REVIEW ARTICLE

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Efficacy and Safety of Testosterone Treatment in Male Hypogonadism: A Systematic Review

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ABSTRACT

Male hypogonadism may occur because of either congenital conditions or dysfunction that arises along the hypothalamic-pituitary-gonadal axis. As part of the lifelong management of male hypogonadism, testosterone replacement therapy (TRT) has been the most important therapy, although its effectiveness and safety are subject to controversy. This systematic review was undertaken to investigate the effectiveness and safety of TRT in men with hypogonadism. Searches were conducted in the literature through MEDLINE, CENTRAL, and ScienceDirect. The inclusion criteria were restricted to RCTs reported within five years. Out of 2,471 published articles, 16 were found eligible for analysis. Results showed that TRT is effective in raising serum testosterone levels in male with hypogonadism no matter the mode of administration, whether injected, oral or topical as in gels. In addition, TRT has improved body composition by decreasing fat and lean muscle mass. An increase in PSA commonly occurs in most patients, yet no research proves that TRT increases the development of prostate cancer and cardiovascular disease. Most commonly, the adverse effects are arrhythmias and increase in blood pressure, especially among those who undergo oral TRT. Amelioration of different symptoms such as erectile dysfunction, decreased libido, and fatigue in patients with hypogonadism was also achieved by TRT. Overall, it can be concluded that, TRT is generally safe and effective but requires close monitoring, but also one where monitoring should regularly be performed because of possible side effects, more research is needed.

Keywords: Hypogonadism, testosterone replacement therapy, safety, efficacy, systematic review.

INTRODUCTION

Male hypogonadism, acquired or congenital, can be caused by defects that interfere with the hypothalamic-pituitary-testicular axis. It is imperative to differentiate between primary and secondary forms of hypogonadism. The presence of decreased spontaneous erections, nocturnal penile flaccidity, diminished libido, and reduced testicular volume are highly suggestive of hypogonadism.[1]

Prevalence of hypogonadism varies widely (between 2.1% and 38.7%) in middle-aged and older men.[2] In Asia, the estimated prevalence of late onset hypogonadism (LOH) was 7.8% among

middle-aged and elderly males in China and significantly increased with age [3]. One method of treatment for hypogonadism is testosterone replacement therapy, but Testosterone therapy has been controversial since its synthesis in the 1930s to the present day [4].

Currently, TRT is available in a variety of ways, including injections, oral medication, and a recently introduced gel formulation. As with any pharmaceutical treatment, TRT carries a certain risk of adverse effects such as mood changes (such as depression), acne, weight gain, arrhythmia, increase risk of acute kidney injury and increase risk of prostate cancer. [5]. Therefore, the purpose of this systematic review is to summarize and determine the efficacy and safety of the use of TRT in patients with male hypogonadism.

METHOD

A total of 1,460 articles from MEDLINE, 828 articles from CENTRAL, and 183 articles from ScienceDirect were identified through the search terms "hypogonadism," "testosterone," and "treatment." The search was limited to five years and 38 journals that met the criteria for free full-text articles and randomized controlled trials (RCTs). Of these, 16 journals were selected for further screening and analysis. This systematic review has been registered PROSPERO CRD42024628103.

