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Prevalence of lower urinary tract symptoms in patients with cardiovascular disease

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Introduction The presence of lower urinary tract symptoms (LUTS) might be linked with elevated cardiovascular risk. There is a lack of data showing the prevalence of LUTS in the population of patients with cardiovascular diseases. The current study aimed to determine the prevalence of LUTS in patients hospitalized due to a cardiovascular disease.

Material and methods Patients hospitalized in a tertiary cardiology department due to a primary diagnosis of cardiovascular disease (including coronary artery disease, heart failure and arrhythmia) were included in the study. All patients were screened for LUTS and assessed using the International Prostate Symptoms Score (IPSS).

Results From 166 patients (age 62.8 ±12.1 years), moderate to severe LUTS was diagnosed in 62 patients (37.3%). Patients with LUTS were significantly older, but there were no other factors associated with LUTS. When we divided patients according to LUTS severity, we saw an increasing prevalence of arterial hypertension (69.5% vs 72.9% vs 100%), diabetes mellitus (29.5% vs 33.3% vs 38.5%), coronary artery disease (68.6% vs 72.9% vs 92.3%), but the observations were not statistically significant. Patients with coronary artery disease had significantly higher severity of LUTS compared to patients with arrhythmia or heart failure (mean IPSS 8.88 vs 5.6 vs 5.5, p = 0.004).

Conclusions The prevalence of LUTS in patients with cardiovascular diseases is high, affecting 37.3% of the studied population. Patients with coronary artery disease have significantly higher severity of LUTS compared to other cardiovascular diseases.

Key Words: lower urinary tract symptoms ‹› cardiovascular risk ‹› risk scores

INTRODUCTION

A major cause of premature death throughout the world are cardiovascular diseases (CVD) [1]. For this reason, cardiovascular risk estimation is an important part of the clinical approach. Cardiovascular risk is the probability of developing cardiovascular disease within a certain period. Current guidelines recommend assessing CVD risk based on all cardiovascular risk factors present in an individual and adapting cardiovascular disease prevention to individual total CVD risk: "the higher the risk, the more intense the action should be" [2, 3]. In recent years, more attention has been drawn towards the non-classical CVD risk factors like periodontal diseases, autoimmune diseases, obstructive sleep apnoea, or erectile dysfunction. The number of investigated factors still increases, and lower urinary tract symptoms (LUTS) seems to be one of them. It has been suggested that patients with LUTS are at higher cardiovascular risk than the one resulting from traditional risk assessment scores, and the risk increases with the severity of lower urinary tract symptoms. This study aimed to establish

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the prevalence of LUTS in patients hospitalised for cardiovascular diseases.

MATERIAL AND METHODS

The study protocol was approved by the Bioethics Commission by the Medical University of Warsaw (KB/152/2017) and was performed in accordance with the Declaration of Helsinki. All patients enrolled in the study signed written informed consent. The study included continuous male patients hospitalised in a tertiary cardiology department due to a primary diagnosis of cardiovascular disease. The criteria for inclusion were male gender and present hospitalisation due to cardiovascular disease. Exclusion criteria were:

- age <18 and >85 years,
- coexisting illness with a predicted survival rate <6 months,
- a coexisting inflammatory illness that requires antibiotic therapy or antifungal treatment,
- current immunosuppressive or hormonal cancer therapy.

The first stage of the study included taking the clinical history, physical examination, body measurements, blood test, and imaging studies were made, in order to confirm the diagnosis of cardiovascular diseases and describe the risk factors. After that, patients were evaluated for the presence of lower urinary tract symptoms (LUTS).

The research was performed using validated questionnaires for assessing lower urinary tract symptoms and sexual dysfunction. Questionnaires used in the study included the International Prostate Symptoms Score (IPSS). The IPSS was calculated for all men who responded to the seven symptom questions (items). Each item has response categories of 0 (not at all) to 5 (almost always); the IPSS is the sum of the seven items, with a total score of 0–35. In the analysis, we categorised LUTS according to total score as no symptoms (IPSS 0), mild (1–7), moderate (8–19) or severe symptoms (20–35), according to recommendations made by the developers of the IPSS [3].

