Title

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Journal

Investigative Urology, 196(1)

ISSN

0021-0005

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Publication Date

2016-07-01

DOI

10.1016/j.juro.2016.02.081

Peer reviewed

HHS Public Access

Author manuscript

J Urol. Author manuscript; available in PMC 2017 July 01.

Published in final edited form as:

J Urol. 2016 July ; 196(1): 166–172. doi:10.1016/j.juro.2016.02.081.

Lower urinary tract symptoms and risk of non-spine fractures among older community dwelling US men

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Abstract

Purpose—Among older men, moderate and severe lower urinary tract symptoms (LUTS) are associated with increased fall risk compared to mild LUTS. Falls are a major risk factor for fractures. Therefore, we assessed associations of LUTS with fracture risk in community dwelling U.S. men aged 65 years or older.

Materials and Methods—We conducted a prospective study in the Osteoporotic Fractures in Men (MrOS) cohort. Men were enrolled at six U.S. sites. The American Urological Association Symptom Index (AUA-SI), LUTS medication use, fracture risk factors and potential confounders were recorded at baseline and every two years thereafter for a total of four assessments. LUTS severity was categorized from the AUA-SI as mild (0–7 points), moderate (8–19 points), or severe (≥20 points). Associations of LUTS severity with fracture rate were estimated with hazard ratios (HR) and 95% confidence intervals (CI) from extended proportional hazards regression.

Results—Among 5,989 men with baseline AUA-SI score and hip bone mineral density (BMD) measures, 745 incident non-spine fractures occurred during 43,807 person-years of follow-up. In a

multivariable model adjusted for age, enrollment site, baseline hip BMD, falls in the past year, and prevalent fracture before baseline, there were no significant associations of moderate (HR 0.9, 95% CI 0.8–1.1) or severe (HR 1.0, 95% CI 0.8–1.3) LUTS with fracture risk. None of the individual LUTS assessed on the AUA-SI including nocturia and urgency was associated with increased fracture risk.

Conclusions—In this cohort of older US men, LUTS were not independently associated with fracture risk.

Keywords

lower urinary tract symptoms; male; aged; fractures; bone

Introduction

Moderate to severe lower urinary tract symptoms (LUTS) occur among 1 in 3 men over age 40 years in the United States (US).[1] LUTS prevalence rises with age, to at least 25% of men age 60 years or older and to 70% of men aged 80 years or older having moderate or severe symptoms.[1–3] In addition to their well-characterized urological morbidities, moderate and severe LUTS exert a substantial negative impact on non-urologic aspects of health including quality of life, instrumental activities of daily living, depression, and mortality.[2, 4–7] Given the expected increase in the size of the elderly male population,[8] further elucidating the negative consequences of LUTS on overall health may substantially improve health care delivery in this population.

LUTS also are associated with increased risk of falls in older men.[9–11] Bone fractures are one of the most serious injuries resulting from a fall.[12] Therefore, we reasoned that LUTS may be positively associated with fracture risk in this population as well. Adaptive behaviors to symptoms that prompt potentially risky physical reactions and could cause a fall would be the most likely mechanism by which LUTS would increase fracture risk. For example, urinary urgency may provoke sudden, impulsive movements to avoid social embarrassment, and nocturia may disrupt sleep patterns and compel affected individuals to rise repeatedly from a recumbent position to navigate darkened environments.[13]

The possible association of LUTS with fracture risk has received limited attention. Two small prospective studies have suggested positive associations of nocturia with risk of hip fracture.[14,15] However, in the absence of larger studies assessing other urinary symptoms and controlling for confounding effects of age, comorbidities, and established risk factors for fractures, associations of LUTS with fracture risk in older men remain unclear. Therefore, we investigated the association of LUTS severity with risk of incident fractures in a large cohort of older U.S. men. LUTS information was obtained with American Urological Association Symptom Index (AUA-SI), a validated instrument widely used in clinical practice and epidemiologic studies to assess the severity and bother of LUTS.[16] We hypothesized that moderate or severe LUTS would be associated with increased fracture risk compared to mild LUTS, independently of established fracture risk factors.

