

Perioperative Management of Patients with Hypothyroidism

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Abstract

Hypothyroidism is an endocrine disorder characterized by reduced thyroid hormone production and may increase the risk of perioperative complications due to cardiovascular, respiratory, metabolic, and altered anesthetic responses. Perioperative management should therefore be tailored to the severity of hypothyroidism and the urgency of surgery. In elective surgery, optimization of thyroid function with levothyroxine and achievement of a euthyroid state are generally recommended before surgery, particularly in patients with overt or severe hypothyroidism. Anesthetic management requires careful selection and dosing of anesthetic agents, adequate hemodynamic and respiratory monitoring, maintenance of body temperature, and prevention of factors that may precipitate cardiovascular or respiratory compromise. Postoperative care should include close monitoring for cardiovascular, respiratory, metabolic, and neurological complications, including myxedema coma. In emergency surgery, the need for timely surgical intervention should be balanced against the severity of hypothyroidism. Surgery may proceed when clinically necessary, with appropriate perioperative thyroid hormone replacement and supportive management; intravenous levothyroxine may be considered in severe hypothyroidism when oral administration is not feasible. A structured approach based on the severity of thyroid dysfunction and surgical urgency is essential to reduce perioperative morbidity and mortality. Achieving a euthyroid state remains the preferred goal before elective surgery whenever clinically feasible.

Keywords: Hypothyroidism, Perioperative, Management

Abstrak

Hipotiroidisme merupakan gangguan endokrin yang ditandai oleh penurunan produksi hormon tiroid dan dapat meningkatkan risiko komplikasi perioperatif akibat gangguan kardiovaskular, respirasi, dan metabolik, serta perubahan respons terhadap obat anestesi. Oleh karena itu, manajemen perioperatif perlu disesuaikan dengan derajat keparahan hipotiroidisme dan urgensi tindakan pembedahan. Pada pembedahan elektif, optimalisasi fungsi tiroid dengan levotiroksin dan pencapaian keadaan eutiroid umumnya direkomendasikan sebelum pembedahan, terutama pada pasien dengan hipotiroidisme nyata atau berat. Manajemen anestesi memerlukan pemilihan dan penyesuaian dosis obat anestesi secara cermat, pemantauan hemodinamik dan respirasi yang adekuat, pemeliharaan suhu tubuh, serta pencegahan faktor-faktor yang dapat memicu gangguan kardiovaskular atau respirasi. Perawatan pascaoperasi harus mencakup pemantauan ketat terhadap komplikasi kardiovaskular, respirasi, metabolik, dan neurologis, termasuk koma miksedema. Pada pembedahan emergensi, kebutuhan untuk melakukan intervensi bedah segera harus dipertimbangkan secara seimbang dengan derajat keparahan hipotiroidisme. Pembedahan dapat tetap dilakukan apabila terdapat indikasi klinis yang kuat, disertai pemberian terapi pengganti hormon tiroid dan tata laksana suportif yang sesuai. Levotiroksin intravena dapat dipertimbangkan pada hipotiroidisme berat apabila pemberian secara oral tidak memungkinkan. Pendekatan yang terstruktur berdasarkan derajat disfungsi tiroid dan urgensi pembedahan sangat penting untuk menurunkan morbiditas dan mortalitas perioperatif. Pencapaian keadaan eutiroid tetap menjadi tujuan utama sebelum pembedahan elektif apabila secara klinis memungkinkan.

Kata kunci: Hipotiroidisme, Perioperatif, Manajemen

I. INTRODUCTION

Hypothyroidism is a clinical syndrome resulting from thyroid hormone deficiency. It is characterized by an elevated serum concentration of thyroid-stimulating hormone (TSH). Hypothyroidism affects approximately 4–10% of the global population, with substantial variation across countries and demographic groups. The prevalence of hypothyroidism among patients undergoing surgery varies according to the type of procedure. It has been reported more frequently among patients undergoing cardiovascular surgery, with some studies reporting prevalence rates of up to 11–13%. In orthopedic surgery, Padur et al. (2016) reported a prevalence of approximately 6%. Several studies have indicated that 1–2% of surgical patients may have undiagnosed hypothyroidism.¹⁻⁴

