ORIGINAL ARTICLE

Andropausal syndrome in men with systolic heart failure

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KEY WORDS

anabolic hormone deficiency, andropausal syndrome, heart failure, male aging, testosterone

ABSTRACT

INTRODUCTION Andropausal syndrome (AS) is an element of male aging, being associated with the age-related decline in circulating androgens.

OBJECTIVES We investigated the prevalence of AS, the severity of andropausal symptoms, and their clinical and hormonal determinants in men with heart failure (HF) and healthy peers.

PATIENTS AND METHODS We examined 232 men with systolic HF aged from 40 to 80 years (New York Heart Association [NYHA] class I/II/III–IV: 17%/54%/29%, left ventricular ejection fraction: 30% ±8%) and 362 healthy peers. The severity of 17 andropausal symptoms were assessed using the Aging Males' Symptoms Rating Scale.

RESULTS In men with HF aged from 40 to 59 years, the prevalence of AS and the severity of andropausal symptoms were greater than in healthy peers (28% vs. 7%; 40 ±14 vs. 35 ±10 points; both P <0.001), while in the age group of 60 to 80 years, there were no differences in the prevalence of AS and the severity of andropausal symptoms between men with HF and healthy peers (31% vs. 40%; 44 ±12 vs. 46 ±10 points; respectively; both P >0.1). In men with HF aged from 40 to 59 years, advanced NYHA class, low hemoglobin, increased platelet number, and low serum dehydroepiandrosterone sulphate were independently associated with the greater prevalence of AS (all P <0.05). In men aged from 60 to 80 years, only reduced hemoglobin was borderline related to the higher prevalence of AS (P = 0.07).

CONCLUSIONS AS affects almost one-third of men with HF regardless of the age group. The clinical and hormonal determinants of the severity of andropausal symptoms differ between younger and older male patients. Endocrinological and sexual counseling is recommended in men with HF.

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INTRODUCTION Improved living conditions and the enormous progress of medicine and healthcare have resulted in a significantly increased life expectancy.[1,2] Over the last 50 years, life expectancy in the European Union has risen by approximately 10 years. In 2009, a new-born European was expected to live to the age of 80 years.[1] However, the advanced age of the population is inevitably associated with numerous health problems that occur in elderly patients,[2,3] and the increasing healthcare expenditures associated with the aging process constitute an important socioeconomic

challenge.[3,4] One of the conditions associated with male aging is the andropausal syndrome (AS; other terms include androgen deficiency in the aging male and late-onset hypogonadism).[5,6]

AS refers to a clinical syndrome with characteristic psychosomatic signs and symptoms usually attributed to the age-related decline in circulating testosterone, dehydroepiandrosterone, and other male hormones.[5,7] Although andropausal symptoms are quite common in elderly men,[8] the causal relationship between the progressively diminished serum testosterone level (and other anabolic hormones) and the symptoms affecting the aging male is still controversial.[6] Further, it is unclear whether concomitant chronic diseases (for example, cardiovascular diseases) could affect the magnitude of andropausal symptoms in the elderly.

Heart failure (HF) is one of the leading medical and socioeconomic problems in the developed countries[9-13]; its prevalence progressively increases with age from 0.7% in persons aged from 45 to 54 years to 8.4% in those aged 75 years and older (United States data).[14] In Europe, HF affects more than 10% of the population aged 85 years and older,[15] and some authors describe this cardiovascular disease as a cardiogeriatric syndrome.[16] Advanced age is considered as one of the major risk factors for developing HF.[17] There are hypotheses that HF may be related to the senescence of the cardiomyocytes (aging at the cellular level associated with the shortening of the telomeres).[7]

The deficiencies of anabolic hormones are common in men with systolic HF[18] and have several consequences; they are associated with reduced exercise capacity,[19] greater severity of depressive symptoms,[20] and poor patient prognosis.[18] Therefore, in this study we aimed to compare the prevalence of AS and the severity of andropausal symptoms between men with systolic HF and the local cohort of age-matched healthy men, and to investigate the clinical and hormonal determinants of the severity of andropausal symptoms in younger compared with older men with systolic HF.

PATIENTS AND METHODS

Study populations

The study was conducted among male patients with chronic systolic HF attending the outpatient clinic or admitted electively to the tertiary referral center (Center for Heart Diseases, Military Hospital, Wrocław, Poland). The inclusion criteria were: 1) a documented history of chronic HF of ≥6 months; 2) left ventricular ejection fraction (LVEF) ≤45% assessed by echocardiography, using the Simpson's planimetric method to determine LVEF; 3) clinical stability of the patient and an unchanged list of medications for ≥1 month preceding the study. The exclusion criteria were as follows: 1) acute coronary syndrome, coronary revascularization, and/or any other major surgery within the 3 months preceding the study; 2) unplanned hospitalization due to deterioration of HF and/or any other cardiovascular reason within 1 month preceding the study; 3) any hormonal treatment, either during the study or in history; 4) lack of informed written consent.

The reference population consisted of 362 healthy men, 40- to 80-years-old, living in the same area, who were examined in 2000 at the Silesian Centre for Preventive Medicine (DOLMED; Wrocław, Poland). These individuals had no history of any chronic disease and no abnormalities present during the physical examination.[8,18]

The study protocol was approved by the local ethics committee, and all subjects gave written informed consent. The study was conducted in accordance with the Helsinki Declaration.

Assessment of andropausal symptoms

Data on the intensity of andropausal symptoms was assessed using the Polish version of the Aging Males' Symptoms Rating Scale (AMS).[8,21,22] The AMS scale includes 17 symptoms divided into 3 groups: psychological (discouraged, depressed, irritable, anxious, nervous); sexual (disturbed potency, impaired erectility, problems with libido, decrease in beard growth, feeling of "having passed the zenith of life"); and somatovegetative (joint and muscle complaints, sweating, need for more sleep, sleep disturbances, weakness, exhaustion, impaired well-being).[21] The questionnaire was completed by a respondent individually, where the intensity of each symptom was rated between 1 (low) and 5 points (high).[21] We analyzed the severity of the 3 subgroups of androupausal symptoms (3 subscores for each cluster) and the total severity of AS symptoms (total AMS score, sum of 3 subscores). AS was diagnosed if the total AMS score was 50 points or higher.[21,22] We need to emphasize that we investigated the clinical syndrome of andropausal symptoms,[5] which differs from the syndrome of late-onset hypogonadism. The latter is based on the concomitance of reduced circulating testosterone and the clinical features (andropausal symptoms).[6]

Laboratory measurements

In all men with systolic HF, venous blood samples were taken in the morning after an overnight fast and supine rest of at least 15 minutes. After centrifugation, the serum was collected and frozen at –70°C until analysis. The serum levels of total testosterone (TT), dehydroepiandrosterone sulphate (DHEAS), and insulin-like growth factor 1 (IGF-1) were measured with immunoassays (Diagnostic Products Corp, San Francisco, California) and expressed in ng/ml (to convert the values for TT to nmol/l, multiply by 3.467; DHEAS to μmol/l, multiply by 0.00271; IGF-1 to nmol/l, multiply by 0.131). Serum concentration of estradiol (E2) was measured by using electrochemiluminescence on the Elecsys 1010/2010 System (Roche Diagnostics GmbH, Mannheim, Germany) and expressed in pg/ml (to convert to pmol/l, multiply by 3.671). The interassay and intraassay variability coefficients were 9.8% and 7.4% for TT, 12.0% and 6.8% for DHEAS, 6.2% and 3.1% for IGF-1, and 2.0% and 3.3% for E2, respectively.

