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Is thyroid disease associated with post-operative complications after total joint arthroplasty? A systematic review of the literature

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- *Background*: This comprehensive systematic review aims to assess the literature regarding the risk of postoperative complications in patients undergoing total joint arthroplasty (TJA) with concomitant thyroid dysfunction.
- *Methods*: Studies were identified by searching PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Scopus, and ClinicalTrials.gov (end of search: May 2022).
- *Inclusion criteria*: Randomized control and case-control studies, cohort and observational clinical studies were included, which focused on postoperative complications and outcomes of patients undergoing TJA operations of major joints (knee, hip, ankle, elbow). All studies were assessed according to their level of evidence, the number and age of patients, and treatment complications.
- *Analysis*: Nine studies were included in this review that demonstrated a higher risk of postoperative anemia, perioperative blood loss, hemoglobin decrease, and transfusion rates in hypothyroid patients after TJA.
- *Results*: Hypothyroidism has been identified as a potential but modifiable risk factor for increased rates of deep venous thrombosis, acute kidney injury, pneumonia, and non-specified cardiac complications among hypothyroid patients who underwent TJA as well as increased rates of periprosthetic joint infection. No significant differences in the prosthesis-related mechanical complication rates have been calculated when comparing hypothyroid and euthyroid patients.

Keywords
- arthroplasty
- hip
- knee
- ankle
- elbow
- hypothyroidism
- complications

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Introduction

Total joint arthroplasty (TJA) is the most effective healthcare intervention to treat end-stage joint osteoarthritis (1, 2). TJA is a highly cost-effective procedure for improving the quality of life of patients with joint osteoarthritis when both short- and long-term outcomes are considered (2, 3).

TJA implementation is constantly growing and it is likely that it will continue its upward trend due to population growth and increasing life expectancy.

It is imperative to stress, however, that a number of variables can influence the precision of forecasts of future demand such as increased population heterogeneity, expansion of joint replacement criteria of feasibility and indications as well as the increase in the proportion of people over 40 years of age in the population (4).

For reference, Australia is expected to experience a 73% increase in primary total hip replacements between 2013 and 2046. This will represent an increase of 198% in the total number of procedures performed. In the case of total knee replacements, a 31% increase is anticipated by 2046, equating to a 126% increase in procedures performed (5). An estimated 20% increase in the volume of primary total hip replacements and a 17% increase in total knee replacements are expected in Sweden by 2030 (4). On the contrary, more lenient estimations projected an increase of primary total hip arthroplasty (THA) in the United States by 284% and primary total knee arthroplasty (TKA) by 401% in 2040 (6).

Hospital readmissions after TJA represent a massive economic burden on healthcare systems. Almost half of the readmissions are due to medical complications unrelated to the TJA (7). Osteoarthritis is an age-related disease; patients diagnosed with osteoarthritis, one of the most common joint disorders requiring TJA, are twice as likely to have comorbidities than a control group of the same age (7, 8). Attention has recently focused on recognizing modifiable risk factors of perioperative complications. Perioperative identification and optimization of the risk factors could improve outcomes and decrease the substantial economic burden of readmissions on the healthcare system (9, 10).

Endocrine dysfunctions, such as thyroid disorders and diabetes, were recently recognized as risk factors for postoperative complications after orthopedic procedures (11, 12). Thyroid hormones exert widespread and complex action in almost all human tissues, including bone remodeling and articular cartilage health. However, understanding the impact of thyroid gland disturbances in TJA patients remains incomplete (9). The reported prevalence of hypothyroidism in the TJA population is up to 18%, significantly higher than in the general population (10). However, the evaluation of thyroid dysfunction influence on primary TJA outcomes is limited. Recent data demonstrated an increased risk of multiple postoperative complications and higher care costs among patients with hypothyroidism following TJA (7).

Research is required to improve our understanding of the risk factors, prophylactic measures, and specific treatment modalities which may prevent complications and enhance TJA outcomes. This comprehensive systematic review aims to assess the literature regarding the risk of postoperative complications in patients undergoing TJA with concomitant thyroid dysfunction.

Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement and in line with the protocol agreed by all authors. The review protocol was registered in the International Prospective Register of Systematic Reviews 'PROSPERO' under registration number CRD 42022296896.

