Validity of the AMS questionnaire for screening hypogonadism in men with type 2 diabetes: A cross-sectional study

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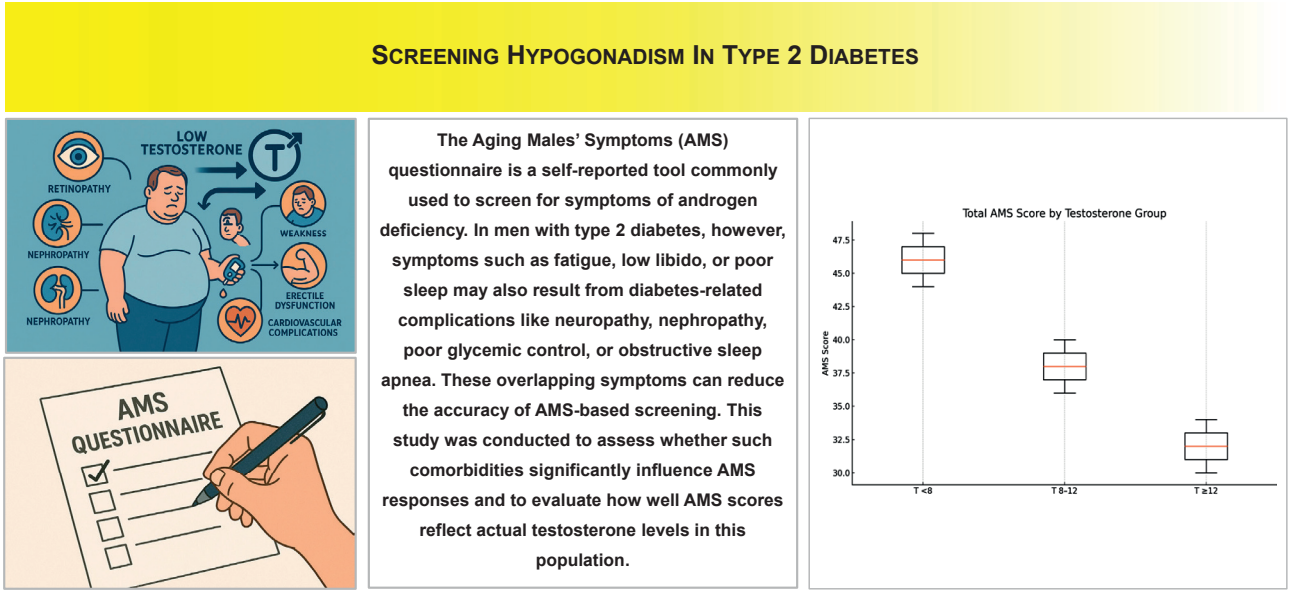
Background. Hypogonadism is common among men with type 2 diabetes mellitus (T2DM), but diagnosis can be confounded by overlapping symptoms from diabetic complications. The Aging Males' Symptoms (AMS) questionnaire is widely used for screening, yet its validity in this specific population remains unclear.
Objective. To evaluate the relationship between AMS scores and serum testosterone levels in men with T2DM, assess diagnostic accuracy at various AMS cut-offs, and examine the influence of diabetic comorbidities on AMS scores.
Methods. We conducted a cross-sectional study in 158 men with T2DM. Participants completed the AMS questionnaire and underwent morning testosterone measurement. Comorbidities such as neuropathy, nephropathy, and obstructive sleep apnea were assessed. AMS diagnostic performance was evaluated using different cut-off values (≥27, 30, 35, 40).
Results. AMS total score showed a modest inverse correlation with testosterone (ρ = –0.16, *P*=0.047), primarily driven by the physical subscale. Neuropathy and nephropathy were associated with higher sexual subscale scores. An AMS ≥27 cut-off had high sensitivity (91%) but poor specificity (21%) for testosterone <12 nmol/L.
Conclusion. AMS scores correlate weakly with testosterone levels in men with T2DM. Diabetic complications can elevate AMS scores independently, suggesting the need for caution and possibly higher cut-offs when using AMS for hypogonadism screening in this population.