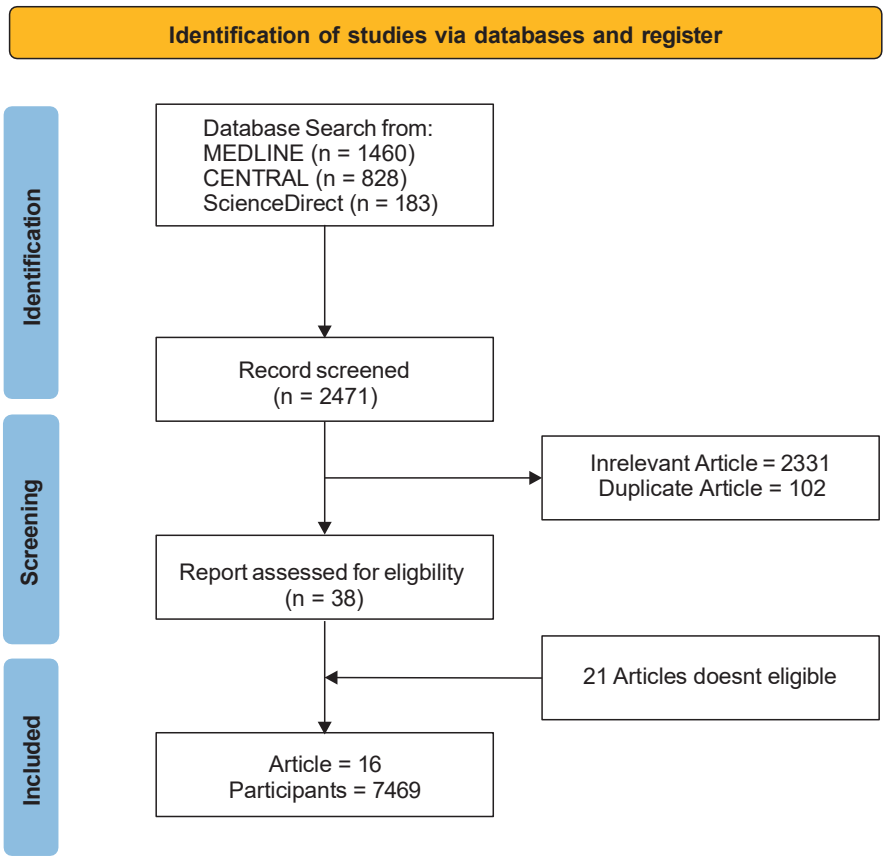

Figure 1. Study selection and inclusion process of safety and efficacy TRT in hypogonadism men

RESULTS

Table 1. Study Characteristic and Outcomes

Author (year)	Sample size		Age (year,mean)		Study design	Testesterone administration	Efficacy	Safety
	IG*	CG*	IG*	CG*				
Dudek et al. (2020)	20	20	54.2	55.6	Randomized clinical trial	testosterone enanthane intramuscular injection every 2 weeks for 12 months	- TRT increased serum testosterone and reduced luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels. BMI decreased from 26.6 ± 2.1 to 26.1 ± 1.8 kg/m² ($p < 0.05$), and fat mass decreased from 17.0 ± 4.4 to 15.6 ± 4.0 kg ($p < 0.05$).Serum leptin decreased from 6.2 ± 1.4 to 4.0 ± 1.2 µg/L ($p < 0.05$).Adiponectin increased from 7.6 ± 2.5 to 9.4 ± 2.8 µg/mL ($p < 0.05$).hsCRP decreased from 1.4 ± 1.2 to 1.0 ± 1.0 mg/L ($p < 0.05$). - In the placebo group serum leptin, adiponectin, and hsCRP levels did not change significantly.	- PSA levels increased in the testosterone-treated and the placebo group: from 0.9 ± 0.4 to 1.2 ± 0.5 ng/mL, $p < 0.05$, and from 0.9 ± 0.5 to 1.1 ± 0.5 ng/mL, $p < 0.05$, respectively. Differences between the groups were not statistically significant at any time point - PSA increases did not exceed 1 mg/year or reach levels >4 mg/L in either group.
Bhasin et al. (2023)	2601	2603		63.3	Randomized, placebo-controlled trial	Topical 1.62% testosterone gel	- Change in IPSS did not differ between groups.	- The incidence of high-grade prostate cancer (5 of 2596 [0.19%] in the TRT group vs 3 of 2602 [0.12%] in the placebo; HR 1.62; 95% CI, 0.39-6.77; P = 0.51) did not differ significantly between groups; - The incidences of any prostate cancer, acute urinary retention, invasive surgical procedures, prostate biopsy, and new pharmacologic treatment also did not differ significantly.