Studies were identified by searching the PubMed database, Cochrane Central Register of Controlled Trials (CENTRAL), ScienceDirect/Scopus, and ClinicalTrials.gov (end of search date: January 2022) using the following search strategy: ('Thyroid Diseases' [Mesh] OR 'thyroid function' [tiab] OR 'thyroid' [tiab] OR 'thyroid disease' [tiab] OR 'hyperthyroidism' [tiab] OR 'hypothyroidism' [tiab] OR 'thyroiditis' [tiab]) AND ('Arthroplasty' [Mesh] OR 'Arthroplasty, Replacement, Hip' [Mesh] OR 'Arthroplasty, Replacement, Shoulder' [Mesh] OR 'Arthroplasty, Replacement, Knee' [Mesh] OR 'Arthroplasty, Replacement, Ankle' [Mesh] OR 'arthroplasty' [tiab] OR 'knee arthroplasty' [tiab] OR 'hip arthroplasty' [tiab] OR 'Total Joint Arthroplasty' [tiab] OR 'total shoulder arthroplasty' [tiab]) AND ('Risk' [Mesh] OR 'Postoperative Complications' [Mesh] OR 'Intraoperative Complications' [Mesh] OR 'Pathologic Processes' [Mesh] OR 'Complications' [tiab] OR 'survival rate' [tiab] OR 'survival' [tiab]). We also manually used combination of the abovementioned 'Mesh' terms during our search strategy.

Randomized control and case-control studies, cohort and observational clinical studies were included. Case reports, letters to the editor or editorial comments, reviews, animal or cadaveric studies, and studies with no full-text available were not included. The selected studies included adult patients with thyroid dysfunction undergoing elective TJA, reporting data on perioperative and postoperative complications. No sample size or year of publication restrictions were applied.

The primary outcomes were the rate of postoperative complications in patients undergoing TJA with thyroid dysfunction. These were divided into four categories: implant-related, blood loss, infection, and postoperative medical complications. Comparative data on the rate of postoperative complications in non-thyroid populations were also recorded.

Two independent investigators (ST, VFP) searched the literature using the strategy provided. Two reviewers independently analyzed and selected the article titles and abstracts from the search strategy based on the inclusion criteria. A senior author (EK) resolved all disagreements by consensus.

The Newcastle–Ottawa Scale was used to evaluate the methodological quality of the case-control and cross-sectional studies (13). The evaluation is based on selection bias, comparability, and outcome measure assessment. Studies can be granted up to nine stars for case-control and ten stars for cross-sectional studies.

Results

Search results

The electronic database search yielded 1412 articles after screening for duplicates. After assessing titles and abstracts, 20 articles were deemed possibly suitable and examined in full text. Eleven studies were disqualified since they did not match the inclusion criteria. Finally, nine articles were eligible and included in this systematic review (Fig. 1).

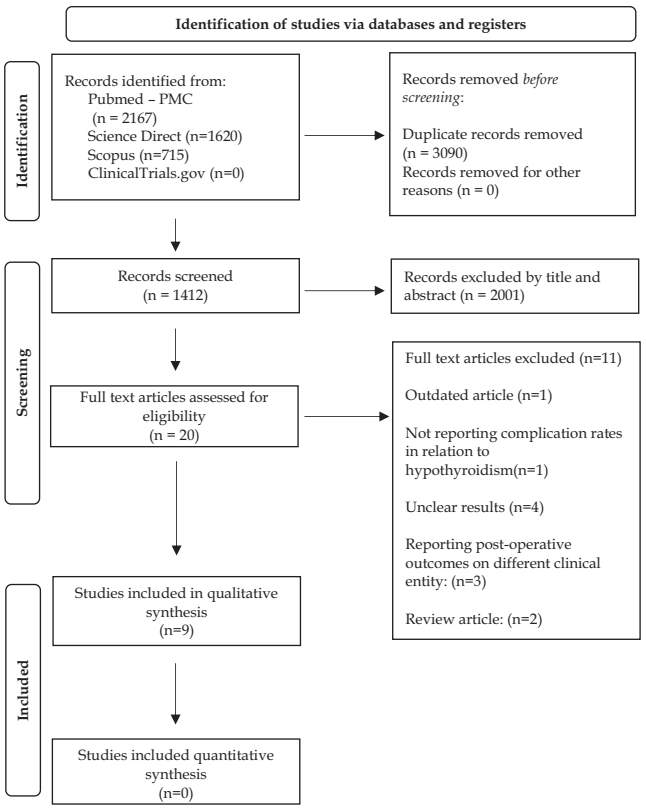

Figure 1
Flow diagram of search strategy.

