REVIEW ARTICLE

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The impact of hyperthyroidism on sexual functions in men and women: a systematic review and meta-analysis

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This study aimed to review the current knowledge on sexual dysfunction in men and women with hyperthyroidism through a systematic review and meta-analysis. Available clinical trials from the MEDLINE database were searched using a prerecorded protocol (Protocol Prospero ID: CRD42022340587), and obtained data were analyzed and reported according to the PRISMA guidelines. Pooled effect estimates were computed using a random-effects model. Twenty eligible studies were identified, of which 15 were included in this meta-analysis. The prevalence of erectile dysfunction was significantly higher in participants with hyperthyroidism than that in controls [odds ratio = 9.16 (95% confidence interval [CI], 5.0–16.5)]. Treatment of hyperthyroidism alone improved erectile functions [effect size, ES = 0.36 (95% CI, −0.01–72)] and mean intra-vaginal ejaculation latency time [ES = 0.63 (95% CI, 0.27–98)] among men with erectile dysfunction and/or premature ejaculation. The prevalence of premature ejaculation also decreased with treatment of hyperthyroidism [odds ratio = 0.11 (95% CI, 0.04–28). Women with hyperthyroidism demonstrated higher odds in female sexual dysfunction than controls [odds ratio = 4.34 (95% CI, 2.63–7.18)]. Female sexual function index scores in women with hyperthyroidism were also significantly lower than those in the controls with moderate effect sizes. An evident and reversible disruption of sexual functions under hyperthyroidism conditions was observed in both sexes.

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INTRODUCTION

Hyperthyroidism, also known as thyrotoxicosis, is the physiological manifestation of excessive thyroid hormone levels [1]. It is generally considered overt or subclinical depending on its biochemical severity, although the disease represents continuously active thyroid function [2]. Hyperthyroidism has a 10-fold higher prevalence among women (1%–2%) than that among men (0.1–0.2%) [1]. Over the last two decades, researchers have reported growing evidence of an association between hyperthyroidism and sexual dysfunction in both sexes [3–8]. Sexual dysfunction is a common public health problem that is increasing in importance and affects both genders cognitively and emotionally. Sexual dysfunction is a common public health problem that is increasing in importance and affects both genders cognitively and emotionally [9]. Emerging evidence from recent studies investigating the association between hyperthyroidism and sexual dysfunction has revealed that hyperthyroidism is associated with increased odds of premature ejaculation (PE) and erectile dysfunction (ED) in men and impaired sexual function in different domains in women [5, 8, 10–14]. The heterogeneity of current clinical reports, unstandardized diagnostic and prognostic evaluations, and lack of quantitative clinical evidence with sufficient sample sizes have limited the establishment of overall evidence-based conclusions and future projections. Here, we aimed to review the current evidence and quantitatively evaluate the current clinical data regarding the relationship between hyperthyroidism and sexual dysfunction in men and women.

MATERIALS AND METHODS

Protocol and registration

The study protocol has been recorded in the International Prospective Register of Systematic Reviews (Prospero: CRD42022340587).

The review and meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews guidelines [15].

Eligibility criteria/study selection

Participants. The participants were those included in the studies investigating the effects of hyperthyroidism and/or its treatment on sexual function. Women and men who had a heterosexual relationship for at least 6 months without any age or ethnicity restrictions were considered trial participants in the current study. Comorbidities, as confounders for sexual dysfunction, apart from hyperthyroidism, were handled as stated in the specific study rather than being rendered as a constant criterion for exclusion.

Interventions. Any type of treatment targeting the removal of the effects of hyperthyroidism was evidenced by low serum thyrotropin (TSH) levels among the participants.

Comparison groups. In the included studies, healthy controls, participants with euthyroidism as evidenced by normal serum TSH levels, and individuals with normal sexual or ejaculatory functions were compared to discriminate the effects of hyperthyroidism on sexual function.

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Outcomes. The primary outcomes (PROs) were erectile and ejaculatory dysfunction in male participants and any sexual dysfunction symptoms expressed or evaluated by questionnaires or PRO measures in female participants. The scores of the PRO measures, such as the PE profile, index of PE, PE diagnostic tool, female sexual function index (FSFI), Sexual Health Inventory of Men (SHIM), International Index of Erectile Function (IIEF) questionnaires, or presence or expression of any sexual complaint as a dichotomous variable, were considered additional outcome measures depending on the retrieved study in our review protocol [16–20].

Study characteristics. The study inclusion criteria were as follows: (i) published in English; (ii) included participants with a stable heterosexual relationship for at least 6 months; (iii) included participants aged between 18 and 80 years; and (iv) randomized and non-randomized controlled clinical trials, cross-sectional studies, case–control studies or case series, and pre- and post-treatment evaluation studies of achieving euthyroid states. Reviews, letters, commentaries, books, book chapters, abstract-only papers, conference proceedings, and dissertations were excluded.

Information sources and search

The MEDLINE database (PubMed) was searched for relevant studies. Clinical trials published in English were analyzed without any restrictions. The following medical subject headings were used as the search terms: hyperthyroidism, sexual dysfunction, ejaculation, orgasm, sexual arousal, sexual desire, dyspareunia, and sexual aversion. The reference lists of all the retrieved articles were also examined as candidate trials for inclusion.

Data collection process

Initial screening via keyword review in PubMed was performed by the first author, and the titles and abstracts of journal articles were evaluated for eligibility. Irrelevant reports were rejected, and candidate studies within the scope of the current review were evaluated for eligibility using full-text files. Finally, the relevance of the studies was assessed by the review authors who were not blinded to the names or institutions of the study authors. The same two authors extracted data from each of the included studies and imported them into Microsoft Excel.

Data items

The extracted items for each study included the author and year of publication, study design, participants, demographic characteristics, intervention protocol, number of participants who dropped out or were withdrawn from the study, activity in which the control group participated, measurements, outcomes, and measured methods.

Risk of bias in individual studies

We established a risk of bias assessment tool for eligible studies specific to the current review and classified all included studies according to their grade and type of bias based on GRADE recommendations to evaluate the certainty of evidence [21].

