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Diagnostics and treatment of differentiated thyroid carcinoma in children — Guidelines of the Polish National Scientific Societies, 2024 Update

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Abstract

The rapid progress made in recent years in thyroid cancer research has necessitated the systematic updating of current clinical recommendations. This update presents the evidence-based management of differentiated thyroid carcinoma (DTC) and medullary thyroid carcinoma in children, including preoperative diagnostics, surgical management, radioiodine therapy in DTC treatment with L-thyroxine, disease monitoring, treatment of advanced disease, and finally, consequences of thyroid cancer treatment. Each recommendation is evaluated regarding its strength (Strength of Recommendation; SoR) and the quality of supporting data (QoE — Quality of Evidence).
(Endokrynol Pol 2024; 75 (6): 565–591)

Key words: *differentiated thyroid cancer; papillary thyroid cancer; medullary thyroid cancer; total thyroidectomy; thyroid lobectomy; radioiodine; L-thyroxine therapy; guidelines; recommendations*

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GUIDELINES

Contents

Introduction

The update of the guidelines "Diagnostics and Treatment of Thyroid Cancer in Adults", published in the Polish Journal of Endocrinology in 2022 [1], necessitated an update of the Polish recommendations for the treatment of thyroid cancer in children. It is worth recalling that the first and most recent version was published in 2016 [2]. The rapid progress in diagnostic and therapeutic methods in recent years has significantly modified the understanding of the course and treatment of thyroid cancer, as reflected in numerous scientific studies. The specificity of thyroid cancer in children has led to the publication, in recent years, of separate recommendations by American and European scientific societies addressing the treatment of thyroid cancer in adults and children [3, 4].

Since the amount of scientific evidence for thyroid cancer in children is limited, the preparation of recommendations requires careful work and the consensus of a multidisciplinary team of experts [5].

Creating the authors' team

The establishment of the authorial team took place during the Polish nationwide congress "Thyroid Cancer and Beyond", organised in 2022 by the team of the M. Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch. The goal of the team was to prepare Polish recommendations for managing thyroid cancer in children, meeting the requirements of evidence-based medicine (EBM). It was decided that the editorial team meetings would be held via teleconference.

The editorial team consisted of the authors of the previous thyroid cancer recommendations, supplemented by the authors of the 2022 recommendations for adults [1], who represented additional and necessary competencies. When assembling the team, attention was given to ensuring representation from all medical specialties involved in diagnosing and treating children with thyroid cancer. Thus, the editorial team's composition was gradually expanded. It was decided that the primary authors would be Prof. Daria Handkiewicz-Junak and Prof. Marek Niedziela. Coordinating and organising the teleconference was entrusted to Prof. Barbara Jarząb.

To whom are the recommendations addressed?

The guidelines are addressed to physicians of all specialties involved in the diagnosis of nodular goitre in children, especially those differentiating between benign and malignant tumours, as well as to doctors treating thyroid diseases and those who wish to learn about the latest evidence-based recommendations. The guidelines are also directed to interested nurses and other healthcare professionals, particularly those organising healthcare in this field. Additionally, the recommendations can serve interested patients and their families and provide a basis for establishing principles for financing medical services.

It was also determined that, due to the progress in medicine, the current recommendations need to be updated every 2 years.

Which patients are addressed by the current recommendations?

The authors of the recommendations decided that these guidelines should apply to children suffering from all histotypes of thyroid cancer. However, since anaplastic thyroid cancer is extremely rare in children, with only isolated cases reported to date, the recommendations focus on differentiated thyroid cancer and medullary thyroid cancer.

The authors also believe that for patients who have completed their growth and sexual maturation processes, it is possible to apply the recommendations for adults [1] (see Part I of the Recommendations, Section 1).

While these recommendations can also be addressed to children and adolescents, the authors adopted the definition from the Act of 6 January 2000 on the Ombudsman for Children, which states that "a child is every human being from conception until reaching adulthood".

What scientific evidence are Polish guidelines based on?

In view of the publication of the European Recommendations [4] on thyroid cancer in children and earlier American guidelines [3], members of the editorial team carefully reviewed their content and the cited scientific publications on which they were based. They decided that in this current update, they would not re-search for scientific evidence but would instead rely on the current works that meet the standards of evidence-based medicine (EBM) and adapt them to the epidemiological and legal-financial Polish context. However, it was decided to search for the latest scientific publications on thyroid cancer in children. The cut-off point was set as May 2020, which marks the period when the collection of scientific publications for the European recommendations was completed.

