The prevalence and predictors of androgen deficiency in Taiwanese men with lower urinary tract symptoms

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ABSTRACT

Objective: To evaluate the prevalence and associated factors of androgen deficiency (AD) in men with lower urinary tract symptoms (LUTS).

Materials and methods: From November 2011 to March 2012 in a single institute, we enrolled 122 men with LUTS. AD was defined as having a total testosterone level less than 3 ng/mL. The underlying disease and associated factors related to AD were analyzed with univariate and multivariate methods.

Results: Of the 122 patients, 55.3% reported having AD. The AD group had a larger waist circumference (WC) and higher blood white cell count (WBC) in the univariate analysis but in multivariate analysis, only WC > 90 cm was an independently associated factor of AD (OR: 2.864, p = 0.042).

Conclusion: A considerable portion of men with LUTS had AD. The major associated factor of AD was WC > 90 cm in order to identify and treat these patients earlier to improve symptoms of LUTS and life quality.

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1. Introduction

Hypogonadism in men is a clinical syndrome that results from failure to produce physiological levels of testosterone (androgen deficiency, AD), which is usually defined as a testosterone level below 3 ng/mL. Diagnosis of AD in men poses several challenges since the symptoms and signs are nonspecific and depend on age, severity, and duration of AD, and medical comorbidities. One health screening study of aging Taiwanese men over 40 years of age revealed that the prevalence of AD and symptomatic AD were 24.1% and 12.0%, respectively. Older age, obesity, and diabetes mellitus were associated with increased incidence of AD and symptomatic AD. Another study by Liu et al., 3 which evaluated the prevalence and predictors of AD in Taiwanese men with Type 2 diabetes mellitus (T2DM), found that one third of Taiwanese men with T2DM have AD. Obesity is the major predictor and potential modifiable risk factor of AD. AD is associated with visceral fat accumulation, metabolic syndrome, T2DM, increased inflammatory cytokines, and coagulation factors. There is also increasing evidence linking AD with an increased risk of cardiovascular disease and all-cause mortality. It is therefore important for clinicians to recognize this high risk population as early as possible.

Lower urinary tract symptoms (LUTS) are experienced by individuals with disorders that affect the lower urinary tract, such as benign prostate hyperplasia, sensory bladder disorders, sphincter weakness, and other neurologic diseases. The European Prospective Investigation into Cancer and Nutrition study showed that LUTS was found to occur in 62.5% of men and 66.6% of women aged ≥ 40 years. 6 Since LUTS has been linked to metabolic syndrome, people with LUTS may have an increased risk of cardiovascular disease. One nationwide population-based study in Taiwan reported that compared with people who do not have LUTS, those who do face a 1.29-fold higher risk of developing acute cardiovascular events. 8

Since AD and LUTS are only reportedly associated with metabolic syndrome and cardiovascular disease, the relationship between the two diseases remains undetermined. Estimates of the prevalence of AD in men with LUTS have been inconsistent, depending on the study sample and design, as well as the definition...
of AD. One study by Schatzl et al. revealed that hypogonadism was prevalent in approximately one-fifth of elderly men with LUTS. However, another study by Litman et al. found that plasma total and bioavailable testosterone were not related to urological symptoms in men with LUTS. Due to the inconsistent reports as well as the scarcity of reports of the prevalence and predictors of AD in men with LUTS in Taiwan, we conducted a cross-sectional study to identify the prevalence and other associated factors in such patients.

2. Materials and methods

2.1. Patient enrollment and data collection

This study was approved by the institutional review board at the Chang Gung Memorial Hospital. We enrolled 122 consecutive patients with LUTS in the Urologic Out-clinic Department at Kaohsiung Chang Gung Memorial Hospital from November 2011 to March 2012. Exclusion criteria consisted of patients having active infection, urological malignancy (prostate cancer or bladder cancer), or using hormones, antifungal drugs, or steroidal agents. The measured biochemical data included fasting blood sugar, triglycerides, low density lipoprotein-C, high density lipoprotein-C, glycosylated hemoglobin, blood white blood cell (WBC), serum creatinine, prostate-specific antigen, and serum total testosterone. AD was defined as having a level of total testosterone less than 3 ng/mL. Recorded baseline characteristics included age, body weight, body height, and waist circumference (WC), and underlying diseases [prediabetes (pre-DM), hypertension, coronary heart disease, stroke, and hyperlipidemia].

2.2. Statistical analyses

The data were analyzed using SPSS 17.0. The comparison between the groups was performed with Pearson’s Chi-square test for categorical variables and independent t test for continuous variables. Binary logistic regression for multivariate analysis was applied to assess the contribution of predictive factors of AD. The level of significance was taken to be \( p < 0.05 \).

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>1.048 (0.994—1.105)</td>
<td>0.083</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>1.006 (0.934—1.083)</td>
<td>0.878</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.348 (0.893—2.035)</td>
<td>0.180</td>
</tr>
<tr>
<td>WBC</td>
<td>1.351 (0.895—2.039)</td>
<td>0.153</td>
</tr>
<tr>
<td>HTN</td>
<td>1.146 (0.382—3.443)</td>
<td>0.808</td>
</tr>
<tr>
<td>Waist &gt; 90 cm</td>
<td>2.864 (1.041—7.878)</td>
<td>0.042</td>
</tr>
</tbody>
</table>

BMI = body mass index; CI = confidence interval; HTN = hypertension; OR = odds ratio; WBC = white blood cells.

