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Basics of prevention and management of iodine-based contrast media-induced thyroid dysfunction — position paper by the Polish Society of Endocrinology

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Abstract

Medical practice involves a high number of radiological examinations using iodinated contrast media (ICM). Therefore, it is crucial for doctors of different specialties to be aware of possible adverse effects associated with ICM use. The most common and well characterized adverse effect is contrast-induced nephropathy, whereas thyroidal adverse reactions remain a diagnostic and therapeutic dilemma. ICM-induced thyroid dysfunction represents a highly heterogenous group of thyroid disorders. Due to supraphysiological iodine concentration, ICM can induce both hyper- and hypothyroidism. In most cases, the ICM-induced thyroid dysfunction is oligo- or asymptomatic, mild, and transient. In rare cases, however, the ICM-induced thyroid dysfunction may be severe and life threatening. Recently, the European Thyroid Association (ETA) Guidelines for the Management of Iodine-Based Contrast Media-Induced Thyroid Dysfunction were published. The authors advise an individualized approach to prevention and treatment of ICM-induced thyroid dysfunction, based on patient's age, clinical symptoms, pre-existing thyroid diseases, coexisting morbidities, and iodine intake. There is a geographic variation of ICM-induced thyroid dysfunction prevalence, which is linked to iodine intake. The prevalence of ICM-induced hyperthyroidism, which may pose a serious therapeutic challenge, is greater in countries with iodine deficiency. Poland is a region with a history of iodine deficiency, contributing to an increased prevalence of nodular thyroid disease, especially in the elderly. Therefore, the Polish Society of Endocrinology has proposed national, simplified principles of ICM-induced thyroid dysfunction prevention and treatment. **(Endokrynol Pol 2023; 74 (1): 1–4)**

Key words: *iodine; contrast media; iodinated contrast media; thyroid; hyperthyroidism; hypothyroidism; prevention*

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Introduction

Medical practice involves a high number of radiological examinations using iodinated contrast media (ICM). Therefore, it is crucial for doctors of different specialties to be aware of possible adverse effects associated with ICM use. The most common and well characterized adverse effect is contrast-induced nephropathy [1–4], whereas thyroidal complications have not been described in detail. The first European Thyroid Association (ETA) Guidelines for the Management of Iodine-Based Contrast Media-Induced Thyroid Dysfunction were published in 2021. The authors of the ETA guidelines reviewed existing scientific evidence and developed recommendations to address the most frequently asked clinical questions regarding the diagnosis and management of ICM-induced thyroid dysfunction [1]. Unfortunately, the strength of most recommendations was weak, due to insufficient or inconclusive scientific evidence. Therefore, additional clinical trials with clinically significant endpoints are needed to improve the recommendations and simplify clinical decision-making in patients with ICM-induced thyroid dysfunction [5].

ICM-induced thyroid dysfunction denotes a highly heterogenic group of thyroid disorders. Due to the non-physiological iodine concentration in the contrast medium, ICM can induce both hyper- and hypothyroidism. In most cases, the ICM-induced thyroid dysfunction is mild, oligo-, or asymptomatic [1, 6–9]. Moreover, it is often self-limiting, lasts for 1-18 months, and subsides without treatment. In rare cases, however, the dysfunction can have a severe course, posing a serious therapeutic challenge.

Recommendations regarding the management of ICM-induced thyroid dysfunction essentially address the effects similar to those expected after prophylactic use of potassium iodide (KI) to block the iodine uptake by the thyroid following radioactive iodine exposure. Regardless of the consequences, certain population groups must be administered KI in recommended doses (12.5–100 mg) to prevent thyroid cancer. Anticipated adverse effects should not discourage the administration of prophylactic KI dose [10].

At present, the prevalence and/or clinical significance of ICM-induced thyroid dysfunction worldwide remains largely unknown. It ranges between 0.05% and 15%, depending on iodine intake and concomitant thyroid dysfunction [1, 7, 8, 11]. However, in a recently published meta-analysis [12] and in the largest population-based retrospective cohort study, it was described as low [13]. Thus, an individual approach to both prevention and treatment of ICM-induced thyroid dysfunction is needed in most cases [1,14]. The geographic variation of ICM-induced thyroid dysfunction prevalence, linked to iodine intake, was also noted. Poland is a region with a history of iodine deficiency, contributing to an increased prevalence of nodular thyroid disease, especially in the elderly. ICM-induced hyperthyroidism is most common in countries with known (past or present) iodine deficiency. Therefore, the Polish Society of Endocrinology has proposed national, simplified practical management principles to prevent and treat iodine-based contrast media-induced thyroid dysfunction.