After analysing the recent European recommendations, we decided to include in the bibliography only those publications released after May 2020. However, we occasionally add older publications if we deem them particularly important for preparing the Polish recommendations. Similarly, we proceeded with publications by Polish authors concerning Polish patients. The review of publications on thyroid cancer in children was concluded in February 2024.

The members of the editorial team also decided that, in formulating recommendations for children, they would base them on the Polish recommendations for adults from 2022 [1], adapting them only in cases where recommendations for children require separate specifications. Team members were asked to submit Polish publications on the diagnosis and treatment of thyroid cancer in children that should be considered when preparing the recommendations. In the adopted method of updating, we drew upon the experience of updating the Polish recommendations for adults [1].

Analogously to the recommendations for adults, it was established that in preparing the recommendations for children, we would follow the AGREE II protocol [6,7] and use as the working material the text of the previous recommendations published in 2016, as well as, the text of "Diagnostics and Treatment of Thyroid Cancer in Adult Patients 2022" [1] mentioned above. It was decided that when adapting European recommendations to Polish conditions, the ADAPTE protocol would be utilised. We believed that by conveying universally accepted international arrangements, we would limit ourselves to evaluating the strength of the recommendations without assessing the quality of the evidence. Similarly, we adopted this approach for the recommended Polish terminology and the proposed methods of proceeding.

Selected experts developed and presented scientific arguments for changing or updating the existing recommendations to the entire team. Meetings were held via teleconference from 21 September 2022, to 3 January 2023. Subsequently, thematic teams were formed to update the assigned sections of the Recommendations text. The thematic teams' work was summarised on 8 February 2023. The unified text was reviewed during a teleconference on 29 March 2023 during the harmonisation of all the sections prepared by the thematic teams. Further work on the text was carried out via electronic correspondence. The text was approved during a teleconference on 10 January 2024. The lead authors then proceeded to translate the final text into English. All authors approved the final text in November 2024.

Assessment of the strength of recommendations and quality of evidence

The choice of methodology for assessing the strength of recommendations and the quality of scientific evidence was guided by the evaluation methods adopted by the National Comprehensive Cancer Network (NCCN) and the National Oncology Strategy. Table 1 outlines the principles and decisions while preparing the updated Polish recommendations for adults [1]. The evaluation methods are presented in Tables 1–4.

Table 1. ***Strength of Recommendations According to the National Comprehensive Cancer Network (NCCN) [87]. Modified According to the Guidelines of the National Oncological Strategy [1]***

Strength of Recommendations	Comment
1	Recommendations based on high-quality evidence, for which unanimity or a high degree of consensus was reached among the expert panel
2A	Recommendations based on lower-quality evidence, for which unanimity or a high degree of consensus was reached among the expert panel
2B	Recommendations based on lower-quality evidence for which a moderate degree of consensus was reached among the expert panel
3	Recommendations based on evidence of any quality level, for which no consensus was reached among the expert panel

Table 2. *Quality of evidence according to the National Comprehensive Cancer Network (NCCN) [87] and the European Society of Medical Oncology (ESMO) [88, 89]. Modified According to the Guidelines of the National Oncological Strategy [1]*

Quality of Evidence	Comments
I	Evidence from at least one large randomised controlled trial (RCT) of high methodological quality (low risk of bias) or a meta-analysis of well-designed RCTs without significant heterogeneity
II	Small RCTs or large RCTs with a risk of systematic bias (lower methodological quality) or meta-analyses of such studies or RCTs with significant heterogeneity
III	Prospective cohort studies
IV	Retrospective cohort studies or case-control studies
V	Studies without a control group, case reports, expert opinions

Table 3. *Interpretation of recommendations regarding therapeutic interventions based on the strength of evidence, developed based on the recommendations of the American Thyroid Association (ATA 2015), modified [62]*

Strength of Recommendation (SoR)	Benefits to Risks Balance	Implications
Strong **SoR 1**	Benefits clearly outweigh the risks	**Patients:** An intervention strongly recommended provides clear benefits for most patients **Physicians:** The intervention should be applied to most patients
Weak **SoR 2**	Benefits balance the risks	**Patients:** An intervention recommended with weak evidence may be effective for many patients, but the decision may depend on individual circumstances **Physicians:** The intervention may be effective in many patients, but decisions should be made individually, taking into account the patient's preferences and indications
No recommendations **SoR 3**	Unable to determine the balance of benefits to risks	Unable to decide based on scientific evidence