To estimate the circulating fraction of free testosterone (FT) and free E2, we also measured the serum level of sex hormone-binding globulin (SHBG) in all subjects using an immunoassay (Diagnostic Products Corp, San Francisco, California), and SHBG was expressed in nmol/l. The interassay and intraassay variability coefficients for SHBG were 5.2% and 3.0%, respectively. The serum level of estimated FT (eFT; expressed in pg/ml; to convert to pmol/l, multiply by 3.467) was calculated with the validated equation of Vermeulen et al.[23] The serum level of estimated free E2 (eFE2; expressed in pg/ml; to convert to pmol/l, multiply by 3.671) was calculated with the validated equation of Södergård et al.[24]

Plasma level of N-terminal pro-B-type natriuretic peptide (NT-proBNP; pg/ml) was measured with an immunoassay based on electrochemiluminescence on the Elecsys 1010/2010 System (Roche Diagnostics GmbH, Mannheim, Germany). The estimated glomerular filtration rate (eGFR, ml/min/1.73 m^2) was estimated using the Modification in Diet in Renal Disease equation.[25] The serum level of high-sensitivity C-reactive protein (hsCRP, mg/l) was assessed using kinetic nephelometry (Dade Behring, Siemens Healthcare Diagnostics, Inc.).

Statistical analyses Most continuous variables had a normal distribution, and were expressed as a mean ± the standard deviation of the mean. The intergroup differences were tested using the *t* test for unpaired samples. Plasma NT-proBNP, serum DHEAS, and serum hsCRP had a skewed distribution, and were log-transformed (a natural logarithm, ln) to normalize their distribution. They were expressed as a median with lower and upper quartiles (an interquartile range), and the intergroup differences were tested using the *t* test for unpaired samples for normalized values. Categorized variables were expressed as a number and a percentage, and the intergroup differences were tested using the χ^2 test.

Univariable and multivariable linear regression analyses were applied to establish variables determining the severity of andropausal symptoms (3 AMS subscores for psychological, sexual, somatovegetative symptoms, and a total AMS score – all andropausal symptoms), separately in younger (40–59 years) and older (60–80 years) age groups of men with systolic HF. In the univariable analyses, as the potential determinants of the severity of andropausal symptoms we included: 1) anthropometric parameters: age, body mass index (BMI); 2) parameters describing the severity of HF: New York Heart Association (NYHA) functional class, LVEF, plasma NT-proBNP, serum sodium, ischemic HF etiology, heart rate, systolic blood pressure; 3) other laboratory parameters: hemoglobin, white blood cells (WBC), platelets (PLT), eGFR, plasma total cholesterol, serum uric acid, serum hsCRP; 4) serum hormones: TT, eFT, DHEAS, IGF-1, E2, eFE2; 5) major comorbidities: previous myocardial infarction, arterial hypertension, atrial fibrillation, diabetes mellitus, previous stroke, and/or transient ischemic attack, chronic obstructive pulmonary disease (COPD), and peripheral vascular disease; 6) administered medications: angiotensin-converting enzyme inhibitor or/and angiotensin receptor blocker, β-blocker, spironolactone, loop diuretic, thiazide diuretic, digoxin, statin, and acetylsalicylic acid. During the construction of multivariable models, we included all variables that had been shown to be significant (P <0.05) determinants of the severity of andropausal symptoms in the univariable analyses.

Univariable and multivariable logistic regression analyses were applied to establish the variables associated with the higher prevalence of AS (defined as described above), separately in younger (40–59 years) and older (60–80 years) age groups of men with systolic HF. In the univariable analyses, as the potential risk factors for the higher prevalence of AS we included the same groups of variables as in linear regression analyses. During the construction of multivariable models, we included all the variables that had been shown to be significant risk factors for the higher prevalence of AS in univariable models (P <0.05). A P value less than 0.05 was considered statistically significant. Statistical analyses were performed using the STATISTICA 9.1. data analysis software system (StatSoft, Inc).

RESULTS

Baseline characteristics of men with systolic heart failure and healthy men We examined 279 healthy men aged from 40 to 59 years (mean BMI, 27.3 ±3.6 kg/m^2) and 83 healthy men aged from 60 to 80 years (mean BMI, 27.6 ±3.0 kg/m^2).

The baseline characteristics of men with HF are shown in TABLE 1. Men with HF aged from 60 to 80 years had lower values of heart rate, hemoglobin, WBC count, eGFR, uric acid, total cholesterol, and serum DHEAS, and higher values of serum sodium compared with men with HF aged from 40 to 59 years (all P <0.05). Men with HF aged from 60 to 80 years presented with more common ischemic etiology of HF and the prevalence of previous myocardial infarction, arterial hypertension, diabetes and COPD as well as the therapy with statin was higher in this age group (all P <0.05).

Severity of andropausal symptoms in men with systolic heart failure and healthy men In the younger age group (40–59 years), the severity of sexual, somatovegetative, and all andropausal symptoms (but not psychological ones) was greater in men with HF compared with healthy men (all P <0.001). In the older age group (60–80 years), the severity of psychological, somatovegetative, and all andropausal symptoms (but not sexual ones) was similar in men with HF and healthy peers (FIGURE 1).

Among men with HF, only the sexual symptoms were more severe in the older compared with the younger group of patients (P <0.001, TABLE 1).