Rasmussen RS et al. (2024)	44	34	≥ 70		double-blind, randomized, placebo-controlled intervention trial with a 2 × 2 factorial design	testosterone undecanoate injections for 52 weeks with or without progressive resistance training	- No significant differences between PSA levels. - Comparing performances within a group at baseline, and at weeks 4, 20 and 52 (Friedman Test), only the Combo group improved in the 30-s Sit to Stand Test ($p<0.001$). - Testosterone levels at week 52 correlated with the 30 s Sit to Stand Test performances only in the Combo and TU groups	NA
Cunningham GR et al. (2019)	395	395	72.3	72.1	Double-blinded, placebo-controlled trial.	Testosterone gel for 12 months.	NA	- Testosterone treatment resulted in a significantly greater increase in PSA levels compared to placebo ($P < 0.001$). Serum PSA levels increased from 1.14 ± 0.86 ng/mL (mean ± SD) at baseline by 0.47 ± 1.1 ng/mL at 12 months in the testosterone group and from 1.25 ± 0.86 ng/mL by 0.06 ± 0.72 ng/mL in the placebo group. - Five percent of men treated with testosterone had an increase of PSA ≥1.7 ng/mL and 2.5% of men had an increase of PSA ≥3.4 ng/mL.
Miner M et al. (2024)	210	105	52.6	54.2	multicenter, phase 3, randomized, open-label, active-controlled study	2:1 to oral testosterone undecanoate or 1.62% topical testosterone gel	- 87.4% of patients taking oral testosterone undecanoate (TU) had an average 24-hour testosterone level within the normal male range (300–1140 ng/dL) by week 13. - Oral testosterone undecanoate (TU) showed significantly greater improvements than 1.62% topical testosterone gel in the SF-36 mental component summary (mean change: 3.82 vs. 0.55; $p = 0.009$). - Oral TU also demonstrated numerically greater improvements in vitality (6.89 vs. 3.82), social role functioning (2.17 vs. 0.64), emotional role functioning (0.65 vs. 0.38), and physical role functioning (0.85 vs.0.24).	- The mean change in PSA levels from baseline was 0.2 ng/mL in both the treatment and placebo groups, indicating no significant difference.

Narukawa T et al. (2020)	23	20	59.5	54.9	open-label, randomized, crossover study	intramuscular injection monotherapy (IMIM) of 250 mg testosterone enanthate every 3 weeks over a period of 12 weeks, followed by 12 weeks combination therapy (CT) of TRT with tadalafil (10 mg)	- There was no significant statistical difference in patients preferences between IMIM and CT.	-Patients who experience polycythemia from IMIM, which may hinder continued treatment, might find CT to be an alternative for testosterone replacement.
Pencina KM et al. (2023)	Same sample with Bhasin et al. (2023)				Randomized, placebo-controlled trial	Topical 1.62% testosterone gel	- Testosterone treatment corrected anemia in a significantly higher percentage of men compared to placebo at : 6 months (41.0% vs. 27.5%), 12 months (45.0% vs. 33.9%), 24 months (42.8% vs. 30.9%), 36 months (43.5% vs. 33.2%), and 48 months (44.6% vs.39.2%) (P = 0.002). - Among participants without anemia, a significantly smaller proportion of testosterone-treated men developed anemia.	NA
Bøgehave et al. (2023)	11	20	54	53	double-blinded, placebo-controlled study	24 weeks of testosterone injections	NA	- TRT affects the coagulation system in an anticoagulant direction through suppressed TF pathway. - Between-group differences at 24 weeks were observed for endogenous thrombin potential (P = 0.036), Factor VII (P = 0.044), Factor X (P = 0.015), prothrombin (P = 0.003), protein C (P = 0.004), and protein S (P = 0.038). Within the TRT group, ETP, peak thrombin, FVII, FX, prothrombin, TFPI, protein C, and FXII decreased and protein S increased (all P < 0.05). - Within the placebo group, coagulation outcomes were unchanged.