Materials and Methods

The Osteoporotic Fractures in Men (MrOS) Study is a prospective cohort study designed to identify risk factors for falls, fractures, and prostate disease among community-dwelling older U.S. men. As described previously,[17] men age 65 years or older, able to walk unassisted by another person, and possessing at least one natural hip (for bone density measurement) were eligible. From March 2000 through April 2002, 5,994 participants completed the baseline questionnaire and in-person visit at one of six academic medical centers in Birmingham AL, Minneapolis MN, Palo Alto CA, Pittsburgh PA, Portland OR, and San Diego CA. Participants alive and active in MrOS were contacted about every two years to update their information in 2002–2004, 2005–2006, 2007–2009, and 2009–2011 (Figure 1). At each assessment, 96% or more participated. Institutional Review Boards at each institution approved the study. All participants gave written informed consent.

Self-reported items obtained only at baseline were race, education, history of problem drinking,[18] history of fracture after age 50 years, history of prostate cancer, and daily average dietary intake of vitamin D (IU/day), calcium (mg/day), and caffeine (mg/day) estimated from food frequency questionnaire.[19]

The AUA-SI,[16] prostatitis history, BPH history, medications, health history, and most other self-report measures were obtained at all four assessments from baseline through 2007–2009 (Figure 1). LUTS were defined from the AUA-SI score as mild (0–7 points), moderate (8–19 points) or severe (20–35 points).[16] Urinary bother were categorized as 0–2 (low), 3, and 4–6 (high).[16] BPH history included treatment with medications or with laser surgery or transurethral resection of the prostate.

Prescription medications and supplements were inventoried from containers at each assessment and matched to ingredients based on the Iowa Drug Information Service IDIS Drug Vocabulary (College of Pharmacy, University of Iowa, Iowa City, IA).[20] Urologic medications were defined as inventory listing of alpha-blockers, urinary antispasmodics, anticholinergics, or 5-alpha-reductase inhibitors. Herbal supplements for LUTS was classified as self-report or inventory listing of saw palmetto, South African star grass, stinging nettle, rye grass pollen, pumpkin seed, or African plum. Because of their association with fracture, diuretics (thiazide, loop, and potassium sparing), statins (HMG-CoA reductase inhibitors), and central nervous system (CNS) medications (antiepileptics, benzodiazepines, antidepressants, opioids, sedatives) were also coded.[21–23]

Other repeat self-reported items used in this analysis included marital status, living situation; history of physician-diagnosed hypertension, major heart diseases, diabetes, chronic obstructive pulmonary disease, stroke, and osteoporosis; and falls in the past 12 months. Lifestyle factors included cigarette smoking, current alcohol consumption, and physical activity obtained with the Physical Activity Scale for the Elderly (PASE).[24] Self-rated health and health-related quality of life were obtained with the Short Form-12 (SF-12) Physical Component (PCS) and Mental Component (MCS) scores.[25] Depressive symptoms were defined as MCS ≤50 points.[26] Mobility limitation was defined as self-report of difficulty walking 2–3 blocks outside or climbing 10 steps without aids.[27]

In-person measures were obtained at the baseline, 2005–2006, and 2007–2009 visits as described previously.[17, 21] Briefly, total hip bone mineral density (BMD) (g/cm^2) was obtained by dual energy x-ray absorptiometry (QDR 4500W, Hologic Inc., Waltham MA USA). Body mass index (kg/m^2) was calculated from height and weight measured by study staff and categorized as normal (<25.0 kg/m^2), overweight (25.0–29.9 kg/m^2), or obese (≥ 30 kg/m^2). Physical performance measures (balance, repeated chair stand time, and grip strength) were assessed by study staff.

Fracture follow-up and other endpoints

Every four months after their baseline visit, participants report fractures and new prostate cancer diagnoses by brief questionnaires or by telephone with study staff. Reports of these events were centrally adjudicated with medical records and fracture radiographs. Date of death was confirmed with death certificates. Endpoint ascertainment was over 99% complete.

Study cohort and analyses

From the 5,994 participants, we excluded 4 missing baseline AUA-SI and 1 missing a hip BMD measure, leaving 5,989 for analysis. Distributions of baseline factors were examined according to LUTS severity status using chi-square tests for categorical variables, one-way analysis of variance for normally distributed continuous variables, and the Kruskal-Wallis test for nonnormally distributed continuous variables.

