

Increased Risk of Adverse Events Following Burn Injury in Patients with Hypothyroidism

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Introduction

- Thyroid hormone is essential in the healing of soft tissue wounds, as it has been shown to promote the proliferation of keratinocytes, production of keratin, dermal thickening, and deposition of mature type 1 collagen.¹
- Hypothyroidism has been associated with delayed wound healing that may worsen surgical outcomes.
- Many key roles of thyroid hormone exist in the respiratory, cardiac, vascular, renal, and nervous systems, all of which can be compromised by systemic manifestations of burns.² Thus, hypothyroidism could have vast implications in burn injuries.
- However, the impact of hypothyroidism as a pre-existing condition prior to burn injury has not been directly studied.
- This study evaluated the role of hypothyroidism on acute outcomes after burn injury.

Methods

- A retrospective cohort analysis was conducted using TriNetX, a federated health research network database. This report was generated on a subset network called US Collaborative Network and included 56 HCOs.
- Using validated ICD-10 codes, the experimental group, cohort 1, identified patients with a pre-existing diagnosis of hypothyroidism (ICD-10-CM:E02-03) before any instance of burn injury (T31-32).
- The control group, cohort 2, identified patients with a diagnosis of thermal or chemical burn injury (T31-32) who have never had a previous diagnosis of hypothyroidism.
- A 1:1 matched propensity score analysis was conducted adjusting for demographics, comorbidities, and percent total body surface area burned.
- The following post-burn outcomes were selected for analysis: skin graft complications, infection of the skin and subcutaneous tissue, hyperglycemia, volume depletion, ICU admission, kidney failure, ARDS, pulmonary edema, pneumonia, pulmonary collapse, respiratory failure, acute MI, acute embolism and thrombosis of the lower extremity, sepsis, and mortality.
- Each post-operative burn outcome was selected and assessed at 30-days after the initial burn injury occurred.
- Adjusted Risk Ratios (RR) with 95% CI were utilized to demonstrate the significance of the increased risks of negative acute outcomes in the hypothyroidism cohort compared to those without hypothyroidism who experience burn injuries.

Demographic or Diagnosis	Cohort	Mean +/- SD	Patients	% of Cohort	P-Value	Std. Diff.
Age at Index	1	55.7 +/- 20.1	33,532	100	0.977	<0.001
	2	55.7 +/- 20.1	33,532	100		
White	1		26,280	78.4	0.785	0.002
	2		26,309	78.5		
American Indian or Alaska Native	1		137	0.4	0.384	0.007
	2		123	0.4		
Hispanic or Latino	1		1,981	5.9	0.922	0.001
	2		1,975	5.9		
Not Hispanic or Latino	1		27,351	81.6	0.952	<0.001
	2		27,357	81.6		
Black or African American	1		3,016	9.0	0.914	0.001
	2		3,008	9.0		
Asian	1		797	2.1	0.829	0.002
	2		699	2.1		
Unknown Race	1		3,368	10.0	0.878	0.001
	2		3,380	10.1		
Unknown Ethnicity	1		4,200	12.5	1.000	<0.001
	2		4,200	12.5		
Male	1		8,034	24.0	0.978	<0.001
	2		8,037	24.0		
Female	1		25,270	75.4	0.986	<0.001
	2		25,272	75.4		
T31- (Thermal) Burns according to TBSA	1		4,244	12.7	0.954	<0.001
	2		4,239	12.6		
T32- Corrosions according to TBSA	1		1,359	4.1	0.875	0.001
	2		1,351	4.0		

Table 1. Characteristics of Cohort 1 and 2 After Propensity Score Matching: Two extremely balanced cohorts of 33,532 patients each were created

