The Risk of Coronary Heart Disease in Men with Erectile Dysfunction

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Abstract

Objectives: Erectile dysfunction (ED) is a common disorder of aging male and about 50% of the ED sufferers consult a physician in the Netherlands. As ED is strongly correlated with cardiovascular diseases, we explored how many patients with ED aged 40 to 69 years will develop cardiovascular disease in the Netherlands and, philosophize if and which preventive measures are available to reduce cardiovascular risks in this specific population.

Methods: 158 patients were included and were comprehensively evaluated. All patients underwent a penile-pharmacoduplex ultrasonography to evaluate the penile vascular status and a cut-off value for acceleration time of 100 ms was used to distinguish between patients with and without cavernous arterial insufficiency. Framingham risk functions were used to determine the 4 to 12 year coronary heart disease risk. The results were extrapolated to the Dutch ageing male population.

Results: In the age group 40 to 49 years and 60 to 69 years no significant difference was detected in coronary heart disease risk between patients with and without cavernous arterial insufficiency. In the age group 50 to 59 years patients with cavernous arterial insufficiency showed a significantly increased risk to develop coronary heart disease. It is estimated that in total, more than 25,000 ageing men with ED will develop coronary heart disease within 4 years and increases to almost 75,000 men within 12 years in the Netherlands.

Conclusions: Screening on cardiovascular risk factors and taking preventive measures is recommended in men with ED. Men with cavernous arterial insufficiency aged 50 to 59 years are especially prone to develop coronary artery disease.

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Keywords: Erectile dysfunction; Coronary heart disease; Prevention; Duplex ultrasonography

1. Introduction

With a prevalence of 13% in men above the age of 40 years in the Netherlands, erectile dysfunction (ED) is a common but underreported disorder [1]. Before the introduction of sildenafil, the first effective oral medication for ED, only about 25% of men consulted their general practitioner [1]. This remarkable difference between prevalence and care seeking behaviour has several reasons. The most important explanation is that ageing men are not so much bothered by ED. In the Boxmeer study, 64% of men between the age of 40 and 49 years were bothered by their dysfunction whereas only 27% of men above the age of 70 experienced bother [1]. The lack of a sexual partner and acceptance of a natural decline of sexual function in both the man and his partner are plausible reasons for this phenomenon. Moreover, many men think that ED is not a medical problem and are embarrassed to raise the issue of sexuality with their physician. Finally, the notion of the (un)availability of effective treatment may have prevented that men seek help. This notion is confirmed by the fact that the number of men consulting their general practitioner because of ED doubled in The Netherlands after the introduction of sildenafil [personal communication].

Amongst health care professionals the introduction of sildenafil and the subsequent medicalization of ED has led to ambivalent feelings. On the one hand
it placed an additional burden on their overburdened practices, on the other hand it offered them an excellent opportunity to reach a group of as yet for health care unreachable men. After all, as ED in the ageing population is strongly correlated with cardiovascular risk factors [1–5], two pivotal questions had been raised. Firstly, how many men with ED will develop cardiovascular disease and, secondly, are additional measures to reduce cardiovascular risks in this specific population warranted.

In this study amongst men older than 40 years and younger than 70 years, consulting our urological outpatient department with the complaint of ED we addressed these questions by assessing the risk of coronary heart disease within 4–12 years using the Framingham equations and by extrapolating the results to the Dutch ageing male population. Finally, we philosophise about the advisability of a cardiovascular prevention program for men with ED.

2. Patients and methods

Except selection for age, patients visiting our urological outpatient department were randomly included in the study. We enrolled 160 consecutive patients aged 40 to 69 years with complaints of ED between January 2000 and December 2001. Data of two patients are missing. Thirty-two patients had a history of traumatic vasculogenic ED (pelvic or perineal trauma/surgery). All 126 men without known cardiovascular disease were comprehensively evaluated using medical and sexual history, physical examination, and blood analysis. Special emphasis was put upon cardiovascular risk factors and disease. Physical examination included measurement of blood pressure, smoking habits, total and HDL cholesterol, and diabetic status. We used ANOVA to test the differences in risk between patients with and without cavernous arterial insufficiency on significance for each age category.

