Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2026**; 53(6): 48995
https://doi.org/10.31083/CEOG48995

Original Research

Mendelian Randomization Study of the Causal Relationship Between Thyroid Disorders and Uterine Fibroids

Min Zhou[1,†], Tianmei Wang[1], Xiaodong Luo[2], Cong Li[1,*,†]

[1]Department of Gynecology, The First Affiliated Hospital of Chongqing Medical University, 400016 Chongqing, China
[2]Department of Gynecology, The Second Affiliated Hospital of Chongqing Medical University, 400010 Chongqing, China
*Correspondence: licong@hospital.cqmu.edu.cn; b05104@126.com (Cong Li)
[†]These authors contributed equally.

Academic Editor: Michael H. Dahan
Submitted: 10 December 2025 Revised: 11 February 2026 Accepted: 18 March 2026 Published: 23 June 2026

Abstract

Background: Both the uterus and the thyroid are regulated by the hypothalamic-pituitary axis, and this study aimed to investigate whether thyroid disease is a risk factor for uterine fibroids. **Methods:** We performed a two-sample MR analysis utilizing summary-level data from genome-wide association studies (GWAS). Genetic instruments, specifically single-nucleotide polymorphisms (SNPs), robustly associated with each thyroid disorder were selected as instrumental variables (IVs). The primary analysis employed the inverse-variance weighted (IVW) method, supplemented by Mendelian Randomization Egger regression (MR-Egger), weighted median, and weighted mode estimators. Heterogeneity was assessed using Cochran's Q test, horizontal pleiotropy was evaluated via MR-Egger intercept and Mendelian Randomization Pleiotropy RESidual Sum and Outlier (MR-PRESSO) tests, and sensitivity analyses were conducted using a leave-one-out approach. To control potential false positives from multiple testing, false discovery rate (FDR) correction was applied across the groups. **Results:** In the initial analysis, genetically predicted thyroid disorders (odds ratio [OR] = 1.15, 95% confidence interval [CI]: 1.04–1.27, $p = 6.05 \times 10^{-3}$) and hypothyroidism (OR = 1.07, 95% CI: 1.00–1.13, $p = 2.72 \times 10^{-2}$) were both significantly associated with the risk of UFs. In the sensitivity analysis performed after removing overlapping SNPs between exposure datasets, the associations for thyroid disorders (OR = 1.12, 95% CI: 0.99–1.28, $p = 0.082$) and hypothyroidism (OR = 1.07, 95% CI: 1.00–1.15, $p = 0.049$) were no longer significant, and none of the associations remained significant after FDR correction. **Conclusion:** This study indicates a potential shared genetic basis between overall thyroid disorders and UFs. However, rigorous MR analyses did not support a causal role for thyroid disorders or their major subtypes. Future studies using more refined phenotypic data are warranted.

Keywords: mendelian randomization; thyroid disorders; uterine fibroids; GWAS

1. Introduction

Uterine fibroids (UFs), the most common benign tumors of the female reproductive system, predominantly affect women aged 30–50 years, with incidence increasing with age. The estimated prevalence among women aged 40–50 years ranges from 51.2% to 60%, reaching 70%–80% by age 50 years of age [1]. Although benign, UFs can lead to complications such as menorrhagia, pelvic pain, infertility, recurrent miscarriage, and preterm labor, constituting a primary indication for hysterectomy [2]. In the United States, UFs account for 40%–60% of all hysterectomies [3]. Between 1990 and 2019, the global incidence of UFs increased by approximately 6.87% [4]. As a major reproductive and endocrine organ, the uterus contributes to local physiological regulation through the secretion of functional proteins, cytokines, and enzymes. Hysterectomy, by eliminating local receptors, may disrupt endocrine balance [5], alter hormone levels, and potentially induce or exacerbate perimenopausal symptoms, thereby affecting patients' psychological well-being and behavior. Therefore, identifying risk factors for UFs is essential for early prevention. Established risk factors for UFs encompass a range of demographic, genetic, metabolic, and lifestyle factors. These include: (1) demographic and genetic factors, such as African ancestry, family history, and genetic predisposition; (2) reproductive and hormonal factors, including early menarche, nulliparity, polycystic ovary syndrome (PCOS), endometriosis, and estrogen/progesterone dependence; (3) metabolic and comorbid traits, such as obesity (elevated body mass index), hypertension (elevated systolic and diastolic blood pressure), insulin resistance, diabetes-related traits (elevated fasting blood glucose, fasting insulin, 2-hour postprandial blood glucose, and glycated hemoglobin A1c), and vitamin D deficiency; and (4) lifestyle factors, including alcohol consumption and smoking [6].