LUTS was defined as suggested by the International Continence Society (ICS) and included: slow stream, splitting, intermittency, hesitancy, straining, terminal dribble, perceived frequency, urgency, urgency with fear of leaking, urgency urinary incontinence (UUI), stress urinary incontinence (SUI), leak for no reason, nocturnal enuresis, leak during sexual activity, incomplete emptying, and post-micturition dribble [4].

Statistical analysis was performed using SPSS Statistics (SPSS version 26, Inc., Chicago, IL) for macOS. Data were tested for normality using the Kolmogorov-Smirnov test. Continuous data were presented as mean and standard deviation or, in the absence of such distribution, as confidence intervals for the median. Comparisons were performed with the Mann-Whitney test or Student's t-test. A comparison for categorical variables was made using the χ^2 or Fisher's exact tests. For comparison of mean values between more than two independent groups, depending on the distribution, analysis of variance (ANOVA) or the Kruskal-Wallis test was used. A p-value of less than 0.05 was considered statistically significant.

RESULTS

The study population comprised of 166 men with a mean age of 62.8 ±12.1 years. Over 79% of patients (n = 132) were overweight. Arterial hypertension was diagnosed in 72.9% (n = 121), diabetes mellitus in 31.3% (n = 52) and dyslipidemia in 75.9% of patients (n = 126). A majority of patients (n = 119, 71.7%) had coronary artery disease, and almost 45% of patients (n = 75) had a history

Table 1. *Demographic and clinical characteristics of all patients (n = 166)*

Parameter	Value (mean ±SD)
Age (years)	62.8 ±12.1
BMI (kg/m^2)	28.8 ±16.6
Arterial hypertension	121 (72.9%)
Atrial fibrillation	51 (30.7%)
Coronary artery disease	119 (71.7%)
History of myocardial infarction	75 (45.2%)
History of stroke	11 (6.6%)
Heart failure	79 (47.6%)
Diabetes mellitus	52 (31.3%)
Peripheral artery disease	13 (7.8%)
Laboratory test results	
Glucose (mg/dL)	123 ±55.3
HbA_{1C} (%)	6.2 ±1.4
Urea (mg/dL)	42.8 ±21.5
Creatinine (mg/dL)	1.2 ±0.5
eGFR (ml/min/1.73 m^2)	73.6 ±21.2
Uric acid (mg/dL)	6.3 ±1.8
NT-proBNP (pg/mL)	1567.9 ±3369.8
CRP (mg/L)	8.5 ±17.1
PSA (ng/mL)	2.3 ±8.6
TSH (µIU/mL)	1.9 ±1.1

BMI – body mass index; HbA_{1C} – hemoglobin A_{1C}; SD – standard deviation; eGFR – estimated glomerular filtration rate; NT-proBNP – N-terminal B-type natriuretic peptide; CRP – C-reactive protein; PSA – prostate-specific antigen; TSH – thyroid-stimulating hormone

Table 2. *Demographic and clinical characteristics – comparison of subgroups separated based on the presence of LUTS*