Table 4. *Interpretation of recommendations regarding diagnostic interventions, developed based on the recommendations of the American Thyroid Association (ATA 2015), modified [62]*

Nr	Strength of Recommendations (SoR)	The significance of the diagnostic test result about the risk and burden imposed on the patient by the test	Implications
1	Strong **SoR 1**	Obtaining information through the test is very significant for further treatment and clearly outweighs the risk and burden to the patient	**Patients:** A test recommended with strong evidence is clearly beneficial for diagnosing the disease and planning its treatment. This benefit significantly outweighs the risk and burden incurred by the patient to undergo the test **Physicians:** The physician should offer a diagnostic test recommended with strong evidence to most patients, as the benefit of an accurate diagnosis and an adequate treatment plan significantly outweighs the risk and burden incurred by the patient to undergo the test
2	Weak **SoR 2**	Obtaining information through this test is balanced against the risk and burden to the patient	**Patients:** A test recommended with weak evidence requires consideration, as it may prove useful for proper disease diagnosis and adequate treatment planning. This benefit is balanced against the risk and burden incurred by the patient to undergo the test **Physicians:** The physician may offer the patient a test recommended with weak evidence, because the benefit of an accurate diagnosis and an adequate treatment plan balances the risk and burden incurred by the patient to undergo the test
3	No recommendation **SoR 3**	There are no clear data allowing comparison of diagnostic benefits against the risk and burden to the patient	No basis for decision according to scientific evidence

Part I. Diagnostics of differentiated thyroid cancer in children

1. The authors of the guidelines believe that for patients who have completed their growth and sexual maturation, it is possible to apply the recommendations for adults. The presented guidelines primarily concern children who have not completed the process of growth and sexual maturation [8–11]. The authors of the recommendations did not choose to specify a particular age limit.
SoR: 2A QoE: V

2. The most common manifestation of differentiated thyroid cancer (DTC) in children is a thyroid nodule. However, papillary thyroid cancer (PTC) may present as cervical lymphadenopathy with or without a palpable thyroid nodule, or as an incidental focus (incidentaloma) in the thyroid identified during neck imaging or surgery initially unrelated to the thyroid [12–18].
SoR: 2A QoE: IV

3. The risk of thyroid cancer among children undergoing surgery for nodular goitre is significantly higher than in adults, amounting to 26.4–32.5% (around 1/4–1/3 of operated children) [19, 20].
SoR: 2A QoE: IV

4. High-risk factors for the development of DTC in children/adolescents include the following:
4.1. Exposure to ionising radiation (external and internal) is a high-risk factor [21, 22]. The peak incidence following external exposure occurs approximately 15–25 years later. The younger the child at the time of exposure and the higher the dose of ionising radiation, the greater the future risk of developing PTC and the shorter the latency period. The latency period is significantly longer following external exposure [23].
SoR: 2A QoE: IV

4.2. Genetic syndromes include familial adenomatous polyposis (FAP), Carney complex, DICER1 syndrome, PTEN hamartoma tumour syndrome (PHTS), Werner syndrome, Beckwith-Wiedemann syndrome, hereditary paraganglioma syndrome, Li-Fraumeni syndrome, McCune-Albright syndrome, and Peutz-Jeghers syndrome [24–30].
SoR: 2A QoE: IV

5. Thyroid ultrasound in a child without palpable changes in the thyroid gland or suspicious cervical lymph nodes is indicated in the following cases:
5.1. Children at high risk of developing thyroid cancer (Part I, 4.1 and 4.2),
5.1.1. After exposure to ionising radiation,
5.1.2. In the aforementioned genetic syndromes,
5.1.3 In dyshormonogenesis.
SoR: 2A QoE: IV

5.2. Ultrasound examination of the thyroid is not a screening test for the entire population.
5.3. Patients with an increased risk of DTC developing in the course of genetic syndromes (4.2) should be referred to reference centres for proper evaluation, monitoring, and genetic counselling.
SoR: 2A QoE: IV

5.4. Neck ultrasound should always be performed in the case of palpable nodules, thyroid asymmetry, and/or cervical lymphadenopathy detected during physical examination [27, 31, 32].
SoR: 2A QoE: IV

