Effect of weight reduction on the severity of lower urinary tract symptoms in obese male patients with benign prostatic hyperplasia: A randomized controlled trial

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Purpose: We assessed whether weight reduction is an effective intervention for the management of lower urinary tract symptoms (LUTS) and investigated the relationship between obesity and LUTS.

Materials and Methods: This was a prospective randomized controlled trial that enrolled obese men older than 50 years with LUTS. The study period was 52 weeks. All patients received standardized alpha-adrenergic blocker therapy for the treatment of benign prostatic hyperplasia (BPH) during the run-in period. Patients were randomized to receive either a standardized prerecorded video program on the general principle of weight reduction or a comprehensive weight reduction program. Patients were assessed at different time points with symptom assessment, uroflowmetry, transrectal ultrasound, and metabolic assessment.

Results: Sixty-five patients were allocated to each study arm. After the study period, no significant difference in weight reduction was found between the two arms. When the pre- and postintervention parameters were compared, none were statistically different between the 2 arms, namely nocturia, International Prostate Symptom Score, quality of life assessment, and uroflowmetry parameters. When the whole study population was taken as a single cohort, these parameters were also not significantly different between the group with a body mass index of 25 to <30 kg/m² and the group with a BMI of 30 to 35 kg/m².

Conclusions: We found no association between obesity and LUTS. This could have been due to the less marked weight difference in our cohort. Whereas weight reduction may be an effective measure to improve LUTS, the implementation of a successful program remains a challenge.

Keywords: Exercise; Lower urinary tract symptoms; Obesity
suggested that obese men are more likely to have LUTS [34], weight reduction could be one such intervention. Body size and composition have long been hypothesized to influence the risk of prostate hyperplasia [5]. While some data have suggested that weight gain worsens LUTS, few data are available to address whether the reverse is true, i.e., if weight loss can improve LUTS. Furthermore, the postulated relationship between obesity and LUTS remains controversial. Contradictory evidence about this relationship is present in the literature [6]. With this background, we conducted a prospective randomized controlled trial to investigate whether weight reduction would be an effective intervention for LUTS and assessed the relationship between obesity and LUTS among patients with BPH.

MATERIALS AND METHODS

This was a prospective randomized controlled trial. The study was approved by the local ethics and research committee. Written informed consent was given by all participants before entering the study. Obese men older than 50 years who attended our urology clinic for LUTS were enrolled. A standard investigation protocol that included a general clinical evaluation with digital rectal examination, transrectal ultrasound (TRUS), blood tests, prostate-specific antigen (PSA) measurement, uroflowmetry, and assessment of International Prostate Symptom Score (IPSS) and quality of life (QoL) score was performed during enrolment. Baseline medical history was documented. Details of the inclusion and exclusion criteria are listed in Table 1.

The study period was 52 weeks. Before the study, patients had been using different alpha blockers for relief of LUTS. Standardized alpha-adrenergic blocker therapy (tamsulosin 0.4 mg oral controlled absorption system) for the medical treatment of BPH/LUTS was given to all patients during the run-in period. Subjects were reassessed at 4 weeks after the run-in period for assessment of baseline parameters. After these assessments, patients were randomly assigned to receive either a standardized pre-recorded video program on the general principle of weight reduction or a comprehensive weight reduction program.

The comprehensive weight reduction program included 3 aspects, namely, an integrated assessment, a weight reduction protocol, and medical nutrition therapy. The integrated assessment included assessment of dietary and activity patterns together with appropriate counseling. Then a weight reduction protocol was devised and supervised by a registered physiotherapist with an American College of Sports Medicine exercise specialist background. The protocol consisted of an initial stage, an improvement stage, and a maintenance stage. Concerning the medical nutrition therapy, it was formulated by dietitians to address individual needs for weight reduction.

After randomization, patients were assessed at different time points over the course of 48 weeks with symptom assessment, EuroQol visual analogue scale (EQ VAS), uroflowmetry, TRUS, and metabolic assessment. The EQ VAS is a visual scale from 0 to 100 for a patient’s subjective assessment of his or her own health state. The higher the score, the better the patient perceives his health state. The follow-up protocol of the study is illustrated in Fig. 1.

With the aim of assessing the effect of a comprehensive weight reduction program on the severity of LUTS, the primary end point was a change in IPSS at the end of the trial compared with baseline. Secondary end points included change in uroflowmetry parameters, change in nocturia episodes, and change in prostate volume.

On the basis of our center's database of more than 1,000 patients with LUTS, the mean total IPSS for patients with moderate to severe symptoms is 19 with a standard deviation of 7. A sample size of 65 in each group would have 80% power to detect a 4-point difference in means, with a 0.05 two-sided significance level and a loss to follow-up rate of 30%.

