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BACKGROUND PAPER

Correlations between lower urinary tract symptoms, erectile dysfunction, and cardiovascular diseases: Are there differences between male populations from primary healthcare and urology clinics? A review of the current knowledge

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Abstract

Objective: To evaluate the correlation between lower urinary tract symptoms, erectile dysfunction, and cardiovascular diseases in different male populations. **Methods:** Data sources: PubMed (Medline), clinical evidence, Embase, Cochrane reviews, and articles from reference lists. Selection criteria: Selection criteria in search databases were lower urinary tract symptoms, LUTS, comorbidity (MeSH), impotence (MeSH), sexual dysfunction, aging, primary care (MeSH), and male. Studies on these subjects, and concerning men aged 40 years or older, were eligible for inclusion in this review. Both community-based and clinical-based studies were included. **Results:** 20 studies were eligible for inclusion, representing 71 322 men. These studies showed a significant positive correlation between lower urinary tract symptoms and erectile dysfunction. The odds ratios varied from 1.4 to 9.74. All studies were community or clinical based. Just one study based on a primary care population was described. The association between erectile dysfunction and cardiovascular diseases is not proven in primary care.

Conclusions: The evidence of a positive correlation between lower urinary tract symptoms and erectile dysfunction is significant in community- and clinical-based studies. It is at present unknown whether these correlations are significant in the patient population of primary healthcare. We need more evidence to prompt the general practitioner to screen every man with initial presentation of erectile dysfunction for standard cardiovascular risk factors and, as appropriate, start initial cardioprotective interventions.

Key words: *Lower urinary tract symptoms, erectile dysfunction, cardiovascular diseases, primary healthcare*

Introduction

With an increasing proportion of older people, cardiovascular diseases, cancer, osteoporosis, and frailty are major health problems that will become more and more prevalent (1,2). Advancing age in men affects the lower urinary tract, and therefore more men will present with lower urinary tract symptoms, prostate disease, and erectile dysfunction. All of these conditions are often dismissed as lifestyle issues. However, these common ageing-related conditions significantly affect quality of life and may even be symptomatic of underlying cardiovascular or metabolic diseases (3–8).

In the mid-1990s, both male sexual dysfunction and lower urinary tract symptoms were known to

be age dependent, although the association between these two conditions had not been investigated. In the last decade, cross-sectional studies have collected data from large samples of men.

Worldwide, about 100 million men are affected by erectile dysfunction (9–11). The worldwide prevalence varies from 11 to 52% (12). In the Dutch population, the prevalence of erectile dysfunction increases from 14% for men aged 41–50 years to 42% for men aged 71–80 (13,14). Many studies describe erectile dysfunction as a somatic condition, with vasculopathy as the most common cause of erectile dysfunction (15–18). The ENIGMA study describes the prevalence of erectile dysfunction in

Dutch primary care. Psychogenic and somatic erectile dysfunction are equally prevalent in men visiting their general practitioner for sexual dysfunction. In young men, erectile dysfunction is mostly caused by a psychological condition, compared to older men, in whom a somatic cause is more common (19,20).

Erectile dysfunction is nowadays considered a readily treatable disorder and is described in several studies as a powerful risk marker for cardiovascular disease, because erectile dysfunction and cardiovascular diseases share similar aetiology and pathophysiology (15–18,21,22). Identification of erectile dysfunction as a predictive symptom for cardiovascular diseases could allow even earlier intervention, possibly further reducing morbidity and mortality due to the diseases.

The present review aimed to assess the relationships between lower urinary tract symptoms and erectile dysfunction, and between erectile dysfunction and cardiovascular disease. The second objective was to identify differences among these relationships between populations from primary healthcare and urology clinics.

Methods

Two search strategies were used. Using key words, the following literature databases were searched: Embase, Cochrane, and Pubmed. Additionally, we made use of the so-called “snowball method”, whereby the reference sections of already selected articles were used to help locate other relevant articles. We selected articles written in English, Dutch, or German. Articles from 1997 up to and including 2007 were included.

The inclusion criteria were: 1) that the research populations were community based, clinical based, or primary care based; 2) that the study was empirical; 3) that (part of) the study investigated the correlation between lower urinary tract symptoms and erectile dysfunction, or between erectile dysfunction and cardiovascular diseases; 4) that (part of) the population was male and 5) at least 40 years of age; and 6) a research population of more than 100 subjects.