3. Results

Data from a total of 122 male patients with LUTS were collected. Among the patients, 55.7% (68 patients) had AD. The baseline demographic data and univariate analysis are shown in Table 1. The prevalence of hyperlipidemia, pre-DM, coronary artery disease, and hypertension in Taiwanese men with AD were 23.5%, 48.5%, 4.4%, and 46.3%, respectively. Compared with the non-AD group, there was no statistical difference among these associated factors, but there was a trend of higher age in the AD group (62.5 ± 7.9 years vs. 60.3 ± 7.2 years, \( p = 0.114 \)).

In the univariate analysis of associated factors, the AD group had a larger WC (91.2 ± 7.7 cm vs. 87.8 ± 9.0 cm, \( p = 0.027 \)) and higher WBC level (6.7 ± 1.5 \( \times \) 10³/mm³ vs. 6.1 ± 1.1 \( \times \) 10³/mm³, \( p = 0.019 \)). Both predictors were found to be statistically significant. However, in the multivariate analysis, only WC > 90 cm was an independent factor associated with AD, which, when compared with WC < 90 cm, conferred a 2.864-fold risk for AD. Age had a borderline association of AD (odds ratio: 1.048, \( p = 0.083 \); Table 2).

4. Discussion

This was a hospital-based study investigating the prevalence and predictors of AD in men with LUTS in a medical center in Taiwan. We found that the prevalence of AD was estimated to be 55.7% in men with LUTS in our Urology Outpatient Clinic. There was a considerable portion of patients both with LUTS and AD that had hyperlipidemia, pre-DM, coronary artery disease, and hypertension (23.5%, 48.5%, 4.4%, and 46.3%, respectively). Although there was no statistical difference in the prevalence of these associated factors compared with those of the non-AD group, we still need to pay attention to these baseline conditions to identify potential AD patients. As for the other parameters, elevated WBC and WC were significantly associated with AD and increased body weight was borderline associated with AD in the univariate analysis. In the multivariate analysis, however, only men with LUTS with elevated WC revealed a significantly higher risk for AD, and elderly men with LUTS showed a borderline risk for AD. Men with LUTS and WC > 90 cm had a 2.86-fold higher risk for AD than those who had WC < 90 cm. Given that some previous studies found a positive association between metabolic syndrome and LUTS, we11 while other studies reported conflicting data, we11,15 analyzed the parameters in metabolic syndrome (including hyperglycemia, hypertension, triglycerides, high density lipoprotein-C, WC) separately and determined that WC can be seen as an indicator of AD in men with LUTS in Taiwan.

Although previous studies have investigated the relationship between AD and LUTS, no consistent correlations were found. In the Third National Health and Nutrition Examination Survey, Rohmann et al.15 evaluated the association of circulating sex steroid hormone with LUTS. No consistent associations were observed between circulating and free testosterone and risk of LUTS. In Kim et al.’s investigation of the relationship between nocturia and decreased serum testosterone in men with LUTS in Korea,
decreased testosterone was a significant independent risk for overall nocturia, especially nocturnal polyuria, and patients with low serum testosterone showed increased nocturnal urine output. Yassin and colleagues proposed the potential role of testosterone in the urinary tract in that testosterone may interact with LUTS via several possible mechanisms, such as by acting on nonopiate synaptic receptors in the bladder detrusor muscle and by stimulating nitric oxide production in the urinary tract and bladder. Despite the inconsistencies so far observed in the relationship between AD and LUTS, replacement for testosterone for AD being able to improve the life quality in men with LUTS.

In our study, increased WC rather than body mass index is an independent indicator of AD and in men with LUTS. One epidemiological investigation by Svartberg et al. enrolled 1548 men aged 25–84 years surveyed the correlation between serum steroid hormones and central obesity. They found that all hormone associations were stronger for WC than for body mass index and suggested that WC should be the preferred anthropometric measurement in predicting endogenous testosterone levels. Measuring WC is a simple way to predict intra-abdominal fat volume or area and where it is placed around the body and increased intra-abdominal fat is associated with an increase in insulin resistance and systemic inflammation, which may contribute to low testosterone levels. In addition, total and free testosterone levels have been observed to decrease with increasing age in longitudinal studies, and thus it is not surprising in our study that older age was associated with a borderline rise in the risk of AD.

This study still has certain limitations. Firstly, since these patients were recruited from a single medical center in Taiwan, selection bias should be considered. The phenotype and disease severity of patients with LUTS might be different from those that were followed by primary physicians in local clinics. Further studies enrolling patients from different levels of medical facility may provide more comprehensive and detailed information. Secondly, this study was not designed as a prospective study and could not detect any causal relationship between WC and AD in men with LUTS. Since it was not our aim to find the underlying mechanism between WC and AD, our study nonetheless provides clues for the clinician to detect AD in men with LUTS early and improve their life quality. Finally, the case number of this study is relatively small and includes a wide variety of patients, so further research is necessary to determine the risk factors of AD in LUTS men.

In conclusion, this study found that increased WC is a marker or indicator of AD in men with LUTS. We suggest that WC be measured routinely in men with LUTS, and that more attention be paid to those of older age and WC > 90 cm. Physicians should be alerted to this association so that they may be able to identify and treat these patients earlier to improve symptoms of LUTS and life quality.

Conflicts of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in the manuscript.

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