Groti Antonic K. (2020)	28	27	58	62	two-part prospective observational clinical study (first year: double-blind randomized placebo-controlled trial employing testosterone undecanoate; second year: open-label follow-up with all participants receiving TTh)	intramuscular testosterone undecanoate administered at first visit (baseline), second injection 6 weeks later (second visit), and each subsequent injection 10 weeks after the previous injection.	Bone turnover markers C-telopeptide of type I collagen (CTX) and procollagen I N-terminal propeptide(PINP) levels significantly decreased in both groups after the first year: for CTX from 1055 (mean) to 453 (mean) pmol/L in group P ($p < 0.001$) and from 897 (mean) to 523 (mean) pmol/L in group T ($p < 0.001$). PINP decreased by 4.30 ± 8.05 µg/L in group P ($p = 0.030$) and 4.64 ± 8.86 µg/L in group T ($p < 0.023$). Lumbar spine BMD increased (by 0.075 ± 0.114 g/cm2; $p = 0.019$) in treatment group following 2 years of treatment. No femoral neck BMD changes were observed in both groups.	No adverse events or side effects of TRT have been observed over the course of this trial.
Cauley JA et al. (2021)	105	92	≥ 65		Multicentre placebo-controlled, double-blind trial	Testosterone gel for one year 5g daily	. There was no difference in the percent change in TBS (trabecular bone score) by randomized group: 1.6% (95% CI 0.2-3.9) in the testosterone group and 1.4% (95% CI 0.2-3.1) in the placebo group. In contrast, vBMD (volumetric bone mineral density) increased by 6% (95% CI 4.5–7.5) in the testosterone group compared to 0.4% (95% CI −1.65–0.88) in the placebo groups	NA
Bischoff-Ferrari HA et al. (2024)	46	45	71.8	72.5	2 × 2 factorial design randomized controlled trial	transdermal testosterone at a dose of 75 mg per day and/or monthly 24’000 IU Vitamin D	Transdermal testosterone did not reduce fall risk but improved appendicular lean mass ((0.21 kg/m2 [0.06, 0.37])) and gait speed (0.11 m/s, [0.03, 0.20]) in pre-frail older men.	NA

Swerdloff RS et al. (2020)	151	48	51.6	53.4	Randomized, active-controlled, open-label study.	Oral testosterone undecanoate (TU) vs. topical testosterone product once daily for 3 to 4 months.	- 87% of patients in both groups achieved mean average Testosterone concentration (TCavg) in the eugonadal range. Sodium fluoride-ethylenediamine tetra-acetate plasma T Cavg (mean ± SD) for the oral TU group was 403 ± 128 ng/dL; serum T equivalent, ~489 ± 155 ng/dL; and topical T, 391 ± 140 ng/dL.	- Blood pressure measured by ABPM showed that the oral TU group had significantly greater increases in daytime, nighttime, and 24-hour systolic BP compared to the topical testosterone group. The 24-hour average systolic BP rose by 4.9 ± 8.7 mm Hg in the oral TU group versus 0.2 ± 9.4 mm Hg in the topical group (P = 0.0013). Diastolic BP increases were higher in the oral TU group but not statistically significant. Clinic (cuff) systolic BP increased from baseline to the end of the study in both treatment groups (mean ± SD:oral TU, 2.8 ± 11.8 mmHg; topical Testosterone, 1.8 ±10.8 mm Hg), whereas diastolic blood pressure was essentially unchanged at the final visit for both groups. - Safety profiles were similar in both groups, but oral TU was associated with a mean increase in systolic BP of 3 to 5 mm Hg.
Lincoff AM et al. (2023)	Same sample with Bhasin et al. (2023)				Randomized clinical trial	Topical 1.62% testosterone gel	-	The main cardiovascular safety measure was the first occurrence of death from heart-related causes, a nonfatal heart attack, or a nonfatal stroke, analyzed over time. A secondary measure included these events plus coronary revascularization. With a follow-up period of 33.0 months, primary cardiovascular events occurred in 7.0% of patients in the testosterone group and 7.3% in the placebo group, showing no significant difference (HR 0.96, 95% CI:0.78–1.17; P < 0.001).

