of erectile dysfunction is high (5–20%) in the general population and increases with age, i.e. from 2% in men <40 years to 86% in men

80 years (Jackson et al., 2010). Coronary artery disease (CAD) and erectile dysfunction have common pathways and risk factors (Katsiki et al., 2014).

The prevalence of erectile dysfunction is very high, i.e. >70% among patients

with cardiovascular disease (CVD) including CAD, stroke, peripheral artery disease (PAD) and in patients with diabetes mellitus suggesting a link between erectile dysfunction and these disorders. A previous consensus proposed that CAD symptoms may present 2–3 years after the incidence of erectile dysfunction in men with no known vascular disease at the time of diagnosis, whereas a CVD event may occur in 3–5 years (*Jackson et al., 2010*).

The penile circulation includes smaller arteries than the coronary ones and this may explain the earlier clinical manifestation of erectile dysfunction, thus supporting the potentiality of erectile dysfunction as a marker of premature atherosclerosis predisposing to CAD (*Banks et al., 2013* and *Gandaglia et al., 2014*).

## PATIENTS AND METHODS

This study included Egyptian patients admitted to Ahmed Maher teaching hospital during the period from May 2018 to January 2019 with acute coronary syndrome (ACS) and history of erectile dysfunction (ED) and underwent coronary angiography. Patients considered potentially eligible who agreed to participate and provided written consent. They were subdivided into 3 groups: group 1 (control group G1, n= 30) have a normal coronary angiography or non-atherosclerotic coronary artery disease, group 2 (G2, n= 36) have a single coronary artery disease and group 3 (G3, n= 34) have more than one coronary artery disease.

Coronary artery disease assessment was done through coronary angiography

and scored via Gensini score, erectile dysfunction assessment through International Index of Erectile Function (IIEF) and penile artery duplex. All patients with symptoms suggestive of erectile dysfunction equal to or older than 18 years of age were admitted at our hospital with ACS (history of chest pain during last 24 hours prior admission and ECG changes denoting coronary artery ischemia plus or minus positive cardiac enzymes) were included in our study. Patients were excluded if there was an absolute contraindication for coronary angiography or intervention (e.g. acute ischemic stroke, severe anemia and decompensated congestive heart failure), any patient refused to participate in the study, patients with old myocardial infarction or previous history of revascularization procedures, patients who presented with complicated ACS such as cardiogenic shock or acute heart failure, patients with diseases that could alter sexual activity such as liver cirrhosis, renal failure, thyroid disease (hypo- and hyperthyroidism on replacement treatment), major depression on long-term pharmacological treatment, and spinal cord injuries, and those with previous pelvic, penile, urethral, or prostate trauma or surgery, and patients with primary erectile dysfunction (psychogenic erectile dysfunction due to troubled marriage or relationship, psychiatric disorders or socioeconomic factors).

Risk factors (when not previously known) were defined according to the European Society of Cardiology guidelines as follows: hypertension as blood pressure  $\geq 120/80$  mmHg in three consecutive readings at rest, hypercholesterolemia as total and/or LDL

cholesterol level  $\geq 5$  mmol/L ( $\geq 190$  mg/dL) and 3 mmol/L ( $\geq 114$  mg/dL), respectively; diabetes as fasting glucose level  $\geq 7.0$  mmol/L ( $\geq 125$  mg/dL); obesity as body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>.

All patients were prepared according to the American College of Cardiology/American Heart Association (AHA/ACC) task force on cardiac catheterization laboratory standards. Coronary angiography was performed according to the Judkin's technique. In the vast majority of patient's coronary angiography was performed with a dedicated 6 french sheath and 6 french diagnostic plus 6 french guiding catheters for PCI for both left and right coronaries. The severity of coronary artery disease was classified according to Gensini Score into two groups; mild atherosclerosis (Gensini score  $< 25$  points) and severe atherosclerosis (Gensini score  $> 25$  points) (*Gensini, 1987*).

**International Index of Erectile Function (IIEF):** Fifteen item self-administered questionnaires which assessed erectile function. The IIEF-5 score is the sum of the ordinal responses to the 5 items.

**Penile artery duplex:** The procedure has been fully explained to the patients; 60 mg of papaverine (2 mL ampoule of 30 mg/mL) was injected intracavernosally, post-injection measurements (at 5, 10, 15, 20 minutes): peak systolic velocity, end diastolic velocity, visual tumescence and erection. According to penile artery Duplex results were divided into 5 sub-groups (full erection, tumescence and rigidity sufficient for sexual intercourse, tumescence and rigidity not sufficient for sexual intercourse, tumescence alone or no erection).