Thyroid disorders encompass a spectrum of structural and functional abnormalities, primarily including hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid malignancies. An estimated 2 billion people worldwide are affected by thyroid diseases, with a particularly high prevalence among women [7]. Experimental studies by Rajoria et al. [8] demonstrated that estrogen promotes thyroid cell proliferation, suggesting a potential role in thyroid pathology. Both uterine physiology [9] and thyroid

function [10] are regulated by the hypothalamic–pituitary axis and are influenced by estrogen signaling, supporting a potential pathophysiological link between these conditions. However, epidemiological findings regarding their association have been inconsistent, and observational studies remain susceptible to confounding and reverse causality.

Mendelian randomization (MR) uses genetic variants as instrumental variables (IVs) to strengthen causal inference by minimizing confounding [11]. This study applied a two-sample MR approach to evaluate the causal relationship between thyroid diseases and UFs, including subgroup analyses of specific thyroid disorders.

2. Materials and Methods

2.1 Study Design

A two-sample MR study was conducted using data obtained from genome-wide association studies (GWAS). Strongly associated single-nucleotide polymorphisms (SNPs) were extracted from the exposure data as IVs. The effects of genetic variants randomly assigned at conception on phenotypes were then utilized to infer the causal effects of the corresponding phenotypes on disease outcomes. This approach was applied to investigate the potential causal relationship between the exposure factors and the outcomes.

2.2 Data Sources

Data were obtained from the GWAS Catalog (https://www.ebi.ac.uk/gwas/) and the FinnGen consortium (https://www.finngen.fi/en). The outcome of interest was UFs, whereas the exposures comprised multiple thyroid phenotypes, including thyroid disorders, hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid malignancies. These specific phenotypes were defined according to the corresponding International Classification of Diseases, 10th Revision (ICD-10) codes. To minimize population heterogeneity, all datasets were derived from individuals of European ancestry. Details are provided in **Supplementary Table 1**.

2.3 Selection of IVs

IVs were selected based on three core assumptions: (1) a strong association between the IV and the exposure ($p < 5 \times 10^{-8}$); (2) no association between the IVs and known confounders; and (3) the IVs influence the outcome exclusively through the exposure. In practice, linkage disequilibrium (LD) clumping was performed ($r^2 < 0.001$, distance window = 10,000 kb) using the Phase 3 European reference panel from the 1000 Genomes Project via the clump_data function. Only strong instruments with an F-statistic >10 were retained (**Supplementary Fig. 1**).

2.4 Statistical Analysis

2.4.1 Two-sample MR Analysis

All analyses were conducted in R (v4.5.0, https://www.R-project.org). A two-sample MR analysis was performed using the TwoSampleMR package (v0.6.15, Bristol, UK) to assess the causal effects of five thyroid disease phenotypes on UFs. Primary causal estimates were derived using the inverse-variance weighted (IVW) method. To ensure robustness, the IVW analysis was supplemented with weighted median, simple mode, weighted mode, and Mendelian Randomization Egger regression (MR-Egger) methods. A causal association was considered supported when the IVW result was statistically significant ($p < 0.05$), and the direction of effect was consistent across the supplementary methods. Results are presented as odds ratios (ORs) with 95% confidence intervals (CIs), where OR >1 indicates an increased risk and OR <1 indicates a protective effect.

2.4.2 Sensitivity and Pleiotropy Analyses

To examine potential pleiotropy and heterogeneity, MR-Egger regression and Cochran's Q test were performed. Additionally, the MR-PRESSO (Mendelian Randomization Pleiotropy RESidual Sum and Outlier) method (MRPRESSO package 1.0, https://github.com/rondolab/MR-PRESSO) was applied to detect and correct for outlier variants. A leave-one-out analysis was also performed to evaluate whether the overall results were driven by any single influential genetic instrument.

2.4.3 False Discovery Rate (FDR) Correction

To control the potential false-positive risk arising from multiple comparisons, FDR correction was applied to the MR results across all thyroid disease phenotypes. Using the standard Benjamini–Hochberg (BH) procedure, the primary *p*-values derived from IVW MR tests were adjusted for the number of phenotypes tested. The FDR threshold was set at $\alpha = 0.05$, and associations with a BH-adjusted *q*-value < 0.05 were considered statistically significant.