Synthesis of results

We used the "Review Manager (RevMan)" computer program Version 5.4 for windows from "Cochrane Collaboration, 2020" [22]. Pooled effect estimates were computed by comparing scores between participants with hyperthyroidism and controls and changing scores between those at baseline and the end of the intervention aimed at achieving the euthyroid state, their standard deviations, and the number of participants. Missing standard deviations of changing values, not provided by e-mail to contact the authors, were computed based on the Cochrane Handbook recommendations [22]. The effect size (ES) for each study was expressed using a standardized mean difference with 95% confidence intervals (CIs) and was calculated by subtracting the measure of the exposed group from the control group. Statistical significance was set at $P < 0.05$. Forest plots were generated to demonstrate the standardized mean difference with the corresponding CIs for each study and the overall estimate of the pooled ESs. Odds ratios for the presence of sexual dysfunction in participants with hyperthyroidism and controls were also issued for meta-analysis if appropriately stated. The overall estimates were computed using a random-effects model. According to Cohen's guidelines, ESs are commonly categorized as small (0.2–0.49), moderate (0.50–79), or large (≥ 0.8) [23].

Additional analysis

Heterogeneity among the included studies, which was considered low, moderate, or high, with cutoff points of 25%, 50%, and 75%, respectively, was assessed using the I^2 statistic [22].

RESULTS

In the current review, 20 studies were included, of which 15 were included in the meta-analysis. The flow diagram of the study selection process is presented in Fig. 1. The characteristics of the included studies are summarized in Supplementary Table 1. The assessment results for the risk of bias within and across studies are presented in Figs. 2 and 3, respectively. The results of the individual studies and our synthesis of the results by topic are discussed below.

ED in men with hyperthyroidism

Velazquez et al. were the first to report on sexual dysfunction in 1997, with ~70% of men with hyperthyroidism suffering from decreased libido [24]. Carani et al. have reported that the prevalence of hypoactive sexual desire and ED in 34 men with hyperthyroidism was 17.6% and 14.7%, respectively [3]. Veronelli et al. have reported a 76% prevalence rate in a small group of individuals with hyperthyroidism ($n = 13$) and that the ED scores of patients with hyperthyroidism and diabetes were worse than those of controls [25]. In patients with hyperthyroidism, the ED score is not associated with the duration of thyroid disease, presence of thyroid antibodies, TSH levels, treatment type, or other medical conditions [25]. Krassas et al. have reported that 70.3% of patients with hyperthyroidism have had a SHIM score of ≤21 (indicating some degree of ED) compared to that of 33.8% in the control group ($P < 0.0001$), [4]. The SHIM scores of the patients with hyperthyroidism at baseline were lower than those of the controls [17.0 [7–25] vs. 24.0 [8–25]; $P < 0.0001$] [4]. In their study, SHIM scores did not correlate with either FT4 or TSH levels in patients with hyperthyroidism [4]. Cihan et al. detected the prevalence of ED in patients with hyperthyroidism as 55.8% (24 of 43) in their cohort [10]. Another retrospective database study from Taiwan identified hyperthyroidism in 3.3% of ED cases and in 1.90% of controls [5]. Conditional logistic regression analysis (conditioned on age group, urbanization level, and index year) revealed that cases were 1.74 (95% CI = 1.46–2.07; $P < 0.001$) times more likely to have been previously diagnosed with hyperthyroidism [5]. The conditional logistic regression analysis further revealed that the odds ratio of prior hyperthyroidism among cases was 1.64 (95% CI = 1.37–96, $P < 0.001$) compared to that of controls [5]. Corona et al. have reported that the absence of erection was more common among participants with hyperthyroidism than that among euthyroid participants (62.3% vs. 10.3%, $P < 0.0001$) in the general population [26]. Furthermore, logarithmically transformed TSH levels were inversely related to ED prevalence (adjusted $r = -0.066$, $P = 0.002$) [26]. Their analyses of the population with ED revealed that among 3202 eligible participants, 108 men (3.4%) had low TSH levels and 7 (0.3%) had overt hyperthyroidism [26]. Sex hormone-binding globulin