TABLE 1 Baseline characteristics of men with systolic heart failure divided according to age

Clinical and laboratory variables	Men aged 40–80 years (n = 232)	Men aged 40–59 years (n = 120)	Men aged 60–80 years (n = 112)
age, y	60 ±9	53 ±5	68 ±4
BMI, kg/m^2	28.0 ±4.7	28.1 ±5.4	28.0 ±3.8
HR, bpm	76 ±13	78 ±13	73 ±13[b]
SBP, mmHg	121 ±19	118 ±18	123 ±19
HF etiology (CAD)	161 (69)	62 (52)	99 (88)[c]
NYHA class (I/II/III–IV)	40 (17)/125 (54)/67 (29)	27 (22)/63 (52)/30 (25)	13 (12)/62 (55)/37 (33)
LVEF, %	30 ±8	30 ±9	31 ±7
NT-proBNP, pg/ml	1258 (388–3222)	1265 (299–3490)	1220 (534–2879)
sodium, mmol/l	141 ±3	141 ±4	142 ±3[a]
hemoglobin, g/dl	14.3 ±1.5	14.7 ±1.4	13.9 ±1.5[c]
WBC, 10^9/l	7.2 ±2.0	7.6 ±2.2	6.8 ±1.6[b]
PLT, 10^9/l	201 ±57	208 ±55	195 ±58
eGFR, ml/min/1.73 m^2	75 ±21	80 ±20	69 ±20[c]
total cholesterol, mg/dl	184 ±54	193 ±62	174 ±44[a]
uric acid, mg/dl	6.86 ±2.11	7.35 ±2.18	6.38 ±1.92[b]
hsCRP, mg/l	2.39 (1.27–6.23)	3.08 (1.20–7.30)	2.12 (1.31–5.68)
serum hormone levels			
TT, ng/ml	4.12 ±1.88	4.31 ±1.89	3.93 ±1.87
eFT, pg/ml	73.4 ±40.0	78.6 ±42.7	68.1 ±36.5
DHEAS, ng/ml	546 (183–1081)	681 (281–1340)	374 (153–846)[b]
IGF-1, ng/ml	92.4 ±42.5	94.1 ±44.7	90.6 ±40.2
E2, pg/ml	31.1 ±12.8	29.6 ±12.3	32.6 ±13.3
eFE2, pg/ml	0.91 ±0.42	0.88 ±0.41	0.95 ±0.44
comorbidities			
previous myocardial infarction	135 (58)	52 (43)	83 (74)[c]
arterial hypertension	126 (54)	53 (44)	73 (65)[b]
atrial fibrillation	81 (35)	42 (35)	39 (35)
diabetes	65 (28)	26 (22)	39 (35)[a]
previous stroke and/or TIA	19 (8)	9 (8)	10 (9)
COPD	21 (9)	5 (4)	16 (14)[b]
peripheral vascular disease	35 (15)	16 (13)	19 (17)

Continued on page 5.

Determinants of the severity of andropausal symptoms in younger and older men with systolic heart failure In men with systolic HF aged from 40 to 59 years, in multivariable linear regression models, the more severe psychological symptoms were independently associated with the advanced NYHA class, low hemoglobin, high PLT count, and with the presence of COPD; the more severe sexual symptoms: with the advanced NYHA class, low hemoglobin, and the therapy with spironolactone; the more severe somatovegetative symptoms: with the advanced NYHA class and low hemoglobin; and the more severe andropausal symptoms (in total): with the advanced NYHA class; low hemoglobin, and the presence of COPD (all P <0.05, TABLE 2).

In men with systolic HF aged from 60 to 80 years, in multivariable linear regression models, the more severe psychological symptoms were independently associated with high total cholesterol and E2 and with the therapy with loop diuretic; the more severe sexual symptoms: with low LVEF and hemoglobin; the more severe somatovegetative symptoms: with low serum TT; and the more severe andropausal symptoms (in total): with low serum TT and the therapy with loop diuretic (all P <0.05, TABLE 3).

Prevalence of andropausal syndrome in men with systolic heart failure and healthy men In the age group of 40 to 59 years, the prevalence of AS was higher in men with HF compared with healthy men (28% vs. 7%, P <0.001, FIGURE 2). In the age group of 60 to 80 years, the prevalence of AS did not differ between men with HF and healthy peers (31% vs. 40%, P = 0.22, FIGURE 2).

Among men with systolic HF, the prevalence of AS was similar in subjects aged from 40 to 59 and those aged from 60 to 80 years (P = 0.53, TABLE 1).

treatment			
ACEI and/or ARB	221 (95)	114 (95)	107 (96)
β-blocker	222 (96)	115 (96)	107 (96)
spironolactone	75 (32)	41 (34)	34 (30)
loop diuretic	124 (53)	60 (50)	64 (57)
thiazide diuretic	58 (25)	33 (28)	25 (22)
digoxin	66 (28)	37 (31)	29 (26)
statin	177 (76)	80 (67)	97 (87)[c]
ASA	139 (60)	65 (54)	74 (66)
andropausal symptoms			
psychological, points	10.4 ±4.5	10.3 ±4.6	10.6 ±4.5
sexual, points	12.9 ±4.8	11.8 ±4.9	14.1 ±4.3[c]
somatovegetative, points	18.6 ±6.1	18.2 ±6.2	19.0 ±5.9
all symptoms, points	41.9 ±13.2	40.4 ±13.7	43.6 ±12.4
andropausal syndrome, n (%)	68 (29)	33 (28)	35 (31)

Data are presented as a mean ± standard deviation of the mean, a median (with lower and upper quartiles) or number (percentage), where appropriate. Andropausal syndrome was diagnosed according to Daig et al.,[20] if the Aging Males' Symptoms Rating Scale total score was ≥50 points.

a $P < 0.05$, **b** $P < 0.01$, **c** $P < 0.001$

For details see the "Methods" section. To convert the values for total cholesterol to mmol/l, multiply by 0.0259; uric acid to μmol/l by 59.48; TT to nmol/l by 3.467; eFT to pmol/l by 3.467; DHEAS to μmol/l by 0.00271; IGF-1 to nmol/l by 0.131; E2 and eFE2 to pmol/l by 3.671.

Abbreviations: ACEI – angiotensin-converting enzyme inhibitor, ARB – angiotensin receptor blocker, ASA – acetylsalicylic acid, BMI – body mass index, CAD – coronary artery disease, COPD – chronic obstructive pulmonary disease, DHEAS – dehydroepiandrosterone sulphate, eFE2 – estimated free estradiol, eFT – estimated free testosterone, eGFR – estimated glomerular filtration rate, E2 – estradiol, HF – heart failure, HR – heart rate, hsCRP – high-sensitive C-reactive protein, IGF-1 – insulin-like growth factor 1, LVEF – left ventricular ejection fraction, NT-proBNP – N-terminal pro-B-type natriuretic peptide, NYHA – New York Heart Association, PLT – platelets, SBP – systolic blood pressure, TIA – transient ischemic attack, TT – total testosterone, WBC – white blood cells

