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European Association of Urology

Benign Prostatic Enlargement

Obesity Is Associated with Increased Prostate Growth and Attenuated Prostate Volume Reduction by Dutasteride

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Article info

Article history:
Accepted February 25, 2013
Published online ahead of print on March 7, 2013

Keywords:
Prostate
Growth and development
Obesity
Dutasteride
5α-reductase inhibitors
Prostatic hyperplasia
Ultrasonography

Abstract

Background: Although obesity has been associated with larger prostate volumes (PV), few studies have actually investigated whether obesity enhances PV growth, especially among men using 5α-reductase inhibitors.
Objective: To examine whether obesity is associated with enhanced PV growth measured by serial transrectal ultrasound (TRUS) measurements.
Design, setting, and participants: We conducted a secondary analysis of the REduction by DUtasteride of prostate Cancer Events (REDUCE) trial, which was originally aimed at cancer risk reduction among high-risk men with a single negative prestudy biopsy.
Intervention: Per-protocol randomization to placebo or dutasteride and mandatory TRUS-guided biopsies at 2 yr and 4 yr.
Outcome measurements and statistical analysis: Percentage change in PV at 2 yr and 4 yr from baseline. We tested its association with baseline body mass index (BMI) groups of <25, 25–29.9, and ≥ 30 kg/m^2 using multivariable linear regression. Secondarily, we tested whether BMI was associated with the likelihood of having no PV reduction among men randomized to dutasteride using multivariable logistic regression.
Results and limitations: Of 8122 participants, we analyzed 71.8% and 54.5% with complete 2-yr and 4-yr PV data, respectively. In multivariable analysis, men on placebo with BMI ≥ 30 versus <25 kg/m^2 had enhanced PV growth from baseline (at 2 yr: 17.0% vs 10.7%, $p < 0.001$; at 4 yr: 29.4% vs 20.1%; $p = 0.001$). Men on dutasteride with BMI ≥ 30 versus <25 kg/m^2 had attenuated PV reduction from baseline (at 2 yr: -14.3% vs -18.5%; $p = 0.002$; at 4 yr: -13.2% vs -19.3%; $p = 0.001$) and higher likelihood of having no PV reduction (at 2 yr: odds ratio [OR]: 1.44; 95% confidence interval [CI], 1.08–1.93; $p = 0.014$; at 4 yr: OR: 1.62; 95% CI, 1.18–2.22; $p = 0.003$). We found no significant interactions between BMI and dutasteride on PV change at 2 yr and 4 yr (p interaction ≥ 0.36). No clinical outcomes or effects of weight change were assessed.
Conclusions: Obesity enhanced PV growth and attenuated PV reduction by dutasteride. The null interaction between obesity and dutasteride for PV change implies that the effect of obesity on dutasteride-treated men is likely a combination of dutasteride-driven PV reduction with obesity-driven PV growth rather than decreased dutasteride efficacy.
ClinicalTrials.gov identifier: NCT00056407.

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0302-2838/$ – see back matter
http://dx.doi.org/10.1016/j.eururo.2013.02.038

1. Introduction

Benign prostatic hyperplasia (BPH) is a pathologic diagnosis highly prevalent among the elderly [1] and usually established in the presence of prostatic enlargement. BPH is a major cause of lower urinary tract symptoms (LUTS) [2] and also associated with an increased risk of falls [3], depression [4], reduced quality of life [5], and elevated costs [2]. Studies on risk factors for BPH and prostatic enlargement traditionally focused on sex hormones, genetic predisposition, and age-related changes [6].

Recent studies indicate that BPH and prostatic enlargement are linked with modifiable factors including obesity [2,6]. In the Baltimore Longitudinal Study of Aging (BLSA), each 1 kg/m^2 increase in body mass index (BMI) corresponded to an increase of 0.41 ml in prostate volume (PV) [7]. Similar results were found by Parsons et al. in a radical prostatectomy series with >16 000 patients [6]. In a cross-sectional study in China, Xie et al. found on age-adjusted analysis that community men with BMI >28 versus 25 kg/m^2 had a 2.3-fold increased risk of having PV >20 ml [8]. Additionally, in the Prostate Cancer Prevention Trial (PCPT), a large chemoprevention trial with up to 7 yr of follow-up, for each increase of 0.05 in waist-to-hip ratio (another measure of adiposity), the BPH incidence (defined by consistently severe urinary symptoms and initiation of medical therapy or surgery) increased by 10% [9].