The key words were lower urinary tract symptoms, LUTS, cardiovascular diseases (MeSH), and sexual dysfunction (MeSH). The combinations of search terms were 1. [(LUTS OR lower urinary tract symptoms) AND (sexual dysfunction)], 2. [(sexual dysfunction) AND (cardiovascular diseases)], 3. [1 AND 2]. Also, the search terms were combined with comorbidity (MeSH), impotence (MeSH), aging, and primary care (MeSH). LUTS was defined as mild with an International Prostate Symptom Score

(IPSS) of 0–7, moderate with an IPSS of 8–19, and severe with an IPSS of 20–35 (23).

Data extraction

Each potentially eligible study was assessed for inclusion and quality. The methodological quality of the studies was assessed by evaluating the design of the study, methods, reliable outcome measures, and also how patients lost to follow-up were handled in the analysis. A checklist to obtain data on topics, study design, setting, number of participants, characteristics of the collaborative strategy, and relevant results was used.

We could not use formal meta-analytical techniques, because the studies used many different effect measures.

Results

The 562 articles resulting from our literature search were examined one by one. The abstracts of 196 articles, which, at first glance, appeared to be relevant to our research question, were analysed. Of these abstracts, 115 were excluded, because closer reading revealed that they did not conform to the inclusion criteria. The full text was obtained for the remaining 81 articles. Fifty-one of these 81 articles did not meet the inclusion criteria.

Two researchers, working independently, judged the remaining 30 articles according to the aforementioned methodological aspects. A third researcher was consulted when a difference of opinion arose, and his opinion decided the matter.

Correlation between lower urinary tract symptoms and erectile dysfunction

Community- and population-based studies. The Krimpen study by Blanker et al. (24) showed a strong age dependency in erectile dysfunction. After multivariate logistic regression analysis, the authors concluded that lower urinary tract symptoms are an independent risk factor for erectile dysfunction. The non-response study showed that the participants in the study were comparable with the non-responders. The age dependency in erectile dysfunction was confirmed by the Multinational Survey of the Aging Male (MSAM-7) (27). This is one of the largest studies to date describing the prevalence of lower urinary tract symptoms and sexual dysfunction in representative samples of ageing males. Moderate-to-severe lower urinary tract symptoms seemed to be strongly related to age, ranging from 22% in men aged 50–59 years to 45% in men aged

70–80 years. Age and lower urinary tract symptom severity showed a higher degree of association with erectile dysfunction than other comorbidities. Mariappan and Chong (26) is the only study reporting a non-significant relationship between lower urinary tract symptoms and erectile dysfunction when controlled for age.

In addition to lower urinary tract symptoms and age, comorbidities such as diabetes mellitus, hypertension, and previous pelvic operations are also independent risk factors for the development of erectile dysfunction, as concluded from the Cologne Male Survey by Braun et al. (25). The Cross National Study on the Epidemiology of Erectile Dysfunction and Its Correlates (37) showed that men with heart disease, hypertension, diabetes, prostate diseases or surgery, depression, gastric or duodenal ulcer, or with hormonal treatment had a 1.64-times higher risk for erectile dysfunction compared with “healthy” men, when controlled for age. Also, the degree of physical activity, current smoking, and educational level were significant predictors. A limit of this study may be that a proportion of the healthy men were undiagnosed with the previously mentioned diseases.

Another cross-national study (28) showed a significant relationship between IPSS and lower urinary tract symptom-induced bother. Men with severe lower urinary tract symptoms had a noticeably higher degree of dissatisfaction (62%) compared to those with moderate lower urinary tract symptoms (14%). When compared with men without lower urinary tract symptoms, the incidence of erectile dysfunction was twice as high in men with moderate lower urinary tract symptoms and more than three times as high in those with severe lower urinary tract symptoms (28).

In the UrEpik study (30), there was a strong difference among four countries in the attitude towards consultation for erectile dysfunction. Factors that influenced consulting a doctor were physical activity, diabetes, high blood pressure, heart attack, prostatitis, and benign prostatic hyperplasia. It is remarkable that just 4.8% of men with erectile dysfunction visited a doctor because of their sexual dysfunction.

Overall, as can be seen in Table I, the results show that men with lower urinary tract symptoms have a higher risk of also having erectile dysfunction. The odds ratios vary from 1.4 to 9.7.