Ramachandran S et al. (2020)	86	103		63	A randomized double-blind trial	testosterone undecanoate 1000 mg intramuscular injection at 0, 6, 18, and 30 weeks.	- In the TRT group, significant reductions were found in waist circumference (−3.0 cm, IQR: −5.30/0.0, P < 0.0001), weight (median: −1.0 kg, IQR: −2.75/0.55, P = 0.0014), body mass index (median:−0.3, IQR:−0.90/0.25, P = 0.0032) and total cholesterol (−0.2, IQR:−0.60/0.10, P = 0.0036). In the placebo group, only HbA1c changed, demonstrating a significant increase after 30 weeks (median: +0.10,IQR: −0.20/0.50, P = 0.032).	NA
Tishova Y. et al. (2024)	81	54	49	53	Double blind randomized controlled trial	testosterone undecanoate parenteral 1000 mg	- -Compared to baseline, HOMA-IR was significantly reduced at almost every time point in men receiving TU after only 18 weeks of TU treatment (p <0.0001); - Placebo was not associated with significant changes in HOMAβIR. - -There was a significant decrease in median values of fasting glucose (30 weeks: −2.1%; 138 weeks: −4.9%) and insulin (30 weeks: −10.5%; 138 weeks: −35.5%) after TU treatment.	NA
Gregori G et al. (2021)	42	41	72.6	72.2	parallel, double-blind randomized controlled trial	Testorone gel 1.62% applied once daily	- Global cognition Z score improved more in the LT + Test group compared to the LT + Pbo group (mean change: 0.49 vs. 0.21; 95% CI : -0.45 to -0.11; Cohen's d = 0.74). Attention processing Z-score (0.55 vs. 0.23; 95% CI: -0.55 to -0.09, Cohen's d = 0.49) and memory Z-score (0.90 vs. 0.37; 95% CI: -0.93 to -0.13, Cohen's d = 1.43) showed greater improvements in the LT + Test group.	NA

*IG : Intervention Group
*CG : Comparison Group
NA: Not Available

DISCUSSION

Swerdloff et al. showed that both oral testosterone undecanoate (TU) and testosterone gel are effective, with 87% of patients achieving mean average testosterone concentration (TCavg) within the eugonadal range. The oral TU group demonstrated a TCavg of 403 ± 128 ng/dL in plasma, equivalent to 489 ± 155 ng/dL in serum, which was comparable to the topical testosterone group (391 ± 140 ng/dL). This emphasizes the oral and topical delivery methods are equally effective in maintaining testosterone levels.[6]

Dudek et al. further supported the efficacy of TU injections, reporting a significant increase in serum total testosterone levels from baseline (3.1 ± 0.4 to 7.2 ± 1.3 ng/mL) after 12 months of treatment. Additionally, TU injections effectively suppressed luteinizing hormone (LH) and follicle-stimulating hormone (FSH) levels ($p < 0.001$), indicative hypothalamic -pituitary-gonadal axis regulation.[7] Similarly, Miner et al. demonstrated the effectiveness of oral TU, with 87.4% of patients achieving average 24-hour testosterone levels within the normal male range (300–1140 ng/dL) by week 13. The confidence interval (CI) for this result was 81.7%–92.7%, and the lower bound (81.7%) exceeded the target of at least 65% of patients achieving normal testosterone levels.[8] These results collectively establish that oral, topical, and injectable testosterone formulations are effective in achieving and maintaining testosterone levels in the eugonadal range.

Prostate safety

TRT appears to be relatively safe concerning prostate health. Bhasin et al. found that the incidence of high-grade prostate cancer was similar between the testosterone gel treated group (0.19%) and the placebo group (0.12%), with no statistically significant difference [HR 1.62, 95% CI: 0.39–6.77, p = 0.51]. The incidence of any prostate cancer was also similar between the testosterone gel treated group (0.46%) and the placebo treated group (0.42%) [HR 1.07, 95% CI: 0.47-2.42, p=0.87].[9]

Most studies observed minimal increases in PSA levels that remained clinically insignificant. Rasmussen et al. and Miner et al. observed there were no significant differences of prostate-specific antigen (PSA) levels.[8,10] Dudek et al. reported PSA levels increased in both the TRT and placebo groups over 12 months, but the differences between the groups were not statistically significant.[7] Cunningham et al. found that TRT led to a significantly greater increase in PSA levels compared to placebo ($p < 0.001$) with PSA rising 0.47 ± 1.1 ng/mL from baseline at 12 months in the TRT group, compared to 0.06 ± 0.72 ng/mL in the placebo group.[11]