#### **Statistical Methods:**

The study data were analyzed using SPSS statistical package. Numeric data were presented as mean and standard deviation and range as appropriate. Categorical variables were presented as frequency and percentage. Comparison between results regarding categorical data was done using Chi-square test, P-value less than 0.05 was considered significant.

## RESULTS

This study enrolled 100 patients admitted with acute coronary syndrome (ACS) and underwent coronary angiography with history of erectile dysfunction which subdivided into 3 groups: Group I included 30 patients in whom coronary angiography identified normal or non-significant CAD, Group II comprised 36 patients in whom coronary angiography documented single significant CAD, and Group III involved 34 patients presented with significant 2-3 CAD. The age of our patients ranged from 45 to 71 years with mean age of  $56.79 \pm 5.2$ ,  $55.3 \pm 4.1$ ,  $60.0 \pm 5.4$  in group I, II and III respectively (P value 0.001). Obese patients based on Body Mass Index (BMI) were 5 (16.7%) in first group, 8 (22.2%) in second group, and 9 (26.5%) in third group (P value 0.250). Smokers were 92; 26 (86%) in first group, 34 (94.4%) in second group, and 32 (94%) in third group (P value 0.44). Hypertensive patients were 77; 20 (66.7%) in first group, 29 (80.6%) in second group, and 28 (82.4%) in third group (P value 0.274). Diabetic patients were 32 patients; 5 (16.7%) in first group, 11 (30.6%) in second group, and 16 (47.1%) in third group (P value 0.000). LDL-C of our patients ranged from 75 to 160 mg/dl (mean  $112.9 \pm 18.3$ ); 75 to 140

mg/dl (mean  $107 \pm 16.5$ ) in control group, 77 to 156 mg/dl (mean  $112.3 \pm 17.5$ ) in second group, and 77 to 160 mg/dl (mean  $118.7 \pm 19.4$ ) in third group (P value 0.039). The number of patients with three risk factors or more were 57; 13 (43.3%) in first group, 21 (58.3%) in second group and 23 (67.6%) in third group (P value 0.146-Table 1).

The total number of patients presenting with acute myocardial infarction (MI) was 57 patients. 27 in second group, and 30 in third group (P value 0.001). Angiographic assessment of coronary arteries of our patients according to Gensini score showed 17 patients (47.2%) with mild atherosclerosis and 16 patients (44.4%) with severe atherosclerosis in second group, and 5 patients (14.7%) with mild atherosclerosis and 29 patients (85.3%) with severe atherosclerosis in third group (**P value 0.001-Table 1**).

The total number of erectile dysfunction patients according to international index of erectile function (IIEF) was 36; 6 (20.0%) in first group, 10 (27.8%) in second group and 20 (58.8%) in third group (P value 0.001). Erectile dysfunction was assessed by penile artery duplex after injection of papaverine intracavernosally (**Table 1**).

**Table (1): Comparison between the study groups according to risk factors, clinical presentation, coronary angiography findings by Gensini score, prevalence of erectile dysfunction by IIEF and penile artery duplex findings**