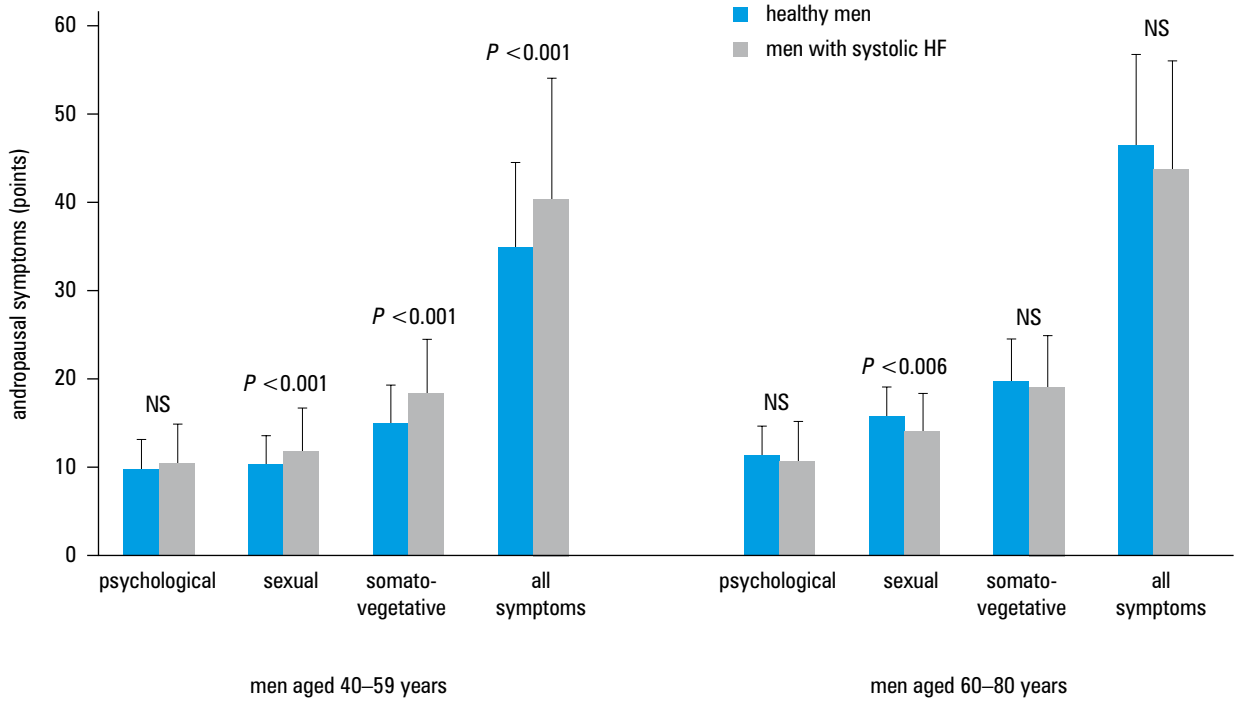

FIGURE 1 Severity of andropausal symptoms (means with standard deviations) in men with systolic heart failure and healthy men
Abbreviations: NS – nonsignificant, others – see **TABLE 1**

TABLE 2 Relationships between clinical and hormonal parameters and the severity of andropausal symptoms in men with systolic heart failure (aged 40–59 years, n = 120)

Variables	Andropausal symptoms							
	psychological		sexual		somatovegetative		all symptoms	
	univariable models	multivariable model corrected $R^2 = 27\%$[c]	univariable model	multivariable model corrected $R^2 = 25\%$[c]	univariable model	multivariable model corrected $R^2 = 30\%$[c]	univariable model	multivariable model corrected $R^2 = 33\%$[c]
age, y	–0.10	–	0.14	–	0.003	–	0.02	–
BMI, kg/m^2	–0.04	–	–0.16	–	–0.07	–	–0.10	–
HR, bpm	0.10	–	0.04	–	0.03	–	0.06	–
SBP, mmHg	0.02	–	–0.13	–	–0.10	–	–0.09	–
HF etiology (CAD vs. non-CAD)	–0.03	–	0.10	–	–0.01	–	0.02	–
NYHA class (I/II/III–IV)	0.41[c]	0.25[a]	0.45[c]	0.24[a]	0.53[c]	0.44[c]	0.54[c]	0.39[c]
LVEF, %	0.08	–	–0.07	–	0.01	–	0.01	–
NT-proBNP, pg/ml (ln)	0.13	–	0.25[b]	–0.03	0.18	–	0.21[a]	–0.09
sodium, mmol/l	–0.18	–	–0.28[b]	–0.09	–0.19[a]	0.07	–0.25[b]	–0.03
hemoglobin g/dl	–0.27[b]	–0.23[a]	–0.24[b]	–0.19[a]	–0.37[c]	–0.27[b]	–0.34[c]	–0.32[b]
WBC, 10^9/l	0.12	–	–0.02	–	0.16	–	0.10	–
PLT, 10^9/l	0.21[a]	0.20[a]	0.09	–	0.15	–	0.17	–
eGFR, ml/min/1.73 m^2	0.01	–	–0.23[a]	–0.05	0.05	–	–0.05	–
total cholesterol, mg/dl	–0.09	–	–0.18	–	–0.25[a]	–0.05	–0.21[a]	0.003
uric acid, mg/dl	0.06	–	0.14	–	0.07	–	0.11	–
hsCRP, mg/l (ln)	0.24[b]	0.02	0.18	–	0.26[b]	–0.04	0.26[b]	–0.02
serum hormone levels								
TT, ng/ml	0.07	–	–0.09	–	–0.05	–	–0.03	–
eFT, pg/ml	0.03	–	–0.13	–	–0.10	–	–0.08	–
DHEAS, ng/ml (ln)	–0.24[a]	–0.16	–0.21[a]	–0.06	–0.26[b]	–0.07	–0.27[b]	–0.10
IGF-1, ng/ml	0.02	–	–0.20[a]	–0.09	–0.11	–	–0.12	–
E2, pg/ml	–0.01	–	–0.05	–	0.001	–	–0.02	–
eFE2, pg/ml	–0.002	–	–0.02	–	–0.03	–	–0.02	–
comorbidities								
previous myocardial infarction, yes vs. no	–0.02	–	0.03	–	–0.03	–	–0.01	–
arterial hypertension, yes vs. no	0.12	–	0.03	–	0.07	–	0.08	–
diabetes, yes vs. no	–0.04	–	0.13	–	0.07	–	0.07	–
atrial fibrillation, yes vs. no	0.08	–	0.19[a]	0.02	0.20[a]	0.08	0.19[a]	0.05
previous stroke and/or TIA, yes vs. no	0.12	–	0.05	–	0.05	–	0.08	–