The estimated risks were extrapolated to the Dutch ageing male population to determine the number of men having potential benefit from a cardiovascular prevention program. Data of Statistics Netherlands (http://www.cbs.nl) and the Boxmeer study [1] were used for extrapolation. The first shows that almost 3 million men aged 40 to 69 years are living in The Netherlands. The latter shows that 13% of men aged 40 years or older had ED with 6% of the men aged 40 to 49 years, 9% in men aged 50 to 59 and 22% in men aged 60 to 69 years.

<table>
<thead>
<tr>
<th>Age</th>
<th>Without CVD</th>
<th>With CVD</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>29</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>50–59</td>
<td>60</td>
<td>12</td>
<td>72</td>
</tr>
<tr>
<td>60–69</td>
<td>37</td>
<td>19</td>
<td>56</td>
</tr>
<tr>
<td>Total</td>
<td>126</td>
<td>32</td>
<td>158</td>
</tr>
</tbody>
</table>

*Cardiovascular disease includes myocardial infarction, angina pectoris, stroke, transient ischaemic accident and peripheral vascular disease.

3. Results

In total, 32 patients had cardiovascular disease in their medical history and a significant increase was seen with age: Three percent of the patients in the age group of 40 to 49, 17% of the patients 50 to 59 years and 34% in the age group 60 to 69 years (Table 1). The remaining 126 patients were included in the subsequent analysis and were free of cardiovascular disease.

Results of the penile-pharmaco duplex ultrasonography indicated that 24% of men aged 40 to 49 years suffered from cavernous arterial insufficiency, 39% of men aged 50 to 59 years and 42% of men aged 60 to 69 years.

The prediction of development of coronary heart disease from 4 to 12 years using the Framingham functions was not significantly different between patients with or without cavernous arterial insufficiency in the age groups 40 to 49 and 60 to 69 years (Fig. 1). After 4 years, the coronary heart disease risk of men aged 40 to 49 years was 5.1% and 5.2% for patients without and with cavernous arterial insufficiency, respectively, and after 12 years the risk was 16.8% and 16.5%. For men aged 60 to 69 years this was 10.0% and 9.8% after 4 years in patients without and with cavernous arterial insufficiency, respectively, and after 12 years the risk was 27.7% and 27.1%. In the age group 50 to 59 years patients with cavernous arterial insufficiency had a significantly increased risk. After 4 years, the estimated risk was 8.3% compared to 6.0% in patients without cavernous arterial insufficiency.
This increases to 24.4% and 19.2% after 12 years, respectively.

Extrapolation of these results to the male population of the Netherlands suggests that more than 25,000 men with ED will develop coronary heart disease within 4 years and almost 75,000 men within 12 years (Table 2).

Global comparison of lifestyle and biochemical physiological characteristics of the patients with and without cavernous arterial insufficiency aged 50 to 59 years showed no significant differences, however a trend in differences was seen for smoking habits, alcohol consumption, systolic blood pressure, body mass index and concentration of serum free testosterone (Table 3).

### Table 2

Estimation of number of men developing coronary heart disease (CHD) among ageing men with erectile dysfunction (ED) in the Netherlands

<table>
<thead>
<tr>
<th>Age</th>
<th>$N_{\text{Netherlands}}^{a}$</th>
<th>$N_{\text{ED}}^{b}$</th>
<th>$N_{\text{CHD4}}^{c}$</th>
<th>$N_{\text{CHD12}}^{d}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>40–49</td>
<td>1,222,094</td>
<td>73,326</td>
<td>37,400</td>
<td>12,245</td>
</tr>
<tr>
<td>50–59</td>
<td>1,070,889</td>
<td>96,380</td>
<td>66,500</td>
<td>20,529</td>
</tr>
<tr>
<td>60–69</td>
<td>685,824</td>
<td>150,881</td>
<td>15,088</td>
<td>41,492</td>
</tr>
<tr>
<td>Total</td>
<td>2,978,807</td>
<td>320,587</td>
<td>25,478</td>
<td>74,266</td>
</tr>
</tbody>
</table>


*b Total number of men with erectile dysfunction in the Netherlands estimated using data of ED prevalence from the Boxmeer study [1].