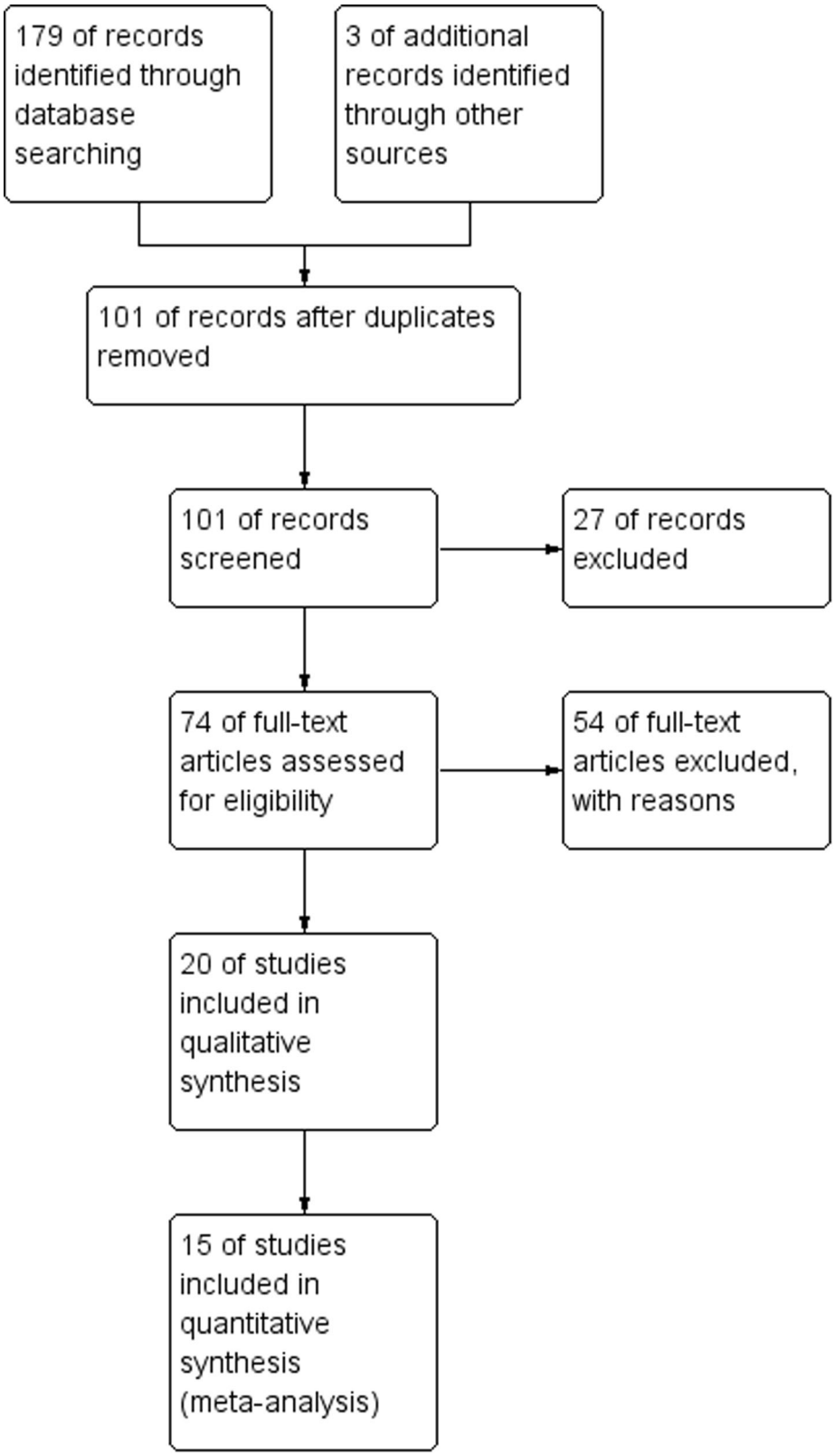

Fig. 1 Flow diagram of the study.

levels were inversely correlated with serum TSH levels (adjusted $r = -0.061$, $P = 0.05$). However, free testosterone levels did not significantly differ between the groups [26]. In the multivariate analysis, serum TSH levels were negatively associated with the ability to have sufficient erections in the study population after adjusting for age, testosterone levels, smoking habits, and chronic disease score (adjusted $r = -0.044$, $P = 0.035$) [26]. Further, overt hyperthyroidism remained a significant predictor of severe ED

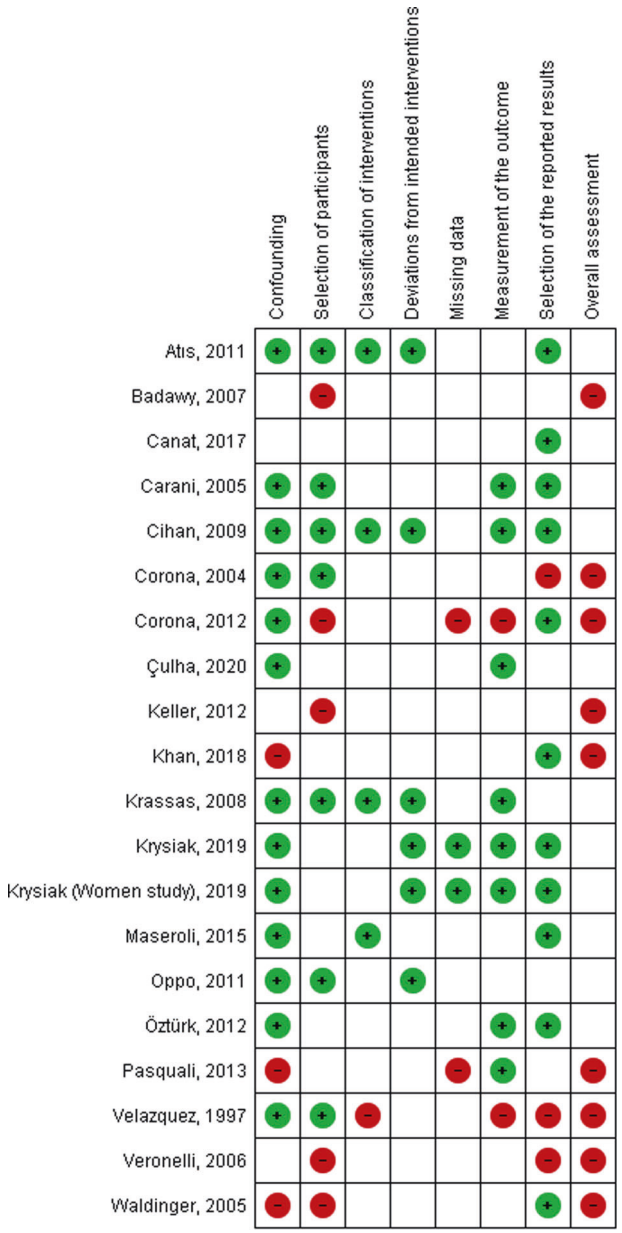

Fig. 2 Risk of bias summary.

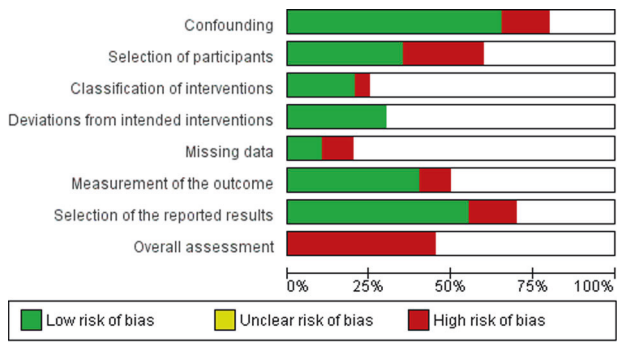

Fig. 3 Risk of bias graph.