Parameter	Patients without LUTS (n = 104)	Patients with moderate to severe LUTS (n = 62)	p value
Age (years)	60.3 ±12.6	66.9 ±10.0	<0.001
BMI (kg/m^2)	28.8 ±6.5	28.7 ±4.2	0.40
Arterial hypertension	72 (69.2%)	49 (79.0%)	0.21
Atrial fibrillation	32 (30.8%)	19 (30.6%)	1.00
Coronary artery disease	71 (68.3%)	48 (77.4%)	0.22
History of myocardial infarction	46 (44.2%)	29 (46.8%)	0.87
History of stroke	9 (8.7%)	2 (3.2%)	0.21
Heart failure	54 (51.9%)	25 (40.3%)	0.15
Diabetes mellitus	30 (28.8%)	22 (35.5%)	0.39
Peripheral artery disease	11 (10.6%)	2 (3.2%)	0.13
Laboratory test results			
Glucose (mg/dL)	126.1 ±59.7	117.8 ±47.1	0.65
HbA_{1C} (%)	6.1 ±1.4	6.3 ±1.4	0.06
Urea (mg/dL)	42.1 ±23	43.9 ±19.2	0.21
Creatinine (mg/dL)	1.2 ±0.5	1.2 ±0.6	0.34
eGFR (ml/min/1.73m^2)	74 ±21.2	73 ±21.4	0.86
Uric acid (mg/dL)	6.3 ±2.0	6.2 ±1.4	0.74
NT-proBNP (pg/mL)	1471.6 ±2747.1	1729.0 ±4232.5	1.00
CRP (mg/L)	7.7 ±16.8	9.7 ±17.6	0.59
PSA (ng/mL)	1.5 ±2.2	3.5 ±13.8	0.32
TSH (μIU/mL)	1.9 ±1.1	2.1 ±1.2	0.18

LUTS – lower urinary tract symptoms; BMI – body mass index; eGFR – estimated glomerular filtration rate; NT-proBNP – N-terminal B-type natriuretic peptide; CRP – C-reactive protein; PSA – prostate-specific antigen; TSH – thyroid-stimulating hormone; HbA_{1C} – hemoglobin A_{1C}; SD – standard deviation

of myocardial infarction. The prevalence of heart failure was also high, amounting to 47.6% of patients (n = 79). Fifty-one patients (30.7%) had atrial fibrillation. Demographic and clinical characteristics of the patients are presented in Table 1.

Moderate to severe LUTS was diagnosed in 62 patients, while none to mild symptoms were presented in 104 patients. The study population was analysed after division into two subgroups: patients with LUTS and patients without LUTS. Detailed data for these patients are presented in Table 2. The incidence of LUTS increased with age (60.3 ±12.6 vs 66.9 ±10.0; p <0.0001) and the mean age of patients increased proportionally with the severity of LUTS (60.3 ±12.5 vs 66.2 ±10.6 vs 70.8 ±6.2; p <0.001). The incidence of LUTS were more common in patients with arterial hypertension (79% vs 69.2%; p = 0.21), diabetes (35.5% vs 28.8%; p = 0.39), coronary artery disease (77.4% vs 68.3%; p = 0.22).

The analysis of the obtained data revealed that with the severity of LUTS have increased with the higher prevalence of arterial hypertension (69.5% vs 72.9% vs 100%, p = 0.07), coronary artery disease (68.6% vs 72.9% vs 92.3%; p = 0.20) and diabetes (29.5% vs 33.3% vs 38.5%; p = 0.76) (Table 3).

Importantly, after dividing the patients according to the cause of hospitalization, we saw that the highest prevalence of LUTS was observed in patients with coronary artery disease rather than in those with heart failure or arrhythmia. Moreover, patients with coronary artery disease had a significantly higher severity of LUTS compared with patients with arrhythmia or heart failure (mean IPSS 8.88 vs 5.6 vs 5.5, p = 0.004) (Figure 1).