Clinic-based and health screening studies. Voiding symptoms correlated significantly with a declining score on the five-item version of the international index of erectile dysfunction (IIEF-5) (38,39). In multivariate analysis, IPSS, voiding symptoms, nocturia, and bother score correlated significantly

with the presence of erectile dysfunction. Overall, men with lower urinary tract symptoms had a two-fold greater risk of erectile dysfunction compared to those without lower urinary tract symptoms. The greatest odds ratios were present in men aged 51–60 years (38).

The strong relationship between age, IPSS severity, and erectile dysfunction was also reported by Vallancien et al. (43). Men aged 70 years or older were nearly six times as likely to experience erectile dysfunction compared to those aged younger than 60 years. Men with severe lower urinary tract symptoms were about twice as likely to have erectile dysfunction compared to those with mild lower urinary tract symptoms. At least 82% of men with erectile dysfunction were bothered by their sexual dysfunction. This bothersomeness significantly decreased with age, but significantly increased with lower urinary tract symptom severity. It should be noted that the men who took part in this study differed from men in the community-based studies, because they had all exhibited some form of health-seeking behaviour relating to lower urinary tract symptoms. Overall, as can be seen in Table II, these studies show similar results compared to the results from community- and population-based studies: men with lower urinary tract symptoms have a higher risk of also having erectile dysfunction. The odds ratios vary from 1.1 to 3.3. The patient population seen by a general practitioner was not specifically described in any of these studies.

Relationship between erectile dysfunction and cardiovascular disease

Endothelial dysfunction, in which damage to the lining of the arterial wall impairs the nitric oxide pathway and vasodilatation, is an important pathophysiological factor underlying both erectile dysfunction and cardiovascular disease (16,17,44–46). Several risk factors, including inflammation, hypoxia, oxidative stress, and homocysteinaemia, are related to this endothelial dysfunction (17). The major cardiovascular risk factors such as smoking, high body-mass index, hypercholesterolaemia, diabetes, and hypertension occur more often in individuals with erectile dysfunction. The prevalence of erectile dysfunction is also directly related to the number of cardiovascular risk factors present, being highest in individuals with more than three (9). One study showed that 19% of men with erectile dysfunction of vascular origin had angiographically documented silent coronary artery disease (47). Among patients who were referred to a clinic because of their erectile dysfunction, left ventricular dysfunction was an independent risk factor for erectile dysfunction,

Table I. Evidence of a significant correlation between LUTS and male sexual dysfunction in community-/population-based studies.

Study	Study type	Country	Sample	Prevalence	Odd ratios (95% CI) No LUTS referent
Blanker et al. 2001 (24)	community based	Netherlands	1688 men, aged 50–70	ED 11%	LUTS mild 1.8 (0.8–4.3) LUTS moderate 3.4 (1.4–8.4) LUTS severe 7.5 (2.5–22.5) IPSS 8–35 1.39 (1.10–1.74)
Boyle et al. 2003 (30)	community based	UK, Netherlands, France, Korea	4800 men, aged 40–79	ED 21.1%	
Braun et al. 2003 (25)	community based	Germany	4489 men, aged 30–80	LUTS 44% LUTS in pts with ED 72.2% LUTS in pts without ED 27.2% ED 19%	LUTS 2.11 (1.75–2.55)
Holden et al. 2005 (1)	population based	Australia	5990 men, aged >40	LUTS 16% ED M/S 21%	NA
Li et al. 2005 (28)	community based	Asia	1155 men, aged 50–80	LUTS 14–59% ED 63%	LUTS mild 1.39 (0.79–2.47) LUTS moderate 2.4 (1.17–4.93) LUTS severe 3.17 (1.8–5.6)
Mariappan et al. 2006 (26)	population based	Malaysia	353 men, aged >40	LUTS 80% ED 71.2%	LUTS M/S 1.4 but age controlled not significant
Nicolosi et al. 2003 (31)	population based	Brazil, Italy, Japan, Malaysia	2412 men, aged 40–70	ED M/S 16.1% (healthy men) 31.5% (in the other men)	LUTS moderate 2.19 (1.24–3.87) LUTS severe 4.91 (1.44–16.73)
Rosen et al. 2003 (27)	population based	US, UK, France, NL, Italy, Germany, Spain	12 815 men, aged 50–80	LUTS M/S 31% ED 48.7%	LUTS mild 1.98 (1.67–2.34) LUTS moderate 3.76 (3.14–4.50) LUTS severe 7.67 (5.87–10.02)
Shabsigh et al. 2005 (29)	population based	USA	28 691 men, aged 20–75	ED 19%	No prostate/urinary problems referent Prostate problems 2.0 (1.8–2.5) Urinary problems 2.1 (1.9–2.7)
Shiri et al. 2005 (35)	population based	Finland	1126 men, aged 50, 60, and 70	NA	LUTS mild 1.4 (0.7–2.7) LUTS moderate 1.9 (0.9–3.8) LUTS severe 3.1 (1.5–6.4)
Stroberg et al. 2006 (36)	population based	Sweden	725 men, aged 60–70	LUTS 51% ED 44%	LUTS mild 4.55 (1.03–20.11) LUTS moderate 9.74 (2.15–44.20) LUTS severe 7.93 (1.36–46.1)