after adjusting for age, smoking habits, testosterone and prolactin levels, chronic disease score (hazard ratio: 11.67, $P = 0.023$), and PE (hazard ratio: 16.02, $P = 0.016$) [26]. Compared with nested controls, severe ED was reportedly higher in participants with overt hyperthyroidism (28.6% vs. 2.9%, $P = 0.02$) [26]. Maseroli et al. have reported that the mean serum TSH (mU/L) [1.39 (0.9–1.9) vs. 1.4 (0.9–1.9] and FT4 levels (pmol/L) [15.94 (14.5–17.4) vs. 13.9 (11.9–15.9)] were similar in the control and ED groups [7]. The prevalence of overt thyroid disorders, including overt hypothyroidism and hyperthyroidism, in the two cohorts [European Male Ageing Study (EMAS) control subjects without ED and subjects with ED from University of Florence study (UNIFI) participants] did not significantly differ [7]. Conversely, subclinical hyperthyroidism (TSH levels <0.35 mU/L and FT4 levels within the normal range) was more prevalent in the EMAS cohort than that in the UNIFI cohort (2 vs. 4.1%, $P < 0.05$) [7]. They concluded that although ED is a symptom frequently observed in patients with overt hyperthyroidism (> 60%), overt hyperthyroidism is infrequent (< 1%) in patients seeking medical care for ED [7]. Krysiak et al. compared 20 men with overt hyperthyroidism due to Graves' disease (Gr A), 21 men with overt hyperthyroidism due to multinodular goiter or toxic adenoma (Gr B), and 23 symptomatic but euthyroid men as the control group (Gr C); their study groups significantly differed in the percentage of patients with ED (85% ($P < 0.001$) in Gr A, 62% ($P < 0.01$) in Gr B, and 26% in Gr C) and in erectile function scores [18.9 ± 6.4 ($P < 0.001$) in Gr A, 22.5 ± 4.8 ($P < 0.01$) in Gr B, and 26.3 ± 2.4 in Gr C] [8]. Our quantitative synthesis of the four eligible studies is depicted in Fig. 4 (A and B are forest plots).

Ejaculatory dysfunction in men with hyperthyroidism

Corona et al. have reported that among 755 patients, those with rapid ejaculation (RE) had significantly low serum TSH levels; this difference was significant even after adjustment for age [27]. Accordingly, logarithmically transformed TSH levels were significantly lower ($P < 0.05$) in the RE group than that in the rest of the sample, even after adjusting for age [27]. The prevalence of RE was 57.1% in patients with abnormally low TSH levels (TSH levels < 0.2 mU/L) and 26.5% in the rest of the sample ($P < 0.05$) [27]. Among patients with ED and TSH levels < 0.2 mU/L, the prevalence of RE was 57.1% and 25.8% in patients with ED and normal TSH levels, respectively ($P < 0.05$). The TSH level of patients with RE was 1.3 [0.9–1.7], while that of those without RE was 1.4 [1,2] ($P = 0.05$) [27]. In the stepwise linear regression analysis, TSH levels were significantly ($P < 0.05$) associated with RE severity (adjusted $r = -0.10$) [27]. Carani et al. have reported a 50% prevalence rate of PE in men with hyperthyroidism [3]. TSH, thyroid hormone, and sex hormone-binding globulin levels are significantly correlated with intra-vaginal ejaculation latency time (IELT) [3]. The measured IELT and serum TSH levels were correlated both before ($r = 0.74$, $P < 0.01$) and after ($r = -0.68$, $P < 0.01$) treatment for thyroid dysfunction [3]. Waldinger et al. have reported their results in a large group of men with lifelong PE but without ED. The geometrical mean TSH concentration was 0.85 mU/L (95% CI: 0.82–90). Of 620 men, 14 (2.2%; 95% CI: 1.3%–3.8%) had a TSH concentration of <0.3 mU/L, while that of 5 men (0.8%; 95% CI: 0.3%–1.9%) was >4 mIU/L [28]. None of the 19 men had any clinical evidence of hyperthyroidism or hypothyroidism, and all fT4 concentrations were normal [28]. The study demonstrated an 11-fold higher prevalence of TSH concentration (< 0.3 mU/L than that of the general population) [28]. In 2009, Cihan et al. demonstrated that according to patient-reported outcome measures, 36 of 43 patients (83.7%) with hyperthyroidism complained of difficulty in controlling ejaculation, ranging from slight to extreme difficulty [10]. The mean IELT was 72.8 ± 83.3 s (median, 38.0; range, 12–404 s) during the initial evaluation [10]. In the hyperthyroidism state, when stopwatch measurements were considered a diagnostic criterion, 30 of 43 patients (69.8%) had definite PE (IELT < 60 s) [10]. Ozturk et al. have reported that the mean TSH level was 1.24 ± 0.78 vs. 1.43 ± 1.23, respectively [29]. Hyperthyroidism was noted in nine (8.4%) patients in the PE group and four (4.25%) in the control group [29]. Canat et al. have

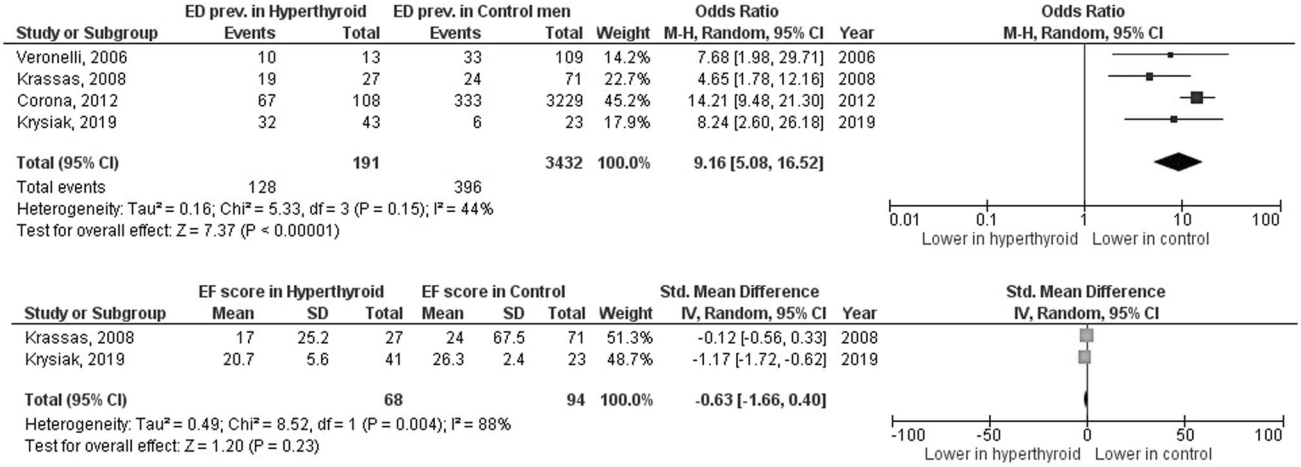

Fig. 4 Erectile dysfunction prevalence and scores of erectile function in men with hyperthyroidism compared to control subjects. **A** Prevalence of erectile dysfunction in men with hyperthyroidism. **B** Erectile function score in men with hyperthyroidism.