For this analysis, participants were followed from their baseline visit date to the date of first non-spine fracture, death, voluntary withdrawal from MrOS, or fifth study assessment, whichever occurred first. LUTS severity was updated at the start of each assessment and person-time allocated accordingly. Incidence rates of non-spine fracture were then calculated as the number of fractures divided by accumulated person-time in each LUTS severity category. The association of LUTS severity with non-spine fracture rates was modeled using hazard ratios (HR) and their 95% confidence intervals (CI). LUTS severity status and other time varying variables were updated in the models. Baseline in-person visit measures were carried forward to the 2002–2004 assessment, for which subjects completed only a questionnaire. To directly control for confounding by age, we used age as the underlying time scale (instead of calendar time).[28] To account for possible bias in fracture rates due to attrition from mortality, we used the Fine-Gray competing risks regression framework[29] with death as the competing event. Multivariable models were first controlled for study enrollment site, and then for major established fracture risk factors (low BMD, prevalent fracture before baseline, and fall history). We further evaluated as potential confounders several other fracture risk factors including white race, physical performance, mobility limitations, obesity, and use of diuretics, CNS medications and statins.

In sensitivity analyses, the adjusted HRs were comparable when baseline hip BMD was fit in place of updated hip BMD. Likewise, HRs also were not materially different when self-reported mobility limitation was fit in place of the physical performance measures. Thus, for parsimony, we present results controlled for baseline BMD and for mobility limitation. Men with missing medication information were coded as non-users, because results with this

coding were similar to results excluding the missing observations. We repeated the main analyses among men with no prostate cancer history and among men with no fracture history. We also estimated HR for each individual symptom item on the AUA-SI. Finally, we conducted analyses stratified by current prescription urologic medications use and by BPH history.

Results

At baseline, 7%, 39% and 54% of the participants reported severe, moderate, and mild LUTS, respectively (Table 1). Compared with men with mild LUTS, men with severe LUTS were older on average and had lower average total hip BMD; the highest percentages with low BMD, fracture history, falls in the past year, mobility limitations, depressive symptoms, and use of CNS medications; and had worse physical performance (Table 1). However, dietary intake of vitamin D and calcium was highest among men with severe LUTS. Additionally, men with severe LUTS generally had a more adverse urological history, higher prevalence of most comorbidities, smoking and problem drinking; and lower average physical activity and quality of life scores (Supplemental Table 1).

During 43,807 person-years of follow-up, 745 men had a confirmed incident non-spine fracture. Fracture rates (number of incident fractures) according to LUTS severity were 16.3/1000 person-years (364 fractures) for none/mild, 17.1/1000 person-years (309 fractures) for moderate, and 21.6/1000 person-years (72 fractures) for severe symptoms.

During follow-up, 13% of the cohort had a first fracture and 20% died with no fracture. Death was a competing risk for fracture regardless of LUTS severity (Figure 2), confirming the need to account for death in the multivariable analysis.

After adjustment for age (time scale) and enrollment site, severe LUTS, but not moderate LUTS, was weakly associated with increased rate of non-spine fracture compared to mild LUTS (Table 2). Adjustment for low baseline total hip BMD, baseline fracture history, and fall history—the major established fracture risk factors—completely attenuated this association. These results were not materially affected by final adjustments for other fracture risk factors (mobility limitation, white race, CNS medication use). Moreover, further adjustment for urinary bother did not materially change these results (data not shown). Results remained null when analyses were restricted to men with no past or incident prostate cancer diagnosis, as well as to men with no history of fractures after age 50 years. Moreover, none of the individual LUTS assessed on the AUA-SI was associated with increased fracture risk (Table 3).

It might be expected that any association of LUTS and fracture risk would be apparent only in men with untreated symptoms. However, we observed no association of LUTS severity with risk of incident non-spine fracture according to current prescription urologic medication use (Supplemental Table 2). Likewise, the association of LUTS and fracture risk remained null in all categories of self-reported history of BPH diagnosis and treatment.

Discussion

Contrary to our hypothesis, neither the unadjusted nor adjusted fracture incidence rates were significantly higher among men with moderate or severe LUTS compared with rates among men with mild LUTS. Nocturia, urgency and other individual LUTS were also not associated with increased fracture risk. Even among men with no previous fracture history and men not currently using prescription urologic medications, the association of LUTS severity and fracture risk remained null.

Despite the high prevalence of LUTS in older men, there is a paucity of prospective data on urinary symptoms and fracture risk in this population. Previous prospective studies have been small, examined only hip fractures, and included younger men in whom fracture rates are low. For example, among 1,820 Austrian men with mean age of 52 years, the association between LUTS severity and hip fracture could not be estimated, because none of the men with severe LUTS had hip fractures despite 6 years of follow-up.[14] Two studies observed that the risk of hip fracture was 2-fold greater among men reporting at least two night-time voids compared with men who had fewer.[14,15] However, due to small numbers of hip fractures (24 in Austrian men and 13 in Japanese men), these associations were compatible with the null and these studies likely were underpowered.[14,15] Moreover, neither of these studies collected information on hip BMD, fall history, or other fracture risk factors which may have confounded the published results.