COPD, yes vs. no	0.20[a]	0.18[a]	0.19[a]	0.16	0.13	–	0.19[a]	0.18[a]
peripheral vascular disease, yes vs. no	0.15	–	0.11	–	0.20[a]	0.05	0.18[a]	–0.01
treatment								
ACEI and/or ARB, yes vs. no	0.21[a]	0.17	0.09	–	0.14	–	0.17	–
β-blocker, yes vs. no	0.03	–	0.06	–	–0.05	–	0.01	–
spironolactone, yes vs. no	0.17	–	0.37[c]	0.23[a]	0.20[a]	0.04	0.28[b]	0.12
loop diuretics, yes vs. no	0.14	–	0.26[b]	–0.01	0.21[a]	0.001	0.24[b]	0.02
thiazide diuretics, yes vs. no	–0.05	–	–0.02	–	–0.06	–	–0.05	–
digoxin, yes vs. no	0.05	–	0.17	–	0.15	–	0.15	–
statin, yes vs. no	–0.13	–	0.01	–	–0.09	–	–0.08	–
ASA, yes vs. no	–0.05	–	–0.03	–	–0.07	–	–0.06	–

Data are presented as standardized regression coefficients β (both in univariable and multivariable models). All variables shown to be significant determinants of the severity of andropausal symptoms in the univariable models ($P < 0.05$) were included in the multivariable models.

a $P < 0.05$, **b** $P < 0.01$, **c** $P < 0.001$

For details see the "Methods" section. For conversion factors see TABLE 1.

Abbreviations: ln – natural logarithm, others – see TABLE 1

FIGURE 2 Prevalence of andropausal syndrome in men with systolic heart failure and healthy men
Abbreviations: see TABLE 1 and FIGURE 1

Risk factors associated with the higher prevalence of andropausal syndrome in younger and older men with systolic heart failure In men with systolic HF aged from 40 to 59 years, in multivariable logistic regression models, the following variables were independently associated with the higher prevalence of AS: the advanced NYHA class, low hemoglobin and serum DHEAS, and high PLT count (all $P < 0.05$). In men aged from 60 to 80 years only reduced hemoglobin was borderline related to the higher prevalence of AS ($P = 0.07$) (TABLE 4 and 5).

DISCUSSION There are two major findings arising from the present study. Firstly, AS was very common in male patients with systolic HF. The prevalence of AS was 4 times higher in men with systolic chronic HF aged from 40 to 59 years compared with healthy men. In contrast, among subjects aged from 60 to 80 years, there was no difference in the prevalence of AS between men with vs. those without HF. Secondly, clinical and hormonal determinants of AS differed between the younger and older age groups of male patients with HF.

To the best of our knowledge, this is the first study reporting the prevalence of AS in chronic cardiovascular disease, while AS and andropausal symptoms have been documented in men with other chronic diseases, such as type 2 diabetes,[26] osteoporosis,[27] and in men treated with hormonal ablation therapy for prostate cancer.[28] We have shown that AS (diagnosed based on the severity of andropausal symptoms using the Polish version of the AMS scale with the highest cut-off, that is, the total AMS score 50 points or more)[21,22] is common in men with HF aged from 40 to 59 years, affecting 28% of these patients, which is significantly higher than in the age-matched local healthy male population (7%). Of note, the prevalence of AS in Polish healthy men in the age group of 40 to 59 years is similar as in a population sample of

TABLE 3 Relationships between clinical and hormonal parameters and the severity of andropausal symptoms in men with systolic heart faillure (aged 60–80 years, n = 112)

Variables	Andropausal symptoms							
	psychological		sexual		somatovegetative		all symptoms	
	univariable model	multivariable model corrected $R^2 = 18\%$[c]	univariable model	multivariable model corrected $R^2 = 8\%$[b]	univariable model	multivariable model corrected $R^2 = 13\%$[b]	univariable model	multivariable model corrected $R^2 = 12\%$[b]
BMI, kg/m^2	–0.10	–	0.09	–	0.05	–	0.02	–
HR, bpm	0.005	–	0.04	–	0.12	–	0.07	–
SBP, mmHg	0.11	–	–0.03	–	0.04	–	0.05	–
HF etiology (CAD vs. non-CAD)	–0.04	–	0.01	–	–0.01	–	–0.02	–
NYHA class (I/II/III–IV)	0.21[a]	0.09	0.07	–	0.22[a]	0.17	0.20[a]	0.12
LVEF, %	–0.11	–	–0.20[a]	–0.19[a]	–0.12	–	–0.17	–
NT-proBNP, pg/ml (ln)	0.06	–	–0.003	–	0.13	–	0.08	–
sodium, mmol/l	–0.04	–	–0.11	–	–0.15	–	–0.12	–
hemoglobin g/dl	–0.14	–	–0.24[a]	–0.23[a]	–0.16	–	–0.21[a]	–0.14
WBC, 10^9/l	–0.05	–	–0.07	–	0.002	–	–0.04	–
PLT, 10^9/l	0.15	–	0.02	–	0.12	–	0.12	–
eGFR, ml/min/1.73 m^2	–0.02	–	–0.08	–	0.03	–	–0.02	–
total cholesterol, mg/dl	0.20[a]	0.24[a]	0.10	–	0.10	–	0.16	–
uric acid, mg/dl	0.01	–	0.05	–	0.03	–	0.03	–
hsCRP, mg/l (ln)	0.01	–	0.02	–	0.12	–	0.07	–
serum hormone levels								
TT, ng/ml	–0.11	–	–0.11	–	–0.26[b]	–0.28[b]	–0.20[a]	–0.19[a]
eFT, pg/ml	–0.08	–	–0.11	–	–0.20[a]	–	–0.16	–
DHEAS, ng/ml (ln)	–0.12	–	–0.06	–	0.003	–	–0.06	–
IGF-1, ng/ml	–0.05	–	0.09	–	–0.03	–	–0.0001	–
E2, pg/ml	0.22[a]	0.24[a]	0.09	–	0.05	–	0.14	–
eFE2, pg/ml	0.22[a]	–	0.07	–	0.07	–	0.14	–
comorbidities								
previous myocardial infarction, yes vs. no	–0.09	–	0.06	–	–0.03	–	–0.03	–
arterial hypertension, yes vs. no	0.03	–	0.03	–	–0.02	–	0.01	–
diabetes, yes vs. no	0.02	–	0.07	–	0.10	–	0.08	–
atrial fibrillation, yes vs. no	–0.05	–	–0.03	–	–0.08	–	–0.06	–
previous stroke and/or TIA, yes vs. no	0.19[a]	0.17	0.03	–	0.01	–	0.09	–
COPD, yes vs. no	0.08	–	–0.16	–	0.06	–	0.002	–

peripheral vascular disease, yes vs. no	0.01	–	0.01	–	0.15	–	0.08	–		
treatment										
ACEI and/or ARB, yes vs. no	0.0003	–	–0.03	–	0.11	–	0.04	–		
β-blocker, yes vs. no	0.08	–	0.05	–	0.06	–	0.07	–		
spironolactone, yes vs. no	0.11	–	0.08	–	0.10	–	0.12	–		
loop diuretics, yes vs. no	0.27[b]	0.24[a]	0.18	–	0.25[b]	0.19	0.28[b]	0.22[a]		
thiazide diuretics, yes vs. no	–0.06	–	0.12	–	–0.09	–	–0.02	–		
digoxin, yes vs. no	–0.03	–	0.08	–	–0.01	–	0.02	–		
statin, yes vs. no	0.06	–	0.07	–	0.05	–	0.07	–		
ASA, yes vs. no	–0.08	–	–0.10	–	–0.09	–	–0.11	–		

Data are presented as standardized regression coefficients β (both in univariable and multivariable models). All variables shown to be significant determinants of the severity of andropausal symptoms in the univariable models ($P < 0.05$) were included in the multivariable models.

a $P < 0.05$, b $P < 0.01$, c $P < 0.001$

For details see the "Methods" section. For conversion factors see TABLE 1.