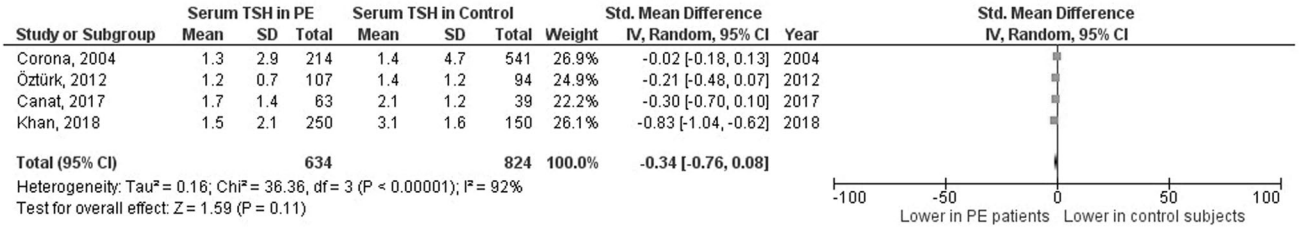

Fig. 5 Serum thyrotropin in men with premature ejaculation.

reported that mean serum TSH level was significantly lower in the PE group than that in the control group [1.7 ± 1.4 vs. 2.1 ± 1.2 mIU/mL ($P = 0.017$)] [30]. Khan et al. have also reported a significant difference in the mean serum TSH levels of men with acquired PE plus diabetes compared with those without PE [serum TSH (mIU/L) level, 1.56 ± 2.1 vs. 3.19 ± 1.6 ($P = 0.001$)] [31]. Culha et al. have reported that hyperthyroidism was diagnosed in 15.09% of patients with acquired PE [14]. The mean duration of PE complaint was 34.1 ± 36.7 months. The mean self-estimated IELT of the patients was 38.2 ± 30.7 s [14]. Compared with other comorbidities, patients with hyperthyroidism had the longest complaint duration (57.7 ± 42.3 months) and the shortest self-estimated IELT duration (27.2 ± 22.3 s) [14]. The quantitative syntheses of the four eligible studies are presented in Fig. 5.

Changes after treatment of hyperthyroidism in male sexual functions

Carani et al. first reported that in patients with hyperthyroidism, the most striking effect of treatment was a decrease in the prevalence of PE from 50% to 15%, whereas that in the general population was 14%. Moreover, hypoactive sexual desire and ED were resolved in most patients [3]. The effects of the treatment were also reflected by changes in the IIEF domain scores; a significant improvement was observed in the EF and intercourse satisfaction domains [3]. In patients treated for hyperthyroidism, self-reported IELT doubled from 2.4 ± 2.1 min to 4.0 ± 2.0 min [3]. Krassas et al. have reported that the SHIM score at follow-up at 1 year with euthyroidism improved compared to that at baseline [24.0 [9–25] vs. 17.0 [7–25]; $P < 0.0001$] [4]. Cihan et al. have reported that after achieving euthyroidism, the rate of definite PE decreased from 25% (6 of 24 patients) to 69.8% [10]. After achieving euthyroidism, the mean IELT in the patients significantly increased from 75.8 ± 99.3 s to 123.2 ± 96.4 s ($P = 0.004$), [10]. Beck anxiety scores significantly decreased after hyperthyroidism treatment ($P = 0.002$) [10]. In recovered patients, a significant improvement was observed in all IIEF domains, except for the intercourse satisfaction domain [10]. In the definite PE group, the mean IELT was significantly prolonged from 36.5 to 104.8 s ($P = 0.039$) [10]. Corona et al. have reported that medical therapy induced normalization of thyroid hormone levels and decreased the prevalence of severe ED from 28.6% to 0% [26]. A quantitative synthesis of the results from the two eligible studies is presented in Fig. 6.

Sexual dysfunction in women with hyperthyroidism

Badawy et al. first reported the presence of FSD in 11 of 18 women with hyperthyroidism diagnosed in their cohort [32]. Subsequently, in a prospective case–control study, Oppo et al. revealed that all domains of the FSFI were significantly impaired in women with hyperthyroidism [desire 3.8 ± 1.0 vs. 4.5 ± 0.6 ($P < 0.005$), arousal/lubrication 8.1 ± 1.2 vs. 9.4 ± 1.3 ($P < 0.001$), orgasm 3.9 ± 1.0 vs. 4.8 ± 0.6 ($P < 0.001$), satisfaction 3.9 ± 0.7 vs. 4.4 ± 1.0 ($P < 0.05$), and pain 4.4 ± 0.7 vs. 5.1 ± 0.8 ($P < 0.005$)] compared to those in controls [11]. In patients with hyperthyroidism, correlations between FSFI domains and TSH levels were less evident and reached statistical significance only for desire ($P = 0.02$), arousal/lubrication ($P = 0.003$), and orgasm ($P = 0.03$), whereas FT4 displayed a significant inverse correlation only for desire ($P = 0.003$) [11]. Atis et al. have reported that FSD was diagnosed in 24 of 40 patients with hyperthyroidism (60%) and 13 of 40 controls (32.5%) ($P = 0.014$) [12]. The mean total FSFI scores were 24.2 ± 9.9 and 29 ± 10.4 in the hyperthyroid and control groups, respectively ($P < 0.0001$) [12]. When the subscores of each FSFI domain were evaluated, the scores for desire (3.8 ± 2.1 vs. 4.3 ± 2.3; $P < 0.04$), arousal (3.4 ± 2.3 vs. 4.7 ± 2.2; $P < 0.0001$), lubrication (4.3 ± 1.9 vs. 5.1 ± 1.6; $P < 0.0001$), orgasm (4.0 ± 2.2 vs. 5.1 ± 1.5; $P < 0.0001$), satisfaction (4.2 ± 1.9 vs. 4.9 ± 2.0; $P < 0.0001$), and pain (4.4 ± 2.3 vs. 5.0 ± 2.6; $P < 0.007$) were also significantly lower in women with hyperthyroidism than those in the controls [12]. The FSFI score was significantly negatively correlated with serum