Descriptive statistics were used to characterize the demo-

Table 1. Inclusion and exclusion criteria

| Inclusion criteria                      | Exclusion criteria                                      |
|----------------------------------------|--------------------------------------------------------|
| Men aged ≥50 years old                 | Patients with urethral stricture, neurogenic bladder, or structural abnormality |
| BMI, 25–35 kg/m²                        | Patients on long-term catheterization or intermittent self-catheterization |
| Moderate to severe lower urinary tract symptoms (IPSS>7) | Patients with prostate cancer or bladder cancer |
| Qmax, 5–15 mL/s, PVR<150 mL             | Patients on 5α-reductase inhibitors, phytotherapy, or hormonal therapy |
| TRUS prostate volume>30 mL              | Patients who cannot tolerate tamsulosin OCAS |
|                                        | Patients with poor cardiac status (NYHA class III or above) or other medical |
|                                        | Conditions that are not suitable for intense exercise or weight reduction program |

BMI, body mass index; IPSS, International Prostate Symptom Score; Qmax, maximal flow rate; PVR, post-void residuals; TRUS, transrectal ultrasound; OCAS, oral controlled absorption system; NYHA, New York Heart Association.
graphic data, uroflowmetry results, prostate volume, IPSS and QoL scores, and body mass index (BMI). Comparison of continuous data between the two arms was done with t-tests or analysis of variance if the data were of normal distribution and with the Mann Whitney U test or Kruskal-Wallis test if the data were ordinal or skewed. Values of \( p < 0.05 \) were considered statistically significant. The IBM SPSS Statistics ver. 22.0 (IBM Co., Armonk, NY, USA) was used for all calculations.

**RESULTS**

A total of 180 patients were assessed for eligibility, 50 patients were excluded for various reasons, and in the end 130 patients were randomly assigned into the two study arms (Fig. 2). Sixty-five patients were allocated to...
general weight reduction advice and 65 patients to a comprehensive weight reduction program. In the end, 117 patients completed the study. Patient characteristics are listed in Table 2. There were no significant differences in baseline characteristics between patients in the control arm and those in the active arm.

After the 48-week study period, we noted changes in BMI of \(-0.4\pm0.9\ kg/m^2\) and \(-0.4\pm0.8\ kg/m^2\) in the control arm and the active arm, respectively. The differences between the pre- and postintervention parameters were compared between these two groups, namely, nocturia episodes, total IPSS, IPSS irritative score subset (sum of score of IPSS questions 2, 4, and 7), and EQ VAS. None of these parameters was significantly different between the control and active arms (Table 3).

In view of these negative results, we looked at the whole study population as a single cohort of obese men with LUTS and tried to identify whether there was a relationship between obesity and LUTS. Subjects were categorized into two groups according to their baseline BMI,

| Table 2. Subject demographics and characteristics |
|------------------|--------|--------|--------|
| Characteristic | Control | Active | p-value |
| No. of subjects | 57 | 60 | |
| Mean age (y) | 63.3±7.8 | 66.5±6.9 | 0.88 |
| Weight (kg) | 75.2±6.6 | 74.3±8.4 | 0.53 |
| Height (m) | 1.66±0.05 | 1.65±0.07 | 0.51 |
| BMI (kg/m²) | 27.4±1.9 | 27.3±2.0 | 0.51 |
| Nocturia episodes | 2.5±1.2 | 2.6±1.2 | 0.63 |
| Total IPSS | 17.6±6.3 | 17.3±6.9 | 0.80 |
| Irritative score | 7.6±3.3 | 8.1±2.9 | 0.44 |
| IPSS QoL score | 3.3±0.9 | 3.2±1.2 | 0.52 |
| EQ VAS | 73.8±15.8 | 74.5±13.8 | 0.81 |
| Qmax (mL/s) | 10.4±4.3 | 10.2±3.9 | 0.81 |
| PVR (mL) | 57.6±79.2 | 37.5±48.1 | 0.27 |
| Prostate size (mL) | 52.1±32.3 | 56.6±31.1 | 0.89 |
| PSA (μg/L) | 4.21±4.62 | 5.14±4.17 | 0.27 |

Values are presented as mean±standard deviation.
BMI, body mass index; IPSS, International Prostate Symptom Score; QoL, quality of life; EQ VAS, EuroQol visual analogue scale; Qmax, maximal flow rate; PVR, postvoid residuals; PSA, prostate-specific antigen.

