



Hypothyroidism and Spine Surgery: a Review of Current Findings

Anitesh Bajaj¹ · Rohan M. Shah¹ · Steven Kurapaty¹ · Alpesh A. Patel¹ · Srikanth N. Divi¹

Accepted: 14 November 2022 / Published online: 10 December 2022

© The Author(s), under exclusive licence to Springer Science+Business Media, LLC, part of Springer Nature 2022

Abstract

Purpose of Review Hypothyroidism is a common medical comorbidity and has been linked to adverse surgical outcomes. However, its effect on spine surgery outcomes is less clear. The aim of this review is to compile current literature to serve as a guide for spine surgeons when treating patients with hypothyroidism.

Recent Findings In both the cervical and lumbar spine, patients with hypothyroidism are at increased risk of postoperative medical complications. Consequently, patients with hypothyroidism experience increased healthcare costs and readmission rates. However, there are some contradictory findings with some studies suggesting that hypothyroidism may have a protective effect in patients undergoing lumbar fusion, specifically against postoperative myocardial infarction and decreased inpatient mortality.

Summary When examining spine surgery outcomes, there are mixed results when considering the effect of hypothyroidism. Some studies have shown increased medical complications, hardware failure, and increased expenditure; however, other recent findings suggest possible protective effects. Future studies are needed to help create concrete guidelines for treating patients with hypothyroidism.

Keywords Hypothyroidism · Spine Surgery · Surgical outcomes · Spine complications

Introduction

Thyroid disorders are the second most common endocrinopathy following diabetes [1]. Clinical hypothyroidism affects 1 out of every 300 people in the USA, with a higher prevalence in female and elderly patients [2, 3]. Thyroid-stimulating hormone (TSH) is upregulated following the release of thyrotropin-releasing hormone, which acts on the anterior pituitary [1]. TSH subsequently binds to the TSH receptor, stimulating the release of thyroid hormones triiodothyronine (T3) and thyroxine (T4) [4].

Thyroid disorders also present with varying degrees of severity: primary, subclinical, and overt. Primary hypothyroidism is characterized by a dysfunctional thyroid gland, resulting in low T4 and high TSH levels [4]. Subclinical hypothyroidism is defined as TSH > 4.0mIU/L with normal T4 levels [5]. Overt hypothyroidism is defined as TSH > 4.0mIU/L and low T4 levels [5].

Hypothyroidism has important clinical ramifications in the surgical setting. It has been associated with greater perioperative risk across many surgical disciplines, especially cardiac surgery [6]. Hypothyroidism within orthopaedic surgery presents a unique challenge due to its crucial role in bone metabolism and formation [7•]. Specifically, hypothyroidism has been linked to significantly increased odds of periprosthetic joint infections [OR: 2.46, 95% CI 1.99–3.05, $p < 0.0001$], greater odds of overall complications following total knee arthroplasty [OR: 1.37, 95% CI 1.32–1.41], and greater odds of medical complications in total hip arthroplasty ($p < 0.001$) [8–10]. While conclusive findings exist in other fields of orthopaedic surgery, the recent literature in spine surgery remains contradictory. The aim of this review is to summarize the current literature on hypothyroidism and outcomes in spine surgery.

This article is part of the Topical Collection on *Updates in Spine Surgery - Techniques, Biologics, and Non-Operative Management*

✉ Anitesh Bajaj
anitesh.bajaj@northwestern.edu

¹ Department of Orthopaedic Surgery, Northwestern University Feinberg School of Medicine, Chicago, IL 60611, USA