1. Assess the risk of developing ICM-induced thyroid dysfunction prior to radiological examinations using iodine-based contrast media (ICM)

— on clinical examination look for: goitre, possible symptoms and signs of hyperthyroidism/hypothyroidism, and past medical history of thyroid disease treatment;
— pay attention to risk factors of developing thyroid dysfunction. ICM-induced hyperthyroidism develops mainly in patients with nodular goitre, those with latent Graves' disease, or living in iodine-deficient regions. Autoimmune thyroiditis (Hashimoto's disease) is the main risk factor for ICM-induced hypothyroidism.

Risk factors for ICM-induced hyperthyroidism

Risk factors for ICM-induced hyperthyroidism include nodular goitre [especially grade 2 goitre according to World Health Organization (WHO) classification), latent Graves' disease (rarely), and endogenous subclinical hyperthyroidism.

Risk factors for ICM-induced hypothyroidism

Risk factors for ICM-induced hypothyroidism include Hashimoto's disease, foetus and neonate, previous thyroid surgery (except for total thyroidectomy), kidney disease, and endogenous subclinical hypothyroidism.

2. Determine serum thyroid-stimulating hormone (TSH) level prior to radiological examination in patients at risk of ICM-induced thyroid dysfunction. If the serum TSH level is abnormal, the thyroid hormones [free thyroxine (FT4) and/or free triiodothyronine (FT3)] should be determined

3. Further management of patients with thyroid dysfunction diagnosed before radiological examination involving ICM use (Tab. 1)

Table 1. *Further management of patients with thyroid dysfunction diagnosed before radiological examination involving ICM use*

Thyroid dysfunction	Management prior to radiological examination involving ICM use
Overt hyperthyroidism TSH↓, FT4↑, and/or FT3↑	Radiological examinations using ICM administration ***are generally contraindicated*** The above does not apply to life-saving procedures* In other cases, alternative imaging procedures should be considered** Commence treatment of hyperthyroidism (anti-thyroid drug with or without sodium perchlorate) prior to or immediately after radiological examination*** (*see Part 5*) *e.g. ST-elevation myocardial infarction (requiring revascularisation), suspected aneurysm **e.g. MRI, non-contrast CT, echocardiography (with exercise echocardiography and transoesophageal echocardiography performed if available and clinically indicated), ultrasound ***in patients already on ATD, consider dose escalation and/or adding sodium perchlorate
Hyperthyroidism in patients on ATD TSH↓ or ↔, FT4↔, FT3↔	Radiological examinations using ICM ***are not contraindicated*** Serum TSH, FT4, and FT3 levels should be determined 3–4 weeks after ICM administration Consider ATD dose escalation and/or adding sodium perchlorate (*see Parts 4 i 5*)
Persistent, endogenous subclinical hyperthyroidism TSH↓, FT4↔, FT3↔	Radiological examinations using ICM ***are not contraindicated*** Prior to elective radiological studies, an endocrine consultation is recommended to determine the aetiology of endogenous subclinical hyperthyroidism Serum TSH, FT4, and FT3 levels should be determined 3–4 weeks after ICM administration Prophylactic treatment may be considered in selected cases (*see Part 4*)
Overt hypothyroidism TSH↑, FT4↓ Subclinical hypothyroidism TSH↑, FT4↔	Radiological examinations using ICM ***are not contraindicated*** Treatment with thyroid hormone (LT4) should be initiated and further monitored according to current guidelines
Hypothyroidism in patients on thyroid hormone replacement with LT4 TSH↔	Radiological examinations using ICM ***are not contraindicated*** Patients with hypothyroidism on thyroid hormone replacement with LT4 are not at risk of developing ICM-induced thyroid dysfunction and do not require endocrine consultation or special management
Euthyroid patients with nodular goitre (non-toxic nodular goitre disease), Euthyroid patients with Graves' disease in remission after ATD therapy TSH↔	Radiological examinations using ICM ***are not contraindicated*** Normal baseline TSH level does not rule out the risk of developing ICM-induced thyroid dysfunction Consider serum TSH level determination 3–4 weeks after the contrast procedure in patients with WHO grade 2 goitre, especially in the elderly In patients with Graves' disease in remission, serum TSH level should be determined if they develop signs and symptoms suggesting thyroid dysfunction