Abbreviations: see TABLES 1 and 2

959 German men aged from 40 to 69 years (7%), which was used to standardize the AMS scale.[21,22] In contrast, in the age group of 60 to 80 years, we found no differences either in the severity of andropausal symptoms (the subscores for 2 symptom clusters and the total AMS score) nor the prevalence of AS between men with systolic HF and healthy (although elderly) male subjects. We hypothesize that the occurrence of HF, a serious disease with multiple endocrine derangements,[18] at a relatively younger age markedly accelerates and enhances the process of male aging, which is associated with the development of andropausal symptoms.

In our study, we have focused exclusively on the clinical syndrome of self-reported andropausal symptoms (that is, associated with male aging) included and assessed in the validated AMS scale.[21,22] The applied methodological approach has enabled us not only to assess the prevalence of AS in men with systolic HF, but also to investigate whether this pathology is associated with hormonal milieu, including androgen deficiencies. We need to emphasize that we have not investigated the late-onset hypogonadism, the definition of which is based on the presence not only of the andropausal symptoms, but also the laboratory confirmation of gonadal hypogonadism.[6] We have observed some associations between the severity of andropausal symptoms and the hormonal status; however, the effects were not as strong as one might expect. There is no consensus regarding the causal relationships between androgen deficiencies and andropausal symptoms in aging men.[5,6] Morley et al.[29] observed that in 148 men aged from 23 to 80 years free and bioavailable testosterone (but not TT) inversely correlated with a total AMS score. Kratzik et al.[30] showed that in 664 manual workers aged from 40 to 60 years, high serum TT level reduced the risk for the presence of severe psychological andropausal symptoms. However, these findings are not unequivocal.[31,32] In men with HF aged from 40 to 59 years, DHEAS deficiency was associated with the higher prevalence of AS, while in those aged from 60 to 80 years reduced serum TT was accompanied by severe andropausal symptoms (high total AMS score). It should be emphasized that, beyond myocardial dysfunction, excessive sympathoexcitation and skeletal myopathy,[33] HF is characterized by the presence of marked anabolic deficiencies (DHEAS, TT, and IGF-1) with several unfavorable consequences (high mortality, impaired exercise capacity, augmented depressive symptoms).[18-20] This study provides another evidence on unfavorable effects of depleted androgen axes in men with systolic HF. These relationships are further supported by the observation that the therapy with spironolactone was independently related to the more severe sexual symptoms in male patients aged from 40 to 59 years. This finding is consistent with the available data on the antiandrogenic effect of this unselective aldosterone antagonist, due to its interference with

TABLE 4 Clinical and hormonal risk factors associated with the higher prevalence of andropausal syndrome in men with systolic heart failure (aged 40–59 years, n = 120)

Variables	Men with AS (n = 33)	Men without AS (n = 87)	Unit	Univariable model				Multivariable model			
				OR	CI	χ^2	*P*	OR	CI	χ^2	*P*
age, y	52 ±6	53 ±5	1 year	0.98	0.91–1.06	0.20	0.66	–	–	–	–
BMI, kg/m^2	26.8 ±5.3	28.6 ±5.3	1 kg/m^2	0.93	0.86–1.01	2.76	0.10	–	–	–	–
HR, bpm	78 ±13	78 ±14	1 bpm	1.00	0.97–1.03	0.00001	0.99	–	–	–	–
SBP, mmHg	116 ±21	119 ±18	5 mmHg	0.96	0.85–1.08	0.52	0.47	–	–	–	–
HF etiology (CAD)	15 (45)	47 (54)	yes vs. no	0.71	0.31–1.60	0.70	0.40	–	–	–	–
NYHA class (I/II/III–IV)	2 (6)/14 (42)/17 (52)	25 (29)/49 (56)/13(15)[c]	III–IV vs. II vs. I	4.25	2.05–8.80	15.53	<0.001	3.07	1.12–8.40	4.90	0.03
LVEF, %	31 ±11	30 ±8	1%	1.02	0.97–1.06	0.45	0.50	–	–	–	–
NT-proBNP, pg/ml	2149 (319–5662)	873 (280–3268)	1 ln pg/ml	1.26	0.96–1.67	2.74	0.10	–	–	–	–
sodium, mmol/l	139 ±5	141 ±3[a]	1 mmol/l	0.90	0.81–1.01	3.50	0.06	–	–	–	–
hemoglobin, g/dl	14.1 ±1.6	14.9 ±1.2[b]	1 g/dl	0.62	0.44–0.86	8.47	0.004	0.61	0.39–0.96	4.76	0.03
WBC, 10^9/l	7.9 ±1.7	7.5 ±2.4	1 10^9/l	1.08	0.91–1.29	0.79	0.37	–	–	–	–
PLT, 10^9/l	224 ±56	202 ±53[a]	10 10^9/l	1.08	1.00–1.17	3.91	0.048	1.17	1.03–1.33	5.92	0.01
eGFR, ml/min/1.73 m^2	79 ±24	80 ±18	1 ml/min/1.73 m^2	1.00	0.98–1.02	0.04	0.84	–	–	–	–
total cholesterol, mg/dl	175 ±46	200 ±65	10 mg/dl	0.92	0.84–1.01	3.46	0.06	–	–	–	–
uric acid, mg/dl	7.39 ±2.99	7.33 ±1.82	1 mg/dl	1.01	0.83–1.25	0.02	0.89	–	–	–	–
hsCRP, mg/l	5.02 (1.49–10.00)	2.06 (1.16–5.10)[b]	1 ln mg/l	2.11	1.24–3.59	7.83	0.005	1.00	0.44–2.25	0.0001	0.99
serum hormone levels											
TT, ng/ml	4.17 ±2.16	4.37 ±1.79	1 ng/ml	0.94	0.74–1.20	0.23	0.63	–	–	–	–
eFT, pg/ml	73.9 ±37.5	80.3 ±44.6	1 pg/ml	1.00	0.98–1.01	0.46	0.50	–	–	–	–
DHEAS, ng/ml	380 (175–677)	825 (428–1593)[b]	1 ln ng/ml	0.58	0.38–0.88	6.66	0.01	0.53	0.28–0.97	4.33	0.04
IGF-1, ng/ml	88.8 ±35.0	96.1 ±47.8	1 ng/ml	1.00	0.99–1.01	0.55	0.46	–	–	–	–
E2, pg/ml	27.6 ±12.5	30.4 ±12.2	1 pg/ml	0.98	0.95–1.02	1.02	0.31	–	–	–	–
eFE2, pg/ml	0.82 ±0.42	0.90 ±0.41	1 pg/ml	0.63	0.21–1.90	0.68	0.41	–	–	–	–
comorbidities											
previous myocardial infarction, yes	12 (36)	40 (46)	yes vs. no	0.67	0.29–1.55	0.90	0.34	–	–	–	–
arterial hypertension, yes	15 (45)	38 (44)	yes vs. no	1.07	0.48–2.43	0.03	0.86	–	–	–	–
diabetes, yes	7 (21)	19 (22)	yes vs. no	0.96	0.36–2.59	0.01	0.94	–	–	–	–
atrial fibrillation, yes	17 (52)	25 (29)[a]	yes vs. no	2.64	1.14–6.07	5.29	0.02	1.62	0.44–5.98	0.54	0.46
previous stroke and/or TIA, yes	3 (9)	6 (7)	yes vs. no	1.35	0.31–5.83	0.17	0.68	–	–	–	–