Cardiovascular safety

Testosterone replacement therapy, through complex mechanisms, is known to increase sodium and fluid retention, which may contribute to elevated blood pressure in some men receiving oral testosterone.[12] Swerdloff et al. highlight significant differences in the impact of testosterone replacement therapies on blood pressure, with oral testosterone undecanoate (TU) showing greater increases in systolic blood pressure compared to topical testosterone.[6] The rise in 24-hour systolic blood pressure observed in the oral TU group (4.9 ± 8.7 mmHg) was significantly higher than in the topical testosterone group (0.2 ± 9.4 mmHg, $p = 0.0013$). These differences were consistent across daytime, nighttime, and 24-hour monitoring. Interestingly, clinic (cuff) measurements did not fully reflect the changes seen in ambulatory blood pressure monitoring (ABPM). Both treatment groups experienced modest increases in clinic systolic blood pressure (oral TU: 2.8 ± 11.8 mmHg; topical testosterone: 1.8 ± 10.8 mmHg), while diastolic pressures remained largely unchanged.

This discrepancy between ABPM and clinic measurements underscores the importance of utilizing ABPM in assessing the cardiovascular effects of testosterone therapy (especially oral), as it provides a more comprehensive evaluation.[6]

Over a follow-up period of 33 months, Lincoff et al. found that there were no significant difference in the occurrence of primary cardiovascular events (death from heart-related causes, a nonfatal heart attack, or a nonfatal stroke) in the testosterone and the placebo group.[13] This finding suggests that while testosterone therapy may influence cardiovascular parameters such as systolic blood pressure, these changes do not necessarily translate to an increased risk of major cardiovascular events.

Hematologic effects

A meta-analysis found that all forms of TRT gels, patches, or injections—cause significant increase in hematocrit (HCt), but no type causes an increase over 4.3%. This finding suggests the risk of excessive red blood cell production can be managed with proper monitoring and patient selection. For patients with low to normal baseline HCt levels, the increase is unlikely to be a concern.[15] Venous thromboembolism and major adverse cardiac events are the most concerning risks associated with increased HCt, necessitating close monitoring.[16] When comparing all testosterone formulations, intramuscular testosterone enanthate showed a significantly greater increase in mean hematocrit compared to the patch. However, no differences in hematocrit were observed between the other formulations.[15] Narukawa suggests that patients who develop polycythemia from intramuscular testosterone, potentially interfering with continued treatment, might consider a combination of intramuscular and patch therapy as an alternative for testosterone therapy.[17]

Pencina found that testosterone treatment has a significant effect in correcting anemia compared to placebo. At each assessed interval—6, 12, 24, 36, and 48 months—a greater proportion of testosterone-treated men achieved anemia correction compared to those receiving placebo, with differences being statistically significant (P = 0.002). Furthermore, testosterone treatment was associated with a reduced incidence of new anemia cases among participants without anemia at baseline. These results suggest that testosterone therapy could be a valuable strategy for managing anemia in men with hypogonadism.[18] Moreover, TRT influences the coagulation system by promoting an anticoagulant effect, primarily through the suppression of the tissue factor (TF) pathway. After 24 weeks, significant between-group differences were observed in key coagulation markers. In the TRT group, several markers decreased, including endogenous thrombin potential, peak thrombin, Factor VII, Factor X, prothrombin, protein C, and Factor XII (all $p < 0.05$), while protein S increased. The placebo group showed no significant changes in coagulation factors.[19]

We expanded the systematic review by adding metabolic and musculoskeletal effects that differ from previous reviews, as well as including more recent studies.[20,21] However, conducting a meta-analysis is not feasible due to the high heterogeneity among included studies.