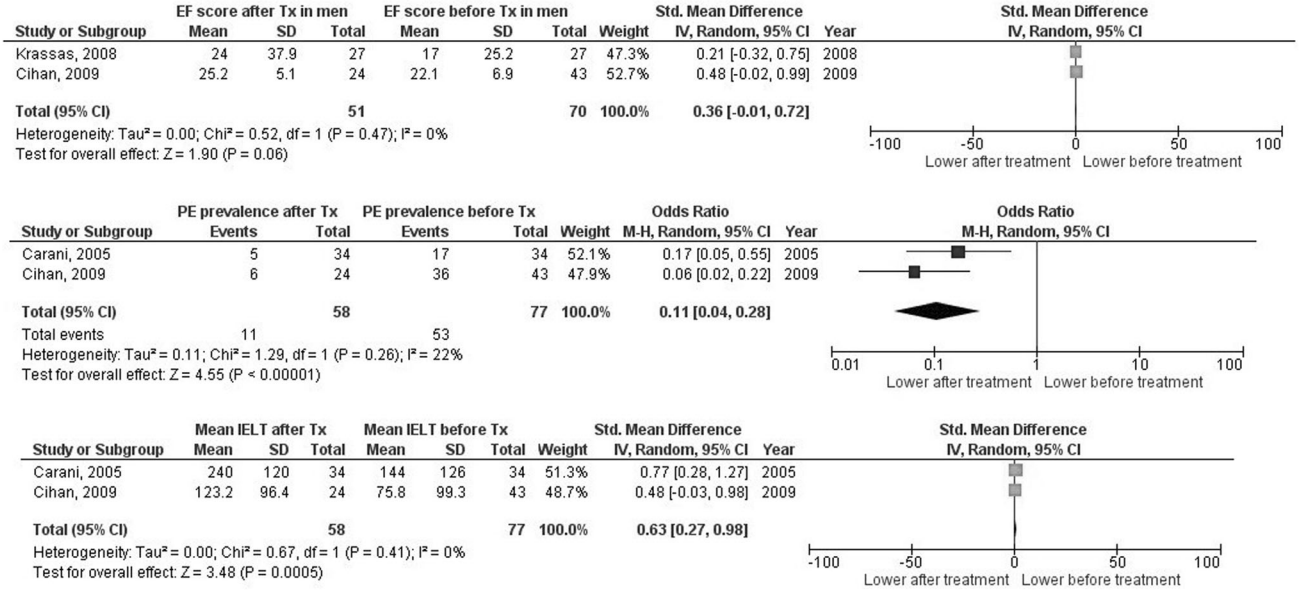

Fig. 6 Changes of parameters related to sexual function with treatment of hyperthyroidism in men. A Change in erectile function score after treatment of hyperthyroidism. **B** Prevalence of PE after treatment of Hyperthyroidism. **C** Mean IELT change after treatment of hyperthyroidism.