Key words: Aging Males' Symptoms questionnaire, hypogonadism, testosterone, type 2 diabetes mellitus, screening, androgen deficiency, diagnostic cut-off, comorbidities

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INTRODUCTION

Most validation studies of the Aging Males' Symptoms (AMS) questionnaire have been conducted in general populations of aging men, without special attention to those with type 2 diabetes mellitus (T2DM) (ref.[1]). However, men with T2DM represent a distinct subgroup, with a higher prevalence of hypogonadism – often reported between 30% and 50% – than in the general population, as well as common complications such as neuropathy, nephropathy, and obesity[2-5]. Hypogonadism in men is characterized by low serum testosterone and a cluster of clinical symptoms including fatigue, reduced libido, erectile dysfunction, muscle weakness, and mood disturbances[6-8]. While diagnosis traditionally requires biochemical confirmation of low testosterone alongside these symptoms, the potential overlap between diabetic complications and androgen-deficiency manifestations can make clinical evaluation challenging.

The AMS questionnaire was originally developed as a self-reported tool to assess health-related quality of life and aging-related symptoms in men[9-11]. It has demonstrated favorable psychometric properties, including internal consistency and sensitivity to changes following testosterone therapy[11]. Nonetheless, in populations with a high burden of comorbidities, such as T2DM, the specificity and overall validity of the AMS for detecting hypogonadism have yet to be clarified. Most prior validation efforts did not incorporate detailed assessments of diabetic complications that could inflate AMS scores independently of testosterone deficiency.

In this study, we aimed to investigate the relationship between AMS scores and serum total testosterone levels among men with T2DM, specifically addressing whether established AMS cut-offs (e.g., ≥27) retain adequate diagnostic performance under the influence of neuropathy, nephropathy, retinopathy, obstructive sleep apnea, hypertension, dyslipidaemia, or hypovitaminosis D. By focusing on this high-risk group and examining the impact of these comorbidities, our work aims to clarify whether the AMS questionnaire can reliably identify true hypogonadism in men with T2DM or whether it may lead to excessive false-positive findings due to overlapping symptomatology.

Symptoms and descriptions	Never	Rarely	Occasionally	Often	Very Often
1. Loss of general sense of well-being (overall health status, subjective feelings)	☐	☐	☐	☐	☐
2. Joint and muscle pain (lower back, joints, hip pain, overall backache)	☐	☐	☐	☐	☐
3. Excessive sweating (sudden, unexpected sweating, hot flushes unrelated to stress)	☐	☐	☐	☐	☐
4. Sleep problems (difficulty falling asleep, waking up during the night, early waking with tiredness, poor sleep quality, insomnia)	☐	☐	☐	☐	☐
5. Increased need for sleep, frequent tiredness	☐	☐	☐	☐	☐
6. Irritability (aggressive feelings, easily upset by small things, moodiness)	☐	☐	☐	☐	☐
7. Nervousness (tension, restlessness, anxiety)	☐	☐	☐	☐	☐
8. Anxiety (feelings of panic)	☐	☐	☐	☐	☐
9. Physical exhaustion/lack of energy (overall decrease in performance, reduced activity, less interest in active rest, diminished efficiency, must force yourself to act)	☐	☐	☐	☐	☐
10. Reduced muscle strength (feeling of weakness)	☐	☐	☐	☐	☐
11. Depressive moods (low mood, sadness, tearfulness, loss of enthusiasm, mood swings, feelings of worthlessness)	☐	☐	☐	☐	☐
12. Feeling that the best times are over	☐	☐	☐	☐	☐
13. Burnout, feeling at your limit	☐	☐	☐	☐	☐
14. Reduced body hair growth	☐	☐	☐	☐	☐
15. Reduced sexual performance/frequency of sexual intercourse	☐	☐	☐	☐	☐
16. Decreased number of morning erections	☐	☐	☐	☐	☐
17. Reduced sexual desire/libido (reduced enjoyment of sex, low desire for sexual activity)	☐	☐	☐	☐	☐

Fig. 1. AMS questionnaire.