3. Results

3.1 Selection of SNPs

Following the initial selection process, we obtained 57, 53, 96, 11, and 10 independent instrumental SNPs for thyroid disorders, thyroid nodules, autoimmune hypothyroidism, autoimmune hyperthyroidism, and thyroid malignancies, respectively. To minimize horizontal pleiotropy, overlapping SNPs were removed, including 21 SNPs shared between thyroid disorders and autoimmune hypothyroidism and 1 SNP shared between thyroid disorders and thyroid nodules. The final analysis proceeded with 35, 52, 75, 11, and 10 independent instrumental SNPs for each phenotype, respectively (**Supplementary Tables 1–8**). All selected IVs were robustly validated (F >10), indicating a low risk

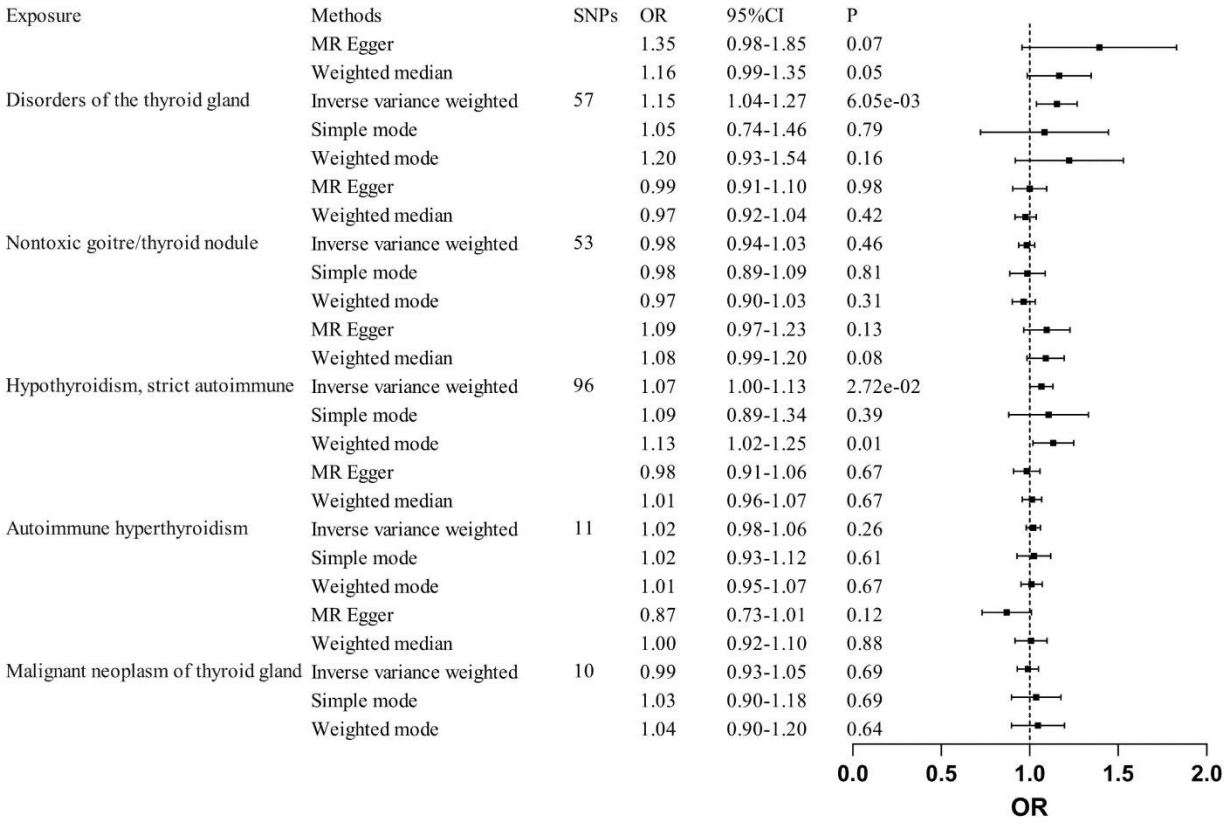

Fig. 1. MR analysis of the association between thyroid disorders and risk of UFs. ORs with 95% CIs were derived from IVW analysis. A causal association was considered significant when the IVW *p*-value was <0.05 and the direction of effect was consistent across supplementary MR methods (MR-Egger, Weighted Median, Simple Mode, Weighted Mode). The vertical line at OR = 1 represents the null. An OR > 1 indicates increased risk, while an OR < 1 indicates a protective factor. Specific estimates were as follows: thyroid disorders, OR = 1.15 (95% CI: 1.04–1.27); hypothyroidism, OR = 1.07 (95% CI: 1.00–1.13). MR, Mendelian randomization; UFs, uterine fibroids; OR, odds ratio; CI, confidence interval; IVW, inverse-variance weighted; SNPs, single-nucleotide polymorphisms.

of weak instrument bias in our analyses.