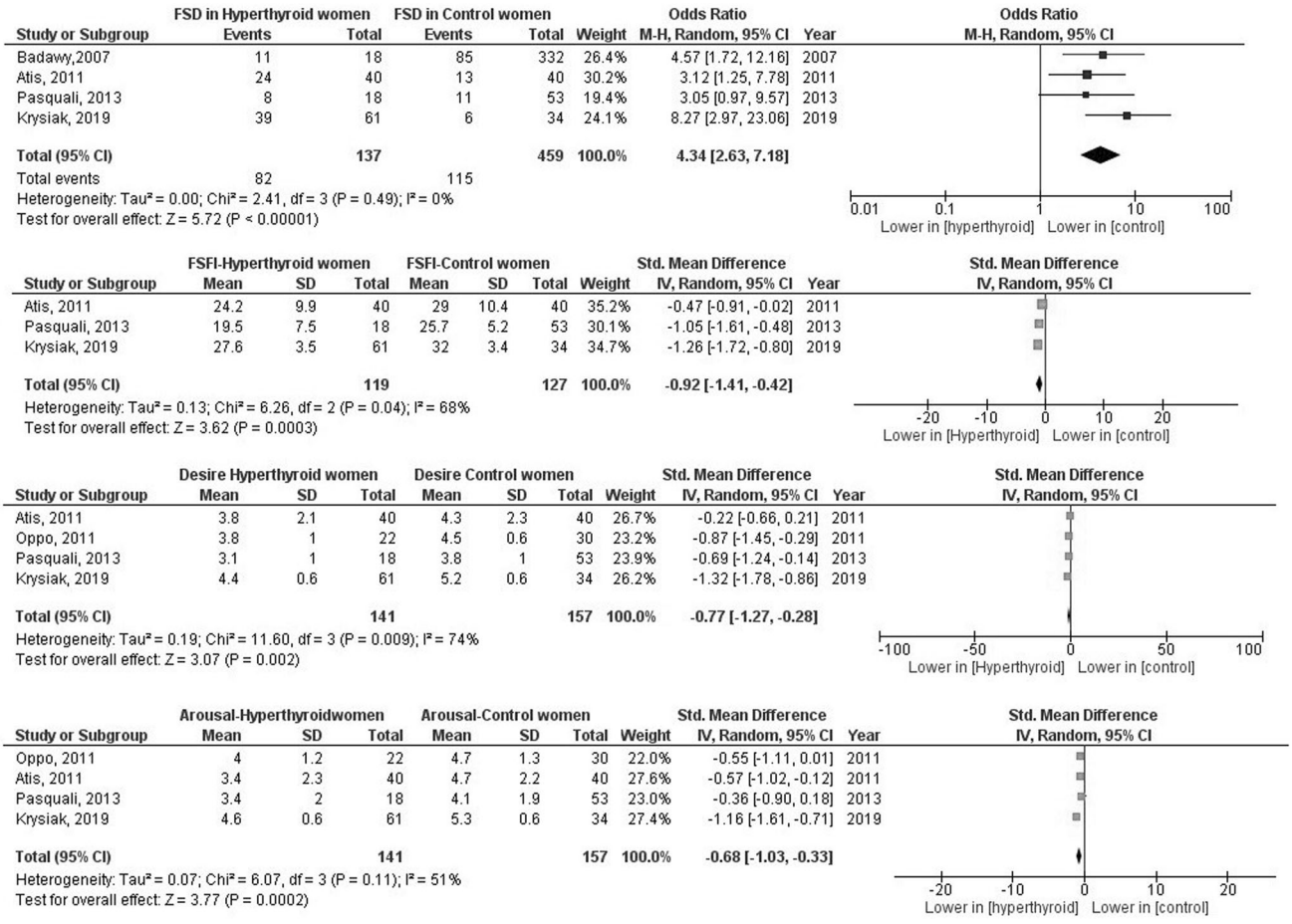

Fig. 7 Parameters related to sexual function in women with hyperthyroidism compared to control subjects. A Prevalence of female sexual dysfunction in women with hyperthyroidism. **B** Female sexual function index in women with hyperthyroidism. **C** Desire in women with hyperthyroidism. **D** Arousal in women with hyperthyroidism.

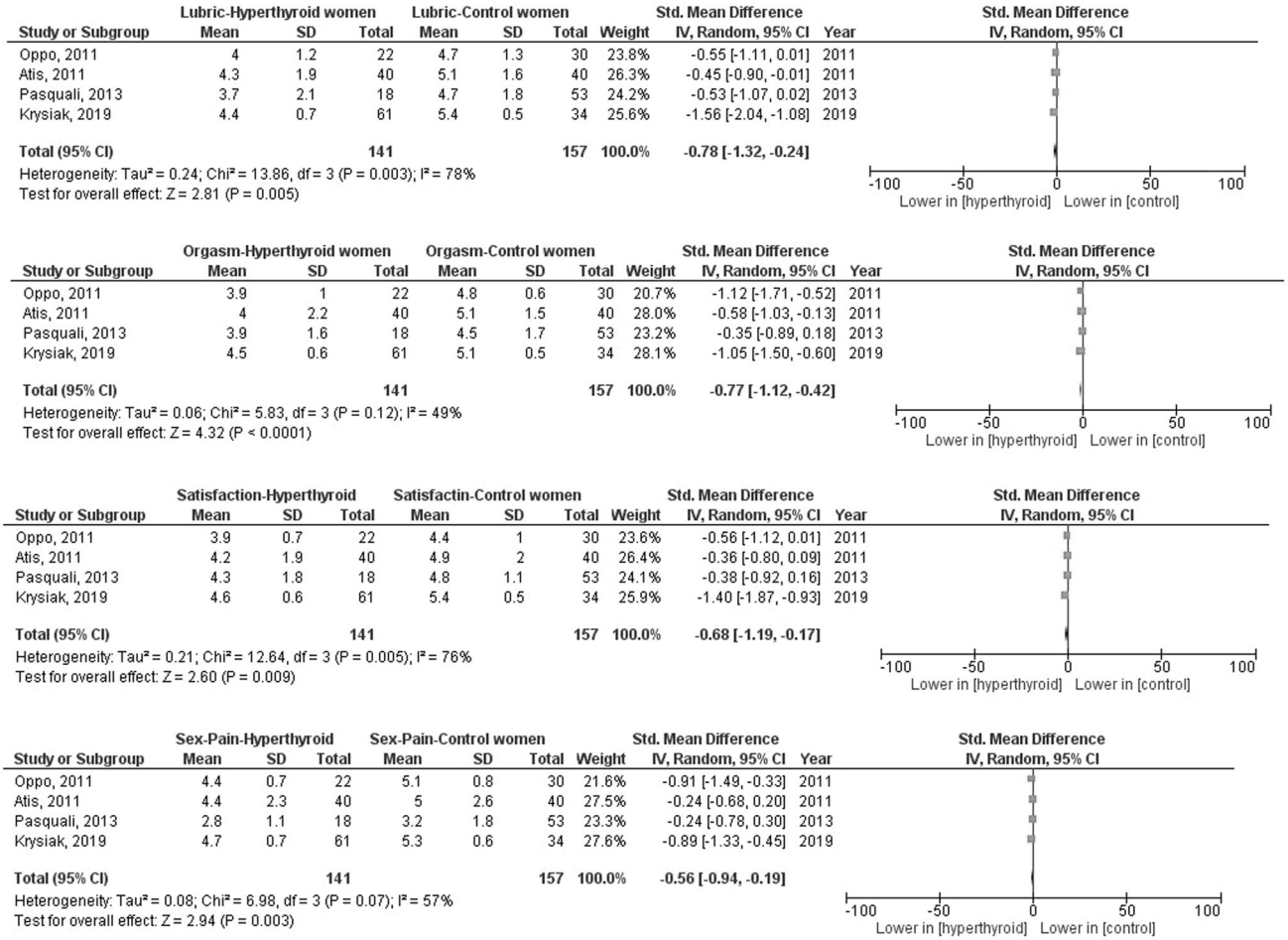

Fig. 8 Some domains of FSFI in women with hyperthyroidism compared to control subjects. A Lubrication in women with hyperthyroidism. **B** Orgasm in women with hyperthyroidism. **C** Satisfaction in women with hyperthyroidism. **D** Sexual pain in women with hyperthyroidism.