MATERIALS AND METHODS

Study design and population

This cross-sectional observational study included 158 men with T2DM, consecutively recruited from a diabetes outpatient clinic. The inclusion criteria were male sex, confirmed T2DM diagnosis, and age over 40 years. Exclusion criteria comprised known hypogonadism under current testosterone therapy, recent acute illness, or any condition interfering with hormonal assessment[12]. All participants provided written informed consent, and the protocol was approved by the local Ethics Committee of University Hospital Olomouc, Czech Republic and was supported by the Internal Grant Agency of Palacký University, grant number IGA: LF_2021_31.

Clinical and laboratory assessment

Anthropometric measurements (weight, height, BMI, waist circumference) were obtained. Morning fasting blood samples (7:00–9:00 a.m.) were analysed for total testosterone using standardized immunoassays[13,14]. Routine parameters, including HbA1c, fasting glucose, and vitamin D levels, were also measured.

AMS questionnaire

Each participant completed the validated Czech version of the Aging Males' Symptoms (AMS) questionnaire (Fig. 1). This 17-item tool uses a 5-point Likert scale covering three subscales: psychological (questions 6, 7, 8, 11, 13), physical/somatic (questions 1, 2, 3, 4, 5, 9, 10) and sexual (questions 12, 14, 15, 16, 17), yielding total scores between 17 and 85 points, with higher scores indicating more severe symptoms. A total AMS score ≥27 is commonly deemed "positive," suggestive of possible androgen deficiency[10,11].

Definition of hypogonadism

Biochemical hypogonadism was defined using two cutoff values for total testosterone: <12 nmol/L (suggesting androgen deficiency) and <8 nmol/L (severe deficiency). Patients were subsequently classified into three groups: T <8, T 8–12, T ≥12 (ref.[6,7,10,11])

Assessment of comorbidities

Diabetes-related complications, including neuropathy, nephropathy, retinopathy, cardiovascular disease, hypertension, and dyslipidemia, were identified using standard clinical criteria based on patient interviews and medical records.

Obstructive sleep apnea: syndrome (OSAS) severity was assessed by overnight monitoring of the apnea-hypopnea index (AHI), the lowest oxygen saturation, and the percentage of time with O_2 saturation below 90%. Home Sleep Apnea Testing (HSAT) is a validated alternative to conventional polysomnography (PSG), which enables the diagnosis of OSA outside the sleep laboratory, typically in the patient's home environment. We performed the home testing using the SomnoCheck micro device (Weinmann/Loewenstein, Germany).

Neuropathy: in addition to patient-reported symptoms, each participant underwent a comprehensive neurological evaluation comprising a 10-g monofilament test (protective sensation), a 128-Hz tuning fork (vibratory perception), and temperature plus sharp-dull discrimination testing.

Nephropathy: defined by albuminuria (≥30 mg/24 h) or eGFR <60 mL/min/1.73 m² for at least three months.

Retinopathy: assessed via a dilated fundus examination performed by an ophthalmologist.

Hypertension: systolic/diastolic blood pressure ≥140/90 mmHg or current antihypertensive therapy.

Dyslipidemia: diagnosed and managed according to European dyslipidemia guidelines or if patients were receiving lipid-lowering medication.

Statistical analysis

Descriptive statistics were generated for all variables. Nonparametric Kruskal-Wallis and Mann-Whitney U tests were used to compare AMS scores across testosterone groups and comorbidity status. Spearman's rank correlation coefficients assessed associations between AMS (total/subscales) and clinical parameters. Logistic regression was applied to examine the relationship between AMS positivity (≥27, 30, 35, 40) and hypogonadism (T <12 or <8 nmol/L). Sensitivity, specificity, and positive and negative predictive values were calculated. Analyses were performed in Python (pandas, scipy, statsmodels), with $P<0.05$ deemed significant.