6. The diagnostics of thyroid nodules in children should be conducted similarly to that in adults [1]. However, there are differences or specific characteristics listed below.
6.1. All children with suspected focal lesions in the thyroid gland or in the neck area require an ultrasound examination of the thyroid and cervical lymph nodes [19, 33, 34].
6.2. Due to the higher risk of DTC compared to adults, children with hyperfunctioning nodules should not be excluded from fine-needle aspiration biopsy (FNAB) [35].
SoR: 2A QoE: IV

6.3. The size of the nodule/lesion should not be the primary criterion for qualifying for targeted FNAB because the thyroid volume changes with age, and the size of the lesion alone does not predict malignancy. For these reasons, ultrasonographic and clinical characteristics should have greater significance than the size of the nodule/lesion itself in selecting cases requiring FNAB. The authors of the recommendations propose the following criteria for FNAB in children: EU-TIRADS-PL categories 4 and 5 (a detailed description of the EU-TIRADS-PL system is included in the 2022 thyroid cancer recommendations for adults [1]).
SoR: 2A QoE: IV

6.4. In centres equipped with the necessary facilities and expertise, elastography can help assess the risk of malignancy of focal thyroid lesions [36, 37].
SoR: 2A QoE: V

6.5. A particular category is paediatric PTC with diffuse infiltration, which leads to enlargement of the affected

Table 5. ***The risk of malignancy in thyroid nodules in children classified as Bethesda III–V in cytological examination - comparison with adult patients [1, 41]***

Bethesda category	Risk of malignancy in children	Risk of malignancy in adults
III	29.6%	6–18%
IV	42.3%	10–40%
V	90.8%	45–60%

lobe or the entire gland, often accompanied by palpable cervical lymph nodes. This form of PTC is typically associated with microcalcifications and requires FNAB. The differentiation between reactive versus "suspicious" lymph nodes follows the same criteria as in adults.
SoR: 2A QoE: IV

7. Cytological and histopathological diagnostics.
7.1. The FNAB cytological diagnoses are classified according to the Bethesda System for Reporting Thyroid Cytopathology [38, 39], hereinafter referred to as the Bethesda system. This system is an effective tool for classifying cytologically diagnosed thyroid nodules in children [38–40].
SoR: 2A QoE: IV

7.2. The risk of malignancy (ROM) in thyroid nodules in children is higher than in adults, at 29.6% for category III, 42.3% for category IV, and 90.8% for category V [41, 42] (Tab. 5).
SoR: 2B QoE: IV

7.3. Cytological diagnosis of thyroid cancer is conducted and signed by a specialist pathologist. The decision to surgically treat a focal lesion/thyroid nodule categorised as Bethesda III, IV, V, or VI is based on 2 independent opinions from pathologists experienced in evaluating thyroid biopsies, similar to the protocol for diagnosed or suspected thyroid cancer in adults. Such a decision may also be made in distinct clinical situations where discrepancies in clinical data exist or where there is a justified clinical suspicion of malignancy.
SoR: 2A QoE: IV

7.4. As stated above, in cytological diagnoses classified as Bethesda categories III and IV, thyroid cancer is postoperatively diagnosed in children significantly more often than in adults. Therefore, in these groups with indeterminate diagnoses, surgical treatment should be considered (proposed scope: removal of the affected lobe — lobectomy along with the isthmus) instead of repeat FNAB. Part II, Section 1.2.2 outlines our recommendations for surgeons when considering the extent of surgery in cases with a high clinical risk of thyroid nodule malignancy.
SoR: 2B QoE: IV

8. Intraoperative examination may be useful for determining the extent of neck lymph node surgery and for the differential diagnosis between parathyroid tissue and a lymph node. Routine use of intraoperative examination is not recommended for the diagnosis of thyroid nodules, particularly follicular nodules and small-sized tumours.
SoR: 2A QoE: IV

8.1. It should be noted that intraoperative examination cannot rule out follicular thyroid carcinoma (FTC).
SoR: 2A QoE: IV

9. Considering indications for molecular testing of thyroid focal lesions, one should take into account the current state of knowledge. It should be noted that research on the molecular basis of thyroid cancer in children is still evolving [17, 29, 43–49]. Available publications document the usefulness of DNA testing for making decisions about surgical treatment. Unfortunately, their value is limited because no prospective multicentre studies have been conducted [21, 50–54]. The authors of the recommendations believe that it is essential to initiate prospective multicentre studies to evaluate the clinical utility of molecular testing in the diagnosis of thyroid cancer in children.
SoR: 2B QoE: IV

