Abstract

Objectives: The aim of this study was to assess erectile dysfunction prevalence, time of onset and association with risk factors in patients with acute chest pain and angiographically documented coronary artery disease.

Methods: 300 consecutive patients with acute chest pain and angiographically documented coronary artery disease were assessed using a semi-structured interview investigating their medical and sexual histories, the International Index of Erectile Function and other instruments.

Results: Patient mean age was 62.5 ± 8 years (range 33–86 years). Mean duration of symptoms or signs of myocardial ischaemia prior to enrolment in the study was 49 months (range 1–200). Coronary angiography showed 1-, 2- and 3-vessel disease in 98 (32.6%), 88 (29.3%) and 114 (38%) patients, respectively. The prevalence of ED among all patients was 49% (147/300). Erectile dysfunction was scored as mild, mild to moderate, moderate and severe in 21 (14%), 31 (21%), 20 (14%), and 75 (51%) of patients, respectively. There was no significant difference between patients with ED (n = 147) or without ED (n = 153) as far as clinical and angiographic characteristics were concerned.

In the 147 patients with co-existing ED and CAD, ED symptoms were reported as having become clinically evident prior to CAD symptoms by 99/147 (67%) patients. The mean time interval between the onset of ED and CAD was 38.8 months (range 1–168). There was no significant difference in terms of risk factor distribution and clinical and angiographic characteristics between patients with the onset of ED before vs. after CAD diagnosis. Interestingly, all patients with type I diabetes and ED actually developed sexual dysfunction before CAD onset (p < 0.001).

Conclusions: Our study suggests that a significant proportion of patients with angiographically documented coronary artery disease have erectile dysfunction and that this latter condition may become evident prior to angina symptoms in almost 70% of cases. Future studies including a control group of patients with coronary artery disease and normal erectile function are required in order to verify whether erectile dysfunction may be considered a real predictor of ischemic heart disease.

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Keywords: Erectile dysfunction; Impotence; Prevalence; Coronary artery disease; Peripheral vascular disease

1. Introduction

Erectile dysfunction (ED) is defined as the recurrent or persistent inability to achieve and/or maintain an erection in order for satisfactory intercourse to occur. The reported prevalence of ED in the general population...
ranges from 19% to 52% [1,2]; this span is likely due to differences in the criteria used in defining ED and to the lack of systematic stratification by age. Despite this significant difference in ED prevalence, the age-related increase of ED and the correlation between ED and vascular risk factors—hypertension, hypercholesterolemia, cigarette smoking, diabetes and obesity—are common findings of several studies [1–6]. These data suggest that ED may be considered a clinical manifestation of a functional (i.e. endothelial dysfunction) and/or a structural abnormality affecting penile circulation as a part of a more generalized vascular disorder [7,8]. So far, little is known about the predictive role of ED as a marker of sub-clinical coronary artery disease (CAD). The aim of this prospective study was to evaluate patients presenting acute coronary syndromes (ACS) in our emergency units—and subsequently diagnosed with documented CAD—in terms of ED prevalence and its chronological and aetiological correlations with heart disease.

2. Material and methods

In two emergency units, between February 2001 and July 2002, we prospectively evaluated 340 consecutive patients (mean age 62.5 ± 8 years; range 33–86) with ACS who subsequently underwent coronary angiography. Both those patients presenting with a first angina episode and those with a known history of CAD underwent full cardiological assessments. For the purpose of this study, the only additional inclusion criterion was the detection (by coronary angiography) of a significant stenosis (>50% diameter stenosis by visual estimation) in at least one major epicardial branch by two different observers. We excluded patients with diseases that could alter sexual activity such as liver cirrhosis, renal failure and thyroid disease. Patients with previous pelvic, penile, urethral or prostate surgery were also excluded from this study.