DISCUSSION

Our study demonstrates the high prevalence of LUTS in patients with cardiovascular diseases (37.3%). The incidence of LUTS increased with age (p <0.0001), was more prevalent in patients with arterial hypertension, diabetes mellitus, atrial fibrillation, and renal insufficiency. Moreover, in our study population, patients with coronary artery disease had significantly higher severity of LUTS, which might suggest

Table 3. *Comparison of patients according to the LUTS severity*

Parameter	LUTS severity according to IPSS			p value
	None or mild n = 104	Moderate n = 49	Severe n = 13	
Age (years)	60.3 ±12.5	66.2 ±10.6	70.8 ±6.2	0.001
BMI (kg/m^2)	28.8 ±6.5	28.9 ±4.5	28.1 ±3.1	0.58
Arterial hypertension	73 (69.5%)	35 (72.9%)	13 (100%)	0.07
Atrial fibrillation	32 (30.5%)	17 (35.4%)	2 (15.4%)	0.38
Coronary artery disease	72 (68.6%)	35 (72.9%)	12 (92.3%)	0.20
History of myocardial infarction	46 (43.8%)	23 (47.9%)	6 (46.2%)	0.89
History of stroke	9 (8.6%)	2 (4.2%)	0 (0%)	0.36
Heart failure	54 (51.4%)	20 (41.7%)	5 (38.5%)	0.42
Diabetes mellitus	31 (29.5%)	16 (33.3%)	5 (38.5%)	0.76
Peripheral artery disease	11 (10.5%)	2 (4.2%)	0 (0%)	0.22
Laboratory test results				
Glucose (mg/dL)	126.1 ±59.4	120.7 ±52.1	106.9 ±23.2	0.83
HbA_{1C} (%)	6.1 ±1.4	6.3 ±1.5	6.4 ±1.4	0.13
Urea (mg/dL)	42.1 ±23	44.4 ±18.2	41.9 ±23	0.38
Creatinine (mg/dL)	1.2 ±0.5	1.1 ±0.4	1.4 ±1.2	0.54
eGFR (ml/min/1.73m^2)	73.8 ±21.1	74.2 ±20.9	69.2 ±24.2	0.83
Uric acid (mg/dL)	6.3 ±2	6.2 ±1.4	6.1 ±1.5	0.99
NT-proBNP (pg/mL)	1458.6 ±2736.8	1853.9 ±4647.7	1400.2 ±2524.8	0.98
CRP (mg/L)	7.7 ±16.8	8.3 ±15.4	15.3 ±24.4	0.40
PSA (ng/mL)	1.5 ±2.1	3.9 ±15.9	2.3 ±2.3	0.11
TSH (µIU/mL)	1.9 ±1	2.2 ±1.3	1.6 ±0.5	0.25

LUTS – lower urinary tract symptoms; IPSS – International Prostate Symptom Score; BMI – body mass index; eGFR – estimated glomerular filtration rate; NT-proBNP – N-terminal B-type natriuretic peptide; CRP – C-reactive protein; PSA – prostate-specific antigen; TSH – thyroid-stimulating hormone ; HbA_{1C} – hemoglobin A_{1C}; SD – standard deviation

that in many cases LUTS might be closely associated with atherosclerosis.

Most previously published studies were concerned only on CVD risk assessment in patients with LUTS. Our observations are consistent with a systematic review and meta-analysis conducted by Gacci et al. [5]. The authors analysed 15 studies concerning incidence of major adverse cardiac events (MACE) in men with moderate to severe LUTS compared to those with mild LUTS or without LUTS and observed significantly higher incidence of MACE in patients with moderate/ severe LUTS [5].

Furthermore, several studies demonstrated a higher cardiovascular risk in patients with LUTS. Lee et al. assessed CVD risk (using ACC/AHA score and Framingham score) of 2994 ostensibly healthy males, who participated in a voluntary health check [6]. They demonstrated that severe LUTS (based on IPSS score) was more prevalent in patients with intermediate/high CVD risk. Similar results were obtained in a study conducted in a group of men with benign prostatic hyperplasia-related LUTS [7]. It has been noted that with a higher IPSS score, the category of Framingham CVD risk score was increased. Additionally, prostate volume was significantly increased in men with intermediate vs low CVD risk scores.