Demographics, patient characteristics, study design

The studies were published between 2016 and 2021. They mainly were retrospective and prospective observational and cohort studies. One study presented data on total ankle arthroplasty (13); four studies presented data on TKA (7, 14, 15, 16); one study included data on THA (17); and one for total elbow arthroplasty (18). Two studies demonstrated data on both TKA and THA operations (19, 20).

Data regarding 1,472,135 TJA operations were included in the involved studies. The mean age of patients at the time of arthroplasty was 66.9 years, and the mean follow-up ranged from 3 to 78 months. Data regarding the thyroid disease type were not included in any of the examined studies.

Demographic data and further information regarding patients and the studies are presented in Table 1.

Methodological quality assessment

Three cohort studies (7, 14, 16) were measured to be of high methodological quality and one (17) of moderate quality. A cross-sectional study was of high (20), three of moderate (15, 19, 21), and one of low methodological quality (18). The quality assessment outcomes are summarized in Supplementary Appendix 1 and 2 (see

Table 1 General studies information, patients' characteristics, and study design of included studies.

				Thyroid disease, *n*		Sex, *n*		Age at TJA (years)		Follow-up (months)
Reference	Year	Study type	Arthroplasty joint	Patients	Control†	Female	Male	Patients	Control	
Tan *et al.* (20)	2016	RO	Hip+Knee	4008	29,281	18,252	14,037	63.98		N/A
Althoff *et al.* (21)	2018	RO	Ankle	TAA: 6977; Hypothyroid: 2010		N/A	N/A	N/A		N/A
Buller *et al.* (7)	2018	RC	Knee	98,555	98,555	16,261	34,498	N/A		N/A
Shahi *et al.* (19)	2019	RO	Hip+Knee	4873		2714	2159	Hip: 65; Knee: 63.7		12
Somerson *et al.* (18)	2019	RC	Elbow	1452		1132	106	PJI: 62	60	3
Yuan *et al.* (16)	2020	RC	Knee	134	134	232	36	TD: 67.29	65.96	69.6
Yuan *et al.* (17)	2020	RC	Hip	63	63	68	58	TD 53.4	56.1	78
Jing *et al.* (14)	2021	CS	Knee	398	398	700	96	TD: 64.8	65.1	25.4
Yang. *et al.* (15)	2021	RO	Knee	PCR: 8484	1,218,760*	771,385	455,859	PCR: 64	67	N/A

*No PCRs; †includes non-thyroid disease.
CS, cohort study; PCR, prosthesis-related complications; PJI, periprosthetic joint infection; RC, retrospective cohort; RO, retrospective observational; TD, thyroid disease; TAA, total ankle arthroplasty; TJA, total joint arthroplasty.

section on supplementary materials given at the end of this article).

Complications

Medical complications

Five of the included studies reported postoperative medical complications (7, 14, 16, 17, 19). In two studies, the rate of deep venous thrombosis, pneumonia, and non-specified cardiac complications was significantly increased among hypothyroid patients. Wen Jing *et al.* reported that the rate of deep venous thrombosis, pneumonia, and non-specified cardiac complications among hypothyroid patients was 3.3, 2.8, and 3.5%, compared to 0.8, 0.8, and 1% of the control group, respectively (14). Significant increases among hypothyroid patients than the control group were also calculated regarding stroke (3.8 vs 0.8%), urinary tract infections (2.8 vs 0.5%), and pulmonary complications (3 vs 0.8%) (14). Non-significant higher rates of pulmonary embolism (0.28–0.23%), acute kidney injury (0.59–0.45%), and intubation rates (0.1–0.07%) were also recorded in hypothyroid than normal patients (7). Shahi *et al.* reported a significantly higher rate of persistent wound drainage in hypothyroid patients undergoing total ankle arthroplasty than in euthyroid patients (OR: 2.8, 95% CI: 1.3–4.2) (19). Table 2 summarizes the reported rates of postoperative medical complications of the involved studies.

Blood loss-related complications

All studies reporting perioperative blood loss-related complications demonstrated a significantly higher rate

Table 2 Post-operative medical complications of patients in the included studies.