*c Estimation of number of men with ED developing CHD within 4 years.

*d Estimation of number of men with ED developing CHD within 12 years.

### Table 3

| Characteristics of the patients with and without cavernous arterial insufficiency (CAI) aged 50 to 59 years |
|--------------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| $n = 60$                                               | Without CAI, $n = 37$                             | With CAI, $n = 23$                                |
| Diabetes mellitus, n (%)                               | 2 (6%)                                           | 4 (16%)                                          |
| Smoking, pack-years$^a$ ± S.D.                         | 13.0 ± 15.4                                      | 18.5 ± 16.8                                      |
| Alcohol consumption, drinks/week ± S.D.               | 8.7 ± 6.5                                        | 10.9 ± 13.6                                      |
| Diastole, mmHg ± S.D.                                  | 84.6 ± 12.1                                      | 85.5 ± 15.4                                      |
| Systole, mmHg ± S.D.                                   | 138.6 ± 22.8                                     | 148.0 ± 22.6                                     |
| Body mass index, kg/m$^2$ ± S.D.                       | 26.1 ± 3.8                                       | 27.3 ± 4.5                                       |
| Total cholesterol/HDL ratio ± S.D.                    | 5.3 ± 2.0                                        | 5.4 ± 1.4                                        |
| Total testosterone, nmol l$^{-1}$ ± S.D.              | 15.7 ± 6.7                                       | 15.1 ± 4.1                                       |
| Free testosterone, pmol l$^{-1}$ ± S.D.               | 308 ± 88                                         | 264 ± 77                                         |

*a One pack-year was defined as smoking 20 cigarettes a day for a period of 1 year.

### 4. Discussion

The introduction of effective oral medication for the symptomatic treatment for ED led in the Netherlands to a twofold increase of men consulting a physician because of ED. Based on recent population based epidemiological studies it is estimated that about 150,000 out of 300,000 ED sufferers consult a physician with a peak incidence occurring between the age of 55 and 64 years (16.1 per 1000 per year) [personal communication]. Our study demonstrates that one out of four men above the age of 40 years with ED will develop coronary heart disease and that almost one in every two men between the age of 50 and 60, presenting with ED without known cardiovascular disease has a proven cavernosal arterial insufficiency and thus a significantly increased risk of developing a myocardial infarction within 4 to 12 years. Based on these figures it may be concluded that ED in ageing men should be regarded as an (early) marker for incident cardiovascular disease and that it should warrant preventive measures in this relatively large new group of patients consulting a physician.

On basis of current knowledge of the erectile mechanism the close relation between ED and cardiovascular disease does not come as a surprise [10–17]. In fact, ED is often a symptom of endothelial dysfunction. Impaired endothelial function and the consequent decreased capacity of the vascular smooth muscle to relax is regarded as the pivotal precursor of atherosclerosis and subsequent impaired cavernosal and coronary perfusion. In the literature, it even has been suggested that the small cavernosal vessels are more prone to atherosclerotic blockage than the larger coronary vessels [4]. In other words ED may be regarded as a sentinel for symptomatic coronary heart disease.
Patients with ED are of interest with respect to heart disease prevention as one out of four men aged between 40 and 69 years will develop coronary heart disease within 12 years. In contrast to our expectations, a distinction between men with and without cavernous arterial insufficiency did not add substantial information about coronary heart disease risk. Only, a difference in risk was detected between men with and without cavernous arterial insufficiency in the age category 50–59 years. However, the difference was relatively small, i.e. about 5%. So, we may conclude that men with ED above the age of 40 offer an excellent target for cardiovascular risk prevention irrespective their penile arterial status. Therefore, not only the proper choice of symptomatic treatment or sexological counselling should be on the physician’s agenda treating an ageing man with ED, but more importantly, the identification of cardiovascular risk factors and preventive measures for those patients identified as being at risk. To reach this goal, evidence-based guidelines derived from cardiovascular prevention programs, based on long-term intervention studies should be utilized.