Patients with uncontrolled hypothyroidism are at increased risk of perioperative complications, particularly cardiovascular and respiratory complications. However, patients with well-controlled hypothyroidism generally have surgical outcomes comparable to those of euthyroid patients. Patients with hypothyroidism also frequently have comorbidities such as obesity, hypertension, and diabetes, which may further influence perioperative management.⁵

For superficial procedures, such as dental procedures and biopsies, surgery generally does not need to be postponed in patients with hypothyroidism. For minor procedures, including inguinal hernia repair and hand surgery, achieving an euthyroid state may reduce the risk of complications. For intermediate procedures, such as hysterectomy and total joint replacement, and major procedures, including cardiopulmonary bypass, prolonged surgery, and procedures requiring prolonged interruption of oral intake, the risk of complications may be higher when surgery is performed in a hypothyroid state. Potential

complications include myxedema coma; cardiovascular effects such as bradycardia, hypotension, diastolic dysfunction, pericardial effusion, electrolyte disturbances, and heart failure; respiratory effects such as hypoventilation, obstructive sleep apnea, and laryngeal edema; metabolic disturbances including insulin resistance, hyponatremia, and dyslipidemia; coagulation abnormalities; impaired renal function; hypoalbuminemia; altered drug metabolism; delayed wound healing; and increased susceptibility to adverse effects of anesthetic agents.⁵

The risk of complications associated with surgery in patients with hypothyroidism depends on the type and extent of the surgical procedure. In the perioperative setting, the management of patients with hypothyroidism presents particular challenges because of the potential for multiple complications. Therefore, preoperative assessment and optimization of thyroid function, together with appropriate perioperative management, are essential to minimize morbidity and mortality in this patient population.

II. HYPOTHYROIDISM

There are two types of primary hypothyroidism based on the circulating concentration of free thyroxine (fT4): overt hypothyroidism and subclinical hypothyroidism. Overt hypothyroidism is defined as a serum fT4 concentration below the normal reference range, whereas subclinical hypothyroidism is characterized by a serum fT4 concentration within the normal reference range.^{5,7,8}

Based on TSH levels, hypothyroidism can be classified into two categories: mild hypothyroidism, defined as a TSH level of 4–10 mU/L, and severe hypothyroidism, defined as a TSH level ≥ 10 mU/L. Based on clinical severity, patients with hypothyroidism can be categorized as having mild, moderate, or severe disease. Mild

hypothyroidism includes patients with subclinical hypothyroidism, defined as a normal serum fT4 concentration accompanied by an elevated serum TSH concentration. Moderate hypothyroidism includes patients with overt hypothyroidism, characterized by elevated TSH and low fT4 levels, without features of severe hypothyroidism. Severe hypothyroidism includes patients with severe clinical manifestations of chronic hypothyroidism, such as altered mental status, pericardial effusion, heart failure, markedly reduced total thyroxine (T4) levels ($<1.0 \mu\text{g/dL}$) or free T4 levels ($<0.5 \text{ ng/dL}$), or myxedema coma.^{5,7}

The Billewicz Index can be used as an initial screening tool for hypothyroidism by assessing clinical signs and symptoms. A score <-30 indicates that hypothyroidism is unlikely, a score >25 indicates hypothyroidism, and a score of -29 to 24 is considered equivocal. The details of this scoring system are presented in the table 1.⁹

TABLE 1. BILLEWICZ INDEX FOR HYPOTHYROIDISM⁹

Clinical Features	Present	Absent
Symptoms		
Reduced sweating	+6	-2
Dry skin	+3	-6
Cold intolerance	+4	-5
Weight gain	+1	-1
Constipation	+2	-1
Hoarseness	+5	-4
Hearing impairment	+2	0
Clinical Signs		
Slowness of movement	+11	-3
Coarse skin	+7	-7
Cold skin	+3	-2
Periorbital edema	+4	-6
Bradycardia	+4	-4
Ankle jerk	+15	-6