Study/postoperative complications	Hypothyroid group, *n* (%)	Control group, *n* (%)	OR	95% CI	*P*-value
Jing *et al.* (14)					
Sepsis	12 (3)	3 (0.8)	4.10	3.80–4.31	0.037
DVT	13 (3.3)	3 (0.8)	4.45	4.23–4.67	0.023
Pneumonia	11 (2.8)	3 (0.8)	3.76	3.57–3.95	0.037
Cardiac complications	14 (3.5)	4 (1)	3.59	3.41–3.77	0.032
Stroke	15 (3.8)	3 (0.8)	5.16	4.90–5.42	0.009
UTI	11 (2.8)	2 (0.5)	5.63	5.35–5.91	0.025
Pulmonary insufficiency	12 (3)	3 (0.8)	4.10	3.80–4.31	0.037
Readmission	21 (5.3)	6 (1.5)	3.64	3.46–3.82	0.006
Intubation	2 (0.5)	1 (0.3)	2.00	1.90–2.10	0.998
PE	4 (1)	0 (0)	4.12	3.83–4.32	0.180
AKI	4 (1)	1 (0.3)	4.03	3.83–4.23	0.370
Buller *et al.* (7)					
Thrombocytopenia	276 (0.28)	166 (0.17)	1.577	1.303–1.910	<0.001
Intubation	98 (0.10)	69 (0.07)	1.524	1.114–2.084	0.008
PE	276 (0.28)	226 (0.23)	1.206	1.012–1.437	0.036
DVT	650 (0.66)	522 (0.53)	1.252	1.115–1.406	<0.001
Pneumonia	532 (0.54)	335 (0.34)	1.579	1.377–1.810	<0.001
AKI	581 (0.59)	443(0.45)	1.304	1.152–1.477	<0.001
Cardiac complications	39 (0.04)	39(0.04)	0.897	0.569–1.416	0.642
Vascular complications	20 (0.02)	30 (0.03)	0.92	0.522–1.621	0.773
Urinary complications	20 (0.02)	20 (0.02)	1	0.561–1.783	1.00
Pulmonary complications	20 (0.02)	30 (0.03)	0.75	0.426–1.321	0.317
MI	138 (0.14)	108 (0.11)	1.217	0.946–1.564	0.126
Yuan *et al.* (16)			N/A	N/A	
IM venous thrombosis	2 (1.49)	13 (9.70)			0.001
PE	0 (0)	0 (0)			1.00
DVT	0 (0)	0 (0)			1.00
AKI	0 (0)	1 (0.75)			1.00
Cardiac failure	1 (0.75)	1 (0.75)			1.00
Wound complications	3 (2.24)	3 (2.24)			1.00
Urinary complications	0 (0)	1 (0.75)			1.00
Yuan *et al.* (17)			N/A	N/A	
Liver dysfunction	1 (1.59)	1 (1.59)			1.00
HF	1 (1.59)	2 (3.17)			1.00
Pulmonary infection	1 (1.59)	0 (0)			1.00
UTI	0 (0)	1 (1.59)			1.00
Wound complications	2 (3.17)	1 (1.59)			1.00
IM vein thrombosis	2 (3.17)	10 (15.87)			0.015
Readmission rate	1 (1.59)	2 (3.17)			1.00

AKI, acute kidney injury; DVT, deep venous thrombosis; MI, myocardial infarction; N/A, not available; OR, odds ratio; PE, pulmonary embolism; UTI, urinary tract infection.

of postoperative anemia in hypothyroid than euthyroid patients undergoing TJA (7, 14, 16, 17). These studies also showed a significant increase in transfusion rates in patients with hypothyroidism, except for the study by Yuan *et al*. (16).

Yuan *et al.* reported a significant increase in intra- and postoperative blood loss in hypothyroid patients during the first postoperative day. The mean blood loss volume during the first postoperative day was 690.04 ± 442.51 mL in hypothyroid compared to 573.61 ± 326.16 mL in euthyroid patients ($P=0.001$). The intraoperative blood loss volume was 174.03 ± 28.90 mL in hypothyroid and 165.70 ± 26.53 mL in euthyroid patients ($P=0.02$) (16).