The two basic and often in combination advocated tools in these preventive cardiovascular medicine programs are: (1) modification of lifestyle factors such as smoking, body weight and lack of exercise with the aid of counselling and (2) modification of physical and biochemical risk factors (i.e. hypertension, dyslipidaemia and diabetes mellitus) with the aid of pharmacological interventions (i.e. anticoagulant therapy, ACE-inhibition and lipid lowering).

From an economical and ecological point of view, lifestyle modification should be the first step in a cardiovascular prevention program. In the literature, it has shown to result in an almost fifty percent decline of cardiovascular mortality [18,19]. However, in clinical practise efficacy is disappointing low because of failing long-term patient motivation and compliance. For example, quitting smoking results in an estimated risk reduction at 3 years similar to the risk of subjects who have never smoked [20]. Long-term quitting rates however are low: 15%–50%, depending on intensity of the counselling and the length of follow-up [21]. The same counts for modification of physical activity, diet and body weight, three closely linked entities. Pate et al. described a large reduction of cardiovascular risk in sedentary men with only a small increase of physical activity [22]. Correspondingly, a recent study has shown that physical activity, even initiated as late as in midlife reduces the risk of developing ED [23]. The difficulty is that most patients relapse on the long term and regain weight [24].

Although perhaps equally effective as lifestyle modification, a pharmacological preventive intervention appears to be more attractive in clinical practise, because it is less time consuming and less dependent on patient motivation. Its effectiveness in for example regulation of blood pressure or dislipidaemia has been proven in a large number of epidemiological studies [25,26]. For example, an average reduction in plasma total cholesterol concentration of 10% has been found to lead to an average cardiovascular risk reduction of 20% [27,28]. Recently, several studies in asymptomatic patients have established that aggressive cholesterol-lowering therapy or long-term ACE inhibition have a beneficial effect on atherosclerosis progression [29,30]. Similarly, several antihypertensive drugs have been revealed to improve sexual functioning [31–33].

5. Conclusion

Modification of lifestyle should be an integrated part of a men’s sexual health clinic. Moreover, a liberal prophylactic pharmacological approach is advantageous not only in high-risk cardiovascular patients but may also be justified in ED patients with mild cardiovascular risk factors. To prove this hypothesis we currently conduct a randomized double blind, placebo-controlled trial with an ACE inhibitor in patients with ED with cardiovascular risk factors. The outcome parameter is erectile function at one year.

Acknowledgements

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patients should be investigated and possibly corrected.

[10] Pritzker MR. The penile stress test: A window to the hearts of man?


Editorial Comment
Luigi Cormio, Bari, Italy

There is increasing evidence that ED can be a preliminary symptom of serious underlying diseases, particularly cardiovascular. Thus, patients with ED should be carefully evaluated and counselled in this respect.

This paper shows that one out of four men with ED aged 40 to 69 years and without known cardiovascular disease will develop coronary artery disease (CHD) within 12 years. Thus, cardiovascular risk factors in ED patients should be investigated and possibly corrected.

Are patients with ED at higher risk of CHD than patients without ED? Unfortunately this study does not provide an answer, as there is no comparison with a control group, i.e. an age-matched population without ED. Only if such difference is proved one can state that ED is a sentinel of CHD and more aggressive preventive measures than those recommended in male population without ED are justified; if there is no difference, one can only say that ED can be a way to identify and possibly modify risk factors in otherwise unreachable men.
Are patients with arteriogenic ED at higher risk of CHD than patients with non-arteriogenic ED? This study shows that arteriogenic ED is associated with an increased risk for CHD only in men in the sixth decade of life suggesting that this group of patients, often unaware of such risk, should be investigated and counselled in this respect. Although this finding was not much emphasised, another study [1] has shown that arteriogenic ED is an even more reliable risk factor against CHD than cardiovascular risk factors [1]. So the next question is: should we use penile duplex ultrasonography to investigate coronary arterial status together with/rather than cavernous arterial status? Probably yes, if future studies will confirm [2–4] that cardiovascular and erectile function can share benefits from the same therapeutic regimen.

References