Although our results appear to contradict prior reports, the present study has several features that distinguish it from previous work in this field. First, instead of a single urinary symptom, we used the AUA-SI to obtain information on the cluster of urinary disorders that manifest as LUTS. LUTS severity as measured by the validated AUA-SI, provides a robust metric for evaluating the association with fracture risk. Second, to reduce misclassification of LUTS severity which can change over time, we updated LUTS status throughout the follow-up period. Third, we studied all non-spine fractures, not just hip fractures, because other fractures such as of the rib or wrist are also associated with substantial morbidity. Fourth, our analyses accounted for competing risks from death[29] and controlled for confounding by established fracture risk factors not considered in earlier studies. Finally, we captured a large number of fracture events (several times greater than in previous studies), which improved the precision of the HR estimates and increased the statistical power.

Reasons that severe LUTS were not an independent risk factor for non-spine fractures in this cohort deserve consideration. The most likely reason pertains to competing risk from death. Our data show that at older ages, men with severe LUTS were more likely to die than to fracture. A related possibility is confounding by age. Although we observed that the crude non-spine fracture incidence rate was highest among men with severe LUTS, the rate did not differ significantly from that among men with mild LUTS after accounting for age and established fracture risk factors. Further, uncontrolled confounding also could have resulted in spurious association of LUTS and fall risk reported previously.[9–11] Finally, even if severe LUTS are an independent risk factor for falls, it is possible that the types of falls most likely to result in a fracture (e.g. sideways or straight down onto the hip, backward onto the wrist)[30] do not vary by LUTS severity.

There are at least three potential limitations of this study. First, during follow-up, participants intermittently opted to complete only the questionnaire portion of the study assessments due to health or other reasons. This resulted in missing data on bone density and physical performance measures. However, in sensitivity analyses restricted to men with complete data, the LUTS and fracture association remained null. Second, we did not obtain clinical urological metrics in the cohort, such as urinary flow and post-void residual volume. However, these measures would not necessarily have imparted additional insight to this investigation, because our goal was to understand the impact of LUTS as represented by the AUA-SI on fracture risk. Finally, MrOS is comprised of generally healthy community dwelling older Caucasian male volunteers, so these results may not apply to older non-Caucasian men, to younger men, or to women.

Conclusions

LUTS are highly prevalent among older men and have documented impacts on non-urological health, including falls, in this population. However, the association of LUTS severity with fracture risk was null.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Funding Support

This research was supported by a grant from Watson Laboratories Inc (Allergan). The MrOS Study is supported by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), the National Institute on Aging (NIA), and the National Center for Research Resources (NCRR) and the NIH Roadmap for Medical Research through grants U01 AR45580, U01 AR45614, U01 AR45632, U01 AR45647, U01 AR45654, U01 AR45583, U01 AG18197, U01 AG027810, and UL1 RR024140.

References

1. Wei JT, Calhoun E, Jacobsen SJ. Urologic diseases in America project: benign prostatic hyperplasia. J Urol. 2006; 173:1256. [PubMed: 15758764]
2. Kupelian V, Wei JT, O'Leary MP, et al. Prevalence of lower urinary tract symptoms and effect on quality of life in a racially and ethnically diverse random sample: the Boston Area Community Health (BACH) Survey. Arch Intern Med. 2006; 166:2381. [PubMed: 17130393]
3. Parsons JK, Bergstrom J, Silberstein J, et al. Prevalence and characteristics of lower urinary tract symptoms in men aged > or = 80 years. Urology. 2008; 72:318. [PubMed: 18554695]
4. Girman CJ, Epstein RS, Jacobsen SJ, et al. Natural history of prostatism: impact of urinary symptoms on quality of life in 2115 randomly selected community men. Urology. 1994; 44:825. [PubMed: 7527166]
5. Taylor BC, Wilt TJ, Fink HA, et al. Prevalence, severity, and health correlates of lower urinary tract symptoms among older men: the MrOS study. Urology. 2006; 68:804–809. [PubMed: 17070357]
6. Kupelian V, Rosen RC, Link CL, et al. Association of urologic symptoms and chronic illness in men and women: contributions of symptom severity and duration—Results from the BACH Survey. J Urol. 2009; 181:694. [PubMed: 19091335]
7. Kupelian V, Fitzgerald MP, Kaplan SA, et al. Association of nocturia and mortality: results from the Third National Health and Nutrition Examination Survey. J Urol. 2011; 185:571. [PubMed: 21168875]