Perioperative Medical Complications

Cervical Spine

Hypothyroidism has been correlated with adverse events following cervical spine surgery as summarized in Table 1. Vakharia et al. conducted a retrospective study grouping 107,066 patients undergoing ACDF into two groups by thyroid status: those with or without diagnoses of hypothyroidism [11]. Patients were matched based on age, gender, and Charlson-Comorbidity Index. Upon univariate analysis, the authors found that hypothyroid patients had a significantly greater odds of 90-day medical complications compared to euthyroid patients [OR: 1.72, 95% CI 1.58–1.87, $p < 0.001$]. Complications included pulmonary embolism (PE) [OR: 2.16, 95% CI 1.51–3.09, $p < 0.001$], deep venous thrombosis (DVT) [OR: 1.81, 95% CI 1.32–2.49, $p < 0.001$], myocardial infarction (MI) [OR: 2.10, 95% CI 1.43–3.08, $p < 0.001$], non-healing surgical wounds [OR: 2.27, 95% CI 1.11–4.62, $p = 0.0232$], infection [OR: 1.72, 95% CI 1.39–2.13, $p < 0.001$], hemorrhage [OR: 2.14, 95% CI 1.36–3.35, $p < 0.001$], wound complications [OR: 1.86, 95% CI 1.25–2.78, $p = 0.0022$], and hematoma [OR: 2.03, 95% CI 1.57–2.63, $p < 0.001$]. Of note, the study found no significantly increased risk of pseudoarthrosis when comparing cohorts with and without hypothyroidism.

Interestingly, in vivo studies may provide mechanistic support for some of the aforementioned complications. A rat study investigating the link between circulating T3 and T4 and wound healing found lower levels of type-IV collagen and hydroxyproline in states of hypothyroidism, potentially explaining the mechanism for worsened wound healing seen in prior literature [12]. The increased rates of thromboembolic events in hypothyroid patients may be explained by the increased levels of von-Willebrand factor and plasminogen activating inhibitor-1 in these patients [13]. Greater levels of these factors promote a prothrombotic state, potentially explaining the mechanism behind greater odds of PE, DVT and MI observed in the hypothyroid group.

Luther et al. conducted a large retrospective database study analyzing 1,681,805 patients to evaluate the impact of hypothyroidism, identified by diagnosis codes, on cervical fusion outcomes [7•]. The authors excluded patients with a diagnosis of hyperthyroidism and adjusted analyses with Elixhauser comorbidity covariates. Using multivariable models, the study found no significant differences between hypothyroid and euthyroid cohorts for rates of DVT/PE, respiratory, gastrointestinal (GI), or renal complications. However, the study reported that hypothyroid patients experienced significantly greater odds of neurologic complications [OR: 1.13, 95% CI 1.04–1.22, $p = 0.0033$], hardware complications [OR: 1.06, 95% CI 1.03–1.09, $p = 0.0005$], and hematologic complications [OR: 1.16, 95% CI 1.11–1.21, $p < 0.0001$]. Both hematoma and seroma risk were used as proxy markers of wound complications and considering these endpoints together, the authors found greater odds of wound complications in hypothyroid patients [OR: 1.09, 95% CI 1.02–1.16, $p = 0.0066$]. Notably, this study showed no significant difference in the odds of acute MI between the hypothyroid and euthyroid cohorts undergoing cervical fusion. Somewhat contradictory to the increased medical complications noted above, the hypothyroid group experienced significantly lower odds of in-hospital mortality [OR: 0.61, 95% CI 0.51–0.72, $p < 0.0001$].

Both Vakharia et al. and Luther et al. found greater odds of wound complications in their hypothyroid patient cohorts, but as noted above, their studies found differences with regard to the risk of PE, DVT, and neurological and hardware complications [7, 11]. In addition, Vakharia et al. found a difference in MI risk between cohorts, whereas Luther et al. found no significant difference. Given the sparse literature on this topic, the negative effects of hypothyroidism on cervical spine surgery outcomes are still unclear.

Lumbar Spine

The aforementioned authors also examined hypothyroidism following lumbar spine surgery as described in Table 2. Vakharia et al. studied 69,584 Medicare patients with hypothyroidism undergoing a 1 or 2 level lumbar fusion [14•].