Another study also demonstrated a significantly higher drop in postoperative hemoglobin level (35.21 ± 13.25 vs 30.02 ± 12.81 g/L, $P=0.02$) and perioperative blood loss (807.26 ± 367.15 vs 951.32 ± 388.44 g/L, $P=0.003$) in patients with hypothyroidism in comparison to the euthyroid group (17). Table 3 reports the rates of postoperative blood loss-related complications among the two groups in the involved studies.

Mechanical complications

The included studies reported no significantly different rates of aseptic loosening between groups (7, 16, 17) except for the study of Yang *et al.* (15). The periprosthetic fracture rate did not differ significantly among groups in the two studies (7, 14). Buller *et al.* demonstrated significantly different dislocation rates (0.46 vs 0.36%) and non-significantly different implant failure rates among hypothyroid and euthyroid patients (7). In contrast, Yang *et al.* reported a significant increase in prosthesis-related complications, including periprosthetic fracture, dislocation, periprosthetic joint infection (PJI) and aseptic loosening among hypothyroid patients (OR: 0.88, 95% CI: 0.82–0.94, $P=0.0004$) (15). The rates of postoperative prosthesis-related mechanical complications among the two groups are summarized in Table 4.

Infectious complications

Seven studies reported data regarding PJI rates (7, 14, 16, 17, 18, 20, 21). Buller *et al.* and Tan *et al.* showed a statistically significant increase in PJI rates in hypothyroid than euthyroid patients (0.35 vs 0.23%, $P < 0.001$ and 3.4 vs 1.4%, $P=0.07$), respectively (7, 20). The other three studies showed no significant difference in PJI rates among groups (14, 16, 17). However, it should be noted that Buller *et al.* studied the largest sample size compared to other studies.

As mentioned earlier, Yang *et al.* reported, among other complications, a significant increase in PJI among hypothyroid patients (15). Table 5 summarizes the PJI risk in the postoperative period among the two groups of the detailed studies. In addition to the above, Somerson *et al*. reported significantly greater odds of developing PJI among hypothyroid individuals in relation to euthyroid controls undergoing total elbow arthroplasty (OR: 2.04, 95% CI: 1.02–4.08, $P=0.045$) (18). A significantly higher PJI rate in the third (OR: 1.27, 95% CI: 1.02–1.58, $P=0.018$) and sixth postoperative month (OR: 1.32, 95% CI: 1.03–1.69) in hypothyroid than in euthyroid patients was also recorded by Althoff *et al.* (21).

Discussion

This systematic review evaluated the role of thyroid dysfunction as a potential independent complication risk factor following TJA. This study assessed postoperative complication rates in hypothyroid patients than in euthyroid patients undergoing TJA. Our data suggest that hypothyroidism could be associated with a higher risk of postoperative blood loss, PJI and a broad spectrum of postoperative medical complications.

Medical complications

There is insufficient evidence to support the higher risk for postoperative medical complications in hypothyroid

Table 3 Blood-loss related complications of patients in included studies.

Study/complications	Hypothyroid group, ***n*** (%)	Control group, ***n*** (%)	OR	95% CI	***P*-value**
Jing *et al*. (14)					
Transfusion	78 (19.6)	60 (15.1)	1.37	1.30–1.44	0.03
Anemia	29 (7.3)	17 (4.3)	1.76	1.67–1.85	0.039
Buller *et al*. (7)					
Post-operative blood loss	404 (0.41)	315 (0.32)	1.252	1.080–1.451	0.03
Transfusion	1212 (1.23)	848 (0.86)	1.428	1.307–1.561	<0.01
Anemia	1902 (1.93)	1429 (1.45)	1.321	1.237–1.422	<0.01
Yuan *et al*. (16)			N/A	N/A	
Transfusion	10 (7.46)	4 (2.99)			0.1
Anemia	123 (91.79)	107 (79.85)			0.01
Yuan *et al*. (17)			N/A	N/A	
Transfusion	7 (11.11)	2 (3.17)			0.084
Anemia	57 (90.48)	48 (76.3)			0.031

Table 4 Prosthesis-related mechanical complications of patients in the included studies.