8. Ortman, JM.; Velkoff, VA.; Hogan, H. An Aging Nation: the Older Population in the United States, Current Population Reports. Washington DC: U.S. Census Bureau; 2014. p. 25-1140.Available at: https://www.census.gov/prod/2014pubs/p25-1140.pdf [last accessed July 29, 2015]
9. Parsons JK, Mougey J, Lambert L, et al. Lower urinary tract symptoms increase the risk of falls in older men. BJU Int. 2009; 104:63. [PubMed: 19154508]
10. Vaughn CP, Brown CJ, Goode PS, et al. The association of nocturia with incident falls in an elderly community dwelling cohort. Int J Clin Pract. 2010; 64:577. [PubMed: 20456212]
11. Tromp AM, Smit JH, Deeg DJ, et al. Predictors of falls and fractures in the Longitudinal Aging Study Amsterdam. J Bone Miner Res. 1998; 13:1932. [PubMed: 9844112]
12. Appell RA, Sand PK. Nocturia: etiology, diagnosis, and treatment. Neurourol Urodyn. 2008; 27:34. [PubMed: 17924538]
13. CDC. Fatalities and injuries from falls among older adults—United States, 1993–2003 and 2001–2005. MMWR Morb Mortal Wkly Rep. 2006; 55:1221. [PubMed: 17108890]
14. Temml C, Ponholzer A, Gutjahr G et al. Nocturia is an age-independent risk factor for hip fractures in men. Neurorurol Urodyn. 2009; 28:949.
15. Nakagawa H, Niu K, Hozawa A, et al. Impact of nocturia on bone fracture and mortality in older individuals: a Japanese longitudinal cohort study. J Urol. 2010; 184:1413. [PubMed: 20727545]
16. Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. J Urol. 1992; 148:1549. [PubMed: 1279218]
17. Orwoll E, Blank JB, Barrett-Connor E, et al. Design and baseline characteristics of the osteoporotic fractures in men (MrOS) study--a large observational study of the determinants of fracture in older men. Contemp Clin Trials. 2005; 26:569. [PubMed: 16084776]
18. Buchsbaum DG, Buchanan RG, Welsh J, et al. Screening for drinking disorders in the elderly using the CAGE questionnaire. J Am Geriatr Soc. 1992; 40:662. [PubMed: 1607581]
19. Block G, Hartman AM, Naughton D. A reduced dietary questionnaire: development and validation. Epidemiol. 1990; 1:58.
20. Pahor M, Chrischilles EA, Guralnik JM, et al. Drug data coding and analysis in epidemiologic studies. Eur J Epidemiol. 1994; 10:405. [PubMed: 7843344]
21. Washburn RA, Smith KW, Jette AM, et al. The Physical Activity Scale for the Elderly (PASE): development and evaluation. J Clin Epidemiol. 1993; 46:153. [PubMed: 8437031]
22. Ware J Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996; 34:220. [PubMed: 8628042]
23. Gill SC, Butterworth P, Rodgers B et al. Validity of the mental health component scale of the 12-item Short-Form Health Survey (MCS-12) as measure of common mental disorders in the general population. Psychiatry Res. 2007; 152:63. [PubMed: 17395272]
24. Guralnik JM, Ferrucci L, Simonsick EM, et al. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med. 1995; 332:556. [PubMed: 7838189]
25. Lewis CE, Ewing SK, Taylor BC, et al. Predictors of non-spine fracture in elderly men: the MrOS study. J Bone Miner Res. 2007; 22:211. [PubMed: 17059373]
26. Meier CR, Schlienger RG, Kraenzlin ME, et al. HMG-CoA reductase inhibitors and the risk of fractures. JAMA. 2000; 283:3205. [PubMed: 10866867]
27. Ray WA, Griffin MR, Schaffner W, et al. Psychotropic drug use and the risk of hip fracture. N Engl J Med. 1987; 316:363. [PubMed: 2880292]
28. Lamarca R, Alonso J, Gomez G, et al. Left-truncated data with age as time scale: an alternative for survival analysis in the elderly population. J Gerontol Biol Sci Med Sci. 1998; 53:M337.
29. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. JASA. 1999; 94:496.
30. Nevitt MC, Cummings SR. Type of fall and risk of hip and wrist fractures: the study of osteoporotic fractures. J Am Geriatr Soc. 1993; 41:1226. [PubMed: 8227898]

