Obesity Research & Clinical Practice (2013) xxx, xxx.e1–xxx.e11

ORIGINAL ARTICLE

Hypogonadal obese men with and without diabetes mellitus type 2 lose weight and show improvement in cardiovascular risk factors when treated with testosterone: An observational study

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Received 25 May 2013; received in revised form 31 July 2013; accepted 12 October 2013

KEYWORDS
Obesity;
Diabetes mellitus type 2;
Testosterone;
Waist circumference;
Weight loss

Summary
Background: Treatment of obesity with diet and exercise may have short-term success but longer-term maintenance of weight loss is less successful. Obesity is associated with a reduction of serum testosterone, and, vice versa, a reduction in serum testosterone is associated with obesity and features of the metabolic syndrome.
Objective: To investigate whether restoring serum testosterone to normal in hypogonadal obese men is beneficial with regard to weight loss and improvement of the metabolic syndrome.
Methods: A prospective registry accumulated to 181 men over five years (mean serum testosterone 10.06 ± 1.3 nmol/L (N > 12.1), body mass index (BMI) ≥ 30 kg/m^2. Of these men, 72 had diabetes mellitus type 2. All received parenteral testosterone undecanoate 1000 mg/12 weeks for up to five years.
Results: Waist circumference (cm) decreased from 111.2 ± 7.54 to 100.46 ± 7.1, weight (kg) from 114.71 ± 11.59 to 93.2 ± 8.49, BMI (kg/m^2) from 36.72 ± 3.72 to 30.2 ± 2.59 (all variables statistically significant vs. baseline ($p < 0.0001$) and each

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1871-403X/$ – see front matter
http://dx.doi.org/10.1016/j.orcp.2013.10.005

Please cite this article in press as: Haider A, et al. Hypogonadal obese men with and without diabetes mellitus type 2 lose weight and show improvement in cardiovascular risk factors when treated with testosterone: An observational study. Obes Res Clin Pract (2013), http://dx.doi.org/10.1016/j.orcp.2013.10.005

year compared to the previous year ($p < 0.0001$)). In the 72 diabetic men, waist circumference (cm) decreased from 112.93 ± 7.16 to 101.48 ± 7.24, weight (kg) from 116.94 ± 11.62 to 94.42 ± 9.42, BMI (kg/m^2) from 37.71 ± 3.5 to 30.95 ± 2.69 (all variables statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$)).
In all men serum glucose, HbA_{1c}, lipid profiles and blood pressure improved significantly. Testosterone treatment as assessed by hemoglobin, hematocrit, serum prostate specific antigen (PSA) and occurrence of prostate cancer was acceptably safe.
Conclusions: Normalizing serum testosterone in obese hypogonadal men, also in those with diabetes type 2, improved their metabolic state.

Introduction

Obesity is a world-wide problem. It is associated with a strong increase of morbidity [1,2] and mortality [3]. Its economic costs are overwhelming [4]. The obvious remedies, reduction of caloric intake and exercise, the latter also to prevent loss of lean body mass while dieting, may be successful in the short term but maintenance of weight loss is often disappointing [5]. Pharmacotherapy has largely been unsuccessful [6]. There is an urgent need to develop new ways of approaching the problem of obesity and its associated illnesses.

Obesity is strongly associated with adverse cardiometabolic events, even at younger age. In a cohort of men included at the age of 22 years in a 33-year follow-up study in Denmark, young obese men, compared with those of normal weight, had an absolute risk increase for type 2 diabetes, cardiovascular morbidity or premature death of almost 30% before the age of 55 years [7]. Epidemiological research shows that obesity increases with aging (for review: [1]). Over the last decades it has been established that serum testosterone levels in men decline with aging. More detailed analysis has shown that calendar age per se may be a factor but obesity is a major determinant in the decline of serum testosterone at all ages [8,9]. Conversely, weight loss induces a rise of bound and unbound serum testosterone levels [10]. Several studies have found that serum testosterone levels have a predictive value of the presence of the metabolic syndrome, waist circumference and serum triglycerides [11,12]. The relationship between testosterone production and obesity has been analyzed in a number of studies [13—15] and it has been established that obesity induces a lowering of serum testosterone [16—19], reversed by weight loss [10,18] and, vice versa, that low serum testosterone levels have profound negative effects on body composition and a host of metabolic variables (for review: [20]). Testosterone appears to play a critical role in regulating energy utilization including nitrogen retention, carbohydrate and fat metabolism and adipogenesis [21] and testosterone deficiency, best exemplified in androgen deprivation treatment of prostate cancer, impacts negatively on these processes. Androgen deprivation treatment decreases lean mass and increases fat mass. It also decreases insulin sensitivity while increasing low-density lipoprotein cholesterol and triglycerides and has inconsistent effects on high-density lipoprotein cholesterol. Consistent with these adverse metabolic effects, androgen deprivation therapy may be associated with a greater incidence of diabetes and cardiovascular disease [22,23]. Interventions aimed at normalizing circulating testosterone have shown to be efficacious [13,24] and acceptably safe [25]. In these studies it has also become clear that inflammatory mechanisms associated with visceral obesity play a significant role in the relationship between obesity and cardiovascular disease and the role of testosterone therein [26].