Table 1 Cervical Spine Surgery

Author	Year	Sample Description	Findings
Vakharia et al.	2018	Patients undergoing anterior cervical discectomy and fusion with/without hypothyroidism N = 107,666	Patients with hypothyroidism had significantly greater odds of medical complications, readmissions, and higher charges than euthyroid counterparts
Luther et al.	2021	Patients undergoing cervical fusion surgery, divided into hypothyroid and euthyroid cohorts N = 1,681,805	Hypothyroid patients had greater likelihoods of experiencing several medical complications, readmissions, and prolonged length of stay. Notably, hypothyroid patients had decreased odds of mortality

Table 2 Lumbar Spine Surgery

Author	Year	Sample description	Findings
Vakharia et al.	2020	Medicare patients undergoing 1- or 2-level lumbar fusion, divided by hypothyroid status <i>N</i> = 417,483	Hypothyroid patients had greater odds of medical complications, readmissions, higher healthcare costs, and longer length of stay
Luther et al.	2021	Patients undergoing lumbar fusion surgery, divided into hypothyroid and euthyroid cohorts <i>N</i> = 2,467,320	Hypothyroid patients were more likely to experience hematologic complications, readmissions, and longer length of stay. Hypothyroid patients had lower odds of in-hospital mortality, neurologic complications, and acute myocardial infarctions

Each patient in the hypothyroid group was matched to 5 controls based on age, sex, and comorbidities (chronic obstructive pulmonary disease, diabetes mellitus, hyperlipidemia, hypertension, obesity, and tobacco use). At 90 days post-operation, comparison of matched cohorts showed that hypothyroid patients had significantly higher odds of medical complications [OR: 3.53, 95% CI 3.40–3.67, $p < 0.0001$], including anemia [OR: 6.47, 95% CI 5.78–7.24, $p < 0.0001$], thrombocytopenia [OR: 6.42, 95% CI 4.66–8.84, $p < 0.0001$], MI [OR: 4.51, 95% CI 2.89–7.04, $p < 0.0001$], acute kidney failure [OR: 3.12, 95% CI 1.89–5.15, $p < 0.0001$], DVT [OR: 1.97, 95% CI 1.59–2.44, $p < 0.0001$], wound complications [OR: 1.30, 95% CI 1.14–1.48, $p < 0.0001$], PE [OR: 2.36, 95% CI 1.73–3.21, $p < 0.0001$], pneumonia [OR: 4.60, 95% CI 3.83–5.54, $p < 0.0001$], and nerve complications [OR: 3.35, 95% CI 3.13–3.58, $p < 0.0001$].

Luther et al. also studied lumbar fusion outcomes in 2,467,320 patients grouped by pre-operative thyroid status [7•]. After excluding patients with hyperthyroidism and adjusting for Elixhauser comorbidity variables, the study found no significant differences in odds of developing DVT/PE, respiratory complications, acute kidney injury, GI, or wound complications between hypothyroid and euthyroid cohorts. Hypothyroid patients in the lumbar fusion group had higher odds of hematologic complications [OR: 1.176, 95% CI 1.16–1.19, $p < 0.0001$]. Luther et al. reported that the hypothyroid group in the lumbar fusion cohort had lower odds of in-hospital mortality [OR: 0.643, 95% CI 0.55–0.75, $p < 0.0001$], neurologic complications [OR: 0.919, 95% CI 0.884–0.955, $p < 0.0001$], and acute MI [OR: 0.851, 95% CI 0.81–0.89, $p < 0.0001$].

An unexpected finding from Luther et al. was a significantly decreased likelihood of MI in the hypothyroidism cohort [7•]. A study by Dhital et al. using the National Inpatient Sample (NIS) found that hypothyroidism was associated with higher odds of coronary heart disease but lower odds of acute coronary syndrome [15]. The researchers theorized that, although hypothyroidism increases vascular resistance and low-density lipoprotein (LDL), cardiac conditioning may occur downstream of milder, chronic ischemia, resulting in