III. EFFECTS OF EMERGENCY SURGERY IN PATIENTS WITH HYPOTHYROIDISM

Hypothyroidism affects multiple organ systems, including the cardiovascular, homeostatic, respiratory, renal, gastrointestinal, hematologic, and central nervous systems. The perioperative risks in untreated patients with hypothyroidism vary according to the severity of thyroid dysfunction. In severe hypothyroidism, several complications may occur, including myxedema coma, cardiac dysfunction, and respiratory impairment.⁵

Cardiovascular complications include a 30%–50% reduction in cardiac output, intraoperative hypotension, arrhythmias, and prolongation of the QT interval, which may result in ventricular tachycardia and torsades de pointes. In addition, hypothyroidism increases peripheral vascular resistance, leading to increased cardiac afterload, a reduced pulse pressure due to increased diastolic pressure, and decreased systolic blood pressure. Despite elevated catecholamine levels, patients with hypothyroidism are prone to hypotension during anesthesia, possibly due to downregulation of β -adrenergic receptors. Hypothyroidism is also associated with an increased risk of coronary artery disease, which may be related to elevated cholesterol levels, prolonged coagulation factor half-lives, and anemia.^{5,10}

Respiratory complications include hypoxemia, hypercapnic respiratory failure, respiratory muscle weakness, and an increased prevalence of obstructive sleep apnea. Difficult airway management may occur because of laryngeal myxedema, macroglossia, and increased sensitivity to anesthetic agents.^{5,11}

Impaired renal excretion may prolong the effects of anesthetic agents, opioids, and other medications. Deposition of

extracellular glycosaminoglycans may exacerbate the reduction in oncotic pressure caused by hypoalbuminemia, resulting in fluid shifts into the extracellular space. This reduces effective circulating filling pressure and renal perfusion. In addition, increased antidiuretic hormone (ADH), decreased atrial natriuretic factor (ANF), and reduced activity of the renin–angiotensin–aldosterone system (RAAS) may contribute to hyponatremia. Hyponatremia may impair consciousness and potentiate the effects of anesthetic agents.¹¹

Gastrointestinal effects include reduced gastrointestinal motility, most commonly manifesting as constipation in patients with hypothyroidism, thereby increasing the risk of postoperative ileus. Hypothyroidism-associated gastrointestinal atony and hypomotility may exacerbate postoperative paralytic ileus and delay the initiation of enteral nutrition. This is particularly concerning because postoperative pain management commonly involves opioids, which independently contribute to constipation. Intestinal wall edema may also

impair the absorption of amino acids and glucose.⁵

Hypothyroidism is associated with several hematologic abnormalities. The most commonly described is normochromic, normocytic anemia. However, because pernicious anemia is more prevalent among patients with hypothyroidism, autoimmune-mediated vitamin B12 deficiency may result in macrocytosis. In addition, in premenopausal women, hypothyroidism-associated menorrhagia may cause iron-deficiency microcytic anemia. Other hematologic manifestations of hypothyroidism include reduced factor VIII activity, prolonged partial thromboplastin time (PTT), and acquired von Willebrand disease. These abnormalities may increase the risk of bleeding at the surgical site. Conversely, the half-lives of coagulation factors such as factors II, VII, and X are prolonged, which may require prolonged anticoagulation with heparin and higher doses of warfarin for postoperative deep vein thrombosis prophylaxis.¹¹