Waist circumference provides a unique indicator of body fat distribution, which can identify patients who are at increased risk of obesity-related cardiometabolic disease, above and beyond the measurement of BMI [27]. The significance of waist circumference to assess the accumulation of abdominal fat has been well documented now [28]. Després et al. showed a linear relationship between waist circumference and visceral fat tissue expressed in cm^2, superior to BMI as a

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quantifier. The same paper showed that 5–10% weight loss led to an improvement of the cardiovascular risk profile, and that loss of weight is to be preferred over pharmacological treatment of the pathologies resulting from visceral obesity, such as hypertension, dyslipidemia and diabetes mellitus. Waist circumference is a better predictor of serum testosterone than body mass index or the waist hip ratio [29] and of cardiovascular disease and diabetes mellitus [30]. Both general adiposity and abdominal adiposity are associated with an increasing risk of death and studies support the use of waist circumference or waist-to-hip ratio in addition to BMI in assessing the risk of death [31,32], also confirmed in another study [33]. Conversely, serum testosterone is at all ages a reliable predictor of the metabolic syndrome, waist circumference and serum triglycerides [11].

Elevated waist circumference by itself does not always identify individuals with increased visceral fat. But the presence of elevated triglycerides, along with an elevated waist circumference, defined as the hypertriglyceridemic waist phenotype, is able to identify a subgroup with higher amount of visceral fat, with hyperinsulinemia and elevated apo B and small, dense LDL particles. This allows a better identification of men with a high risk for cardiovascular disease [34,35].

Subjects and methods

In a cumulative registry study of 255 mainly elderly men, aged between 33 and 69 years (mean 59.11 ± 6.06) (of whom the results have been published [36]), a subgroup analysis of 181 men, selected for obesity, was performed. All subjects had sought urological consultation in a single urologist's office for various medical conditions; e.g. erectile dysfunction, decreased libido, questions about their testosterone status, or a variety of urological complaints. A number of subjects, for instance, men with osteoporosis, had been referred by other specialists suspecting they might have testosterone deficiency. Upon clinical and laboratory investigation, the subjects were found to have subnormal plasma total testosterone levels (mean: 10.06 ± 1.3; range: 5.89–12.13 nmol/L) as well as at least mild subjective symptoms of hypogonadism assessed by the Aging Males' Symptoms scale [37]. Fifteen patients had Klinefelter's syndrome; eight patients had undergone unilateral testicular ablation; two of those eight had had a contralateral cryptorchidism, one of those eight a bilateral cryptorchidism; two had a history of unilateral cryptorchidism, one had a history of bilateral cryptorchidism. This is a total of 26 patients (14%) with known primary hypogonadism. Maldescensus testis may have been underreported.

All men received treatment with parenteral testosterone undecanoate 1000 mg (Nebido®, Bayer Pharma, Berlin, Germany), administered at baseline and 6 weeks and thereafter every 12 weeks for up to 60 months. The cut-off level for below-normal serum testosterone was determined on the basis of the following considerations: although there is no international consensus as to the normal range of testosterone, clinical data suggest that the normal range of testosterone in adult men is between 12 and 40 nmol/L [38]. A threshold of 12.1 nmol/L was recently confirmed by Bhasin et al. in an analysis of a number of important studies such as Framingham Heart Study generations 2 and 3, European Male Aging Study (EMAS), and the Osteoporotic Fractures in Men Study [39].

Measurements of anthropometric parameters were performed at baseline (height, weight, waist circumference) and at each visit (weight, waist circumference) and blood samples drawn at each visit, prior to the next injection of testosterone. Therefore, testosterone levels were trough levels at the end of an injection interval. Waist circumference (WC) was measured midway between the last rib and the uppermost border of the right iliac crest. Testosterone was measured by standard laboratory measurement as described previously [36].

A cumulative, prospective, registry of 181 men (mean age: 59.11 ± 6.06 years) with testosterone levels below 12.1 nmol/L and a body mass index (BMI) of $\geq 30\,kg/m^2$ was built up. After one year, 181 obese men were included in the registry, after two years, 159 men, after three years, 133 men, after four years, 114 men, after five years, 89 men. The declining numbers do not reflect drop-out rates but are a result of the registry design. Of the 181 men, 178 fulfilled the harmonized criteria for the metabolic syndrome [40].

The data of this study were collected during a careful follow-up of the men receiving testosterone to gather long-term experience in a real-life setting, and the quality of the data collection lends itself to an analysis of the effects of normalizing testosterone on the variables of the metabolic syndrome.