Patients with significant coronary artery stenosis underwent a detailed cardiological assessment in order to identify co-morbidities and risk factors, and to define on-going medical therapies, and sexual histories. Anginal chest pain was defined as any discomfort in the chest or adjacent area, spreading to the left arm, infra-scapular area or lower jaw, lasting 5–15 minutes, triggered by physical or emotional stress, and subsiding with rest or after sublingual nitrates in 15–20 minutes. A positive non-invasive test response was defined as: >1 mm ST-segment horizontal or down-sloping depression during exercise stress test or ambulatory ECG monitoring and reversible perfusion defects during exercise or a pharmacological myocardial scintigraphy. The onset of coronary artery disease was established at the first episode of typical chest pain or the first objective demonstration of myocardial ischaemia by non-invasive tests.

Hypertension was defined as blood pressure >140/90 mmHg in 3 consecutive recordings, at rest. Hypercholesterolemia was defined as a total cholesterol level >200 mg/dl (>7.73 mmol/l) (in patients not taking specific drugs) and diabetes as a fasting plasma glucose level >140 mg/dl (>7.8 mmol/l) (in patients without a previous diagnosis).

Patients also underwent a full urological assessment (including a semi-structured interview aimed at evaluating their medical and sexual histories) through the administration of the International Index of Erectile Function (IIEF) [9] and Beck’s Inventory for Depression [10].

In all the patients enrolled, an ED diagnosis was made on the basis of the value of the erectile function domain score of the IIEF, according to the classification by Cappelleri et al. [11]. Possible correlations between erectile function and CAD were investigated by targeted questions routinely included in the semi-structured interview mentioned above. The study was approved by the Ethics Committee and a written informed consent was signed by all patients. Statistical analysis was based on the Student’s t-test for unpaired data, the χ²-test and the Fisher exact test.

3. Results

Twenty-seven out of 340 (12%) successive patients refused to enter the study and did not sign the informed consent. Thirteen out of the 313 remaining patients (4%) were excluded from the study due to unsatisfactory completion of the self-administered questionnaires. Three hundred patients completed the study protocol and were included in the data analysis. The clinical characteristics of the patient population are reported in Table 1.

Patient mean age was 62.5 ± 8 years (range 33–86 years). The vast majority of them (249 patients; 83%) had been previously diagnosed with symptomatic CAD and presented a recurring episode of ACS. Mean duration of either symptoms or signs of myocardial ischaemia prior to enrolment was 49 months (range 1–200). Recognized vascular risk factors for CAD (i.e. hypertension, hypercholesterolemia, diabetes, smoking), were present in all patients: one risk factor was found in 87/300 patients (29%), two risk factors in 101/300 patients (34%) and 3 or more in 112/300 patients (37%). Coronary angiography showed 1-, 2- and 3-vessel disease in 93 (33%), 88 (29%) and 114 (38%) patients, respectively. The prevalence of ED among all patients was 49% (147/300). Erectile dysfunction was scored as mild, mild to moderate, moderate and severe in 21 (14%), 31 (21%), 20 (14%), and 75 (51%) of patients, respectively. There was no significant difference between patients with ED (n = 147) or without ED (n = 153) as far as risk factor distribution, clinical and angiographic characteristics, and drugs potentially affecting sexual function (beta-blockers, diuretics [thiazides, potassium-sparing], digoxin, antidepressant agents) were concerned.

In the 147 patients with co-existing ED and CAD, ED symptoms were reported as becoming clinically evident prior to anginal or non-invasive detection of CAD in 99/147 (67%) patients. The mean time interval between the onset of ED and CAD in these patients was 38.8 months (range 1–168). Initial CAD manifestation in patients with previous ED was AMI in 40/99 patients.
and stable/unstable angina in 59/99 patients (60%). When we compared patients with the onset of ED preceding or following the onset of CAD in terms of risk factor distribution and clinical and angiographic characteristics, we did not find any significant differences except in all those patients with ED, type I diabetes and CAD, who reported that they had become impotent prior to developing any angina symptoms (p < 0.001).