| Table 3. Difference between pre- and postintervention parameters |
|------------------|--------|--------|
| Parameter | Control | Active | p-value |
| BMI (kg/m²) | \(-0.4\pm0.9\) | \(-0.4\pm0.8\) | 0.88 |
| Nocturia episodes | \(-0.1\pm0.9\) | \(-0.1\pm0.9\) | 0.78 |
| Total IPSS | \(-0.7\pm6.4\) | \(-1.8\pm6.6\) | 0.38 |
| IPSS irritative score | \(-0.2\pm2.6\) | \(-0.6\pm2.7\) | 0.35 |
| IPSS QoL score | \(-0.3\pm1.0\) | \(-0.2\pm1.2\) | 0.52 |
| EQ VAS | 0.4±14.8 | \(-4.0\pm15.8\) | 0.12 |
| Qmax (mL/s) | \(-0.1\pm4.8\) | \(-0.2\pm3.7\) | 0.92 |
| PVR (mL) | \(-0.2\pm91.6\) | 25.2±70.5 | 0.06 |
| TRUS prostate volume (mL) | 2.8±12.6 | 6.2±19.3 | 0.26 |
| PSA (μg/L) | 0.1±0.3 | 0.1±0.4 | 0.17 |

Values are presented as mean±standard deviation.
BMI, body mass index; IPSS, International Prostate Symptom Score; QoL, quality of life; EQ VAS, EuroQol visual analogue scale; Qmax, maximal flow rate; PVR, postvoid residuals; TRUS, transrectal ultrasound; PSA, prostate-specific antigen.

| Control arm: general weight reduction advice; active arm: comprehensive weight reduction program. | Irritative score: sum of score of IPSS questions 2, 4, and 7. | p-value signifies the difference between the control arm and the active arm. | p-value signifies the difference between different BMI groups. |
namely, a BMI of 25 to <30 kg/m$^2$ and a BMI of 30 to 35 kg/m$^2$. A total of 101 subjects had a BMI of 25 and <30 kg/m$^2$, and 13 subjects had a BMI of 30–35 kg/m$^2$ (Table 2). When we looked at the baseline characteristics of these two groups, we did not notice any significant differences in terms of nocturia episodes, total IPSS, IPSS irritative score subset, IPSS QoL score, EQ VAS, or uroflowmetry parameters. As for prostate size, the group with a higher BMI had a relatively smaller prostate than did the group with a lower BMI (40.1±15.3 mL vs. 56.8±28.4 mL, respectively, $p=0.03$).

We further identified all subjects who had lost weight during the study period, and categorized this group of patients into four quartiles according to the percentage of weight reduction (Table 4). When we compared LUTS parameters and total IPSS across these four groups, we did not find any statistically significant differences.

### DISCUSSION

A number of studies have been carried out to address the relationship between obesity and LUTS, and these have produced mixed results. Kristal et al. [7] reported that each 0.05 increase in waist-to-hip ratio (a measure of abdominal obesity) is associated with a 10% increased risk of IPSS$>$14 ($p<0.003$) and IPSS$>$20 ($p<0.02$). A similar positive correlation was also observed by Parsons et al. [4] and Mondul et al. [8]. To account for such observations, some have hypothesized that obesity may be linked to increased sympathetic nervous system activity, leading to increased irritative LUTS from smooth muscle contraction [9]. In addition, obese men have an increased estrogen-to-testosterone ratio, which may play a role in prostatic tissue hyperplasia.

However, such a relationship was not demonstrated in our study. In our whole cohort of obese male subjects, there was no significant difference in LUTS between the group with BMI of 25 to <30 kg/m$^2$ and the group with BMI of 30–35 kg/m$^2$. Such absence of association between obesity and LUTS was also echoed in the studies by Kok et al. [10] and Wong et al. [11]. These contradictory results concerning obesity and LUTS could be in part due to the different degree of obesity in different studies. Mondul et al. [8] compared the risk of LUTS between 2 extreme BMI groups, namely BMI$\geq$35 kg/m$^2$ and BMI 23 to <25 kg/m$^2$. However, in an average Asian population, there are relatively fewer severely obese (BMI 35 to <40 kg/m$^2$) or morbidly obese (BMI$\geq$40 kg/m$^2$) men [12]. In our cohort, 101 subjects fell into the group of overweight (BMI 25 to <30 kg/m$^2$), whereas only 13 subjects belonged to the obese group (BMI 30–35 kg/m$^2$). Without a significant difference in BMI, a subtle relationship between obesity and LUTS might fail to be demonstrated in Asian-population-based studies, including our current study. However, it is worthwhile to note that in our cohort, although overweight and obese patients had a similar IPSS, obese patients actually had a smaller mean prostate size (40.1±15.3 mL vs. 56.8±28.4 mL, respectively). This might present a clue to the subtle relationship between obesity and LUTS.