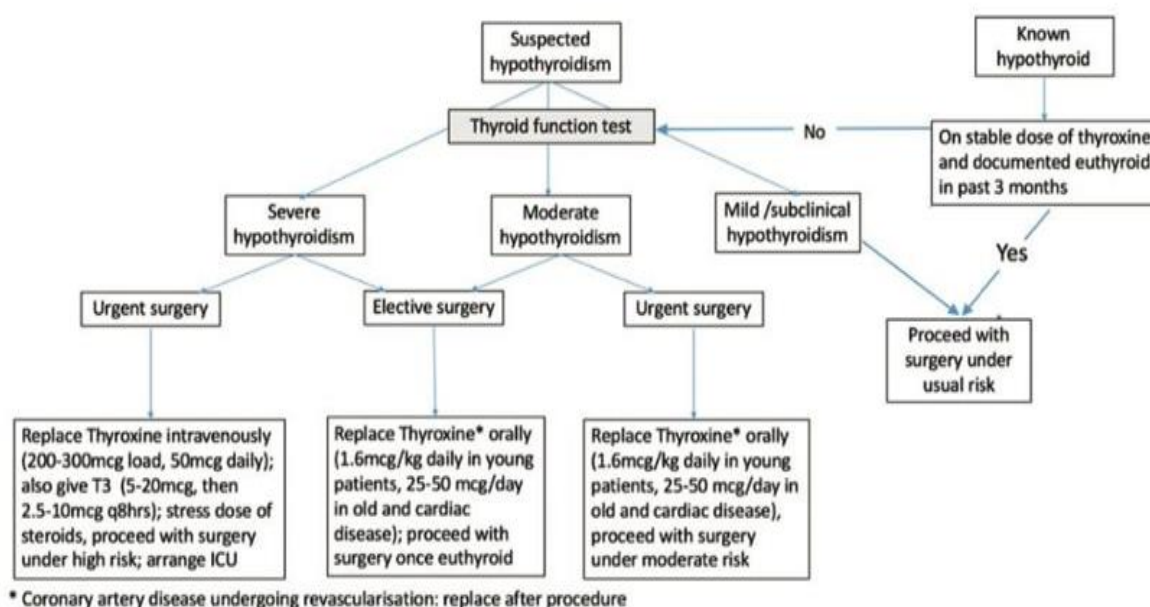


FIGURE 1. PERIOPERATIVE MANAGEMENT OF HYPOTHYROIDISM
(SOURCE: MALHOTRA AND BHADADA, 2022)⁵

A feared complication of severe hypothyroidism following surgery is myxedema coma, which may be associated with mortality rates of up to 80%. It is characterized by altered mental status, hypotension, bradycardia, hypothermia, and metabolic disturbances.⁵

IV. PERIOPERATIVE MANAGEMENT OF HYPOTHYROIDISM

Perioperative management of patients with hypothyroidism should be guided by the severity of the clinical condition, as illustrated in the algorithm in Figure 1.

A. EMERGENCY SURGERY

1. Preoperative Management

In patients with severe hypothyroidism requiring emergency surgery, the procedure may proceed despite the increased operative risk. Intravenous levothyroxine should be administered at an initial dose of 200–300 µg, followed by 50 µg daily for 3–5 days. If intravenous levothyroxine is unavailable, an oral LT4 regimen consisting of a loading dose of 300–500 µg, followed by a gradual dose reduction over the subsequent 3–5 days, may be administered. If there is concern for myxedema coma or potential precipitating factors, intravenous liothyronine may be administered concomitantly, with an initial dose of 5–20 µg followed by 2.5–10 µg every 8 hours. Lower doses of thyroid hormone should be used in elderly patients, patients with cardiac disease, or those undergoing emergency cardiac revascularization. Addison's disease may coexist with primary Hashimoto's hypothyroidism, while secondary hypothyroidism may be associated with secondary adrenal insufficiency. If adrenal insufficiency is suspected, stress-dose corticosteroids should be administered perioperatively.^{6,11,12}

The stress-dose corticosteroid regimen should be determined according to the type

of surgery being performed. Patients undergoing minor procedures, such as hernia repair or colonoscopy, should receive a single intravenous dose of 25 mg hydrocortisone before surgery. For intermediate procedures, such as cholecystectomy, colorectal resection, hysterectomy, or total joint replacement, 50 mg of intravenous hydrocortisone should be administered for 1–2 days. For major procedures, such as abdominoperineal resection or pancreaticoduodenectomy, 100 mg of intravenous hydrocortisone should be administered for 2–3 days.¹³

Supplemental corticosteroids are recommended without the need for additional testing in patients with primary adrenal insufficiency or secondary adrenal insufficiency due to hypopituitarism; patients with clinical Cushing syndrome secondary to corticosteroid exposure; patients receiving oral corticosteroids at a dose exceeding 5 mg of prednisone daily (or equivalent) for more than 3 weeks within the preceding 3 months; and patients receiving high-dose inhaled glucocorticoid therapy, such as beclomethasone 1.5 mg/day or fluticasone >8 mg/kg/day.¹³

