

Risk Factors for Progression or Improvement of Lower Urinary Tract Symptoms in a Prospective Cohort of Men

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Abbreviations and Acronyms

BPH = benign prostatic hyperplasia
CV = coefficient of variance
HDL = high-density lipoprotein
LUTS = lower urinary tract symptoms
OSA = obstructive sleep apnea

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Purpose: We determined the metabolic, lifestyle and physical factors associated with progression or improvement of storage and voiding lower urinary tract symptoms in a population based cohort of men.

Materials and Methods: After the exclusion of men with prostate or bladder cancer and/or surgery from the study, progression and improvement of storage and voiding lower urinary tract symptoms was assessed using the AUA-SI (American Urological Association symptom index) in 780 men, age 35 to 80 years at baseline, who attended 5-year followup clinics.

Results: Storage and voiding lower urinary tract symptoms progressed in 39.8% (308) and 32.3% (250) of men, and improved in 33.1% (256) and 23.4% (181), respectively. In final adjusted regression models greater bother and physical activity at baseline predicted improvement in storage and voiding lower urinary tract symptoms, while greater income, high-density lipoprotein cholesterol and lower triglycerides predicted improvement of storage lower urinary tract symptoms only. Being widowed, higher plasma estradiol and depression at baseline predicted the progression of storage and voiding lower urinary tract symptoms, while greater abdominal fat mass and obstructive sleep apnea risk predicted the progression of storage lower urinary tract symptoms only. Older age, lower high-density lipoprotein cholesterol, testosterone, income, previous benign prostatic hyperplasia and erectile dysfunction at baseline predicted the progression of voiding lower urinary tract symptoms only. The initiation or continued use of α -blockers or anticholinergics (storage lower urinary tract symptoms), and 5 α -reductase inhibitors (voiding lower urinary tract symptoms), were associated with symptom improvement.

Conclusions: Lower urinary tract symptoms may progress or remit. Even accounting for medication use, progression may be associated with modifiable disease, or metabolic or behavioral factors, which are also risk factors for type 2 diabetes and cardiovascular disease. These factors should be looked for and managed.

Key Words: prostatism, epidemiology, urinary tract physiological phenomena, cohort studies, men's health

ALTHOUGH common and associated with reduced quality of life and increased health care expenditure,¹

there are only limited data relating to the outcome of lower urinary tract symptoms in men over time.²⁻⁵ While

usually assumed to worsen, LUTS may also improve.^{3,6} A number of risk factors and health conditions other than age and BPH associate with LUTS in men,⁷ suggesting that the lower urinary tract is susceptible to systemic influences outside of the prostate. Furthermore, these associations vary according to specific clusters of urinary symptoms.⁸ In a study of elderly men from the MrOS (Osteoporotic Fractures in Men) Study with clinically significant LUTS at baseline, more than a quarter reported significant symptom improvement at followup.³ In an earlier study of Swedish men 45 to 99 years old, 20.2% and 9.5% had remitting urinary incontinence and overactive bladder, respectively, although only an overall symptom score was obtained.⁴ Few studies have simultaneously examined the contribution of multiple risk factors to the progression or improvement of specific symptom clusters in men.

In this study we determined the prevalence, incidence and improvements of storage and voiding LUTS in a population based cohort of men with detailed psychosocial, health related and behavioral assessments during 5 years. We tested the hypothesis that the onset and course of LUTS are determined, at least in part, by potentially remediable factors.

METHODS

Study Design and Sampling

Data were obtained from the FAMAS (Florey Adelaide Male Ageing Study), a population based study of randomly selected men from the northern and western suburbs of Adelaide, Australia.⁹ A total of 1,620 men 35 to 80 years old at recruitment completed a telephone interview (sample response rate 67.8%) and 1,195 attended a clinic visit (T1, clinic response rate 45.1%) between 2002 and 2005. Written, informed consent was obtained from all participants. All protocols were approved by the Royal Adelaide Hospital Research Ethics Committee, with funding currently provided through the Australian National Health and Medical Research Council (Project Grant #627227).

Comparisons to the 2001 Australian Census data showed that FAMAS participants matched the population for most key demographics, although younger groups and never married men were underrepresented and older participants were overrepresented.⁹ Followup clinic visits using identical protocols were conducted between 2007 and 2010 (T2, 899), as near as practical to 5 years after the initial visit (mean followup 5.0 ± 0.2 years). Comparison to the 2006 Australian Census data showed that FAMAS participants were more likely to be older, married and have a higher level of post-secondary school education.¹⁰

Lower Urinary Tract Symptoms

The 7-item AUA-SI was used to evaluate the presence of LUTS. Subjects were classified as having storage

symptoms if the sum of the score on AUA-SI items 2, 4 and 7 was 4 or greater (and the score on item 4, urgency, was 1 or greater), and as having voiding symptoms if the sum of the score on AUA-SI items 1, 3, 5 and 6 was 5 or greater. Subjects were classified as having mild, moderate or severe LUTS if the total LUTS score was 0 to 7, 8 to 19, or 20 to 35, respectively. Given the absence of standardized definitions for LUTS progression and improvement, we defined these outcomes based on previous studies³ and AUA management guidelines.¹¹ Men who reported an increase in AUA-SI score for voiding symptoms of 3 or more and for storage symptoms 2 or more were classified as having voiding and storage LUTS progression, respectively. Men who reported a decrease in AUA-SI score for voiding symptoms of 3 or less and for storage symptoms 2 or less were classified as having voiding and storage LUTS improvement, respectively (with a -2 to 2 and -1 to 1 -point absolute changes in voiding and storage symptoms classified as stable).

Demographic Factors, Health Status and Medication Use

Information on age, education, and marital, occupational, smoking and disease status was obtained by self-report questionnaire.⁹ Medication use was determined by self-report and data linkage with a national medication registry. The presence of depression was assessed using the Beck Depression Inventory (BDI-1A¹²) or a report of physician diagnosed depression and/or use of antidepressant medication. The probability of obstructive sleep apnea was determined using a multivariate prediction equation.¹³

Plasma Assays

Morning fasting venous blood samples were obtained by venipuncture at clinic and stored at -80°C . Serum total testosterone was measured by validated stable isotope dilution liquid chromatography-tandem mass spectrometry (interassay CV 9.3% at 0.43 nmol/l, 8.6% at 1.66 nmol/l, 4.0% at 8.17 nmol/l) as was estradiol (E_2) (interassay CV 14% at 23 pmol/l, 4.0% at 83 pmol/l, 6.0% at 408 pmol/l). HDL, low-density lipoprotein cholesterol and triglycerides were measured enzymatically using a Hitachi 911 (Boehringer Ingelheim, Ingelheim, Germany; interassay CV triglyceride 3%, total cholesterol 2.3%, HDL 6.7% and low-density lipoprotein 3.7%). Plasma glucose was determined using an automated chemistry analyzer system (Olympus AU5400TM, interassay CV 2.5% at 3.5 mmol/l and 3.0% at 19.6 mmol/l). Glycated hemoglobin (HbA1c) was measured by high-pressure liquid chromatography using a spherical cation exchange gel (CV 2% at 6% of total hemoglobin).

Body Composition

Anthropometric measures, blood pressure, grip strength and body composition (by dual energy x-ray absorptiometry) were obtained as previously published.⁹

Statistical Analysis

In the present study only men who had completed the AUA-SI at T1 and T2 (822) were included in the study. Men with a history of bladder cancer (8) or prostate cancer (17) or prostate surgery (12) and those with a current

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