3.2 Main MR Analysis Results

Genetically predicted predisposition to overall thyroid disorders was significantly associated with an increased risk of UFs (OR = 1.15, 95% CI: 1.04–1.27, $p = 6.05 \times 10^{-3}$). In subgroup analyses, hypothyroidism showed a nominally significant association with UFs (OR = 1.07, 95% CI: 1.00–1.13, $p = 2.72 \times 10^{-2}$) (Fig. 1). Following FDR correction across the 5 thyroid disease phenotypes, the association for overall thyroid disorders remained significant (adjusted $*q* = 0.030$), whereas the associations for the 4 specific subtypes were no longer significant (all $*q* > 0.05$) (Table 1). However, due to sample overlap among the 5 exposure datasets, a sensitivity MR analysis was performed after removing overlapping SNPs. In this analysis, the association between overall thyroid disorders and UFs was no longer significant (IVW $p = 0.082$). The association for strict autoimmune hypothyroidism was borderline significant (IVW $p = 0.049$) (Fig. 2), but did not remain significant after subsequent FDR correction.

3.3 Heterogeneity and Pleiotropy Tests

Cochran's Q test showed no evidence of heterogeneity among the SNPs in the thyroid disease group (Q = 49.3, df = 56, $p = 0.72$). Similarly, no heterogeneity was observed among the SNPs in the hypothyroidism group (Q = 99.2, df = 95, $p = 0.36$). In both groups, no residual heterogeneity (MR-Egger, Q_*p*-value > 0.05) or horizontal pleiotropy (pleiotropy test, $p > 0.05$). Furthermore, the MR-PRESSO global test (NbDistribution = 3000) detected no significant outliers indicative of horizontal pleiotropy (all $p > 0.05$) (Table 2). For the marginally significant association observed for hypothyroidism group after pruning overlapping SNPs (IVW $p = 0.049$), Cochran's Q test detected no significant heterogeneity (Q = 12.5, df = 10, $p = 0.25$), supporting the consistency of the causal estimate (**Supplementary Table 9**).

Table 1. Comparison of FDR-corrected MR analyses for thyroid diseases before and after SNP pruning.

Exposure	Before SNP removal		After SNP removal		Change in significance
	IVW *p*-value	FDR *q*-value	IVW *p*-value	FDR *q*-value	
Disorders of the thyroid gland	0.006	0.030	0.082	0.205	Yes → No
Hypothyroidism, strict autoimmune	0.027	0.068	0.049	0.205	No → No
Autoimmune hyperthyroidism	0.263	0.438	0.263	0.438	No → No
Nontoxic /thyroid nodule	0.463	0.579	0.430	0.538	No → No
Malignant neoplasm of thyroid gland	0.688	0.688	0.688	0.688	No → No

The FDR threshold was set at $\alpha = 0.05$, and associations with a BH-adjusted q-value < 0.05 were considered statistically significant. The only association that was initially FDR-significant ("Disorders of the thyroid gland") became non-significant after pruning, with its q-value increasing from 0.030 to 0.205. FDR, false discovery rate; BH, Benjamini–Hochberg; SNP, single-nucleotide polymorphism. IVW, inverse-variance weighted.