Of these 181 men, 72 (40%) had type 2 diabetes mellitus, which had been diagnosed before entering the study and was being treated by their primary care physician. Data are available for 72 men for one year, 58 for two years, 50 for three years, 43 for four years and 33 for five years. Declining numbers do not reflect drop-outs but are a result of

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the registry design. We performed also a subgroup analysis in these obese diabetic men.

The 72 diabetic patients were on various anti-diabetic drugs. Of the total group, 121 men were on anti-hypertensives, 106 on lipid-lowering drugs.

Ethical guidelines as formulated by the German ''Ärztekammer'' (the German Medical Association) for observational studies in patients receiving standard treatment were followed. All subjects consented to be included in the research of their treatment protocol which is in accordance with the Declaration of Helsinki (http://www.wma.net). All procedures were carried out with the adequate understanding and written consent of the subjects.

All men in the study received parenteral testosterone undecanoate 1000 mg/12 weeks following an initial 6-week interval for up to five years [36].

Statistical analyses

For continuous variables, the mean, median, standard deviation, range, minimum, maximum, and sample size for the overall sample and various groups were reported at each time point. For categorical variables the frequency distribution was reported. We tested the hypotheses regarding change in outcome scores across the study period by fitting a linear mixed effects model to the data. Time (to indicate follow-up interviews) was included as fixed effect in the model. A random effect was included in the model for the intercept. Estimation and test of change in scores were determined by computing the differences in least square means at baseline versus the score at each follow-up interview. For the correlation study, Pearson correlation was calculated between baseline changes in outcomes at various time points. The significance of each correlation was tested using Fisher's test.

Results

Table 1 presents an overview of co-morbidities at baseline assessment of the 181 obese hypogonadal men, attesting to the high degree of pathology associated with obesity and hypogonadism. Some of the comorbidities had been known and reported by the patient at baseline, others were diagnosed by our own measurements at baseline. For instance, in a large proportion of the patients with dyslipidemia and hypertension, men had not been aware of their conditions. Our diagnostic criteria were based on the cut-off values in the harmonized definition of the metabolic syndrome [40] (Table 1).

Table 1 Baseline characteristics of 181 obese hypogonadal men undergoing long-term treatment with testosterone undecanoate.

Mean age (years)		59.11 ± 6.06 (min: 33, max: 69)
Comorbidities at baseline	*n*	Proportion (%)
Hypertension	175	97
Type 2 diabetes	72	40
Fasting glucose ≥ 5.6 ≤ 7 mmol/L	27	15
Dyslipidemia	181	100
HDL ≤ 1.03 mmol/L (40 mg/dL)	24	13
Triglycerides ≥ 1.7 mmol/L (150 mg/dL)	181	100
Waist circumference ≥ 94 cm	179	99
Hypertriglyceridemic waist	179	99
Coronary artery disease	39	22
Post-myocardial infarction	35	19
Post-stroke	5	3
Erectile dysfunction	140	77
Osteoporosis	19	10
Klinefelter's syndrome	15	8

Upon treatment with parenteral testosterone undecanoate, trough levels of serum testosterone measured before the new injection were in the range of 17—19 nmol/L.

Testosterone treatment of obese men

All but two of the 181 men fulfilled the criteria of the hypertriglyceridemic waist [34,35].

At the end of the observation period, mean waist circumference (cm) as a measure of abdominal fat had decreased from 111.20 ± 7.54 (min: 89.00; max: 129.00) to 100.46 ± 7.1 (min: 84.00; max: 117.00) (Fig. 1A). Mean change from baseline was 9.87 ± 0.17 cm. The mean percentage reduction of waist circumference was 3.29 ± 0.12% after one year, 5.44 ± 0.12% after two years, 6.79 ± 0.13% after three years, 7.92 ± 0.13% after four years, and 8.87 ± 0.15% after five years. All decreases were statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$).