increased coronary collateral circulation. Thus, a lower rate of acute MI could be explained by this increased circulation. However, another study evaluating patients with subclinical hypothyroidism and stable angina found that TSH levels >9 $\mu\text{IU/mL}$ predicted poor coronary collateral circulation, refuting the prior explanation [16]. A second explanation for the decreased likelihood of ACS may be that hypothyroidism has been associated with a hypo-coagulable state [17, 18]. Low levels of FT4 can also have a protective effect against venous thromboembolism and high levels may have a positive association [18]. On the other hand, patients with subclinical hypothyroidism also demonstrate a pro-coagulative effect with higher levels of Factor VII, PAI-1, and t-PA than healthy controls [18]. Thus, there is conflicting literature regarding the effect of hypothyroidism on the coagulative environment in patients. The findings from Luther et al. are strengthened by the large sample size used and variety of operations included [7•]. Furthermore, the power of the NIS database lies in its size and breadth: it is a nationwide database and includes data from several insurers, and is therefore relatively heterogeneous, increasing the external validity of the study. Future investigations can help clarify the cardiac pathophysiology in hypothyroid patients and assist clinicians in pre-operative risk assessments.

Impact on Readmissions

Cervical Spine

Although there is contention surrounding the impact of hypothyroidism on various post-operative medical complications, there is a consensus that hypothyroidism increases the risk of readmission. In line with prior literature, Vakharia et al. reported readmission rate at the 30-, 60-, and 90-day time points, along with an aggregate measure that captured total readmissions across the three periods [11]. Hypothyroid patients had significantly greater risk of readmission at 30 days [adjusted relative risk (aRR): 1.56, 95% CI 1.46–1.66, $p < 0.001$] and in the total readmissions measure [aRR: 1.45, 95% CI 1.41–1.49,

$p < 0.001$] [11]. Similarly, Luther et al. found a higher probability of 30-day readmission for hypothyroid patients using the Elixhauser readmission index after cervical fusion ($p < 0.0001$) [7•].

Lumbar Spine

Vakharia et al. found increased odds of 90-day readmissions in hypothyroid patients undergoing lumbar fusion [OR: 1.18, 95% CI 1.16–1.20, $p < 0.0001$] [14•]. Similarly, Luther et al. also reported that hypothyroid patients in their lumbar fusion cohort had a higher probability of 30-day readmission using the Elixhauser readmission index ($p < 0.0001$) [7•]. Overall, hypothyroidism is linked to increased readmission rates following both cervical and lumbar spinal fusions and should be cautiously managed.

Effect on Total Healthcare Costs

Cervical Spine

Given the increased risk of complications found in the hypothyroid patient population, and the increased healthcare costs associated with postoperative medical complications, overall healthcare expenditure in this population is increased [19]. Vakharia et al. reported that average charges were higher for hypothyroid patients on day of ACDF surgery (\$75,044.06 vs. \$66,948.35), at 30 days postoperative (\$80,887.25 vs. \$70,374.41, $p < 0.001$), 60 (\$85,442.97 vs. \$73,095.65, $p < 0.001$), and 90 days postoperative (\$90,020.98 vs. \$76,363.64, $p < 0.001$) [11]. Furthermore, Luther et al. reported that hypothyroid patients experienced longer length of stay (LOS) than euthyroid counterparts after cervical fusion (2.6 vs 2.3 days; $p < 0.0001$) [7•].

Lumbar Spine

Examining healthcare spending for lumbar fusion, Vakharia et al. found that hypothyroidism was associated with greater costs on the day of surgery (\$97,304 vs \$95,168; $p = 0.014$) and at 90 days post-operation (\$113,514 vs \$108,861; $p = 0.001$) [14•]. In line with this, Vakharia et al. found that hypothyroid patients undergoing lumbar fusion had significantly longer LOS (8 vs 4 days; $p < 0.0001$) [14•]. Similarly, Luther et al. found that hypothyroid lumbar fusion patients also had longer LOS than their euthyroid counterparts (4.3 days vs 4.0 days; $p < 0.0001$) [7•]. With a shift in the US healthcare system to value-based models, minimizing spending is a primary goal, and spine surgeons should be aware of the requisite financial impact of caring for hypothyroid patients.