<b>Parameter</b>	<b>Group 1 (n=30)</b>	<b>Group 2 (n=36)</b>	<b>Group 3 (n=34)</b>
Age (45-71) (mean 56.8± 5.2)	48-63 (54.9± 4.5)	45- 63 (55.3± 4.1)	49- 71 (60.0 ± 5.4)
Obesity (n= 22) (%)	5 (16.7%)	8 (22.2%)	9 (26.5%)
BMI (21 to 35) (Mean 28.01±3.8)	21 to 35 (27.4 ± 3)	22 to 37(27.7±3.7)	23 to 39 (28.9±4.5)
Smoking (n= 92) (%)	26 (86.7%)	34 (94.4%)	32 (94.1%)
Hypertension (n= 57) (%)	20 (66.7%)	29 (80.6%)	28 (82.4%)
Diabetes mellitus (n=32) (%)	5 (16.7%)	11 (30.6%)	16 (47.1%)
HBA <sub>1</sub> C (4.7 to 12.0) (mean6.58± 1.7)	4.7 to 9.5 (5.8± 1.2)	4.7 to 10 (6.4± 1.5)	4.8 to 12 (7.5± 2)
LDL-C (75 to 160 mg/dl) (mean112.9± 18.3)	75 to 140 (107± 16.5)	77 to 156 (112.3±17)	77 to 160 (118.7±19.4)
TG (110 to 450 mg/dl) (mean220.9± 86.6)	125 to 400 (213± 76.2)	110 to 450 (186.9±63.4)	135 to 450 (263± 99.7)
3 factors or more (n=57) (%)	13 (43.3%)	21 (58.3%)	23 (67.6%)
<b>Clinical presentation</b>			
• Unstable angina (n=43)	30 (100%)	9 (25%)	4 (11.8%)
• NSTEMI (n=41)	0	19 (52.8%)	22 (64.7%)
• STEMI (n=16)	0	8 (22.2%)	8(23.5%)
<b>Gensini score: (n-%)</b>			
• Mild atherosclerosis	-	17 (47.2%)	5 (14.7%)
• Severe atherosclerosis	-	16 (44.4%)	29 (85.3%)
<b>Erectile dysfunction by IIEF (n= 36) (%)</b>	6 (20.0%)	10 (27.8%)	20 (58.8%)
<b>Penile artery duplex:</b>			
• Full erection	30(100%)	28 (77.8%)	15 (44.1%)
• Tumescence and rigidity sufficient for sexual intercourse	-	8 (22.2%)	5 (14.7%)
• Tumescence and rigidity not sufficient for sexual intercourse	-	-	11 (32.4%)
• Tumescence alone	-	-	2(5.9%)
• No erection	-	-	1(2.9%)

## DISCUSSION

Erectile dysfunction (ED) affects 50% of men older than 40 years exerting substantial effects on quality of life. This common problem is complex and involves multiple pathways. Penile erections are produced by an integration of physiologic processes involving the central nervous, peripheral nervous, hormonal and vascular systems. Any abnormality in these systems, whether from medication or disease has a significant impact on the ability to develop and sustain an erection, ejaculate and experience orgasm. A common and important cause of ED is vasculogenic. Many men with ED have comorbid conditions such as dyslipidaemia, tobacco abuse and diabetes mellitus (*Lopushnyan and Chitaley, 2012*).

Erectile dysfunction may be the earliest presentation of atherosclerosis and vascular disease (*Nehra et al., 2012*) which was approved in our study as the percentage of erectile dysfunction patients according to international index of erectile function (IIEF) was 20.0% in first group, 27.8% in second group, and 58.8% in third group. Patients in third group, who had a more aggressive risk factors and higher atherosclerotic burden, had higher erectile dysfunction prevalence and more severe coronary atherosclerosis diagnosed by coronary angiography and assessed by Gensini score which showed a more severe atherosclerosis in coronaries (85.3%). This was also confirmed by the Princeton III Consensus which recommended screening men who present with ED for cardiovascular risk factors (*Miner et al., 2012*).

Initially thought to be a chronic, slowly progressive, degenerative disease, atherosclerosis is a disorder with periods of activity and quiescence. Although a systemic disease, atherosclerosis manifests in a focal manner and affects different organ systems in different patients for reasons that remain unclear. Pooled whole-exome sequencing (WES) appears to have potential for providing insights into the pathogenesis of coronary artery atherosclerosis. In a study that used this technology on patients with multiple cardiovascular risk factors but normal coronary arteries and control subjects with multivessel CAD, investigators found 19 genetic variants that may provide protection from CAD, but whose mechanism remains unclear (*Abramowitz et al., 2016*). Atherosclerotic plaques (or atheroma), which may require 10-15 years for full development, characteristically occur in regions of branching and marked curvature at areas of geometric irregularity and where blood undergoes sudden changes in velocity and direction of flow. Decreased shear stress and turbulence may promote atherogenesis at these important sites within the coronary arteries, the major branches of the thoracic and abdominal aorta, and the large conduit vessels of the lower extremities. A study by Samady and his colleagues (*Samady et al., 2011*) suggests low shear segments in the coronary arteries develop greater plaque and necrotic core progression and constrictive remodeling, whereas high shear segments develop greater necrotic core and calcium progression, regression of fibrous and fibrofatty tissue, and excessive expansive remodeling.

