

# Increased Postoperative Risks After Mohs Surgery in Patients With Hypothyroidism: A Cohort Study

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To the Editor,

A direct relationship between hypothyroidism and delayed wound healing has been demonstrated in both in vivo murine and ex vivo human models.<sup>1,2</sup> Clinical studies further support this association, with higher postoperative complication rates reported among hypothyroid patients, including those seen in cutaneous and other head and neck surgeries such as rhytidectomy or laryngectomy.<sup>3,4</sup> However, the impact of hypothyroidism on outcomes after Mohs micrographic surgery (MMS) remains unclear. This retrospective cohort study evaluates postoperative risks within 30 days of MMS in patients with hypothyroidism.

A global retrospective cohort study was conducted utilizing TriNetX, a database containing records from over 120 million patients across 80 health care organizations. Patients who underwent MMS were categorized based on a history of hypothyroidism (n= 50,284) or no diagnosis of hypothyroidism (n= 406,045). Propensity score matching was used to control for demographics, comorbidities, and medication use (Table 1). Post-surgical complications within 30 days were compared between matched cohorts, with significance at *P*-value <0.05.

TABLE 1.

Baseline Characteristics of the Hypothyroidism Cohort and Control Cohort Before and After Propensity Score Matching

Variable	Hypothyroidism (BPSM) (N= 44,778)	Control (BPSM) (N= 352,241)	<i>P</i> -value (BPSM)	Hypothyroidism (APSM) (N= 44,763)	Control (APSM) (N= 44,763)	<i>P</i> -value (APSM)
<b>Demographics</b>						
Age at Index	73.4 +/- 11.2	67.6 +/- 12.7	<0.0001	73.4 +/- 11.2	73.4 +/- 11.2	0.9384
Female	25,053 (55.95%)	136,567 (38.77%)	<0.0001	25,038 (55.94%)	25,035 (55.93%)	0.9839
Male	19,725 (44.05%)	215,638 (61.22%)	<0.0001	19,725 (44.07%)	19,718 (44.05%)	0.9624
White	42,410 (94.71%)	316,064 (89.73%)	<0.0001	42,395 (94.71%)	42,412 (94.75%)	0.7993
Hispanic	604 (1.35%)	4,987 (1.42%)	0.2575	604 (1.35%)	597 (1.33%)	0.8389
<b>Comorbidities</b>						
Nicotine dependence	2,641 (5.90%)	15,078 (4.28%)	<0.0001	2,636 (5.90%)	2,630 (5.88%)	0.9321
Alcohol related disorders	1,288 (2.88%)	6,031 (1.71%)	<0.0001	1,285 (2.87%)	1,290 (2.88%)	0.9204
<b>Medication use</b>						
Long term use of immunosuppressant therapy	260 (0.58%)	713 (0.20%)	<0.0001	260 (0.58%)	216 (0.48%)	0.432
Long term use of systemic steroids	1,670 (3.73%)	4,571 (1.30%)	<0.0001	1,655 (3.70%)	1,647 (3.70%)	0.8872

Abbreviations: before propensity score matching (BPSM), after propensity score matching (APSM)

TABLE 2.

**Post-Surgical Outcomes 30 Days After MMS After MMS in Patients With Hypothyroidism Compared to Patients With No History of Thyroid Disease**

Category of Outcome	Risk Percentage	Risk Ratio with 95% Confidence Intervals	P-value
Cellulitis and Lymphangitis	0.39%	1.959(1.498,2.561)	<0.0001
Postprocedural Pain	0.32%	2.238 (1.653,3.031)	<0.0001
Rash	0.27%	2.273 (1.613,3.205)	<0.0001
Edema	0.31%	2.899(2.049,4.1)	<0.0001
Pruritus	0.13%	2.554 (1.556,4.192)	<0.0001
Post-operative hematoma and seroma	0.04%	1.056 (0.554,2.012)	0.8678
Wound dehiscence	0.25%	1.194 (0.908,1.571)	0.2044

After propensity matching, hypothyroid patients (n= 44,763) had significantly higher risks of postoperative cellulitis and lymphangitis (0.39%,  $P<0.0001$ ), rash (0.27%,  $P<0.0001$ ), edema (0.31%,  $P<0.0001$ ), pruritus (0.13%,  $P=0.0001$ ), and post-procedural pain (0.32%,  $P<0.0001$ ; Table 2).

These findings align with prior clinical literature showing that inadequate thyroid hormone activity contributes to impaired tissue repair and delayed resolution of inflammation. In a retrospective study of salvage laryngectomy patients, postoperative hypothyroidism was independently associated with a 3.6-fold increase in fistula formation and an 11-fold increase in reoperation rates, demonstrating the direct clinical impact of thyroid dysfunction on wound outcomes.<sup>4</sup> Similarly, a report on face-lift surgery identified prolonged postoperative edema lasting several months among hypothyroid patients despite thyroid replacement therapy, suggesting that even subclinical thyroid impairment may disrupt lymphatic drainage and collagen remodeling.<sup>3</sup>

Experimental data offer insight into the biological mechanisms underlying these clinical outcomes. Safer et al. demonstrated that triiodothyronine (T3) promotes epidermal proliferation through the induction of keratin genes (K6a, K16, K17), which are critical for reepithelialization and barrier repair.<sup>1</sup> Likewise, Zhang et al. found that thyroxine (T4) enhances both angiogenesis and epithelial repair through the fibroblast growth factor (FGF) and fibroblast growth factor receptor 1 (FGFR1) signaling pathway, an effect that occurred in a dose-dependent manner.<sup>2</sup> Collectively, these findings suggest that reduced thyroid hormone activity may weaken both epidermal regeneration and microvascular repair, contributing to the higher rates of infection, edema, and postoperative pain observed in our cohort.

As the prevalence and underdiagnosis of thyroid disease continue to rise, recognition of thyroid status in patients undergoing MMS is increasingly important. Older patients, who represent a large proportion of the MMS population, have a high rate of subclinical hypothyroidism, affecting approximately 8%

to 18% of individuals aged 65 years or older, with many cases remaining unrecognized.<sup>5</sup> Risk mitigation strategies, such as comprehensive preoperative evaluation and patient counseling regarding prolonged healing times, are warranted. Future research should investigate whether structured screening protocols and early thyroid hormone optimization can improve surgical outcomes in this population.

### DISCLOSURES

Dr. Tolkachjov is an investigator and speaker for CASTLE Biosciences, Kerecis, and Boehringer Ingelheim. No relevant COI. Other authors have no COI to disclose.

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