COPD, yes	3 (9)	2 (2)	yes vs. no	4.25	0.66–27.2	2.38	0.12	–	–	–	–
peripheral vascular disease, yes	5 (15)	11 (13)	yes vs. no	1.23	0.39–3.91	0.13	0.72	–	–	–	–
treatment											
ACEI or/and ARB, yes	33 (100)	81 (93)	yes vs. no	–	–	–	–	–	–	–	–
β-blocker, yes	32 (97)	83 (95)	yes vs. no	1.54	0.16–14.7	0.15	0.70	–	–	–	–
spironolactone, yes	18 (55)	23 (26)[b]	yes vs. no	3.34	1.44–7.76	8.02	0.005	2.78	0.78–9.84	2.58	0.11
loop diuretics, yes	19 (58)	41 (47)	yes vs. no	1.52	0.67–3.45	1.04	0.31	–	–	–	–
thiazide diuretics, yes	7 (21)	26 (30)	yes vs. no	0.63	0.24–1.65	0.89	0.34	–	–	–	–
digoxin, yes	13 (39)	24 (28)	yes vs. no	1.71	0.73–3.99	1.55	0.21	–	–	–	–
statin, yes	19 (58)	61 (70)	yes vs. no	0.58	0.25–1.34	1.67	0.20	–	–	–	–
ASA, yes	13 (39)	52 (60)[a]	yes vs. no	0.44	0.19–1.00	3.91	0.048	0.50	0.13–1.86	1.10	0.29

Data are presented as a mean ± a standard deviation of the mean, a median (with lower and upper quartiles) or n (with %), where appropriate. All variables shown to be significant ($P < 0.05$) risk factors for the presence of andropausal syndrome in the univariable models were included in the multivariable models. Andropausal syndrome was diagnosed according to Daig et al.,[20] if Aging Males' Symptoms Rating Scale total score was ≥50 points.

a $P < 0.05$, b $P < 0.01$, c $P < 0.001$

For details see the "Methods" section. For conversion factors see TABLE 1.

Abbreviations: CI – confidence interval, OR – odds ratio, others – see TABLES 1 and 2

the testosterone production, as well as the antagonism with androgen receptors in target tissues.[34]

In conclusion, AS affects almost one-third of men with HF, regardless of the age group. Clinical and hormonal determinants differ between younger and older male patients. There are some links between androgen deficiencies (TT, DHEAS), antiandrogen therapy (spironolactone), and andropausal symptoms. Endocrinological and sexual counseling is recommended in men with HF. Further studies are needed to establish whether the presence of AS is related to the worse outcome in these patients, and whether the androgen supplementation would reduce the severity of andropausal symptoms.

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TABLE 5 Clinical and hormonal risk factors associated with the higher prevalence of andropausal syndrome in men with systolic heart failure (aged 60–80 years, n = 112)

Variables	Men with AS (n = 35)	Men without AS (n = 77)	Unit	Univarable model				Multivariable model			
				OR	CI	χ^2	*P*	OR	CI	χ^2	*P*
age, y	69 ±4	67 ±4	1 year	1.07	0.97–1.17	1.80	0.18	–	–	–	–
BMI, kg/m^2	27.6 ±3.1	28.2 ±4.1	1 kg/m^2	0.95	0.86–1.06	0.72	0.40	–	–	–	–
HR, bpm	74 ±12	73 ±14	1 bpm	1.01	0.98–1.04	0.19	0.67	–	–	–	–
SBP, mmHg	122 ±23	124 ±18	5 mmHg	0.98	0.87–1.10	0.13	0.72	–	–	–	–
HF etiology (CAD)	31 (89)	68 (88)	yes vs. no	1.03	0.28–3.72	0.002	0.97	–	–	–	–
NYHA class (I/II/III–IV)	1 (3)/19 (54)/15 (43)	12 (16)/43 (56)/22 (29)	III–IV vs. II vs. I	2.03	1.03–4.02	4.25	0.04	1.62	0.78–3.37	1.73	0.19
LVEF, %	30 ±8	31 ±7	1%	0.97	0.92–1.03	1.06	0.30	–	–	–	–
NT-proBNP, pg/ml	1430 (533–3926)	1148 (535–2528)	1 ln pg/ml	1.17	0.84–1.64	0.89	0.35	–	–	–	–
sodium, mmol/l	141 ±3	142 ±3	1 mmol/l	0.93	0.80–1.07	1.13	0.29	–	–	–	–
hemoglobin, g/dl	13.5 ±1.7	14.1 ±1.3[a]	1 g/dl	0.73	0.54–0.97	4.67	0.03	0.76	0.57–1.03	3.23	0.07
WBC, 10^9/l	6.7 ±1.6	6.8 ±1.7	1 10^9/l	0.97	0.76–1.25	0.06	0.81	–	–	–	–
PLT, 10^9/l	205 ±72	190 ±50	10 10^9/l	1.04	0.97–1.12	1.53	0.22	–	–	–	–
eGFR, ml/min/1.73 m^2	67 ±23	70 ±19	1 ml/min/1.73 m^2	0.99	0.97–1.01	0.43	0.51	–	–	–	–
total cholesterol, mg/dl	180 ±43	172 ±44	10 mg/dl	1.00	0.99–1.01	0.65	0.42	–	–	–	–
uric acid, mg/dl	6.76 ±1.80	6.22 ±1.97	1 mg/dl	1.16	0.92–1.46	1.68	0.19	–	–	–	–
hsCRP, mg/l	1.95 (1.26–5.40)	2.19 (1.31–5.85)	1 ln mg/l	1.04	0.59–1.86	0.02	0.89	–	–	–	–
serum hormone levels											
TT, ng/ml	3.47 ±1.60	4.13 ±1.95	1 ng/ml	0.82	0.63–1.05	2.58	0.11	–	–	–	–
eFT, pg/ml	60.9 ±27.0	71.2 ±39.7	1 pg/ml	0.99	0.98–1.00	1.64	0.20	–	–	–	–
DHEAS, ng/ml	281 (160–562)	470 (153–1010)	1 ln ng/ml	0.75	0.50–1.12	2.09	0.15	–	–	–	–
IGF-1, ng/ml	89.5 ±49.9	91.1 ±35.7	1 ng/ml	1.00	0.99–1.01	0.03	0.86	–	–	–	–
E2, pg/ml	36.1 ±13.2	31.1 ±13.1	1 pg/ml	1.03	1.00–1.07	2.92	0.09	–	–	–	–
eFE2, pg/ml	1.06 ±0.45	0.90 ±0.42	1 pg/ml	2.38	0.85–6.63	2.81	0.09	–	–	–	–
comorbidities											
previous myocardial infarction, yes	26 (74%)	57 (74)	yes vs. no	1.01	0.38–2.67	0.00	0.98	–	–	–	–
arterial hypertension, yes	22 (63)	51 (66)	yes vs. no	0.86	0.37–2.00	0.12	0.73	–	–	–	–
diabetes, yes	13 (37)	26 (34)	yes vs. no	1.16	0.50–2.69	0.12	0.73	–	–	–	–
atrial fibrillation, yes	11 (31)	28 (36)	yes vs. no	0.80	0.34–1.90	0.26	0.61	–	–	–	–
previous stroke and/or TIA, yes	5 (14)	5 (6)	yes vs. no	2.40	0.64–9.03	1.71	0.19	–	–	–	–
COPD, yes	6 (17)	10 (13)	yes vs. no	1.39	0.45–4.22	0.34	0.56	–	–	–	–