Mean weight (kg) had decreased from 114.71 ± 11.59 (min: 87.0, max: 139.00) to

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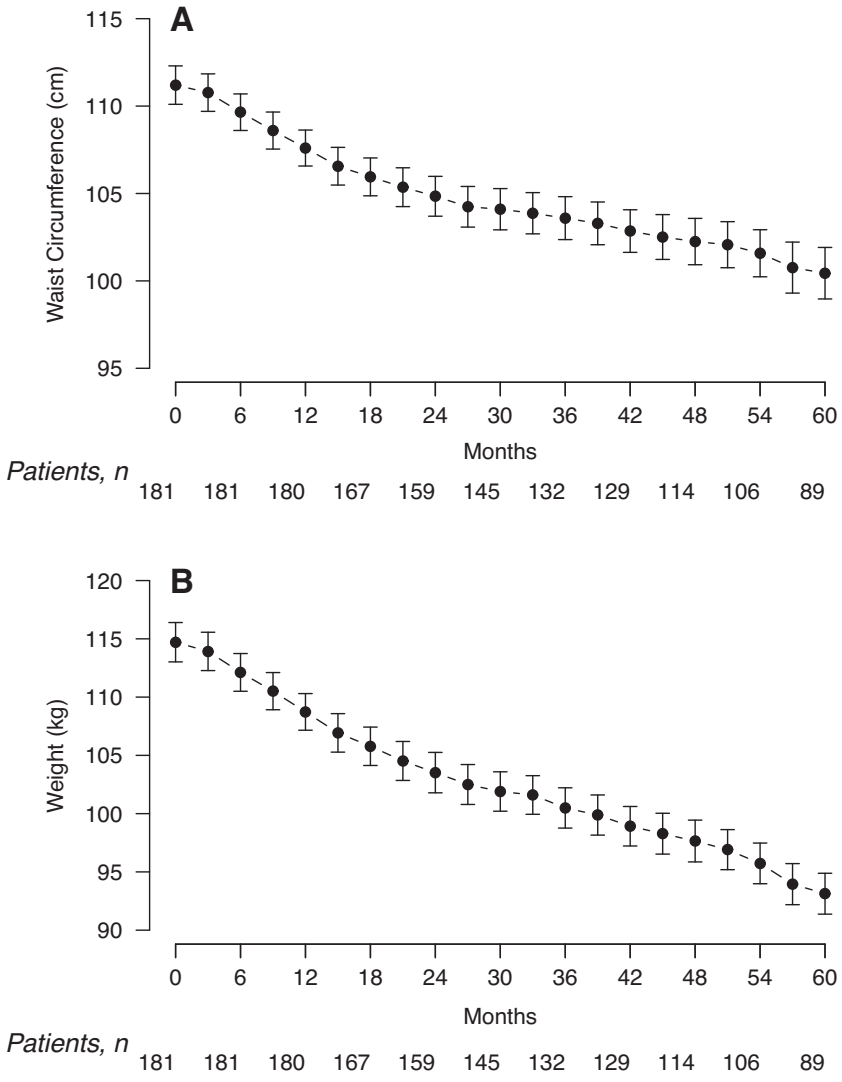

Figure 1 (A) Waist circumference (cm) and (B) weight (kg) in 181 obese hypogonadal men treated with testosterone.

93.2 ± 8.49 (min: 80.0; max: 115.0) (Fig. 1B). This decrease was statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$). Mean change from baseline was 18.86 ± 0.36 kg. The mean percentage weight reduction (and also reduction of BMI) from baseline was 5.2 ± 0.24% after one year, 9.11 ± 0.25% after two years, 11.58 ± 0.27% after three years, 13.78 ± 0.28% after four years and 16.44 ± 0.3% after five years (Fig. 2). This reduction was statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$).

After five years, all men had lost any weight, 99% had lost ≥5 kg, 90% ≥10 kg, 70% ≥15 kg, and 40% ≥20 kg (Fig. 3).

BMI (kg/m^2) decreased from 36.72 ± 3.72 (min: 30.10; max: 46.51) to 30.2 ± 2.59 (min: 25.66; max: 36.71) by 6.06 ± 0.11 kg/m^2. These changes were also statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$).

Fasting serum glucose decreased from 5.84 ± 0.84 to 5.41 ± 0.12 mmol/L (105.30 ± 15.15 to 97.47 ± 2.22 mg/dL) and HbA_{1c} decreased from 7.4 ± 1.47 to 6.02 ± 0.61%. Total serum cholesterol declined from 7.63 ± 0.95 to 4.9 ± 0.28 mmol/L (294.62 ± 36.63 to 189.04 ± 10.79 mg/dL), LDL from 4.47 ± 1.02 to 2.93 ± 0.93 mmol/L (172.58 ± 39.46 to 113.27 ± 35.72 mg/dL), triglycerides from 3.32 ± 0.56 to 2.17 ± 0.13 mmol/L (290.19 ± 49.26 to 189.96 ± 11.52 mg/dL) ($p < 0.0001$ for all). Serum HDL increased from 1.58 ± 0.44 to 1.61 ± 0.44 mmol/L (61.1 ± 17.07 to 62.29 ± 16.9 mg/dL). Systolic blood pressure decreased from 159.17 ± 15.9 to 139.04 ± 10.96 mmHg, diastolic blood pressure