Key Definitions

AUA-SI	American Urological Association Symptom Index
BMD	bone mineral density
BPH	benign prostatic hyperplasia
CI	Confidence Interval
CNS	central nervous system
HR	Hazard ratio
LUTS	Lower urinary tract symptoms
MrOS	Osteoporotic Fractures in Men Study
US	United States

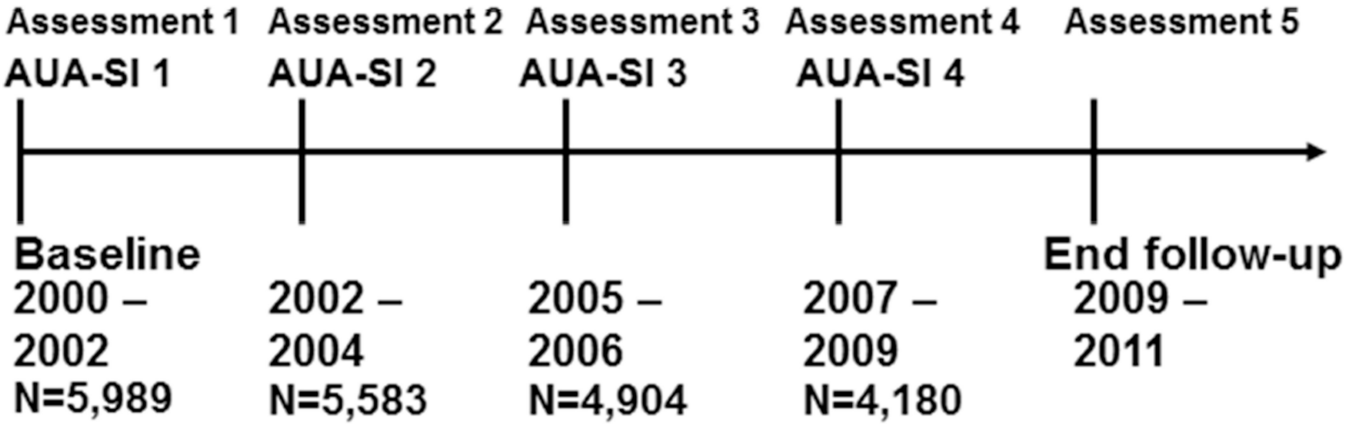

Figure 1.

Timeline of Osteoporotic Fractures in Men Study (MrOS) assessments used in this analysis. The repeated American Urologic Association Symptom Index time points are shown along with numbers of cohort members alive and free from fracture at the start of each assessment interval. During follow-up, 13% of men in the analytic cohort had a first fracture, 20% died with no fracture, and 2% voluntarily withdrew before death or fracture. Refusal to participate in an assessment ranged from 1%–2%; however, men who refused returned to the analysis cohort if they participated in a subsequent assessment.