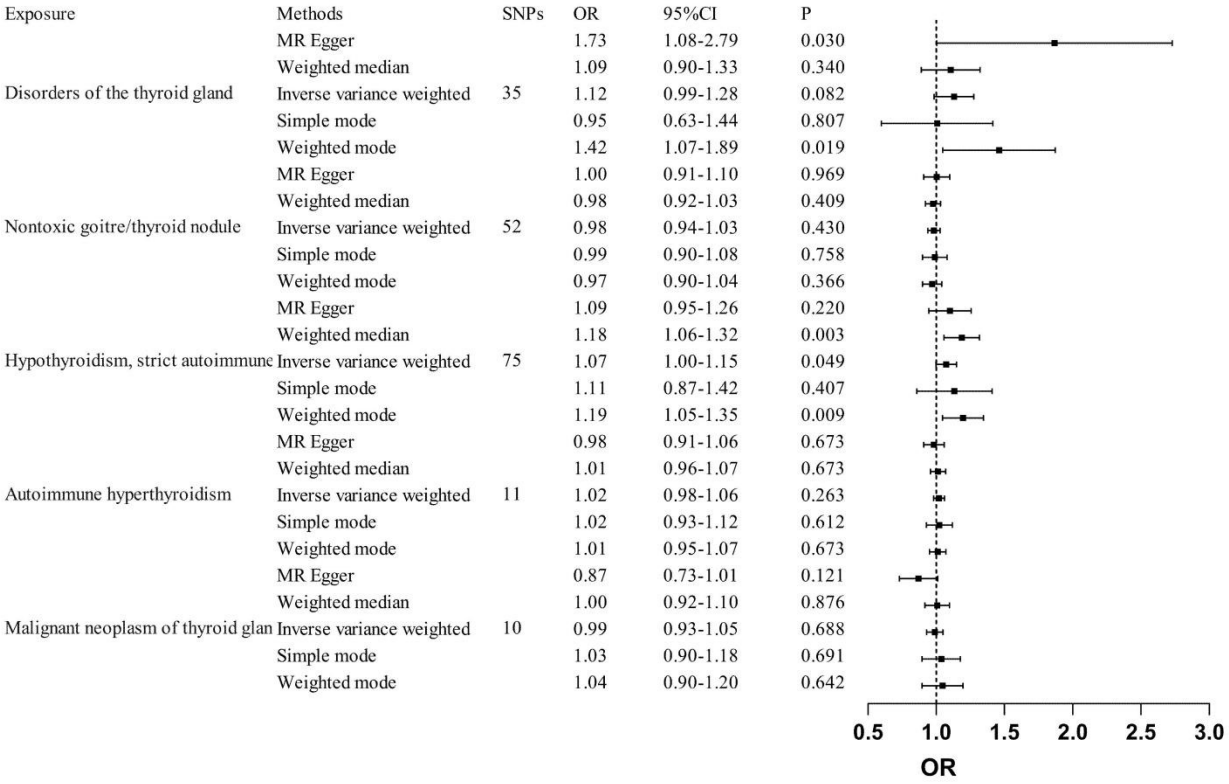

Fig. 2. MR results after removal of overlapping SNPs across exposures. MR, Mendelian randomization; SNPs, single-nucleotide polymorphisms.

3.4 Leave-One-Out Sensitivity Analysis

To assess the influence of individual genetic variants on the overall causal estimate, we performed a leave-one-out sensitivity analysis. As shown in **Supplementary Figs. 2–4** the non-significant results from the main IVW analysis were generally consistent in direction and magnitude across most variants in the leave-one-out sensitivity analysis. However, the identification of potentially influential SNPs suggests that the point estimates may be sensitive to the specific instrument set used.

4. Discussion

Numerous epidemiological studies have reported a co-occurrence of thyroid disorders and UFs. The pathogenesis of UFs has long been attributed to the sex hormone hypothesis, which considers UFs to be hormone-dependent benign tumors [1]. Both the uterus and thyroid glands are regulated by the hypothalamic-pituitary axis and express estrogen receptors, rendering them susceptible to estrogenic influence and potentially contributing to their high comorbidity. At the hypothalamic-pituitary level, thyroid-stimulating hormone (TSH) shares a common α-subunit with luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

Table 2. Heterogeneity and pleiotropy test results.

Exposure	Heterogeneity test MR Egger			Heterogeneity test IVW			Pleiotropy test			MR-PRESSO
	Q	Q_df	Q_*p*-value	Q	Q_df	Q_*p*-value	Egger intercept	SE	*p*-value	Global test *p*-value
Disorders of the thyroid gland	48.2	55	0.73	49.3	56	0.72	–0.0084	0.0084	0.30	0.73
Nontoxic /thyroid nodule	68.5	51	0.05	68.6	52	0.06	–0.002	0.0079	0.72	0.06
Hypothyroidism, strict autoimmune	99.0	94	0.34	99.2	95	0.36	–0.0021	0.0044	0.63	0.36
Autoimmune hyperthyroidism	8.1	9	0.52	9.5	10	0.48	0.0148	0.0128	0.28	0.54
Malignant neoplasm of thyroid gland	6.2	8	0.62	9.1	9	0.42	0.0334	0.019	0.13	0.38

Both the IVW and MR-Egger methods indicated no significant heterogeneity (all Cochran's Q *p*-values > 0.05). The global test for horizontal pleiotropy showed no significant evidence of outliers (all $p > 0.05$). IVW, inverse-variance weighted; SE, standard error; MR, Mendelian randomization.