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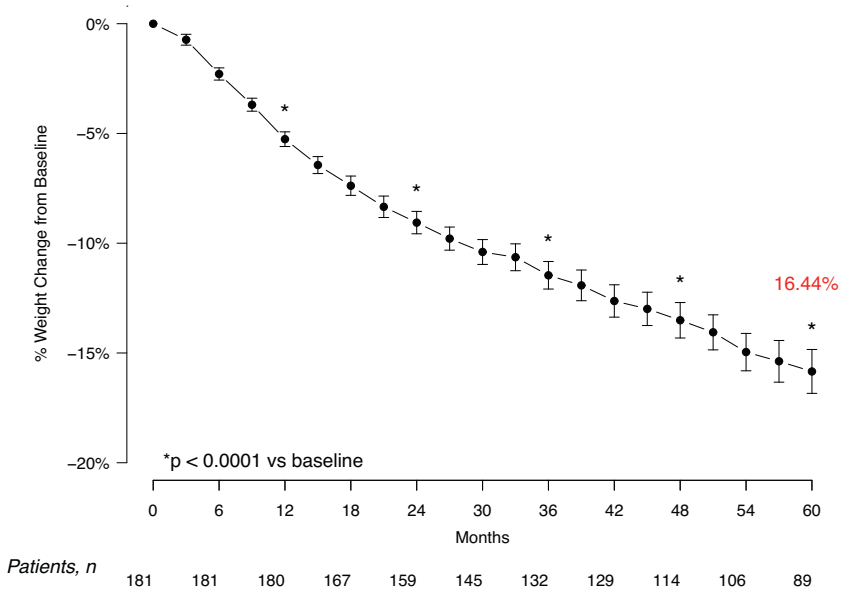

Figure 2 Weight change (%) from baseline in 181 obese hypogonadal men treated with testosterone.

from 96.5 ± 11.01 to 80.36 ± 7.52 mmHg ($p < 0.0001$ for all). Serum C-reactive protein declined from 4.03 ± 4.8 to 0.77 ± 1.53 mg/dL.

With regard to safety: hemoglobin levels rose from 14.54 ± 0.62 to 15.03 ± 0.4 g/dL over the first 24 months to reach stable levels thereafter. Hematocrit increased from 43.71 ± 2.51 to 49.03 ± 1.65% reaching a plateau at 36 months with minor fluctuations thereafter. Prostate volumes rose slightly (less than 10 per cent) over the first 36 months and then stabilized. Prostate volume increased in the first treatment year by 0.18 ± 0.11 ml, in the second year by 1.04 ± 0.11 ml, in the third year by 0.71 ± 0.11 ml, in the fourth year by 0.35 ± 0.12 ml, in the fifth year by 0.14 ± 0.13 ml from 30.52 ± 11.31 ml at baseline to 33.06 ± 11.73 ml at the end of the observation. Mean prostate specific antigen (PSA) was 1.76 ± 0.93 ng/dL at baseline, 1.78 ± 0.92 after one year, 1.8 ± 0.92 after two years, 1.84 ± 0.95 after three years, 1.8 ± 0.94 after four and 1.86 ± 0.93 ng/dL after five years. Changes were 0.02 ± 0.01 in the first year, 0.07 ± 0.02 in the second year, 0.05 ± 0.02 in the third year, 0.03 ± 0.02 in the fourth year and 0.03 ± 0.02 in the fifth year with a mean change of 0.18 ± 0.01 ng/dL and a *p*-value for linear trend of <0.0001. One patient was diagnosed with prostate cancer approximately ten months after initiation of testosterone therapy when two PSA measurements had been above 4 ng/mL. Upon prostate biopsy, a low-risk prostate adenoma was diagnosed and the patient was treated by radical prostatectomy.

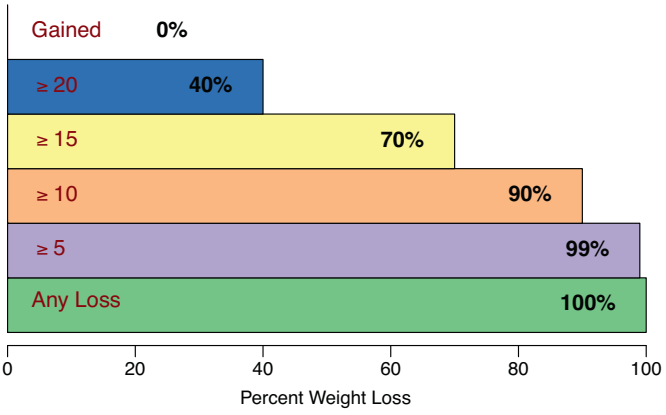

Figure 3 Distribution of weight loss categories in 181 obese hypogonadal men treated with testosterone for up to 5 years.

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Testosterone treatment of men with diabetes mellitus

In the subgroup of patients with diabetes mellitus type 2, mean weight (kg) decreased from 116.94 ± 11.62 (min: 87.0, max: 139.00) to 94.42 ± 9.42 (min: 80.0; max: 114.0) at the end of the observation period (Fig. 4A). This decrease was statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$). Mean change from baseline was 18.55 ± 0.57 kg or 15.97 ± 0.46% (Fig. 4B).