Abbreviations: AUA-SI, American Urological Association Symptom Index

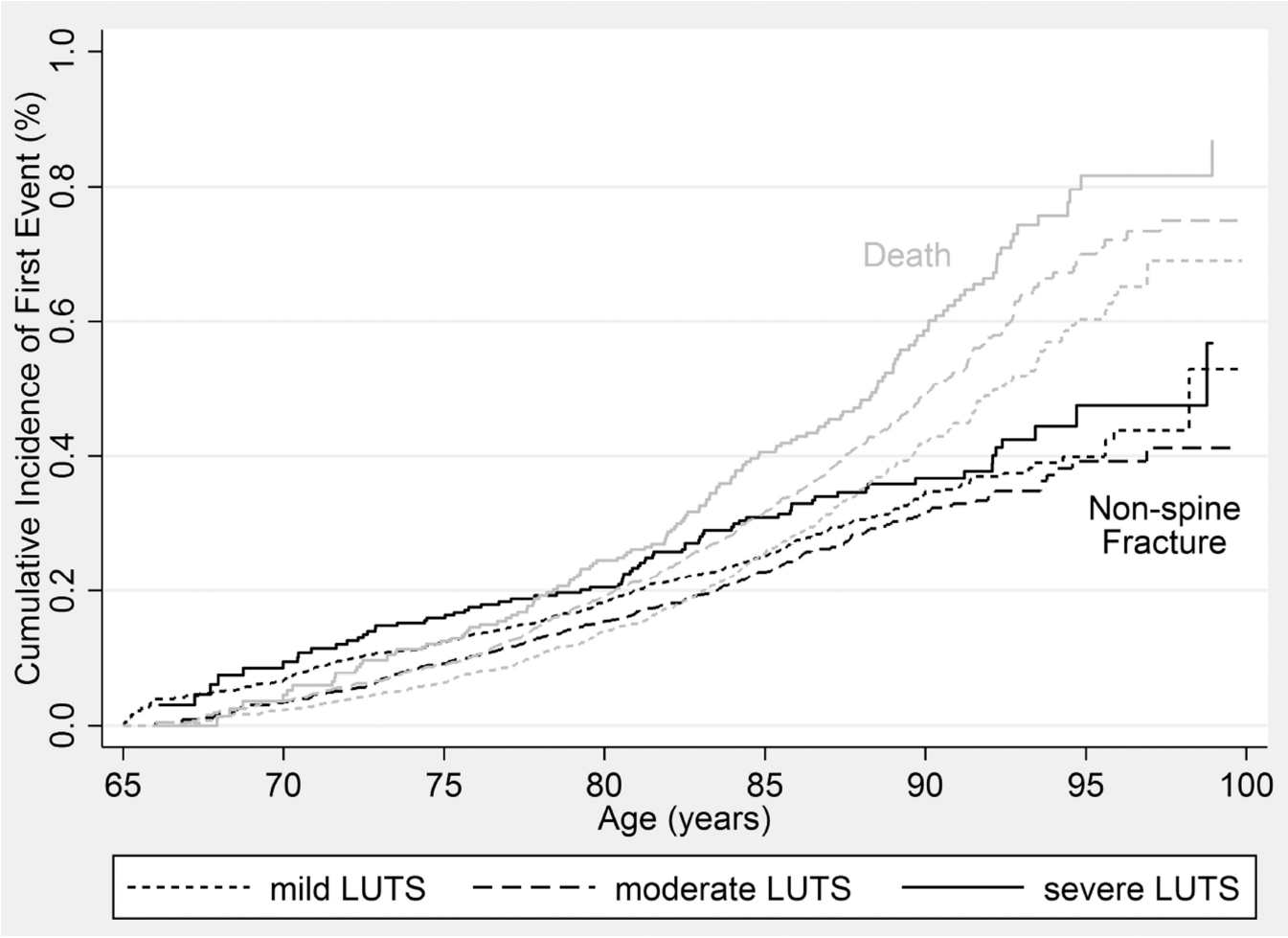

Figure 2.

Cumulative incidence of first non-spine fracture and of death without fracture during follow-up among community dwelling older men: the MrOS study.

Table 1

Distributions at baseline of potential fracture risk factors according to lower urinary tract symptom severity among 5989 community dwelling men aged 65 years or older: the MrOS study.

Baseline characteristic	None/Mild N=3,236 (54%)	Moderate N=2,355 (39%)	Severe N=398 (7%)	P-value
Age, mean (s.d.)	73.2 (5.8)	74.2 (5.9)	74.6 (6.2)	<0.001
Total hip BMD (g/cm^2), mean (s.d.)	0.963 (0.139)	0.950 (0.141)	0.960 (0.148)	0.004
Total hip BMD <1 s.d. below cohort mean (%)	18.1	16.8	13.9	0.003
History of diagnosed osteoporosis (%)	2.5	4.3	7.0	<0.0001
History of fracture after age 50 years (%)	20.4	25.0	27.1	<0.0001
History of falls in the past year (%)	17.8	24.5	28.1	<0.0001
Unable to perform narrow walk (%)	7.2	9.9	12.5	<0.0001
Time to complete 5 chair stands (s), mean (s.d.) *	10.9 (3.1)	11.3 (3.4)	11.8 (4.0)	<0.0001
Unable to complete 5 chair stands (%)	2.6	3.3	4.8	0.03
Grip strength (kg), mean (s.d) *	39.0 (8.1)	38.1 (8.1)	37.4 (8.3)	<0.0001
Unable to perform grip strength (%)	1.2	2.3	2.3	0.005
Mobility limitation (%) †	10.6	16.6	26.0	<0.0001
Depressive symptoms (%) ‡	12.9	19.7	23.6	<0.0001
BMI categories				0.51
<25.0 kg/m^2 (%)	27.9	27.1	24.9	
25.0–29.9 kg/m^2 (%)	50.9	51.7	50.8	
≥30 kg/m^2 (%)	21.2	21.2	24.4	
Dietary vitamin D intake (IU/day), median	422	437	446	0.002
Dietary calcium intake (mg/day), median	975	1023	1061	0.0001
Statin prescription medication use (%)	25.4	26.7	28.4	0.32
CNS active prescription medication use (%)	10.1	14.3	18.6	<0.0001