Study	Mechanical complications	Hypothyroid group, *n* (%)	Control group, *n* (%)	OR	95% CI	*P*-value
Jing *et al.* (14)	Peri-prosthetic fracture	1 (0.3)	0 (0)	1.00	0.95–1.05	0.317
Buller *et al.* (7)						
	Aseptic loosening	69 (0.07)	60 (0.06)	1.119	0.787–1.590	0.531
	Dislocation	453 (0.46)	355 (0.36)	1.258	1.095–1.446	0.01
	Broken implant	20 (0.02)	20 (0.02)	1.05	0.569–1.937	0.876
	Peri-prosthetic fracture	177 (0.18)	148 (0.15)	1.153	0.927–1.434	0.202
	Other	60 (0.06)	39 (0.04)	1.6	1.078–2.376	0.019
Yuan *et al.* (16)	Aseptic loosening	0 (0)	0 (0)	N/A	N/A	1
Yuan *et al.* (17)	Aseptic loosening	0 (0)	0 (0)	N/A	N/A	1

patients. Our analysis demonstrated a potentially increased rate of deep venous thrombosis, acute kidney injury, pneumonia, and non-specified cardiac complications among hypothyroid patients who underwent TJA.

It has been reported that thyroid hormones modulate various biological functions. Hypothyroidism can affect tissue function and immune response through multiple mechanisms such as chemotaxis, phagocytosis, reactive oxygen species (ROS), cytokine synthesis, and release (22). A recent study reported a significantly longer postoperative length of hospital stay (LOS) for hypothyroid patients compared to the predicted LOS determined using a surgical risk calculator (22). Hypothyroid patients had a trend toward a higher incidence of ileus, use of vasopressors, and need for reintubation but equal rates of chronic obstructive pulmonary disease and a lower incidence of obstructive sleep apnea than euthyroid controls (23).

Hypothyroidism is strongly associated with an increased risk of postoperative myocardial dysfunction, atrial fibrillation, and risk of death in patients undergoing cardiac surgery (23, 24, 25, 26). However, Komatsu *et al.* found no association of hypothyroidism with LOS or other complications in patients after cardiac surgery (24).

On the contrary, hypothyroidism was supported to protect against all-cause mortality and may even be cardioprotective in the postoperative period after lumbar spinal fusions (25). A retrospective analysis evaluating outcomes in hypothyroid patients undergoing spinal fusion demonstrated lower rates of inpatient mortality, neurological complications, and acute myocardial infarction than their euthyroid counterparts, but no differences in rates of respiratory, gastrointestinal complications, acute kidney injury, and pulmonary embolism/deep venous thrombosis.

Our data do not support the protective effect of hypothyroidism relative to postoperative medical complications and cardiac dysfunction. Moreover, this study revealed that hypothyroidism might place patients at a higher risk for postoperative medical complications, such as acute kidney injury, pulmonary embolism, cerebrovascular events, and cardiac dysfunction.

Blood loss-related complications

Our study demonstrated a higher risk of anemia, perioperative blood loss, hemoglobin drop, and transfusion in hypothyroid patients after TJA. This increased bleeding risk in hypothyroid patients could be partly explained by the low synthesis or release of VIII, von-Willebrand, and autoimmune factors (27, 28). This lower factor production may result in an acquired von Willebrand syndrome characterized by prothrombin time and activated partial thromboplastin time increase and von Willebrand factor and Factor VIII decreased activity in hypothyroid patients (26, 29). Hypothyroidism may also increase fibrinolysis and reduce thrombin-activatable fibrinolysis inhibitor activity, resulting in shortening clot lysis time (30).

The role of thyroid insufficiency on coagulation factor synthesis and function is emphasized by the reversal of the acquired von Willebrand Syndrome (aVWS) seen after thyroid hormone replacement therapy (29). aVWS with significantly lower free T4 levels has been reported in 33% of 90 hypothyroid patients (31). Although bleeding episodes are often mucocutaneous, the bleeding risk in hypothyroid patients undergoing major surgery should be considered, and every effort should be made to correct thyroid dysfunction preoperatively (31).

Table 5 Periprosthetic joint infection rates of patients in included studies.