Waist circumference (cm) decreased from 112.93 ± 7.16 (min: 89.00; max: 129.00) to 101.48 ± 7.24 (min: 85.00; max: 117.00) by 10.31 ± 0.29 cm (Fig. 4A), BMI (kg/m^2) from 37.71 ± 3.50 (min: 30.10; max: 46.51) to 30.95 ± 2.69 (min: 25.88; max: 35.98) by 6.02 ± 0.18 kg/m^2. These changes were also statistically significant vs. baseline ($p < 0.0001$) and each year compared to the previous year ($p < 0.0001$).

At the end of each year, HbA_{1c} was available for 50, 38, 30, 29 and 24 men, respectively. At baseline, HbA_{1c} was 8.35 ± 0.7% (min: 6.90; max: 11.60), declining steadily and statistically significantly to 6.21 ± 0.6% (min: 5.50; max: 7.20) (Fig. 5) by a mean 2.01 ± 0.07%.

Fasting glucose decreased from 6.58 ± 0.79 to 5.42 ± 0.16 mmol/L (118.64 ± 14.27 to 97.61 ± 2.85 mg/dL) (Fig. 6) by a mean 1.35 ± 0.12 mmol/L (24.28 ± 2.16 mg/dL).

Discussion

It is well known that obesity and its sequels are associated with low serum testosterone. A recent meta-analysis showed that weight loss (diet, physical exercise, bariatric surgery) reverts the obesity-associated hypogonadotropic hypogonadism [10]. Treatment of obesity with diet and exercise may have short-term beneficial effects but it is unfortunate that in the longer term the majority of patients regain weight [5]. In view of the serious deleterious effects of obesity on health, new avenues of managing obesity are needed [2]. Our study focused on the effects of normalizing serum testosterone in a group of hypogonadal men with a BMI of ≥30 kg/m^2 and a subgroup of this cohort of obese men suffering from diabetes mellitus type 2.

In this relatively long-term study over 60 months, a continuous decline of body weight, body mass index and waist circumference was observed. Fasting glucose declined over the first 18 months and then stabilized, with similar patterns for serum total cholesterol, LDL cholesterol and triglycerides. HDL increased slightly but significantly. Diastolic and systolic blood pressure showed a decrease during the first two years but systolic blood pressure declined again after four years of testosterone administration.

Similar patterns of change were encountered in the subgroup of 72 obese men with diabetes mellitus type 2. In them the decline in percentage HbA_{1c} was more pronounced than in the total group of 181 obese men.

The results of our study are in agreement with earlier studies confirming a positive effect of normalizing serum testosterone on variables of the metabolic syndrome [41—44].

A remarkable finding of our study is the continuous decline of body weight, body mass index and waist circumference over the 5-year period of our observation. The continued weight loss trajectory is different from pharmacotherapy where a plateau is reached somewhere between 1—2 years. Also the trajectory with bariatric surgery similarly shows plateaus, but at a different rate which does not seem to occur with testosterone treatment within the first 5 years of treatment.

It is well known that overweight and obese men with metabolic syndrome at baseline have higher risks to regain weight (odds ratio = 2.8, $p = 0.015$) after initial weight loss. In a recent study high baseline retinol-binding protein 4 (RBP4), low total testosterone and low sex hormone binding globulin were identified as significant predictors of regain of weight after earlier weight loss (difference between men with weight regain and weight loss $p = 0.001$, 0.038, 0.044, respectively), and these factors may play roles in the link between the metabolic syndrome and regain of previously lost weight [45]. This observation is supported in a study in mice with a selective knockout of the androgen receptor signaling. It could be shown that androgen action in adipocytes not only protects against high-fat diet-induced visceral obesity but also regulates insulin action and glucose homeostasis, independently of adiposity. Androgen deficiency in adipocytes in mice resembles human type 2 diabetes, with early insulin resistance and evolving insulin deficiency [46]. In our study, serum testosterone levels were maintained in a range above 17—19 nmol/L, so serum testosterone levels were not low at any point of the study.

The subjects in our study did not receive instructions or encouragement to change their lifestyle in terms of diet and/or exercise other than the