RESULTS

Basic characteristics of the study population

A total of 158 men with T2DM participated. The mean age was 63 years (range 42–82), with a median T2DM duration of 10 years. The average BMI was 31.2 kg/m^2, with 89% classified as overweight/obese (BMI ≥25). Mean HbA1c was 7.8%, and fasting glucose averaged 8.4 mmol/L. Median serum total testosterone was 11.2 nmol/L (range 3.2–31.0). Overall, 48.1% (n=76) had T <12 nmol/L, and 13.9% (n=22) had T <8 nmol/L. The median AMS total score was 38 (IQR: 31–45), with 88% (n=139) screening "positive" by the conventional ≥27 cutoff (Table 1).

Comorbidities were frequent: 72% (n=114) had hypertension, 91% (n=144) dyslipidemia, 42% (n=66) neuropa-

Table 1. Basic characteristic of the study population.

Variable	Mean ± SD	Range
Age (years)	63.4 ± 13.9	42–82
BMI (kg/m²)	31.4 ± 6.7	19.6–52.0
Testosterone level (nmol/L)	11.2 ± 5.7	0.5–43.3
HbA1c (NGSP %)	7.8 ± 2.1	5.1–16.4
Total AMS score	40.0 ± 10.9	17.0–69.0
Duration of diabetes mellitus (years)	9.9 ± 8.0	0–42

Table 2. Complications of the study population, AHI (apnoe/hypopnoe Index), OSA (obstructive sleep apnea).

Complication	n (%)	Complication	n (%)
Neuropathy	66 (41.8%)	Dyslipidemia	144 (91.1%)
Retinopathy	16 (9.8%)	No OSA (AHI <5)	43 (27.4%)
Nephropathy	43 (27.2%)	Mild OSA (AHI 5–15)	57 (36.3%)
Ischemic heart disease	28 (18.4%)	Moderate OSA (AHI 15–30)	33 (20.7%)
Hypertension	114 (72.3%)	Severe OSA (AHI >30)	25 (15.6%)

thy, 27% (n=43) nephropathy, 10% (n=16) retinopathy, and 18% (n=28) had cardiovascular disease. The screening for sleep apnea using the Apnea-Hypopnea Index (AHI) revealed that 27.4% of patients were negative (AHI <5), 36.3% had mild sleep apnea (AHI 5–14.9), 20.7% had moderate sleep apnea (AHI 15–29.9), and 15.6% were affected by severe sleep apnea (AHI ≥30) (Table 2).

AMS score and testosterone levels

Serum testosterone showed a significant inverse correlation with the total AMS score (Spearman's ρ=−0.16; *P*=0.047). Among three testosterone groups (<8, 8–12, ≥12 nmol/L), AMS total scores differed significantly (Kruskal-Wallis *P*=0.042) (Fig. 2). Post hoc tests indicated that T <8 nmol/L patients exhibited higher AMS scores than those with T ≥12 nmol/L, whereas the 8–12 nmol/L "gray zone" did not significantly differ from either group.

The physical subscale correlated most strongly with testosterone (Spearman's ρ=−0.19; *P*=0.025), with T <8 nmol/L participants reporting significantly higher physical-symptom scores compared to those with normal testosterone (*P*=0.022). Sexual subscale differences were not statistically significant (*P*=0.108), and psychological subscale scores did not vary across testosterone groups (*P*=0.556).

Influence of comorbidities on AMS scores

Diabetic neuropathy correlated with higher total AMS scores (median 42 vs. 37, *P*=0.045), predominantly driven by the sexual subscale (median 13 vs. 11, *P*=0.017). Similarly, nephropathy was associated with elevated sexual subscale scores (median 13.5 vs. 11, *P*=0.016). Other comorbidities (hypertension, retinopathy, cardiovascular disease) did not significantly influence total or subscale AMS scores. These results suggest that diabetes-related complications, particularly neuropathy and nephropathy, may increase AMS scores independent of testosterone, raising the risk of false-positive screening results.