Metabolic effects

Increased serum testosterone may influence metabolic processes, including body mass index, fat mass, and energy expenditure. Dudek observed that TRT causes significant weight loss and decreases fat mass compared to placebo. TRT also reduces leptin and increase adiponectin level significantly. In addition, highly selective C-reactive protein level decrease significantly in TRT group. The results suggest that TRT may improve systemic metabolic health in patients with hypogonadism.[7]

Similar findings in metabolic effects also observed by Ramachandran who found that in the TRT group, significant reductions were found in waist circumference (−3.0 cm, IQR: −5.30/0.0, P < 0.0001), weight loss (median: −1.0 kg, IQR: −2.75/0.55, P = 0.0014), body mass index (median:−0.3, IQR: −0.90/0.25, P = .0032) and total cholesterol (−0.2, IQR:−0.60/0.10, P = .0036). In the placebo group, only HbA1c changed (median: +0.10, IQR: −0.20/0.50, P = 0.032).[22]

A study conducted by Tishova observed that HOMA-IR was significantly reduced (from baseline) at almost every time point in men after only 18 weeks of Testosterone undecanoate treatment (p <0.0001). There was a significant decrease in median values of fasting glucose (30 weeks: −2.1%; 138 weeks: −4.9%) and fasting insulin (30 weeks: −10.5%; 138 weeks: −35.5%) after TU treatment. Placebo was not associated with significant changes in HOMA-IR. These results suggest that TRT appears to increase insulin sensitivity.[23]

Musculoskeletal effects

Testosterone therapy had a notable impact on bone health, especially in bone mass density. Cauley found that even though there was no difference in the percentage change in TBS (trabecular bone score): 1.6% (95% CI 0.2-3.9) in

the testosterone group and 1.4% (95% CI – 0.2, 3.1) in the placebo group, the vBMD (volumetric bone mineral density) increased by 6% (95% CI 4.5–7.5) compared to 0.4% (95% CI −1.65–0.88) in the placebo group.[24]

Groti found that both groups (testosterone and placebo) experienced a significant reduction in bone turnover marker, indicating reduced bone resorption. However, only the testosterone group had a significant increase in lumbar spine BMD (following 2 years of treatment), with no changes in femoral neck BMD for either group.[25]

Testosterone is found to significantly improve appendicular lean mass and gait speed in pre-frail older men.[26] Rasmussen reveal insights into the effects of strength training and testosterone supplementation on functional performance, specifically measured by the 30-second STS test. The Combogroup (testosterone injection, training, oral vitamin D, calcium, and protein) showed significant improvement in the 30-second STS test at all time points (p<0.001) compared to no intervention, testosterone injection alone, or training with oral vitamin D, calcium, and protein alone. At week 52, testosterone levels were correlated with the performances in the 30-second Sit to Stand Test exclusively for the Combo and TU injection groups; therefore, higher testosterone levels were associated with better physical performance in older men.[10]

Mental Health and Cognitive Function

Gregori et al. found that combination of lifestyle changes (weight management and exercise) with testosterone therapy had consistently larger improvements in cognitive functions (global cognition, attention processing and memory) than lifestyle changes only. A stronger effect size was reported for memory.[27] Miner et al. observed oral TU showed significantly greater improvement in the SF-36 mental component summary (3.82 vs. 0.55; p = 0.009) and numerically greater improvements in vitality, social role functioning, emotional role functioning, and physical role functioning compared to 1.62% topical testosterone gel.[8] These results suggested that oral TU could be the answer to the delivery of testosterone in a way that improves performance in many aspects related to mental health and quality of life. However, the lack of statistical significance in the other aspects warrants further investigation. Limitation: We did not conduct a subgroup analysis due to significant heterogeneity among the studies, which may be attributed to variations in measurement methods, outcome

definitions, and small sample sizes. Moreover, the optimal TRT delivery could not be identified because the different comparators were utilized through the studies. Future research: A longer duration of TRT administration, defined as a minimum of ten years, is required to establish long-term effects.

CONCLUSION

TRT effectively improves testosterone levels, symptoms, overall health, and body composition in male with hypogonadism. While generally safe, TRT has been linked to higher PSA and hematocrit levels, necessitating monitoring. However, there's no evidence that TRT increases the risk of prostate disease and cardiovascular disease. More research is needed to explore long-term outcomes of TRT.

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