### 4. Discussion

Evidence is accumulating in favor of considering ED as a vascular disorder [12,13]. Common risk factors for atherosclerosis have been frequently found in patients with ED; in addition, the extent of ED has been related to the number and severity of vascular risk factors [13,14]. Moreover, abnormal sexual function has been reported in patients with vascular diseases such as myocardial infarction, cerebrovascular accidents, hypertension and peripheral arterial disease [5]. Little is known, however, about the role of ED as a marker of CAD. Apart from the anecdotal report by O’Kane et al. [15] regarding 2 patients who were diagnosed with CAD following an initial evaluation for ED, current available data come from studies of patients originally investigated for ED who subsequently submitted to testing for CAD [6,16–18]. In these studies, the mean prevalence of positive responses to non-invasive tests (mainly exercise stress test) average out at 20%, with the vast majority of patients showing an abnormal electrocardiography response had multiple risk factors for atherosclerosis. Similar mean prevalence of positive stress test has been found in studies addressing the topic of latent CAD in asymptomatic, middle-aged subjects [19–21]. Although no information about ED was reported in these studies, the finding of a similar prevalence of positive responses raises questions about the role of ED as an early marker for CAD. Interestingly, when viewed from the opposite angle (i.e. prevalence of ED in patients with proven CAD), figures change: a prevalence of ED in CAD patients is much higher, ranging from 44 to 65% [22–26]. Differences may be due to varying criteria in defining CAD, the sensitivity-specificity of cardiological test(s) used (mainly the exercise stress test in the ED series vs. coronary angiography in the CAD series) and to CAD’s clinical characteristics. Indeed, initial CAD manifestation in 30–40% of patients is AMI. Since it has been shown that angiographically defined mild rather than critical coronary stenoses are those more prone to

<p>| Table 1 | Patient population characteristics |</p>
<table>
<thead>
<tr>
<th>All patients (n = 300)</th>
<th>Patients with ED (n = 147)</th>
<th>Patients without ED (n = 153)</th>
<th>p valuea</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.5 ± 8</td>
<td>65 ± 6</td>
<td>59 ± 6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.7 ± 1.2</td>
<td>26.9 ± 1.3</td>
<td>26.4 ± 1.3</td>
</tr>
<tr>
<td>Stable angina</td>
<td>265 (83)</td>
<td>135 (92)</td>
<td>130 (85)</td>
</tr>
<tr>
<td>Unstable angina/AMI</td>
<td>35 (17)</td>
<td>12 (8)</td>
<td>23 (15)</td>
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<tr>
<td>Prior AMI</td>
<td>143 (48)</td>
<td>69 (47)</td>
<td>74 (48)</td>
</tr>
<tr>
<td>Symptom onset (months)</td>
<td>49 ± 16</td>
<td>47 ± 14</td>
<td>51 ± 15</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>171 (57)</td>
<td>83 (56)</td>
<td>88 (57.5)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>45 (15)</td>
<td>30/45 (67)</td>
<td>15/45 (33)</td>
</tr>
<tr>
<td>Type I</td>
<td>11 (4)</td>
<td>8/11 (73)</td>
<td>3/11 (27)</td>
</tr>
<tr>
<td>Type II</td>
<td>34 (11)</td>
<td>22/34 (65)</td>
<td>12/34 (35)</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>182 (61)</td>
<td>88 (57)</td>
<td>94 (61)</td>
</tr>
<tr>
<td>Smoking (current)</td>
<td>63 (21)</td>
<td>24 (16)</td>
<td>39 (25)</td>
</tr>
<tr>
<td>Smoking (past)</td>
<td>168 (56)</td>
<td>87 (59)</td>
<td>81 (53)</td>
</tr>
<tr>
<td>Obesity (BMI &gt; 24.9)</td>
<td>214 (71)</td>
<td>108/147 (73)</td>
<td>106/153 (69)</td>
</tr>
<tr>
<td>CAD extension</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-VD</td>
<td>98 (33)</td>
<td>43 (29)</td>
<td>55 (36)</td>
</tr>
<tr>
<td>2-VD</td>
<td>88 (29)</td>
<td>42 (28.5)</td>
<td>46 (30)</td>
</tr>
<tr>
<td>3-VD</td>
<td>114 (38)</td>
<td>62 (42)</td>
<td>52 (34)</td>
</tr>
</tbody>
</table>

Mean values are expressed as ±S.D. Values in parentheses refer to %. AMI: Acute myocardial infarction; BMI: body mass index; CAD: coronary artery disease; ED: erectile dysfunction; VD: vessel disease.