In fact, the degree of weight change with respect to LUTS development was also discussed by St Sauver et al. [6] in their retrospective review of The Olmsted County Study.

| Variable                  | Group 1       | Group 2       | Group 3       | Group 4       | p-value |
|---------------------------|---------------|---------------|---------------|---------------|---------|
| No. of subjects           | 20            | 21            | 20            | 20            |         |
| Total IPSS                | $-1.3\pm6.7$  | $-0.3\pm6.8$  | $-1.8\pm7.4$  | $-0.1\pm5.1$  | 0.83    |
| Irritative score$^a$      | $-0.6\pm1.8$  | 0.2±2.8       | $-1.2\pm3.6$  | $-0.4\pm2.3$  | 0.43    |
| IPSS QoL score            | $-0.4\pm0.9$  | 0±1.3         | $-0.1\pm0.9$  | $-0.3\pm1.5$  | 0.63    |
| Nocturia episodes         | $-0.3\pm1.0$  | $-0.1\pm0.9$  | $-0.4\pm1.0$  | 0.0±0.7       | 0.61    |
| EQ VAS                    | $-4.3\pm16.3$ | $-1.2\pm15.2$ | $-2.2\pm17.4$ | $-2.1\pm13.2$ | 0.93    |
| Qmax (mL/s)               | 0.3±4.6       | $-0.2\pm2.8$  | 0.4±3.9       | $-0.6\pm3.5$  | 0.80    |
| PVR (mL)                  | 24.9±75.5     | 34.3±84.9     | 26.1±61       | $-19.5\pm124.3$ | 0.45    |
| Prostate size (mL)        | 3.1±12.5      | 1.2±17.5      | 8.0±17.6      | 3.6±17.9      | 0.80    |
| PSA (μg/L)                | 0.3±3.4       | 0.7±1.6       | $-0.3\pm1.8$  | 1.2±4.8       | 0.20    |

Values are presented as mean±standard deviation. Patients were categorized into 4 quartiles according to the percentage of weight reduction, with group 1 having the least weight reduction and group 4 having the most weight reduction.

IPSS, International Prostate Symptom Score; QoL, quality of life; EQ VAS, EuroQol visual analogue scale; Qmax, maximal flow rate; PVR, postvoid residuals; PSA, prostate-specific antigen.

$^a$Irritative score: sum of score of IPSS questions 2, 4, and 7.
Weight reduction in obese men with LUTS

An association between obesity, weight loss, and LUTS was not demonstrated in our study. This could have been due to the less marked weight difference and weight loss in our cohort. Although weight reduction might be an effective measure to improve LUTS, the implementation of a successful weight reduction program remains a challenge.

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

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EDITORIAL COMMENT

Recently, obesity has become a significant male health issue that is linked to several diseases such as hypertension [1], coronary heart disease [2], diabetes [3], and dyslipidemia [4]. However, the relationship between obesity and benign prostatic hyperplasia/lower urinary tract symptoms (BPH/LUTS) remains controversial [5]. In the present study, the authors provide significant information to further our understanding of this issue. However, several limitations of the study should be noted.

This is a prospective clinical study dealing with the role of weight reduction in LUTS. The authors intended to assess if weight reduction in obese patients with LUTS might improve their symptoms. However, the comprehensive weight reduction program did not work sufficiently to reduce the weight of the participants, so the authors could not obtain any significant results from the data. In addition, the effect of the program was not validated. Furthermore, there were few truly obese patients in the study population; therefore, no association between body mass index (BMI) and severity of LUTS was identified.

Patients without weight reduction should have been excluded from the study at a particular follow-up point, and the compliance or effectiveness of the weight reduction program should have been considered when calculating the sample size.

Regarding the definition of obesity, the World Health Organization Regional Office for the Western Pacific and the International Association for the Study of Obesity and the International Obesity Task Force published provisional recommendations for adults for the Asia-Pacific region in February 2010. These guidelines defined overweight as a BMI ≥ 23 kg/m² and obesity as a BMI ≥ 25 kg/m² [6]. However, the current study applied the criteria used for western participants to its Asian population. As a result, most participants were defined as overweight, and the number of participants defined as obese was too small to achieve statistical power. Before beginning the study, the patient demographics should have been determined using a preliminary investigation or a review of previous studies.

Though I and reviewers raised some concerning issues, I am sure that this study is valuable for the advance of research on obesity and BPH/LUTS. Both scientific interest and originality should be highly rated.

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