↔ within the normal range, ↑ above the normal range, ↓ below the normal range. Rare, secondary (hypothalamic-pituitary) thyroid dysfunction was not included in the table. ICM — using iodinated contrast media; TSH — thyroid-stimulating hormone; FT4 — free thyroxine; FT3 — free triiodothyronine; MRI — magnetic resonance imaging; CT — computed tomography; ATD — anti-thyroid drugs; LT4 — L-thyroxine; WHO — World Health Organization

4. Prophylactic treatment in patients at risk of developing ICM-induced hyperthyroidism

Prophylactic therapy with methimazole and/or sodium perchlorate can be administered:

— to selected patients at high risk of developing ICM-induced hyperthyroidism (endogenous subclinical hyperthyroidism, large nodular goitre);
— prior to emergency radiological examinations;
— especially to elderly patients or those with cardiovascular comorbidities, in whom hyperthyroidism may pose a significant burden.

There is no single effective prophylactic treatment protocol. You can choose one of the following:

— administer methimazole per os (*p.o.*) (20–30 mg, once a day) the day before scheduled contrast procedure, and continue treatment at the same dose for the next 14 days. Some centres in Poland administer methimazole intravenously (*i.v.*) (40 mg) prior to or immediately after emergency imaging;
— administer 600 mg sodium perchlorate (available in Poland *via* the direct import route) prior to ICM exposure and continue treatment with 300 mg three times a day for the next 7–14 days;
— in selected patients at the highest risk of developing severe hyperthyroidism, use combined therapy with methimazole and sodium perchlorate;
— hydrate patients well prior to and following administration, avoiding overhydration. In patients with

normal kidney function [assessed based on estimated glomerular filtration rate (eGFR)] this intervention may alone shorten the ICM exposure time.

5. Diagnosis and management of ICM-induced hyperthyroidism

ICM-induced hyperthyroidism, subclinical or overt, most often develops within 3-4 weeks following exposure. While the course can be severe in some cases, it is usually self-limiting and lasts between 1 and 18 months. Notably, in elderly patients and those with unstable cardiovascular diseases, serious complications may occur, such as congestive heart failure, angina, atrial fibrillation, and thromboembolic events, secondary to even mild ICM-induced hyperthyroidism.

The diagnosis of ICM-induced hyperthyroidism is based on clinical signs and symptoms of hyperthyroidism and/or laboratory tests results confirming hyperthyroidism as well as a history of recent (i.e. within last 3 months) exposure to ICM.

Treatment

— an endocrine consultation is recommended;
— we recommend an individualized approach to the treatment of ICM-induced hyperthyroidism, based on clinical symptoms and aetiology as well as the patient's age, concomitant diseases (especially cardiovascular comorbidities), and clinical status;
— in most mild cases, we recommend close monitoring, avoidance of further excess iodine exposure, and administration of β-adrenergic blocking drugs;
— in severe cases, we recommend initiation of treatment with ATD (e.g. methimazole dose of 20–40 mg/day). No response or partial response to antithyroid drugs should trigger referral to a highly specialised centre. Dose escalation of methimazole and/or adding sodium perchloride should also be considered.

6. Diagnosis and management of ICM-induced hypothyroidism

ICM-induced hypothyroidism may develop within 2 years following exposure. It is usually subclinical and self-limiting, lasting weeks to months, but it can also be permanent in patients with autoimmune thyroiditis.

The diagnosis of ICM-induced hypothyroidism is based on clinical signs and symptoms of hypothyroidism and/or laboratory tests results confirming hypothyroidism as well as a history of exposure to ICM within the last 1–2 years.

Treatment

— we recommend an individualized approach to the treatment of ICM-induced hypothyroidism, based on clinical symptoms and aetiology [including an anti-thyroid peroxidase (anti-TPO) antibody assay], as well as the patient's age, concomitant diseases, and clinical status;
— in most cases of ICM-induced hypothyroidism, we suggest close monitoring without thyroid hormone replacement;
— temporary L-thyroxine (LT4) treatment should be commenced in line with the current guidelines, especially in patients with overt hypothyroidism, younger patients with subclinical hypothyroidism, those with an underlying chronic autoimmune thyroiditis, and in women planning pregnancy.

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