Abbreviations: BMD, bone mineral density; BMI, body mass index; CNS, central nervous system.

* Among men able to complete the measure.

† Self-report of difficulty walking 2–3 blocks outside on level ground or difficulty climbing 10 stairs.[24]

‡ Depressive symptoms defined as SF-12 mental component score <50 points.[23]

Table 2

Associations of LUTS severity with non-spine fracture among 5,989 community dwelling US men age 65 year or older: the MrOS study.

	LUTS Severity*		
Unadjusted estimates	**None/Mild**	**Moderate**	**Severe**
Person-years	22,386	18,087	3,334
Cases	364	309	72
Fracture rate/1000 person-years	16.3	17.1	21.6
Modelling results—entire cohort	Hazard Ratio (95% confidence interval)		
Adjusted for age and enrollment site†	1.0 (Referent)	1.0 (0.8, 1.2)	1.2 (0.9, 1.5)
Further adjusted for fracture risk factors‡	1.0 (Referent)	0.9 (0.8,1.1)	1.0 (0.8, 1.3)
Fully adjusted§	1.0 (Referent)	0.9 (0.7, 1.0)	0.9 (0.7, 1.2)
Modelling results—restricted cohorts			
No diagnosed prostate cancer§	1.0 (Referent)	0.9 (0.7, 1.0)	1.0 (0.7, 1.3)
No fracture history after age 50 yrs‖	1.0 (Referent)	0.9 (0.7, 1.1)	1.1 (0.8, 1.6)

Abbreviations: BMD, bone mineral density LUTS, lower urinary tract symptoms.

*Defined from AUA-SI score as 0–7 for none/mild, 8–19 for moderate, and 20–35 for severe.[16] LUTS severity category was updated at the start of each assessment.

†Age was adjusted by using it as the time scale.

‡Adjusted for baseline fracture history, baseline total hip BMD <1 s.d. below the cohort mean, and history of falls in past 12 months.

§Adjusted for enrollment site, baseline fracture history after age 50 years, baseline total hip BMD <1 s.d. below the cohort mean, history of falls in past 12 months, mobility limitation, current use of central nervous system active medication, and white race.

‖Adjusted for variables in fully adjusted model except for baseline fracture history after age 50.

Table 3

Associations of individual LUTS frequency with non-spine fracture among older men: the MrOS study.

Lower Urinary Tract Symptom	Hazard Ratios (95% CI)* for Symptom Frequency†		
	Does not have symptom	Less than half the time	Half the time or more
Sense of incomplete emptying	1.0 (Referent)	0.9 (0.8, 1.1)	1.0 (0.8, 1.2)
Frequency	1.0 (Referent)	0.9 (0.8, 1.1)	0.9 (0.7, 1.1)
Intermittent urinary stream	1.0 (Referent)	0.9 (0.7, 1.0)	0.9 (0.8, 1.1)
Urgency to urinate	1.0 (Referent)	1.0 (0.9, 1.2)	1.0 (0.8, 1.2)
Weak urinary stream	1.0 (Referent)	0.9 (0.8, 1.1)	1.0 (0.8, 1.2)
Push or strain to start urination	1.0 (Referent)	1.0 (0.8, 1.2)	1.0 (0.7, 1.4)
	0–1	2–3	4 – 5 or more
Nocturia (times per night)	1.0 (Referent)	1.0 (0.9, 1.2)	1.0 (0.8, 1.3)

*Adjusted for enrollment site, baseline fracture history, baseline total hip BMD <1 s.d. below the cohort mean, and history of falls in past 12 months. Age was adjusted by using it as the time scale.

†Symptoms obtained from the AUA-SI.[16] The symptom frequency category was updated at the start of each assessment.