Furthermore, thyroid hormones (THs) can directly or indirectly regulate the secretion of kisspeptin and gonadotropin-releasing hormone (GnRH) through metabolic signals such as prolactin and leptin [12,13]. These shared regulatory pathways suggest a potential link between thyroid function and the etiology of UFs.

Hypothyroidism, particularly autoimmune hypothyroidism, is the most prevalent thyroid dysfunction. A 2014 retrospective study by Ott et al. [14] reported an association between hypothyroidism and UFs, with women with hypothyroidism exhibiting larger fibroids than those without hypothyroidism. Additionally, studies suggest that a hypothyroid state may promote the expression of systemic chronic inflammatory immune factors, which may stimulate the proliferation of UF cells [15]. Our initial MR analysis suggested a borderline causal relationship between hypothyroidism and UFs. To mitigate potential pleiotropy arising from shared instruments across the five thyroid-related exposures, we identified overlap among the instruments for thyroid disorder and hypothyroidism (22 SNPs), whereas no overlap was observed among the other thyroid disease subtypes. After removal of the overlapping SNPs, the association for the thyroid disorder group became non-significant, whereas the borderline association for hypothyroidism persisted. These findings suggest that the initially significant association observed for thyroid disease may have been driven primarily by instruments related to hypothyroidism. Therefore, this potential relationship should be further explored using larger and more precisely defined datasets.

Among thyroid disorders, autoimmune hyperthyroidism poses significant clinical risks. Studies have shown that plasma estrogen levels are two- to three-fold higher in women with hyperthyroidism across all menstrual phases than in euthyroid women. One potential underlying mechanism involves the upregulation of sex hormone-binding globulin (SHBG) expression by triiodothyronine (T3) and thyroxine (T4), which enhances steroid hormone transport. Elevated SHBG levels increase binding to 17-β-estradiol, thereby reducing its metabolic clearance rate [16]. Women with hyperthyroidism exhibit a two- to three-fold increase in estrogen levels across all phases of the menstrual cycle, accompanied by elevated total and free estradiol (E_2) levels [17]. However, evidence supporting a direct association between hyperthyroidism and UF incidence remains inconclusive. Our MR analysis found no significant causal relationship between hyperthyroidism and UFs. Whether hyperthyroidism influences UF pathogenesis through its effects on sex hormone regulation warrants further investigation through prospective studies or clinical datasets.

Thyroid nodules are the most common structural thyroid disorder, with a higher prevalence in women than in men. Both UFs and thyroid nodules are considered hormone-dependent pathologies, with their development and progression influenced by interactions between sex hormones (e.g., estrogen and progesterone) and THs. Estrogen promotes the proliferation of uterine smooth muscle cells by binding to estrogen receptors in the uterus, thereby contributing to UF formation. A 2022 large-scale study from Korea (JIM et al. [18]) reported that individuals with UFs had a higher risk of developing thyroid nodules compared to those without UFs. Similarly, Li et al. [19] observed that multiple UFs were more common among patients with thyroid nodules than in those without, indicating that thyroid nodules may increase the risk of UFs in Chinese women. However, in our MR analysis, the IVW method showed no significant association between thyroid nodules and UFs ($p = 0.46$). These findings suggest that previously observed correlations in epidemiological studies may have been influenced by confounding factors, such as age, obesity, and metabolic syndrome. In contrast, the MR design leverages genetic instruments to minimize confounding and reverse

causation, thereby providing estimates that more closely approximate causal inference.

Thyroid malignancy represents one of the most severe outcomes among thyroid diseases. Whether malignant transformation of benign thyroid nodules, potentially triggered by radiation exposure, chronic inflammation, or alterations in signaling pathways, affects UF risk remains poorly understood, with evidence currently limited to isolated case reports. In 2019, a study documented a case of papillary thyroid carcinoma in which a thyroid-origin metastasis was identified within a UF six years after surgery and radioiodine therapy [20]. In the present study, although 10 SNPs showed strong associations with both thyroid cancer and UFs, the MR analysis did not support a significant causal relationship between thyroid malignancy and UFs. These findings imply that malignant progression of thyroid disease does not increase the risk of UFs.