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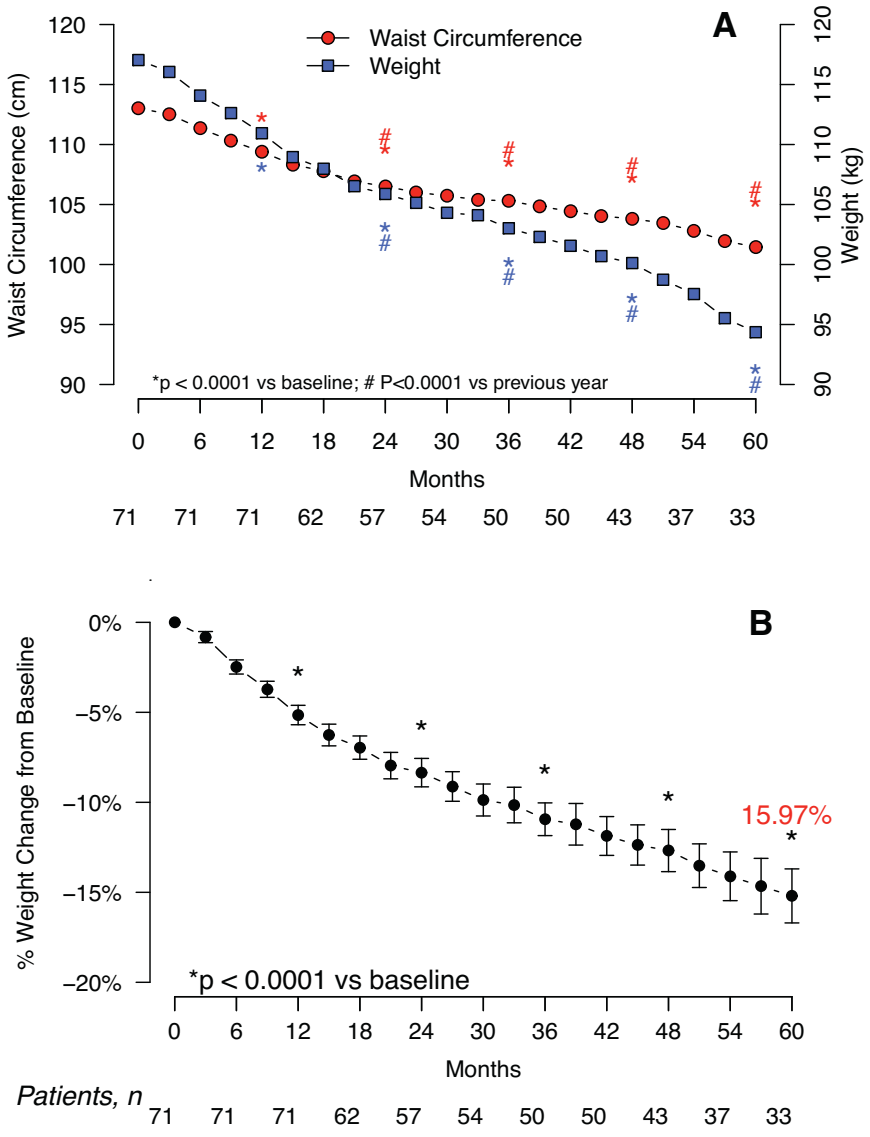

Figure 4 (A) Waist circumference (cm) and weight (kg) in 72 obese hypogonadal men with type 2 diabetes treated with testosterone; (B) weight change (%) from baseline in 72 obese hypogonadal men with type 2 diabetes treated with testosterone.

usual brief advice at baseline that it would be good if they could lose weight by a healthier diet consisting of more vegetables and fruit and less meat. There were no written instructions. The value of exercise has been documented in a number of studies. Even moderate intensity resistance training appeared beneficial [47]. In another study behavioral interventions increasing free-living physical activity/exercise produced clinically significant improvements in long-term glucose control. Future studies should consider increase of ''free living'' physical activity and exercise which were associated with clinically significant improvements in long-term glucose control and HbA_{1c}, pointing to the need of structured training for care providers on the delivery of behavioral interventions [48]. In a study of men newly diagnosed with diabetes mellitus, men were assigned to treatment of diet and moderate exercise or to diet, moderate exercise and testosterone treatment. Diet and exercise appeared beneficial in managing the diabetes but addition of testosterone to treatment delivered a better treatment outcome [49].

The addition of testosterone to diet and exercise of obese men might also be propitious in view of the mood elevating effects of testosterone administration to hypogonadal obese men who often show depressive symptoms [50].

The effects of restoring testosterone levels to normal on the treatment of obesity and its

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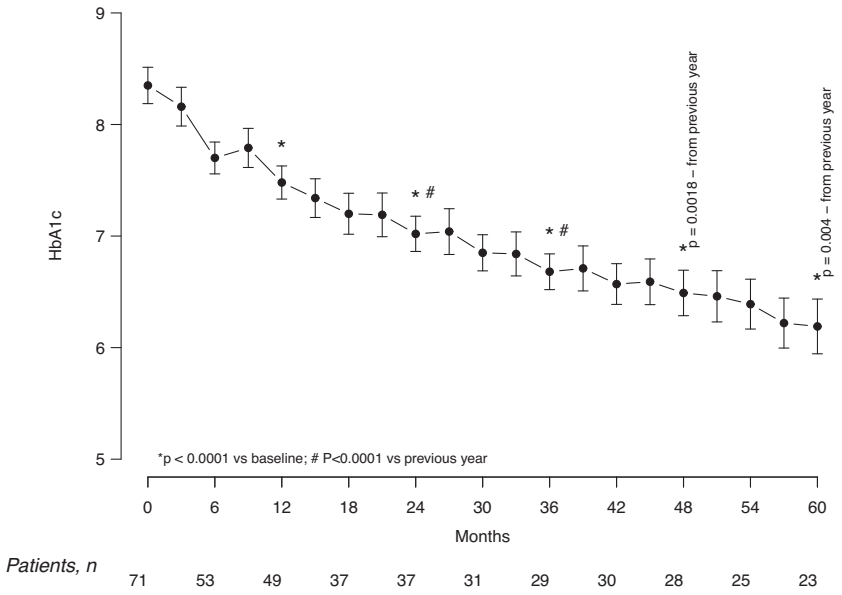