In patients with moderate hypothyroidism, emergency surgery may proceed with an intermediate operative risk. Oral levothyroxine should be administered at a dose of 1.6 µg/kg/day, or at a lower dose of 25–50 µg/day in elderly patients and those with cardiovascular disease. In patients with subclinical hypothyroidism, emergency surgery may also proceed with levothyroxine treatment at the aforementioned doses.⁴

2. Intraoperative Management

During surgery, ketamine may be considered a preferred induction agent because of its sympathomimetic and positive inotropic effects. Thiopental is not an optimal choice because of its effects on systemic vascular resistance and its antithyroid properties. Rapid-sequence induction with

succinylcholine should be considered because of delayed gastric emptying. Rapid-acting nondepolarizing neuromuscular blocking agents may also be used; however, reduced drug metabolism and pre-existing muscle weakness may result in prolonged neuromuscular blockade. Anesthesia may be maintained with nitrous oxide and short-acting opioid supplementation, with or without a volatile anesthetic. The details are presented in the table 2.¹⁴

Table 2. Preferred Anesthetic Agents for General Anesthesia in Patients with Thyroid DYSFUNCTION¹⁵

Agent	Drug
Induction	Ketamine
Maintenance	Nitrous oxide and short-acting opioids/non-opioid analgesics
Intubation	Rapid-sequence induction with succinylcholine or a short-acting non-depolarizing neuromuscular blocking agent

During surgery, intensive monitoring of heart rate, respiratory rate, oxygen saturation, blood pressure, body temperature, and the patient's clinical condition is required. Temperature monitoring is important for assessing perioperative and postoperative risks in patients with hypothyroidism and for maintaining normothermia throughout the procedure. Hypothermia may increase morbidity, length of hospital stay and healthcare costs. Recent studies have also demonstrated an increased incidence of complications among patients who develop hypothermia following head and neck cancer surgery.¹⁶

3. Postoperative Management

The most serious postoperative complication in patients with severe hypothyroidism is myxedema coma. Clinical manifestations may vary among patients but typically include altered mental status, hypothermia, hypotension, bradycardia, hyponatremia, hypoglycemia, and hypoventilation. Laboratory findings may demonstrate markedly elevated TSH and very low fT4

levels. Early diagnosis and prompt treatment are essential for successful management.¹⁷

Myxedema coma may lead to cardiovascular collapse; therefore, early recognition and prompt treatment are potentially lifesaving. Patients with suspected myxedema coma should be treated with intravenous levothyroxine at a dose of 100–500 µg. There is currently no consensus regarding the perioperative management of myxedema coma. Some endocrinologists prefer intravenous liothyronine (10–25 µg every 8 hours) because of its greater biological activity and the impaired conversion of fT4 to fT3 in hypothyroidism. However, excessive administration of fT3 may increase mortality. Alternatively, many clinicians favor an initial dose of levothyroxine 200–500 µg administered intravenously or through a nasogastric tube, followed by 50–100 µg/day, with lower doses recommended for elderly patients. Others recommend combination therapy with fT3 and fT4.¹⁷

The postoperative phase includes monitoring in the recovery room until the patient regains consciousness, followed by continued management during hospitalization until discharge. Postoperative nutritional support can be initiated once the patient is fully conscious and should be advanced gradually, beginning with fluids and progressing to solid food as tolerated. Prolonged withholding of oral nutrition may impair intestinal microbial colonization and increase the risk of infection.¹⁶

Uncontrolled hypothyroidism may increase the risk of postoperative ileus because of reduced gastrointestinal motility. Therefore, the use of opioid analgesics should be carefully considered because opioids may further aggravate constipation. Intravenous opioids are effective analgesics but may increase the risk of respiratory depression, pruritus, urinary retention, ileus, nausea, and vomiting.¹⁶

After surgery, if oral intake cannot be resumed within 5–7 days, T4 should be administered intravenously or intramuscularly. The dose should be approximately 70%–80% of the patient's usual oral dose, corresponding to the fraction of orally administered T4 that is absorbed. This is also related to the long half-life of levothyroxine, which is approximately 7 days. Therefore, if oral intake is not possible for 5–7 days, intravenous or intramuscular levothyroxine should be initiated.⁵