Limitations and Future Directions

This study has several limitations. First, our analysis utilized a pan-European LD reference panel for clumping, which may not fully capture population-specific LD patterns within the Finnish cohort and could potentially leave residual correlations among the selected instruments. Second, as a preliminary investigation, our study did not incorporate multivariable MR or colocalization/fine-mapping analyses. Consequently, we were unable to distinguish whether the observed overall association was driven by generalized thyroid dysfunction or by a specific subtype with limited statistical power. Third, phenotype definitions based on electronic health records (EHR) may be influenced by healthcare-seeking behavior and diagnostic coding patterns. This may lead to inflated co-diagnosis rates and potentially bias the observed associations. Importantly, this source of bias is non-genetic in nature and therefore would not be detectable using standard MR pleiotropy robust methods such as MR-Egger or MR-PRESSO. Fourth, our analysis was confined to five major thyroid disease categories (thyroid disorders, hypothyroidism, hyperthyroidism, thyroid nodules, and thyroid malignancies) and did not extend to other subtypes, such as thyroiditis or goiter. Thus, although our study informs the relationship between several major thyroid phenotypes and UFs, it cannot exclude the possibility of distinct causal effects associated with unexamined subtypes. Fifth, all datasets were obtained from European populations, limiting the generalizability of the findings to other ethnic groups. Future studies should include more diverse populations to validate these findings. Sixth, the exclusion of confounders relied on currently recognized phenotypes, which may have resulted in either incomplete or excessive exclusion. Future research could consider employing multivariable MR approaches to better control for confounding and improve the robustness of the findings.

5. Conclusion

In summary, although our study provides suggestive evidence of an association between overall genetic susceptibility to thyroid disorders and the risk of UFs, the subtype-specific basis of this association remains to be elucidated. Based on our most stringent analyses, the present findings do not support disorders of the thyroid gland or their major subtypes as causal risk factors for UFs. Future studies should aim to assemble larger, subtype-specific GWAS datasets and apply advanced approaches, such as multivariable MR and colocalization analyses, to more precisely define the underlying causal architecture.

Abbreviations

MR, Mendelian randomization; UFs, uterine fibroids; GWAS, genome-wide association studies; SNPs, single-nucleotide polymorphisms; IVW, inverse-variance weighted; IVs, instrumental variables; MR-Egger, Mendelian Randomization Egger regression; OR, odds ratio; CI, confidence interval; FDR, false discovery rate; MR-PRESSO, Mendelian Randomization Pleiotropy RESidual Sum and Outlier; PCOS, polycystic ovary syndrome; TSH, thyroid-stimulating hormone; LH, luteinizing hormone; FSH, follicle-stimulating hormone; THs, thyroid hormones; GnRH, gonadotropin-releasing hormone; T3, triiodothyronine; T4, thyroxine; SHBG, sex hormone-binding globulin.

Availability of Data and Materials

The original contributions presented in the study are included in the article and Supplementary Material. Further inquiries can be directed to the corresponding author.

Author Contributions

MZ and CL designed the research study. MZ performed the research. MZ, TW and XL analyzed the data. MZ and TW wrote the manuscript. XL and CL reviewed and revised the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

Not applicable.

Acknowledgment

We thank the GWAS Catalog and the FinnGen study for providing publicly accessible data, as well as all participants and funding bodies involved in the original studies.

Funding

This work was supported by the Science-Health Joint Medical Scientific Research Project of Chongqing [Grant number 2024GDRC003].

Conflicts of Interest

The authors declare no conflicts of interest. Cong Li is serving as one of the Editorial Board members of this journal. We declare that Cong Li had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Michael H. Dahan.

Declaration of AI and AI-Assisted Technologies in the Writing Process

During the preparation of this work, the authors used the DeepSeek AI tool in order to check spelling and grammar. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/CEOG48995.

References

[1] Uterine Fibroid Diagnosis and Treatment Chinese Expert Consensus Panel. Chinese expert consensus on the diagnosis and treatment of uterine fibroids. Zhonghua Fu Chan Ke Za Zhi. 2017; 52: 793–800. https://doi.org/10.3760/cma.j.issn.0529-567x.2017.12.001 (In Chinese)

[2] Marsh EE, Wegienka G, Williams DR. Uterine Fibroids. JAMA. 2024; 331: 1492–1493. https://doi.org/10.1001/jama.2024.0447

[3] Pavone D, Clemenza S, Sorbi F, Fambrini M, Petraglia F. Epidemiology and Risk Factors of Uterine Fibroids. Best Practice & Research. Clinical Obstetrics & Gynaecology. 2018; 46: 3–11. https://doi.org/10.1016/j.bpobgyn.2017.09.004