Study	Hypothyroid group, *n* (%)	Control group, *n* (%)	OR	95% CI	*P*-value
Jing *et al* (14)	2 (0.5)	0 (0)	2.0	1.90–2.10	0.99
Tan *et al.* (20)	135 (3.4)	348 (1.4)	2.46	1.99–3.05	<0.01
Buller *et al.* (7)	345 (0.35)	227 (0.23)	1.502	1.271–1.775	<0.01
Yuan *et al.* (16)	1 (0.75)	0 (0)	N/A	N/A	1
Yuan *et al.* (17)	1 (1.59)	0 (0)	N/A	N/A	1

Prosthesis-related complications

Thyroid hormones play a vital role in the endochondral ossification process, skeletal growth, and bone density maintenance, primarily through thyroid hormone receptor 1 (TR1) (32). Current research suggests that T3 and T4 hormones indirectly act on osteoblasts and osteoclasts via the membrane, cytoplasmatic, and nuclear receptors. Hyperthyroidism and hypothyroidism are thought to hinder bone development (32) and increase the risk of developing metabolic bone disorders (33).

The role of thyroid hormones during development may be examined to emphasize their importance in bone metabolism. T3 stimulates the osteoblast proliferation–differentiation–apoptosis cycle while upregulating the expression of osteocalcin, type 1 collagen, alkaline phosphatase, metalloproteins, IGF1, and its receptor (IGF1 R). T3 then enhances the production of critical osteoclast lineage distinguishing factors such as interleukin-6 and prostaglandin E2, facilitating bone resorption as well as acting in concert with hormones that promote osteoclast activity such as parathyroid hormone and vitamin D (34). T3 has also been shown to enhance the mRNA production of the ligand of receptor activator of nuclear factor (RANKL) in osteoblasts, which then activates RANK in osteoclast precursors, a critical stage in the creation of osteoclasts (35).

Hypothyroidism is associated with a decreased bone mineral density (BMD) and increased fracture risk (36). Other studies showed that hypothyroidism extends the usual bone remodeling period of around 200–700 days, raising BMD by about 17% throughout each cycle but increasing the fracture risk due to the increased stiffness of the formed bone (37). Subclinical hypothyroidism, on the other hand, did not show any correlation between osteoporosis and fracture risk (36).

Our data indicated no significant differences in the prosthesis complication rates between hypothyroid and euthyroid patients. However, the earlier data indicate the need for further studies to assess whether hypothyroid patients are at a higher risk of prosthesis-related complications such as periprosthetic joint fractures and aseptic loosening.

Infectious complications

While multiple studies have suggested a potentially beneficial role of thyroid hormones in immunity, concrete evidence regarding the exact mechanisms surrounding these effects is lacking. A higher T3:T4 ratio, when T3 remains within the normal range, has been positively correlated with a higher IL-2 receptor density on the lymphocyte surface, indicating a possible connection between the metabolically active T3 and IL2 receptor expression. Higher T3 levels were also linked to a decreased rate of premature lymphocyte apoptosis (38).

In septic patients, decreased free T3 levels have been directly linked to worse patient outcomes (39). On the contrary, higher T4 levels can enhance immune cell migration by stimulating the increased ROS formation, and the replacement of thyroid hormones has been shown to amplify neutrophilic phagocytosis (40, 41).

The data in the studies included in our review suggest a potentially harmful effect of hypothyroidism on the immune response of patients undergoing TJA, with the PJI rates being significantly increased among hypothyroid individuals compared to euthyroid controls.

Limitations

Several limitations of our systematic review may impact the validity of our findings. The main limitation of this systematic review is the low level of evidence of the detailed studies. The majority of the articles are non-randomized retrospective cohorts or case series and thus impart a degree of inherent selection bias and heterogeneity. Another limitation of this study was the minimal number of articles reporting on TJA outcomes of patients with thyroid dysfunction; however, the studies' relatively high sample size strengthens our results. The significant heterogeneity of the studies, including different TJAs, may have influenced our results. Not all studies reported on variables of interest, such as the type of thyroid dysfunction and follow-up. Therefore, all analyses were performed according to the availability of data. However, many reports have published comparative data strengthening the results.

Conclusions

The primary goal of our systematic review was to draw attention to the potentially harmful implications of thyroid dysfunction on TJA patients. Hypothyroidism has been identified as a potential but modifiable risk factor leading to increased perioperative TJA complications, including blood loss and medical complications. The risk of PJI and implant-related complications may also be high but need further studies. Our results suggest that a more robust understanding of the pathophysiologic changes seen in hypothyroid patients is necessary to elucidate better the potential higher risk of complications and outcomes in the TJA population. Prospective high-quality trials are certainly needed.

Supplementary materials
This is linked to the online version of the paper at https://doi.org/10.1530/EOR-22-0085.

ICMJE conflict of interest statement
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