AMS cut-off analysis and screening performance

Using testosterone thresholds <12 and <8 nmol/L, AMS cut-offs of 27, 30, 35, and 40 were evaluated. At AMS ≥27, sensitivity reached 91% for T <12 nmol/L, whereas specificity was only 21% (PPV 52%, NPV 71%). Adjusting the threshold to AMS ≥30 modestly reduced sensitivity (84%) while improving specificity (28%). Higher thresholds (AMS ≥35, ≥40) provided further specificity gains (41% and 62%, respectively) at the expense of sensitivity (67% and 52%). The positive predictive value for detecting T <8 nmol/L remained low (15–24%) across all cut-offs, yet negative predictive values exceeded 90%.

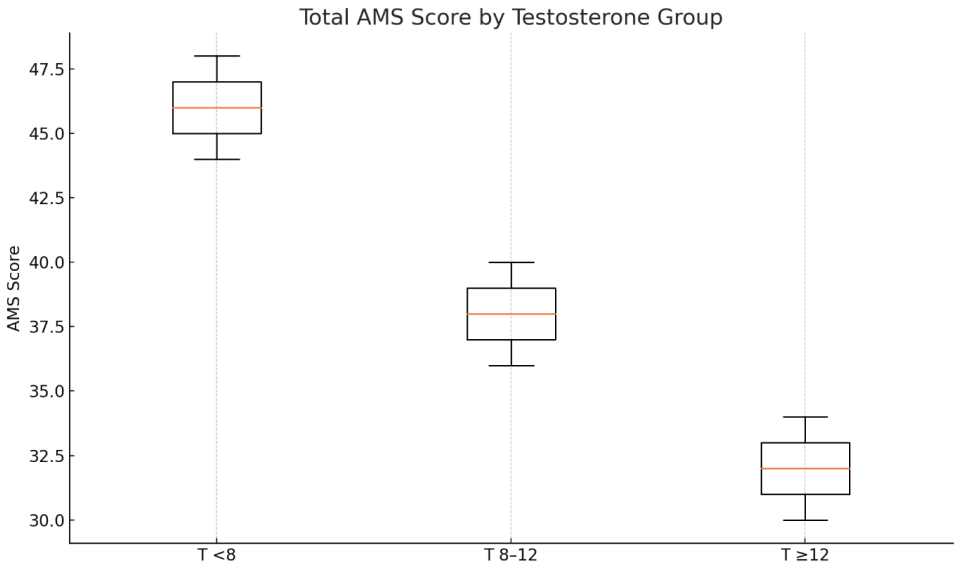

Fig. 2. Total AMS score by testosterone group.

Table 3. Table summarizes the strength and direction of associations between total AMS score and its subscales (physical, sexual, psychological) and selected variables. Statistically significant correlations (P<0.05) are indicated.

Variable 1	Variable 2	Spearman ρ	*P*	Significant (*P*<0.05)	Direction
AMS total	Testosterone	−0.16	0.047	Yes	Negative
AMS total	BMI	−0.00	0.960	No	Neutral
AMS total	HbA1c	0.07	0.400	No	Positive
AMS total	AHI	0.03	0.750	No	Positive
AMS total	Age	−0.12	0.28	No	Negative
AMS total	Duration of DM	0.15	0.18	No	Positive
Physical subscale	Testosterone	−0.19	0.025	Yes	Negative
Sexual subscale	Neuropathy	0.17	0.017	Yes	Positive
Sexual subscale	Nephropathy	0.18	0.016	Yes	Positive
Psychological subscale	Testosterone	−0.09	0.260	No	Negative
Testosterone	AHI/RDI	−0.10	0.240	No	Negative
Testosterone	Vitamin D	0.12	0.140	No	Positive