Another challenge during the postoperative period is the development of non-thyroidal illness syndrome (NTIS), also known as euthyroid sick syndrome, which is commonly observed after major surgery, such as coronary artery bypass grafting (CABG). Euthyroid sick syndrome refers to abnormalities in thyroid function tests occurring in patients with severe non-thyroidal illness, after surgery, or during prolonged fasting, without pre-existing abnormalities of the hypothalamic–pituitary–thyroid axis or thyroid gland. It is characterized by decreased T3, normal or decreased T4, normal, decreased, or mildly elevated TSH, and increased reverse T3 (rT3). The prevalence of NTIS is approximately 11%–18% among hospitalized patients and increases to 70%–75% among patients admitted to the intensive care unit (ICU). The pathophysiology of NTIS involves reduced deiodinase 1 (D1) activity and increased deiodinase 3 (D3) activity in target tissues. Reduced D1 activity decreases peripheral conversion of T4 to T3, whereas increased D3 activity increases rT3 levels, an inactive thyroid hormone metabolite.¹⁸

The pathophysiology of NTIS also involves peripheral processes in target tissues and central processes involving the hypothalamic–pituitary–thyroid axis. Peripheral mechanisms include alterations in thyroid hormone metabolism and action at target tissues, including changes in

deiodinase activity, thyroid hormone receptor expression, transporters, and binding proteins. Central mechanisms involve alterations in the hypothalamic–pituitary–thyroid axis and disruption of negative feedback at the hypothalamic and pituitary levels. An important aspect of management is reassessment of thyroid function after recovery from the underlying illness. Repeat thyroid function testing is recommended approximately 6 weeks after hospital discharge.^{5,18}

B. ELECTIVE SURGERY

1. Preoperative Management

Elective surgery in patients with hypothyroidism should generally be postponed until an euthyroid state is achieved. Oral levothyroxine should be initiated as soon as possible at a dose of 1.6 µg/kg/day, or at a lower dose of 25–50 µg/day in elderly patients and those with cardiovascular disease.⁴

In patients with suspected adrenal insufficiency, appropriate diagnostic evaluation should be performed to establish the diagnosis and determine whether perioperative stress-dose corticosteroids are indicated.⁶

In patients with established hypothyroidism who are receiving a stable dose of thyroxine and have documented euthyroidism within the preceding 3 months, surgery may proceed with relatively low risk, and the previous levothyroxine dose should be continued. In patients with a large goiter, airway evaluation should include ultrasonography and/or thyroid imaging to assess for retrosternal extension.⁵

2. Intraoperative Management

During elective surgery, intraoperative management should include hemodynamic monitoring, with particular attention to intraoperative hypotension, bradycardia, and reduced cardiac output. The response to

vasopressors may be altered because of changes in catecholamine sensitivity.^{15,16}

Patients with hypothyroidism, even when euthyroid, are more susceptible to intraoperative hypothermia. Warming blankets, warmed intravenous fluids, appropriate operating-room temperature control, and continuous temperature monitoring should be used to maintain normothermia.¹⁶

3. Postoperative Management

Recovery from anesthesia may be prolonged in patients with hypothyroidism; therefore, an extended stay in the recovery room may be required. Hypoventilation and carbon dioxide retention should be closely monitored, and patients should be fully awake before extubation. Signs of hypothyroidism precipitated or exacerbated by surgical stress should also be monitored. Oral levothyroxine should be resumed as soon as the patient is able to tolerate oral intake, preferably within 1–2 days. In patients undergoing total thyroidectomy, levothyroxine should be initiated immediately after surgery. In patients undergoing subtotal thyroidectomy, TSH should be assessed 6–8 weeks after surgery and the levothyroxine dose adjusted accordingly.¹⁶

Although myxedema coma is rare in euthyroid patients, it may still be precipitated by severe physiological stress, infection, or hypothermia. Therefore, clinical features suggestive of myxedema coma should remain part of postoperative monitoring.¹⁷

V. CONCLUSION

Surgery performed in patients with hypothyroidism may lead to complications such as myxedema coma, cardiovascular dysfunction, and respiratory complications. Perioperative management should be guided by the severity of hypothyroidism, with the aim of minimizing postoperative

complications associated with the hypothyroid state.

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