Current Recommendations

Currently, no organizational guidelines have been established regarding preoperative recommendations for hypothyroid patients. A recent review recommends that asymptomatic patients without history of thyroid dysfunction should not undergo preoperative TSH screening [20•]. However, for patients showing symptoms or signs of thyroid dysfunction, TSH levels should be taken. In cases of mild or moderate hypothyroidism, postponing elective surgery is not necessary. Mild hypothyroidism was defined as subclinical hypothyroidism whereas moderate hypothyroidism was denoted by elevated TSH and reduced total thyroxine level, $\geq 0.5 \mu\text{g/dL}$. On the other hand, patients with severe hypothyroidism (defined as myxedema coma, severe symptoms, or free thyroxine level $< 0.5 \text{ng/dL}$) should not undergo elective procedures until treatment. In emergent situations, patients with severe hypothyroidism should undergo intravenous hormone therapy preoperatively. Given the limited research surrounding the effect of hypothyroidism on spine surgery, future studies should investigate specific TSH thresholds associated with increased operative risk to help guide more specific recommendations.

Conclusions

Hypothyroidism in cervical and lumbar spine surgery is linked to increased healthcare expenditure as well as higher rates of readmission and complications. However, there is a discrepancy in the literature between studies regarding hypothyroidism and its potential cardioprotective effects and impact on inpatient mortality. Although there are proposed mechanisms, further prospective research could reveal nuanced physiological mechanisms regarding thyroid dysfunction and its cardiovascular implications. Current studies are limited by usage of diagnosis codes, rather than TSH levels, to assess operative risk related to hypothyroidism. Future studies should aim to stratify patients with hypothyroidism into mild, moderate, and severe cohorts to study spine surgery outcomes at a more granular level in this population.

Declarations

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Conflict of interest Anitesh Bajaj, Rohan M. Shah, Steven Kurapaty, Alpesh A. Patel, and Srikanth N. Divi declare that they have no conflicts of interest.

References

Papers of particular interest, published recently, have been highlighted as:

- Of importance
- Of major importance

1. Paschou SA, Bletsas E, Stampoulou PK, Tsigkou V, Valatsou A, Stefanaki K, Kazakou P, Spartalis M, Spartalis E, Oikonomou E, Siasos G. Thyroid disorders and cardiovascular manifestations: an update. *Endocrine*. 2022;75(3):672–83. <https://doi.org/10.1007/s12020-022-02982-4>.
2. Wilson SA, Stem LA, Bruehlman RD. Hypothyroidism: Diagnosis and Treatment. *Am Fam Physician*. 2021;103(10):605–13.
3. Vacante M, Biondi A, Basile F, Ciuni R, Luca S, Di Saverio S, et al. Hypothyroidism as a Predictor of Surgical Outcomes in the Elderly. *Front Endocrinol (Lausanne)*. 2019;10:258. <https://doi.org/10.3389/fendo.2019.00258>.
4. Shahid MA, Ashraf MA, Sharma S (2022) Physiology, Thyroid Hormone. StatPearls. Treasure Island (FL): StatPearls Publishing; Copyright © 2022, StatPearls Publishing LLC
5. Simon C, Weidman-Evans E, Allen S. Subclinical hypothyroidism: To treat or not to treat? *JAAPA*. 2020;33(5):21–6. <https://doi.org/10.1097/01.Jaa.0000660120.03250.55>.
6. Ladenson PW, Levin AA, Ridgway EC, Daniels GH. Complications of surgery in hypothyroid patients. *Am J Med*. 1984;77(2):261–6. [https://doi.org/10.1016/0002-9343\(84\)90701-0](https://doi.org/10.1016/0002-9343(84)90701-0).
7. Luther E, Perez-Roman RJ, McCarthy DJ, Burks JD, Bryant JP, Madhavan K, et al. Incidence and Clinical Outcomes of Hypothyroidism in Patients Undergoing Spinal Fusion. *Cureus*. 2021;13(8):e17099. <https://doi.org/10.7759/cureus.17099> **Reports extensive postoperative complication data for hypothyroid patients undergoing cervical and lumbar fusion.**
8. Tan TL, Rajeswaran H, Haddad S, Shahi A, Parvizi J. Increased Risk of Periprosthetic Joint Infections in Patients With Hypothyroidism Undergoing Total Joint Arthroplasty. *J Arthroplasty*. 2016;31(4):868–71. <https://doi.org/10.1016/j.arth.2015.10.028>.
9. Buller LT, Rosas S, Sabeh KG, Roche MW, McLawhorn AS, Barsoum WK. Hypothyroidism Increases 90-Day Complications and Costs Following Primary Total Knee Arthroplasty. *J Arthroplasty*. 2018;33(4):1003–7. <https://doi.org/10.1016/j.arth.2017.10.053>.
10. Damodar D, Vakharia A, Zachwieja E, Vakharia R, Hernandez V, Roche M. Hypothyroidism Increases 90-Day Complications and Cost Following Primary Total Hip Arthroplasty. *The Journal of Hip Surgery*. 2019;03:062–7. <https://doi.org/10.1055/s-0039-1678748>.
11. Vakharia RM, Vakharia AM, Ameri B, Niedzielak T, Donnally CJ 3rd, Malloy JP. Hypothyroidism increases 90-day postoperative complications in patients undergoing primary single level anterior cervical disectomy and fusion: a matched control analysis. *J Spine Surg*. 2018;4(2):274–80. <https://doi.org/10.21037/jss.2018.05.26>.
12. Natori J, Shimizu K, Nagahama M, Tanaka S. The influence of hypothyroidism on wound healing. An experimental study. *Nihon Ika Daigaku Zasshi*. 1999;66(3):176–80. <https://doi.org/10.1272/jnms.66.176>.
13. Müller B, Tsakiris DA, Roth CB, Guglielmetti M, Staub JJ, Marbet GA. Haemostatic profile in hypothyroidism as potential risk factor for vascular or thrombotic disease. *Eur J Clin Invest*. 2001;31(2):131–7. <https://doi.org/10.1046/j.1365-2362.2001.00777.x>.
14. Vakharia RM, Ehiorobo JO, Mahmood B, Roche MW, Mont MA, Razi AE. Does Hypothyroidism Increase Complications, Lengths of Stay, Readmissions, and Costs Following Primary 1- to 2-Level Lumbar Fusion? *Clin Spine Surg*. 2020;33(10):E559–e62. <https://doi.org/10.1097/bsd.0000000000001002> **Reports data regarding complications after lumbar fusion in hypothyroid patients.**
15. Dhital R, Basnet S, Poudel DR. Impact of Hypothyroidism on Occurrence and Outcome of Acute Coronary Syndrome from the National Inpatient Sample. *Am J Cardiol*. 2017;120(12):2160–3. <https://doi.org/10.1016/j.amjcard.2017.08.035>.
16. Khalfallah M, Draz E, Shalaby K, Hafez YM. Predictors of poorly developed coronary collateral circulation in patients with subclinical hypothyroidism suffered from chronic stable angina. *Glob Cardiol Sci Pract*. 2019;2019(2):e201910. <https://doi.org/10.21542/gcsp.2019.10>.
17. Squizzato A, Romualdi E, Büller HR, Gerdes VE. Clinical review: Thyroid dysfunction and effects on coagulation and fibrinolysis: a systematic review. *J Clin Endocrinol Metab*. 2007;92(7):2415–20. <https://doi.org/10.1210/jc.2007-0199>.
18. Elbers LPB, Fliers E, Cannegieter SC. The influence of thyroid function on the coagulation system and its clinical consequences. *J Thromb Haemost*. 2018;16(4):634–45. <https://doi.org/10.1111/jth.13970>.
19. Stokes SM, Scaife CL, Brooke BS, Glasgow RE, Mulvihill SJ, Finlayson SRG, Varghese TK. Hospital Costs Following Surgical Complications: A Value-driven Outcomes Analysis of Cost Savings Due to Complication Prevention. *Ann Surg*. 2022;275(2):e375–e81. <https://doi.org/10.1097/sla.0000000000004243>.
20. Himes CP, Ganesh R, Wight EC, Simha V, Liebow M. Perioperative Evaluation and Management of Endocrine Disorders. *Mayo Clin Proc*. 2020;95(12):2760–74. <https://doi.org/10.1016/j.mayocp.2020.05.004> **Provides clinical recommendations for varying degrees of hypothyroidism observed in patients.**

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.