Distinction has been made between the anatomic appearance of a stenosis and its

functional significance, with a marked discordance between the two. Using methods such as fractional flow reserve (FFR), it has been shown that only about 1/3 of narrowings within a stenosis range of 50% to 70% display provokable myocardial ischemia that merit intervention. The remainder of narrowings can safely be managed medically (*Tonino et al., 2010*). In the majority of cases AMI occurs due to obstruction of isolated non-critical stenotic coronary artery (low atherosclerotic burden) so infarct related artery (IRA) was not critically obstructed (<50% diameter stenosis) at the time of the coronary angiography in 60–70% of cases which approved by pasupathy and his colleagues through a coronary angiography that was done twice before and soon after AMI which impelled lack of chronic anginal symptoms in 70% of patients (*Pasupathy et al., 2015*).

Analyzing results from several studies showed that erectile dysfunction had a significantly increased risk by 44 % for CV events, 62 % for myocardial infarction and 25 % for overall mortality compared to those without ED (*Banks et al., 2013* and *Vlachopoulos et al., 2013*).

## CONCLUSION

Erectile dysfunction may be considered a possible marker for the development of atherosclerosis and coronary artery disease.

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## العلاقة بين الفشل فى الانتصاب ومدى حدة القصور فى الشرايين التاجية

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**خلفية البحث:** ضعف الانتصاب هو المشكلة الجنسية الأكثر شيوعاً عند الرجال، ويعرف بأنه عدم القدرة على الوصول إلى الانتصاب القضيبى أو الحفاظ عليه كافيًا لممارسة المهبل بنجاح. و يعتبر ضعف الانتصاب من الأمراض الوعائية بشكل أساسي في غالبية الحالات. و العديد من عوامل الخطورة التي تسهم في تطور وبداية الضعف الجنسي هي السبب الرئيسي لتطویر مرض الشريان التاجي.

**هدف البحث:** توثيق العلاقة بين ضعف الانتصاب وحدة القصور فى الشريان التاجي في المرضى الذين يعانون من متلازمة الشريان التاجي الحادة مع التركيز على العلاقة بين بداية ضعف الانتصاب وظهور نقص تروية الشريان التاجي الحاد.

**المرضى و طرق البحث:** شملت هذه الدراسة المرضى المصريين الذين يعانون من متلازمة القصور الحاد فى الشريان التاجي مع وجود تاريخ مرضى من ضعف الانتصاب وخضعوا للتصوير بالصبغة للشرايين التاجية.

و قد تم تقسيمهم إلى 3 مجموعات وفقا للتصوير بالصبغة للشرايين التاجية الى:

المجموعة الاولى تحتوى على ٣٠ مريضا لديهم تصوير طبيعى بالصبغة للشرايين التاجية، المجموعة الثانية تحتوى على ٣٤ مريضا يعانون من قصور فى واحد من الشرايين التاجية اثناء التصوير بالصبغة للشرايين التاجية، المجموعة الثالثة تحتوى على ٣٦ مريض يعانون من قصور فى اكثر من شريان من الشرايين التاجية اثناء التصوير بالصبغة للشرايين التاجية.

و قد تم عمل مقارنة بين الثلاث مجموعات من حيث عوامل الخطورة و الامراض المصاحبة، و تم تقييم مدى القصور فى الشرايين التاجية عن طريق

مؤشر جنسي، و تم تقييم درجة الفشل فى الانتصاب عن طريق المؤشر الدولى للفشل فى الانتصاب.

**نتائج البحث:** كان العدد الإجمالي للمرضى الذين يعانون من متلازمة الشريان التاجي الحادة وتاريخ مرضى ضعف الانتصاب وفقا للمؤشر الدولي لوظائف الانتصاب 36، وكان هذا العدد 6 (20.0%) في المجموعة الأولى، 1 (27.8%) في المجموعة الثانية، وبلغ المجموع 20 (58.8%) في المجموعة الثالثة مع وجود فرق احصائي ملحوظ بين المجموعات. وبالمقارنة بين المجموعات من حيث نتائج حقن البافيرين فى شريان القضيب و تصوير الشريان القضيبي بواسطة الدوبلكس تبين عدم وجود فرق ملحوظ بين مجموعات الدراسة.

**الاستنتاج:** التعرف على الضعف الجنسي هو علامة تحذير من مرض الأوعية الدموية الصامتة، وقد أدى إلى إعتبار الرجل المصاب بالضعف الجنسي وليس له أعراض قلبية هو مريض قصور فى الشرايين التاجية (أو الأوعية الدموية) حتى يثبت العكس.