[4] Li B, Wang F, Chen L, Tong H. Global epidemiological characteristics of uterine fibroids. Archives of Medical Science. 2023; 19: 1802–1810. https://doi.org/10.5114/aoms/171786

[5] De Leo S, Lee SY, Braverman LE. Hyperthyroidism. Lancet (London, England). 2016; 388: 906–918. https://doi.org/10.1016/S0140-6736(16)00278-6

[6] Qu Y, Chen L, Guo S, Liu Y, Wu H. Genetic liability to multiple factors and uterine leiomyoma risk: a Mendelian randomization study. Frontiers in Endocrinology. 2023; 14: 1133260. https://doi.org/10.3389/fendo.2023.1133260

[7] Chaker L, Bianco AC, Jonklaas J, Peeters RP. Hypothyroidism. Lancet (London, England). 2017; 390: 1550–1562. https://doi.org/10.1016/S0140-6736(17)30703-1

[8] Rajoria S, Suriano R, Shanmugam A, Wilson YL, Schantz SP, Geliebter J, et al. Metastatic phenotype is regulated by estrogen in thyroid cells. Thyroid. 2010; 20: 33–41. https://doi.org/10.1089/thy.2009.0296

[9] Yang Q, Ciebiera M, Bariani MV, Ali M, Elkafas H, Boyer TG, et al. Comprehensive Review of Uterine Fibroids: Developmental Origin, Pathogenesis, and Treatment. Endocrine Reviews. 2022; 43: 678–719. https://doi.org/10.1210/endrev/bnab039

[10] Kansakar E, Chang YJ, Mehrabi M, Mittal V. Expression of estrogen receptor, progesterone receptor, and vascular endothelial growth factor-A in thyroid cancer. The American Surgeon. 2009; 75: 785–789.

[11] Spiga F, Gibson M, Dawson S, Tilling K, Davey Smith G, Munafò MR, et al. Tools for assessing quality and risk of bias in Mendelian randomization studies: a systematic review. International Journal of Epidemiology. 2023; 52: 227–249. https://doi.org/10.1093/ije/dyac149

[12] Brown RSE, Khant Aung Z, Phillipps HR, Barad Z, Lein HJ, Boehm U, et al. Acute Suppression of LH Secretion by Prolactin in Female Mice Is Mediated by Kisspeptin Neurons in the Arcuate Nucleus. Endocrinology. 2019; 160: 1323–1332. https://doi.org/10.1210/en.2019-00038

[13] Donato J, Jr, Frazão R. Interactions between prolactin and kisspeptin to control reproduction. Archives of Endocrinology and Metabolism. 2016; 60: 587–595. https://doi.org/10.1590/2359-3997000000230

[14] Ott J, Kurz C, Braun R, Promberger R, Seemann R, Vytiska-Binstorfer E, et al. Overt hypothyroidism is associated with the presence of uterine leiomyoma: a retrospective analysis. European Journal of Obstetrics, Gynecology, and Reproductive Biology. 2014; 177: 19–22. https://doi.org/10.1016/j.ejogrb.2014.03.003

[15] Wegienka G. Are uterine leiomyoma a consequence of a chronically inflammatory immune system? Medical Hypotheses. 2012; 79: 226–231. https://doi.org/10.1016/j.mehy.2012.04.046

[16] Selva DM, Hammond GL. Thyroid hormones act indirectly to increase sex hormone-binding globulin production by liver via hepatocyte nuclear factor-4alpha. Journal of Molecular Endocrinology. 2009; 43: 19–27. https://doi.org/10.1677/JME-09-0025

[17] Krassas GE, Poppe K, Glinoer D. Thyroid function and human reproductive health. Endocrine Reviews. 2010; 31: 702–755. https://doi.org/10.1210/er.2009-0041

[18] Yuk JS, Kim JM. Uterine fibroids increase the risk of thyroid goiter and thyroid nodules. Scientific Reports. 2022; 12: 6620. https://doi.org/10.1038/s41598-022-10625-x

[19] Li S, Li W, Sheng B, Zhu X. Relationship between thyroid disorders and uterine fibroids among reproductive-age women. Endocrine Journal. 2021; 68: 211–219. https://doi.org/10.1507/endocrj.EJ20-0340

[20] Bertrand AS, Iannessi A, Peyrottes I, Lacout A, Thyss A, Marcy PY. Myoma Hot Spot: Tumor-to-Tumor Metastasis of Thyroid Origin into Uterine Leiomyoma. European Thyroid Journal. 2019; 8: 273–277. https://doi.org/10.1159/000501153