LUTS: lower urinary tract symptoms; ED: erectile dysfunction; CI: confidence interval; IPSS: International Prostate Symptom Score (0–7 mild, 8–19 moderate, 20–35 severe symptoms of LUTS) (23); M/S: mild/severe; NA: not assessed.

independent of heart failure symptoms. Moreover, symptoms of erectile dysfunction appeared 3.04 ± 7.2 years prior to the cardiovascular event (42). Ponholzer et al. found a 65% increased risk of developing coronary artery disease within 10 years in patients with erectile dysfunction compared with those without erectile dysfunction (42).

Data from the Prostate Cancer Prevention Trial (a prospective study in a clinical setting) (48) showed that, in 9457 men, aged 55 years and older,

incidental erectile dysfunction was statistically significantly associated with subsequent angina, myocardial infarction, and stroke. The unadjusted risk of an incidental cardiovascular event among men without erectile dysfunction at study entry was 1.5% per person-year compared with 2.4% per person-year for those with erectile dysfunction. Incidental erectile dysfunction also had an equal or greater effect on subsequent cardiovascular events, of the same magnitude as a family history of myocardial infarction

Table II. Evidence of a correlation between LUTS and male sexual dysfunction in clinic/health screening based studies.

Study	Study type	Country	Sample	Prevalence	Odds ratios (95% CI) No LUTS referent
Atan et al. 2006 (40)	clinic based	Turkey	307 men, aged 21–77	LUTS 52.8% ED 76.8%	OR not stated
Chia-Chu Liu et al. 2006 (41)	health screening	Taiwan	160 men, older than 45 years	ED 56.1–84.2%	LUTS mild referent LUTS M/S 3.27 (1.52–7.02)
Elliott et al. 2004 (37)	clinic based	US	181 men, mean age 68.2 years	NA	yes for ED and obstructive LUTS or depression OR not stated
El-Sakka et al. 2005 (38)	office based	Egypt	374 men, aged 45–63	LUTS 80.7% ED 100%	OR not stated
Glina et al. 2005 (32)	clinic based	Brazil	118 men, aged >40	LUTS 16–40% ED 11–29%	age adjusted (Pearson) –0.25
Ponholzer et al. 2004 (42)	health screening	Austria	2858 men, aged 20–80	LUTS 84% ED 32%	LUTS 2.2 (1.8–2.8) nocturia 1.4 (1.1–1.7)
Teraï et al. 2004 (33)	clinic based	Japan	2084 men, aged >18	ED 85.7%	mild LUTS referent LUTS M/S 1.52 (age adjusted)
Vallancien et al. 2003 (43)	clinic based	France, Denmark, Netherlands, Switzerland, UK	927 men, aged 36–92	ED 62%	moderate LUTS 1.18 (0.7–2.0) severe LUTS 1.94 (1.09–3.46)

LUTS: lower urinary tract symptoms; ED: erectile dysfunction; CI: confidence interval; IPSS: International Prostate Symptom Score; M/S: mild/severe; NA: not assessed; SHIM: Sexual Health Inventory for Men (34).

(hazard ratio [HR] 1.46; 95% confidence interval [CI] 1.16–1.83), cigarette smoking (HR 1.46; 95% CI 1.07–1.97), or measures of hyperlipidaemia (HR 1.03; 95% CI 0.98–1.08) (40).