sex hormone-binding globulin levels ($r = -0.309$, $P = 0.005$), fT3 ($r = -0.353$, $P = 0.006$), fT4 ($r = -0.305$, $P = 0.018$) levels, and BDI scores ($r = -0.802$, $P = 0.0001$) and positively correlated with total testosterone ($r = 0.284$, $P = 0.011$), free testosterone ($r = 0.407$, $P = 0.001$), and TSH levels ($r = 0.615$, $P = 0.0001$) [12]. Pasquali et al. have reported that the prevalence of FSD was higher in women with hyperthyroidism than that in controls (44.4% vs. 20.1%, $P > 0.05$) [6]. Compared with controls, the mean FSFI scores of the women with hyperthyroidism were 19.5 ± 7.6 vs. 25.7 ± 5.2, and the domain scores were as follows: 3.1 ± 1.0 vs. 3.8 ± 1.0 for desire, 3.4 ± 2.0 vs. 4.1 ± 1.9 for arousal, 3.7 ± 2.1 vs. 4.7 ± 1.8 for lubrication, 3.9 ± 1.6 vs. 4.5 ± 1.7 for orgasm, 4.3 ± 1.8 vs. 4.8 ± 1.1 for satisfaction, and 2.8 ± 1.1 vs. 3.2 ± 1.8 for pain [6]. Compared with controls, women with hyperthyroidism demonstrated a significant decrease in desire scores only [6]. Krysiak et al. compared 31 women with overt hyperthyroidism due to Graves' disease (Gr A), 30 women with overt hyperthyroidism due to multinodular goiter or toxic adenoma (Gr B), and 34 symptomatic but euthyroid age-matched women in the control group (Gr C) [13]. According to their analysis, sexual dysfunction was identified in 25 women (81%) from Gr A ($P = 0.002$ compared with that from Gr C), 14 women (47%) from Gr B ($P = 0.04$ compared with that from Gr C), and 6 women (18%) from Gr C [13]. The mean total FSFI score [26.42 ± 3.89 in Gr A ($P = 0.0001$), 28.85 ± 3.26 in Gr B ($P = 0.0001$), and 32.03 ± 3.41 in Gr C] and all domain scores were lower in women with overt hyperthyroidism than that in women with normal thyroid function [13]. Significant differences in the overall FSFI and domain scores for desire, arousal, and sexual satisfaction were observed between groups A and B [13].

Our quantitative synthesis of the results from the five eligible studies regarding FSD is depicted in Figs. 7 and 8.

Changes after treatment of hyperthyroidism in female sexual function

According to the first report in the literature, after treatment for hyperthyroidism, only one patient in the hyperthyroid group (1/11) reported improvement in their sexual life [32]. Oppo et al. have reported that following restoration of the euthyroid state, a significant improvement in all domains was observed, except for orgasm, whose increase did not reach statistical significance [11]. Although the pain score significantly improved, it remained significantly higher in patients with hyperthyroidism than that in controls, whereas restoration of the euthyroid state was associated with a complete normalization of desire, arousal/lubrication, and satisfaction scores [desire, 4.3 ± 0.5 vs. 3.8 ± 1.0 ($P < 0.05$); arousal/lubrication, 9.0 ± 1.2 vs. 8.1 ± 1.2 ($P < 0.005$); orgasm 4.3 ± 1.0 vs. 3.9 ± 1.0 (not significant); satisfaction, 4.3 ± 1.0 vs. 3.9 ± 0.7 ($P < 0.05$); and pain, 4. ± 0.7 vs. 4.4 ± 0.7 ($P < 0.05$)] [11].

DISCUSSION

Our systematic review revealed that clinical trials investigating sexual dysfunction in men and women with hyperthyroidism are limited. We obtained comparable data for 191 ED, 634 PE, and 137 FSD cases for quantitative synthesis, except for studies that retrospectively searched databases.

Regarding erectile function (EF), 55–76% of men with hyperthyroidism also suffer from ED. The diagnosis of hyperthyroidism in men was associated with higher odds of ED. By contrast, the prevalence of hyperthyroidism reported in currently available studies is ~10–15-fold higher among patients with ED than that among the general population. Quantitative synthesis of the available data has not revealed sufficient evidence suggesting the difference in PRO measures (IIEF scores) between participants with hyperthyroidism and controls.

Regarding ejaculatory function, 50–83% of men with hyperthyroidism have PE. Despite the small sample sizes in the available studies, the prevalence of hyperthyroidism was 2–11-fold higher among men with PE than that among men in the general population. Our quantitative synthesis of the available data did not reveal sufficient evidence for the difference in mean serum TSH levels between participants with and without PE. Although the current studies are limited, treatment with hyperthyroidism alone significantly decreased the prevalence of PE and ED in men. The EF scores and mean IELT measurements also improved significantly according to our meta-analysis.

Women with hyperthyroidism had fourfold higher odds of being diagnosed with FSD. Among the available studies, the prevalence of FSD varied between 40% and 83% in women with hyperthyroidism. Our quantitative synthesis of available data also revealed that women with hyperthyroidism had worse FSFI and domain scores than euthyroid women with a moderate size of effect.

In conclusion, hyperthyroidism severely affects sexual function in both sexes with moderate-to-large ESs.

Limitations

The main limitations were the high risk of bias arising from the biased selection of participants, measurement of outcomes, and heterogeneity of the available studies.

Implications for research

Our study contributes to the literature and supports the idea that the thyroid gland should be considered a sexual organ, similar to the brain or genitalia. However, further research is necessary to clarify some clinical findings, such as why several domains of sexual function were affected more frequently by hyperthyroidism, why some of them did not appropriately recover at the time of evaluation, the physiological role of thyroxin in the ejaculatory reflex, and the interrelation between the thyroid and gonadal axes through testosterone efficacy.

Implications for clinical practice

Our findings support previous recommendations in the literature [33–35]. Newly diagnosed patients with hyperthyroidism should be adequately counseled that their sexual complaints will improve after achieving a euthyroid state. Moreover, clinicians should investigate TSH levels in men with specific symptoms suggestive of hyperthyroidism. Men who have acquired PE and PE accompanied with anxiety or ED would also be benefitted from TSH measurement. Women who complain of severe sexual dysfunction accompanied with hypoactive sexual desire and specific symptoms suggestive of hyperthyroidism should also be investigated for underlying thyroid hyperfunction.

DATA AVAILABILITY

We analyzed currently published data that were protected according to publisher-specific policies. Therefore, we did not take further action regarding the availability of the data.

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AUTHOR CONTRIBUTIONS

AC: conceptualization, methodology, investigation, data curation, validation, writing and, revisions of the paper. AAE: conceptualization, methodology, validation, and final approval of the paper.

COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL

We analyzed currently published data that were protected according to publisher-specific policies. Therefore, seeking ethical approval was not necessary. Nevertheless, the study was conducted according to the tenets of the Declaration of Helsinki.

ADDITIONAL INFORMATION

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