Despite multiple cross-sectional studies linking obesity with increased PV [7,8,10], only a few studies have actually examined serial PV changes to determine the effects of obesity on PV growth [11,12]. The largest report came from the Olmstead County study, with mixed results [11]. Although BMI ≥30 versus <30 kg/m^2 was associated with higher baseline PV in age-adjusted analysis of the overall cohort, no association was found between obesity and serial PV changes among a smaller subsample of 545 men from that cohort followed with biennial transrectal ultrasound (TRUS) PV measurements for 16 yr [11]. Another important question whose answer is virtually unknown is how obesity affects PV changes among men on dutasteride, which in a prior randomized trial had on average a 28% reduction in PV after 4 yr [13].

We examined whether obesity was associated with enhanced PV growth measured by serial TRUS in a secondary analysis of the REduction by DUtasteride of prostate Cancer Events (REDUCE) trial. REDUCE was a large 4-yr trial of dutasteride versus placebo for risk reduction of prostatic cancer among high-risk men, with per-protocol mandatory TRUS-guided biopsies. REDUCE was unique in examining objectively the association between obesity with serial PV change. We hypothesized that higher BMI levels at baseline are associated with enhanced PV growth among placebo-treated men and attenuated PV reduction among dutasteride-treated men.

2. Patients and methods

2.1. Study population and procedures

Eligible men were age 50–75 yr, had a serum prostate-specific antigen (PSA) ≥2.5 or 3.0 ng/ml (for age groups of 50–60 or 60–75 yr, respectively) but ≤10 ng/ml, one negative prostate biopsy 6 mo before enrollment, PV <80 ml, and International Prostate Symptom Score <25 or <20 on α-blockers [14]. At baseline, medical history and serum

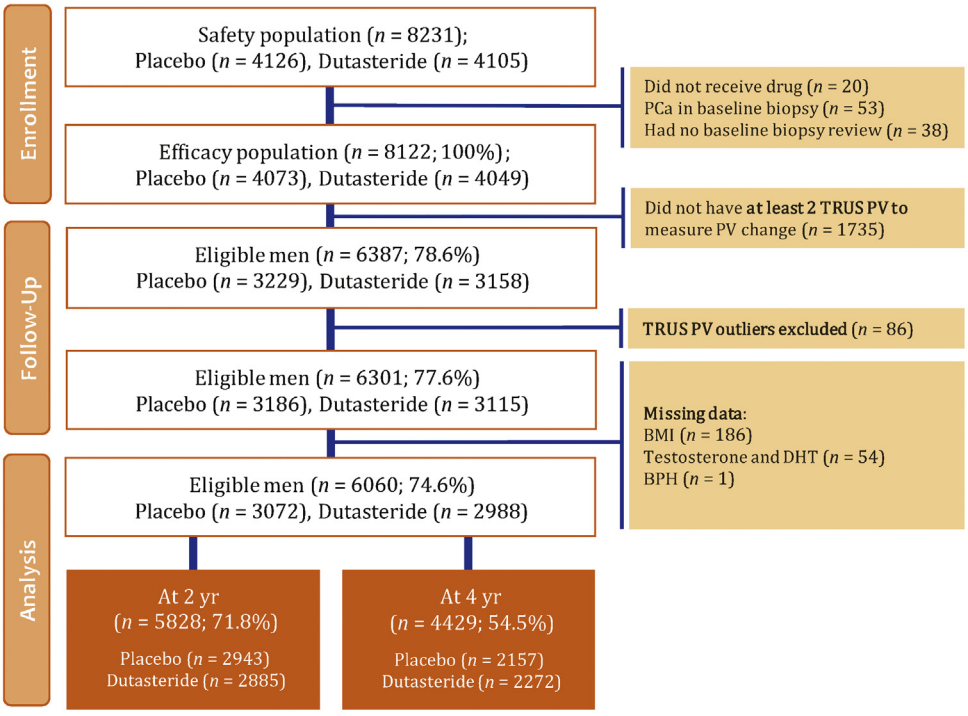

Fig. 1 – Assembly of our study population based on original REDUCE trial participants. BMI = body mass index; BPH = benign prostatic hyperplasia; PCa = prostate cancer; PV = prostate volume; TRUS = transrectal ultrasound.