a Refers to difference between patients with and without ED.
of CAD. We, as others [1,3–5], found common risk factors for atherosclerosis as being well represented and equally distributed between patients with or without ED (see Table 1) except for type 1 diabetes, which was significantly more prevalent in patients with ED. Thus, our data confirm the major role of type 1 diabetes as a risk factor for ED due to its vascular and neural involvement. We did not find any relationship between the severity of ED and the number of coronary vessels involved. On the contrary, Greenstein et al. [28] found patients with 1-vessel disease as having more prolonged and firmer erections than patients with 2- and 3-vessel disease. This discrepancy is likely to be the result of using different criteria in defining ED and angiographically significant stenosis. The more stringent angiographic cut-off adopted (>70–75% diameter stenosis) and the almost double-fold prevalence of diabetes (28% vs. 15%), likely led to the selection of a patient population with severe and diffuse vascular disease that tallies well with severe ED.

The major limitation of this study is the lack of a control group, i.e. patients with ED and no clinically-evident CAD. Thus, we cannot state whether ED is actually more frequent in CAD patients when compared to patients without CAD, and further research is needed to verify the hypothesis that ED is a predictor for CAD. The question whether patients presenting ED and other vascular risk factors should, on meeting with a urologist, undergo further testing for silent CAD remains open and needs future studies in large patient-number populations.

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References

The study by Montorsi and colleagues adds to the evidence of the collision of two important diseases of our time—coronary artery disease and erectile dysfunction (CAD and ED). From a practical standpoint it shows how often CAD patients bring their ED with them to the angiography suite—and so how often ED will add to the misery of CAD and how, for some, prior recognition of the ED could have set vascular if not cardiovascular complications in train.

The data they have collected looks back from the vantage point of the man with clinical CAD to reveal how many of the men with significant proven coronary artery lesions have had a history of ED. They show, in a remarkable series of 300 men, that fully half of the men at the end of the coronary catheter will have had pre-existent ED and for half of those the ED has been severe. When ED has preceded the CAD, as it did in 67% of those with both, it has done so for over 3 years presenting a substantial window of opportunity for anticipation of other vascular problems. To what extent we should recognize ED as a warning sign of cardiac disease to come (the so called sentinel marker) is a more problematic issue and the structure of this already demanding study does not permit this specific assessment.

Of special interest—and perhaps concern—is the fact that the coronary vascular disease of men with or without ED is indistinguishable. In line with this is the absence of distinguishing characteristics in the risk factor profile, the clinical presentation, or the medication list in men with CAD in respect to whether or not they have ED.

There is a suggestion from these, and other [1], data and from an understanding of the underlying clinical [2] and basic science that this overlap is strong enough to justify the search for CAD in men presenting with ED [3]. Whenever a surrogate marker is used to find a disease the questions about specificity and sensitivity have to be asked as do the questions about the costs of finding disease, the benefits and risks of finding disease and the relative value to patient and society. In the Montorsi study there is little doubt that the men studied had important CAD deserving of attention (they had clinical or objective evidence of ischemia). At what level of utility should the cardiologists incorporate ED as a marker for CAD?

There are two reasons why urologists are becoming interested in the interrelationship between ED and CAD: they share common cause in terms of the blood vessels of the organ involved and the prime treatment, PDEI, was evolved with CAD in mind. But this link between ED and CAD is also a conduit to the greater world of vascular disease and its multiple manifestations. This conduit should convey a two way exchange: urologists interested in ED have the opportunity to expand their understanding of ED through the greater world of vascular function, dysfunction and treatment [4]; specialists with vascular knowledge should consider ED as one of the issues not to be
overlooked. Montorsi et al. and others [5] have shown us that ED and CAD are overlapping in terms of risk factors, the pathological basis of disease and the clinical context.

Disease of blood vessels, functional and anatomic, contribute to a broad variety of conditions and sexual dysfunctions are certainly among them. We need to study in a prospective fashion the value of prevention and the links that can be drawn between risk factors and the important vascular diseases including SD and CAD. Montorsi et al. have made an important contribution to these connections.

References