DISCUSSION

Our cross-sectional study in men with T2DM revealed a modest but statistically significant inverse relationship between AMS scores and serum testosterone levels. This link was pronounced in individuals with testosterone <8 nmol/L; those in the 8–12 nmol/L range resembled the ≥12 nmol/L group. Notably, the physical subscale best reflected androgen deficiency, whereas the sexual subscale was less discriminative, possibly due to confounding by diabetes complications. These findings are consistent with previous studies, which also reported that the correlation between AMS scores and testosterone is strongest in men with overt hypogonadism, and that symptom-based questionnaires tend to lose discriminative power in the borderline range of testosterone (8–12 nmol/L) (ref.[2,8]). Similarly, Rastrelli et al. emphasized that comorbid conditions in men with T2DM may blur the clinical picture, particularly in domains related to sexual function[2].

Neuropathy and nephropathy specifically boosted sexual subscale scores, illustrating how certain comorbidities can mimic or amplify androgen-deficiency symptoms. Although obstructive sleep apnea was evaluated via AHI and oxygen saturation[15], we observed no conclusive impact on AMS scores, despite a trend toward lower testosterone with more severe apnea.

The standard AMS ≥27 threshold delivered high sensitivity (91%) for hypogonadism (T <12 nmol/L) but poor specificity (21%). Slightly raising the cut-off to 30 or 35 improved specificity yet reduced sensitivity. These findings mirror concerns about overdiagnosis in comorbid populations[8,9,16], where a balance between sensitivity and specificity is needed to avoid unnecessary follow-up testing. A simplified AMS variant showed promise in general populations, but our data underline the importance of population-specific validation, particularly for men with T2DM (ref.[17]).

Limitations include the cross-sectional design, single total testosterone measurement, and potential confounding from unmeasured factors such as depression or medication effects. Although only total testosterone was measured, free or bioavailable testosterone may offer a better reflection of androgen status in obese individuals[18]. However, the pragmatic scope of this study aligned with current guidelines favoring total testosterone as an initial screening[6-7]. In clinical practice, borderline values (8–12 nmol/L) warrant confirmatory assessment, including SHBG and free testosterone[19-20]. Nonetheless, the chosen approach, a single morning testosterone draw, aligns with practical screening guidelines[6]. While the overall sample size of 158 men provided sufficient statistical power to address the primary study question, it was more limited for secondary or exploratory subgroup analyses, such as stratification by age, where statistical significance may have been attenuated Additional prospective studies could assess whether combining AMS scores with clinical/biochemical markers enhances detection accuracy and cost-effectiveness.

Beyond its diagnostic role, the AMS questionnaire also offers practical advantages in routine care. It provides a structured way to explore a broad spectrum of symptoms, including sensitive areas such as sexual function, which are often not spontaneously discussed during standard diabetes follow-up visits. In this respect, the questionnaire may serve as a useful communication aid, helping clinicians to identify concerns that might otherwise remain unaddressed[21].

CONCLUSION

In men with T2DM, AMS scores correlate only moderately with total testosterone, primarily in severe hypogonadism. Diabetic complications, especially neuropathy and nephropathy, can inflate AMS scores, reducing specificity. Based on our analysis, the conventional cut-off of ≥27 showed high sensitivity but very poor specificity, leading to many false-positive results. A threshold of ≥30 provided the best balance between sensitivity and specificity in this cohort, and may therefore represent a more pragmatic cut-off for clinical use in men with type 2 dia-

betes. Future research should address whether integrating AMS with other clinical and biochemical markers can refine hypogonadism screening in this high-risk population. Besides its diagnostic utility, the AMS questionnaire can serve as a practical tool to open discussion on sensitive issues, such as sexual dysfunction, that are often overlooked in standard diabetes care.

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Author contributions: JO: conceived and designed the study, supervised the project, and drafted the manuscript; KM, ES: recruitment of patients and clinical data collection; MS, LJ: performed clinical examinations and contributed to data interpretation; RA: statistical analyses and results interpretation. All authors critically revised the manuscript, approved the final version, and agree to be accountable for the accuracy and integrity of the work.

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