Figure 5 HbA_{1c} (%) in 72 obese hypogonadal men with type 2 diabetes treated with testosterone.

associated pathology have now been well documented [14,44]. More large-scale studies are needed to prove definitively that restoring testosterone levels to normal levels produces weight loss. Then physicians managing men with overweight and diabetes mellitus could use these new and maybe unfamiliar insights in the treatment of their patients. There are no comparison studies with the more traditional treatments of obesity and diabetes mellitus but the contributions of testosterone administration to hypogonadal men to weight loss could equal those of the more traditional treatment approaches. Fears that testosterone worsens the risks of cardiovascular disease [51] or induces carcinomas of the prostate [25] are no longer tenable.

The present study has a number of limitations. This observational study primarily monitored the effects of normalizing serum testosterone on the traditional androgen-dependent targets in the setting of a urology clinic. The study was not designed to monitor the effects of normalizing serum testosterone in hypogonadal men on weight and other variables of the metabolic syndrome, and, therefore, the men studied are different from groups

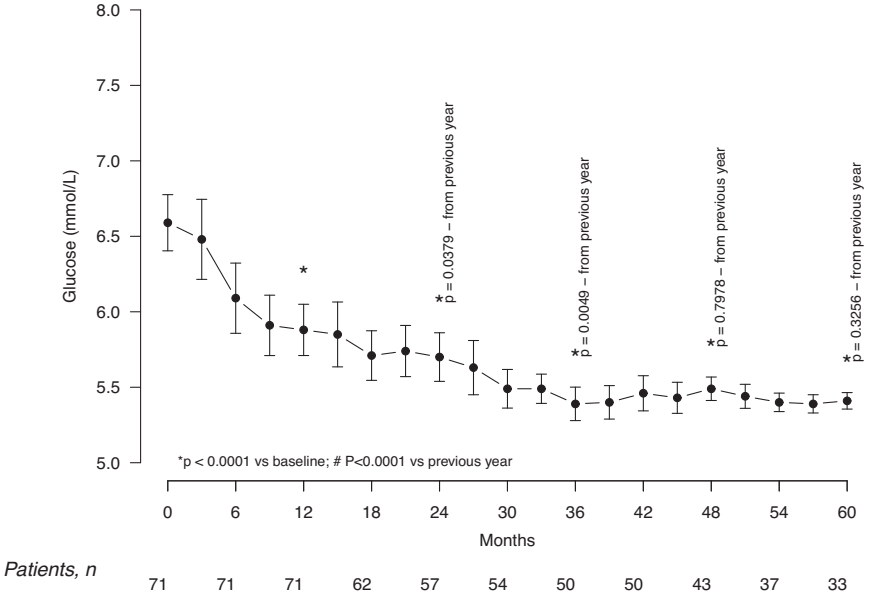

Figure 6 Fasting glucose (mmol/L) in 72 obese hypogonadal men with type 2 diabetes treated with testosterone.

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which enter weight loss trials. Without a matched comparator group it is hard to interpret the magnitude or significance of any effect. It is unlikely but theoretically possible that a similar group would have had improvements without receiving testosterone treatment. However, placebo-control in hypogonadal men is not considered ethical for a prolonged period of time.

The study was observational and not double blind/placebo controlled. There was no formal assessment of diet, exercise and drug treatment by primary care physicians and whether their patterns had changed over the five-year period of the study. It was not possible to obtain information on changes in the treatment of men with type 2 diabetes that their family physician may have prescribed.

Conclusion

In a real-life situation in our urological institution, an unselected group of obese hypogonadal men, with or without type 2 diabetes, showed major beneficial effects of normalizing serum testosterone on obesity, glycemic control, blood pressure and lipid profile. Large, controlled studies are needed to confirm these observations.

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Please cite this article in press as: Haider A, et al. Hypogonadal obese men with and without diabetes mellitus type 2 lose weight and show improvement in cardiovascular risk factors when treated with testosterone: An observational study. Obes Res Clin Pract (2013), http://dx.doi.org/10.1016/j.orcp.2013.10.005

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