An historical cohort study, using medical records of general practices in the Netherlands, concluded that erectile dysfunction could be seen as a marker for cardiovascular diseases before the introduction of sildenafil (odds ratio [OR] 1.7; 95% CI 0.9–3.3) but not so clearly afterwards (OR 1.1; 95% CI 0.6–1.8) (50). However, it is questionable if this is a significant difference. Both confidence intervals contain 1 and cannot be said to differ significantly from 1.

Ströberg et al. (36) do not support the concept that erectile dysfunction is a clinically useful predictor of the more severe cardiovascular diseases such as myocardial infarction. The incidence of erectile dysfunction was higher in the myocardial infarction group (32%) compared to the control group (18%). However, the difference was not significant, and two-thirds of the myocardial infarctions were not preceded by erectile dysfunction. Also, Travison et al. concluded that erectile dysfunction is not a common predictor for cardiovascular diseases. Erectile dysfunction spontaneously disappeared in 35% of the study population (95% CI 30–40%) (49).

Discussion

Different studies describe the correlation between lower urinary tract symptoms and erectile dysfunction.

Men with lower urinary tract symptoms have a higher risk of also having erectile dysfunction. The odds ratios vary from 1.1 to 9.74. Studies differ in terms of their populations: clinical- as well as community-based studies are described. Also, different kinds of questionnaires are used, and sometimes the results were obtained by direct interview instead of self-administered questionnaire. Another difference is the method of statistical analysis: univariate and/or multivariate analysis. However, even though there are differences in the way the previously described studies have been done, in both community- and clinical-based studies the conclusion was the same: men with lower urinary tract symptoms have a higher risk of also having erectile dysfunction. The patient population seen by a general practitioner, however, was not specifically described in any of these studies.

Formerly dismissed as a psychological condition, urologists now assume that erectile dysfunction is a powerful risk marker for cardiovascular diseases. Most studies mentioned previously are based on outpatient populations. The predictive value of erectile dysfunction for consequent cardiovascular diseases is confirmed by most of the studies, but not all. Also, there are almost no studies that have investigated the patient population of a general practitioner.

There is a difference in cause of erectile dysfunction between the male population that visits the urologist, which is mostly somatic, and the male population of the general practitioner, where the distribution between somatic and psychological

erectile dysfunction is almost equal. The prevalences concerning the causes of erectile dysfunction in primary care show a shift from a more psychological condition at younger age to a more somatic disorder in elder men. Nevertheless, it is often a mixture of psychological and somatic causes. This complicates the reasonable suggestion of screening for cardiovascular diseases in men with erectile dysfunction as early as possible (13). The Princeton consensus (51) recommends screening for modifiable cardiovascular risk factors in patients with erectile dysfunction. By doing so, cardiovascular diseases can possibly be prevented. The Dutch guidelines for general practitioners on erectile dysfunction do not recommend screening for cardiovascular diseases in men with erectile dysfunction until more follow-up studies have been done (13).

Only a few men contact their physician for their erectile dysfunction, varying from 5 to 24% (13,44,52). In the Netherlands, general practitioners perform specific case findings, but do not screen for risk factors in their total patient population (53,54). Most people who develop atherosclerotic cardiovascular disease have several risk factors which interact to produce their total fatal cardiovascular risk, which can be estimated directly by using the SCORE risk estimation system (55). General practitioners inquire about erectile dysfunction in less than 10% of their patients (52). If erectile dysfunction is to be a practically useful predictor, there must also be a reason for a man to seek medical attention, which was rarely the case in several study populations (44,52).

The correlations we investigated are studied mainly in clinical- or community-based populations. Data from patient populations in primary care would help healthcare providers decide if and when to screen for cardiovascular diseases in men with erectile dysfunction.

Conclusions

The evidence of a positive correlation between lower urinary tract symptoms and erectile dysfunction, as well as between erectile dysfunction and cardiovascular diseases is significant in community- and clinical-based studies. It is as yet unknown whether these correlations are significant in the patient population of primary healthcare. We need more evidence to prompt the general practitioner to screen every man with initial presentation of erectile dysfunction for standard cardiovascular risk factors and, as appropriate, start initial cardioprotective interventions.

Contributors: IIB and WKH analysed the data. IIB, WKH, JMN, and KM interpreted the data. All authors conceived and designed the study, drafted

and revised the manuscript, and approved the final version. IIB is guarantor.

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