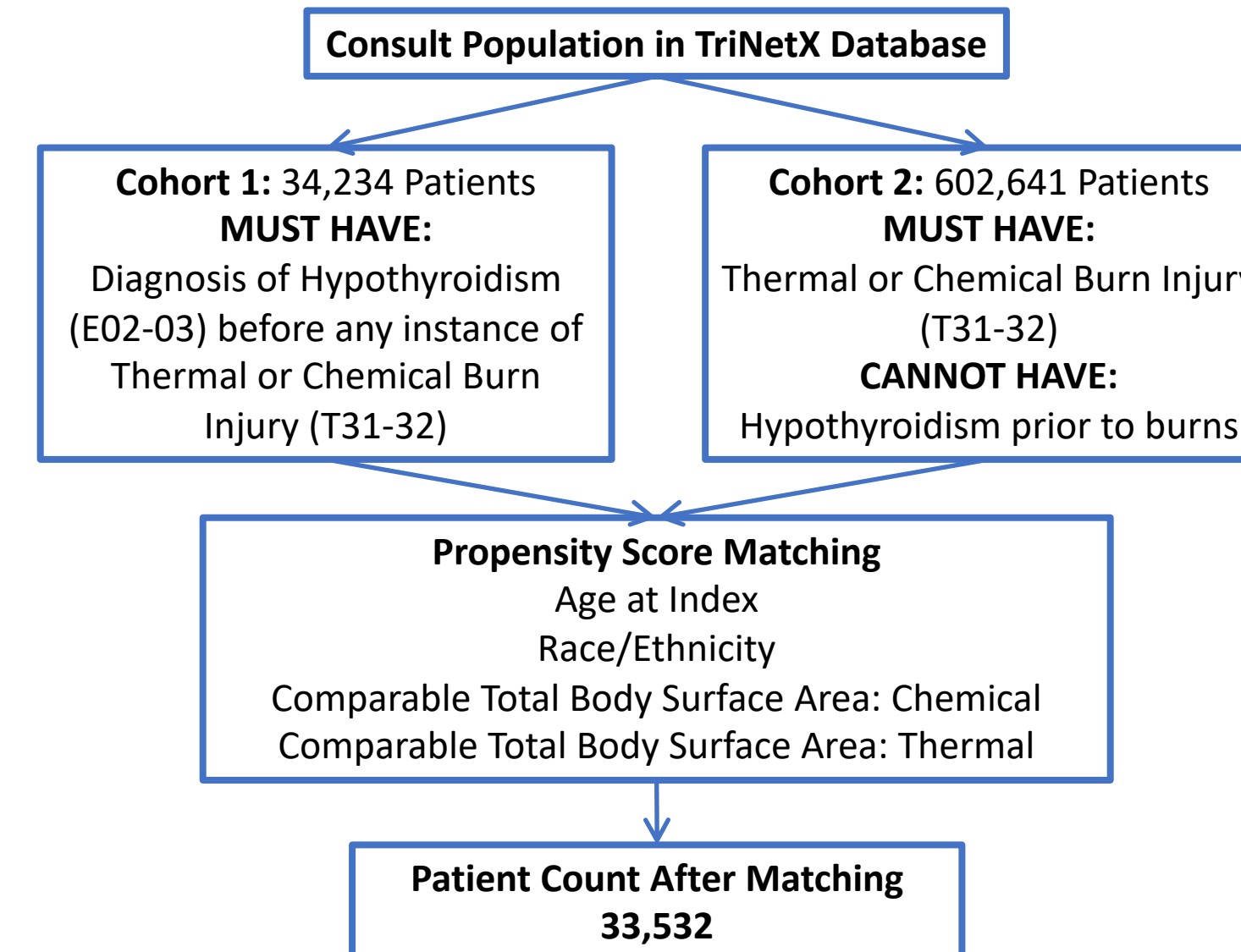


Figure 1. Flow diagram depicting the selection process in the creation of the cohorts for this retrospective cohort study

Acute Complications	UMLS Code	Risk Ratio	95% CI
Skin graft complications	ICD-10-CM:T86.82	1.37	(0.97-1.96)
Infection of the skin and subcutaneous tissue	ICD-10-CM:L00-08	1.28	(1.22-1.34)
Hyperglycemia	ICD-10-CM:R73.9	1.69	(1.50-1.89)
Volume depletion	ICD-10-CM:E86	1.45	(1.33-1.59)
ICU admission	LNC:95420-6	0.512	(0.36-0.74)
Kidney Failure	ICD-10-CM:N17-19	1.83	(1.70-1.97)
ARDS	ICD-10-CM:J80	1.15	(0.73-1.38)
Pulmonary edema	ICD-10-CM:J81	1.27	(1.11-1.45)
Pneumonia	ICD-10-CM:J12-18	1.51	(1.40-1.64)
Pulmonary collapse	ICD-10-CM:J98.1	1.27	(1.15-1.39)
Respiratory failure	ICD-10-CM:J96	1.29	(1.18-1.40)
Acute Myocardial Infarction	ICD-10-CM:I21	1.48	(1.35-1.63)
Acute embolism and thrombosis of lower extremity	ICD-10-CM:I82.4	1.51	1.38-1.65)
Sepsis	ICD-10-CM:A41.9	1.76	(1.59-1.96)
Mortality	Demographics	1.02	(0.87-1.19)

Table 2. Selected Adjusted Risk Ratios (aRR) for the risk of experiencing acute complications post-burn injury in patients with pre-existing hypothyroidism **Bold values indicate P < 0.05**

Results

- Patients with a history of hypothyroidism were found to experience a significantly greater risk of infection of the skin and subcutaneous tissue 1.28 [1.22-1.34]), hyperglycemia (1.69 [1.50-1.89]), volume depletion (1.45 [1.33-1.59]), kidney failure (1.83 [1.70-1.97]), pulmonary edema (1.27 [1.11-1.45]), pneumonia (1.51 [1.40-1.64]), pulmonary collapse (1.27 [1.15-1.39]), respiratory failure (1.29 [1.18-1.40]), acute MI (1.48 [1.35-1.63]), acute embolism and thrombosis of the lower extremity (1.51 [1.38-1.65]), and sepsis (1.76 [1.59-1.96]).
- There was a significantly lower risk of ICU admission (0.51 [0.355-0.739]) in the hypothyroidism cohort.
- The following outcomes showed no significant differences: skin graft complications, ARDS, and mortality.

Discussion

- 12 out of 15 risk ratios in this study were significantly increased in the hypothyroidism cohort versus control.
- It has been previously shown that thyroid hormone plays a key role in soft tissue wound healing¹ which may explain the increased skin complication risks shown here including infection.
- A robust regenerative response is vital in minimizing secondary complications, thus, the diminished wound healing is likely implicated in prolongation of a dangerous post-burn state where volume status, temperature, and immune response is abnormal.
- Disrupted hormone and cytokine levels are also culprits in decreased ability to maintain or overcome the cutaneous, respiratory, hematologic, and renal risks demonstrated here.³
- Hypothyroidism already predisposes to many cardiac and pulmonary complications, including reduced respiratory drive, which may play a role in the largely increased risks in all studied respiratory complications.²
- ICU admission was the only complication with a significantly reduced risk, which is surprising, warranting future investigation.

Conclusions

- These results postulate that burned patients with a history of hypothyroidism are significantly more likely to experience severe acute adverse events and should be monitored closely.
- Additionally, this highlights the need for more research to help elucidate the mechanism for this relationship and allow physicians to be more aware of the unique risks in this group.

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