peripheral vascular disease, yes	7 (20)	12 (16)	yes vs. no	1.35	0.48–3.84	0.33	0.56	–	–	–	–
treatment											
ACEI and/or ARB, yes	33 (94)	74 (96)	yes vs. no	0.67	0.10–4.28	0.18	0.67	–	–	–	–
β-blocker, yes	34 (97)	73 (95)	yes vs. no	1.86	0.20–17.7	0.30	0.58	–	–	–	–
spironolactone, yes	12 (34)	22 (29)	yes vs. no	1.30	0.55–3.10	0.37	0.54	–	–	–	–
loop diuretics, yes	25 (71)	39 (51)[a]	yes vs. no	2.44	1.02–5.80	4.13	0.04	1.86	0.74–4.69	1.76	0.18
thiazide diuretics, yes	6 (17)	19 (25)	yes vs. no	0.63	0.23–1.77	0.78	0.38	–	–	–	–
digoxin, yes	11 (31)	18 (23)	yes vs. no	1.50	0.61–3.69	0.81	0.37	–	–	–	–
statin, yes	32 (91)	65 (84)	yes vs. no	1.97	0.51–7.59	0.99	0.32	–	–	–	–
ASA, yes	21 (60)	53 (69)	yes vs. no	0.68	0.29–1.57	0.83	0.36	–	–	–	–

Data are presented as a mean ± a standard deviation of the mean, a median (with lower and upper quartiles) or n (with %), where appropriate. All variables shown to be significant ($P < 0.05$) risk factors for the presence of andropausal syndrome in the univariable models were included in the multivariable models. Andropausal syndrome was diagnosed according to Daig et al.,[20] if Aging Males' Symptoms Rating Scale total score was ≥50 points.

a $P < 0.05$, **b** $P < 0.01$, **c** $P < 0.001$

For details see the "Methods" section. For conversion factors see **TABLE 1**.

Abbreviations: see **TABLES 1**, **2**, and **4**

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Zespół andropauzalny u mężczyzn ze skurczową niewydolnością serca

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SŁOWA KLUCZOWE

niedobór hormonów anabolicznych, niewydolność serca, starzenie się mężczyzn, testosteron, zespół andropauzalny

STRESZCZENIE

WPROWADZENIE Starzenie się mężczyzn jest związane z występowaniem zespołu andropauzalnego (ZA), zależnego od postępującego z wiekiem zmniejszania się stężenia androgenów we krwi.

CELE Zbadano częstość występowania ZA, nasilenie objawów andropauzalnych i ich kliniczne oraz hormonalne determinanty u mężczyzn z niewydolnością serca (NS) i zdrowych mężczyzn.

PACJENCI I METODY Zbadano 232 mężczyzn ze skurczową NS w wieku 40–80 lat (klasa czynnościowa wg New York Heart Association [NYHA] I/II/III–IV: 17/54/29%, frakcja wyrzutowa lewej komory: 30 ±8%) i 362 zdrowych mężczyzn. Nasilenie 17 objawów andropauzalnych oceniono przy użyciu skali Aging Males' Symptoms Rating Scale.

WYNIKI U mężczyzn z NS w wieku 40–59 lat częstość występowania ZA i nasilenie objawów andropauzalnych było większe niż u zdrowych mężczyzn (odpowiednio: 28 *vs* 7%, 40 ±14 *vs* 35 ±10 punktów, wszystkie p <0,001), podczas gdy w grupie wiekowej 60–80 lat nie zaobserwowano różnic w częstości występowania ZA i nasileniu objawów andropauzalnych między mężczyznami z NS i zdrowymi mężczyznami (odpowiednio: 31 *vs* 40%, 44 ±12 *vs* 46 ±10 punktów, wszystkie p >0,1). U mężczyzn z NS w wieku 40–59 lat zaawansowana klasa NYHA, niskie stężenie hemoglobiny, duża liczba płytek krwi i niskie stężenie siarczanu dehydroepiandrosteronu w surowicy były niezależnie związane z częstszym występowaniem ZA (wszystkie p <0,05). U mężczyzn z NS w wieku 60–80 lat niskie stężenie hemoglobiny było granicznie związane z częstszym występowaniem ZA (p = 0,07).

WNIOSKI ZA występuje u 1/3 mężczyzn z NS niezależnie od grupy wiekowej. U młodszych i starszych pacjentów kliniczne i hormonalne determinanty nasilenia objawów andropauzalnych są odmienne. Poradnictwo endokrynologiczne i seksuologiczne jest zalecane u mężczyzn z NS.

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