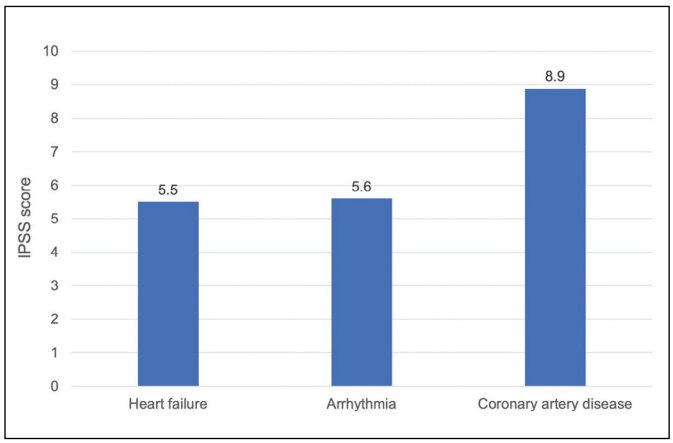

Figure 1. *IPSS score according to the chief complaint on admission.*

Multivariate logistic regression analysis showed that intermediate and high-risk scores were independently associated with moderate-severe LUTS.

Numerous studies demonstrate that traditional risk factors like arterial hypertension or hypercholesterolemia are more prevalent in LUTS patients. Kim et al. conducted detailed health evaluations in 280 men aged more than 50 years taking part in the Hallym Aging Study (HAS) [8]. The authors were concerned about the prevalence of vascular risk factors (hypertension, diabetes mellitus, hyperlipidemia, smoking) and LUTS. The LUTS were more severe (based on IPSS score) in men with ≥3 vascular risk factors compared with no and one or two vascular risk factors ($p < 0.05$). Multiple logistic regression analysis demonstrated that men with 3 or more vascular risk factors compared with no risk factors were 3 times more likely to have moderate/severe LUTS ($p < 0.05$) [8]. In another study, it was shown that the IPSS score was higher in men with hypertension, diabetes mellitus, chronic stress, and unmotivated fatigue compared with the general population [9, 10].

Most studies concerning LUTS focus on males. Nevertheless, it is worth mentioning that a correlation between LUTS and CVD risk was also observed in studies including both sexes. The Boston Area Community Health (BACH) Survey was a population-based cohort study of urologic symptoms conducted among 4144 men and women [10, 11, 12]. Additionally, the presence of diabetes mellitus and heart disease was assessed in all patients. It was observed that the presence of moderate to severe LUTS was associated with increased risk of earlier onset of diabetes mellitus among younger participants, and a moderate increase in the risk of heart disease.

Several factors might be responsible for the relationship between CVD and LUTS: metabolic syndrome, chronic inflammation, atherosclerosis-induced pelvic ischemia, increased Rho-kinase activation, impaired nitric-oxide synthase pathway in the endothelium, autonomic hyperactivity with sympathetic dysregulation, declining testosterone levels [13, 14]. It should be underlined that LUTS are not only common chronic conditions in elderly men. There is the association between the prevalence and severity of LUTS and cardiovascular risk factors such as diabetes and arterial hypertension. Higher LUTS severity in patients with coronary artery disease may indicate a significant role of atherosclerosis in the pathophysiology of LUTS. The recent studies indicate that healthy lifestyles, antihypertensive therapy with angiotensin II receptor blockers and lipid-lowering therapy (statins) reduce not only cardiovascular mortality but also might reduce prevalence and severity of lower urinary tract symptoms [13]. Patients with LUTS need a holistic approach and cooperation of a urologist and cardiologist to diagnose concomitant cardiovascular diseases as early as possible and implement appropriate treatment.

CONCLUSIONS

Our study demonstrates a high prevalence of LUTS in patients with cardiovascular diseases (37.3%). Patients with coronary artery disease had significantly higher severity of LUTS compared to patients with arrhythmia or heart failure. The increasing severity of LUTS was associated with an increasing mean age, concentration of metabolic biomarkers and prevalence of arterial hypertension.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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