10. Table 6 presents the 2022 histopathological classification of thyroid tumours according to the World Health Organisation (WHO) [55].
Due to the lower technical quality of the examination and the necessity of preserving diagnostically valuable tissue material for paraffin block analysis, capsular invasion and angioinvasion should be assessed based on serial examinations of paraffin blocks.
SoR: 2A QoE: IV

Table 6. *2022 World Health Organization (WHO) classification of thyroid neoplasms*

Developmental abnormalities
Thyroglossal duct cyst
Other congenital thyroid abnormalities
Follicular cell-derived neoplasms
Benign tumours
Thyroid follicular nodular disease
Follicular thyroid adenoma
Follicular thyroid adenoma with papillary architecture
Oncocytic adenoma of the thyroid
Low risk neoplasms
Non-invasive follicular thyroid neoplasm with papillary-like nuclear features
Thyroid tumours of uncertain malignant potential
Hyalinising trabecular tumour of thyroid
Malignant neoplasms
Follicular thyroid carcinoma
Invasive encapsulated follicular variant papillary carcinoma
Papillary thyroid carcinoma
Oncocytic carcinoma of the thyroid
Follicular-derived carcinomas, high-grade
a) Differentiated high-grade thyroid carcinoma
b) Poorly differentiated thyroid carcinoma
Anaplastic follicular cell derived thyroid carcinoma
Thyroid C-cell derived carcinoma
Medullary thyroid carcinoma
Mixed medullary and follicular cell derived carcinomas
Salivary gland-type carcinomas of the thyroid
Mucoepidermoid carcinoma of the thyroid
Secretory carcinoma of salivary gland type
Thyroid tumours of uncertain histogenesis
Sclerosing mucoepidermoid carcinoma with eosinophilia
Cribriform morular thyroid carcinoma
Thymic tumours within the thyroid
Thymoma family
a) Spindle epithelial tumour with thymus-like elements
b) Thymic carcinoma family
Embryonal thyroid neoplasms
Thyroblastoma

Part II. Treatment of differentiated thyroid cancer in children

1. Surgical treatment

1.1. Essential examinations to prepare patients for surgical treatment in cases of confirmed or suspected malignant thyroid tumours include the following:

1.1.1. Medical history and physical examination;

1.1.2. Neck ultrasound:

1.1.2.1. Thyroid;

1.1.2.2. Lymph nodes;

1.1.3. Ultrasound-guided FNAB of:

1.1.3.1. Suspected thyroid lesions (according to the principles given above);

1.1.3.2. Suspected lymph-nodes.

1.1.4. Thyroid-stimulating hormone (TSH) and free thyroxine (fT4) tests to exclude functional thyroid abnormalities.

1.1.5. Basic tests: haematology, electrolytes with calcium, coagulation system, blood typing, securing blood supply (packed red blood cells — PRBC), in some circumstances calcitonin level measurement in cases of medullary thyroid cancer (see also Part V);

1.1.6. Laryngological examination to assess vocal cord function;

1.1.7. Other examinations, including imaging studies [X-ray, computed tomography (CT), magnetic resonance imaging (MRI)], depending on clinical status and disease advancement.

SoR: 2A QoE: V

1.2. Surgical management in cases of suspected malignant thyroid nodules.

1.2.1. The management should resolve diagnostic uncertainties as effectively as possible while minimising potential postoperative complications. For patients under the age of 16 years, the physician must obtain consent from the parents or legal guardians each time. Additionally, the patient may be informed about the health status with the consent of the parents or legal guardians. If the patient is 16 years or older, it is necessary to obtain consent for the proposed procedure.

SoR: 2A QoE: V

1.2.2. We believe that in the case of a cytological diagnosis of Bethesda category III or IV (Tab. 5), the surgeon may choose one of the options, considering the clinical risk of malignancy for the tumour in each patient as well as the patient's preferences:

1.2.2.1. The complete removal of one lobe along with the isthmus — provided that the parents/guardians of the patient and the patients themselves are informed about the risk of a postoperative diagnosis of thyroid cancer, which would necessitate a second surgery to remove the remaining lobe of the thyroid, and that they accept this course of action.

SoR: 2A QoE: IV

1.2.2.2. Total thyroidectomy, after explaining to the patient and their parents/guardians that postoperative histopathological examination may not confirm a diagnosis

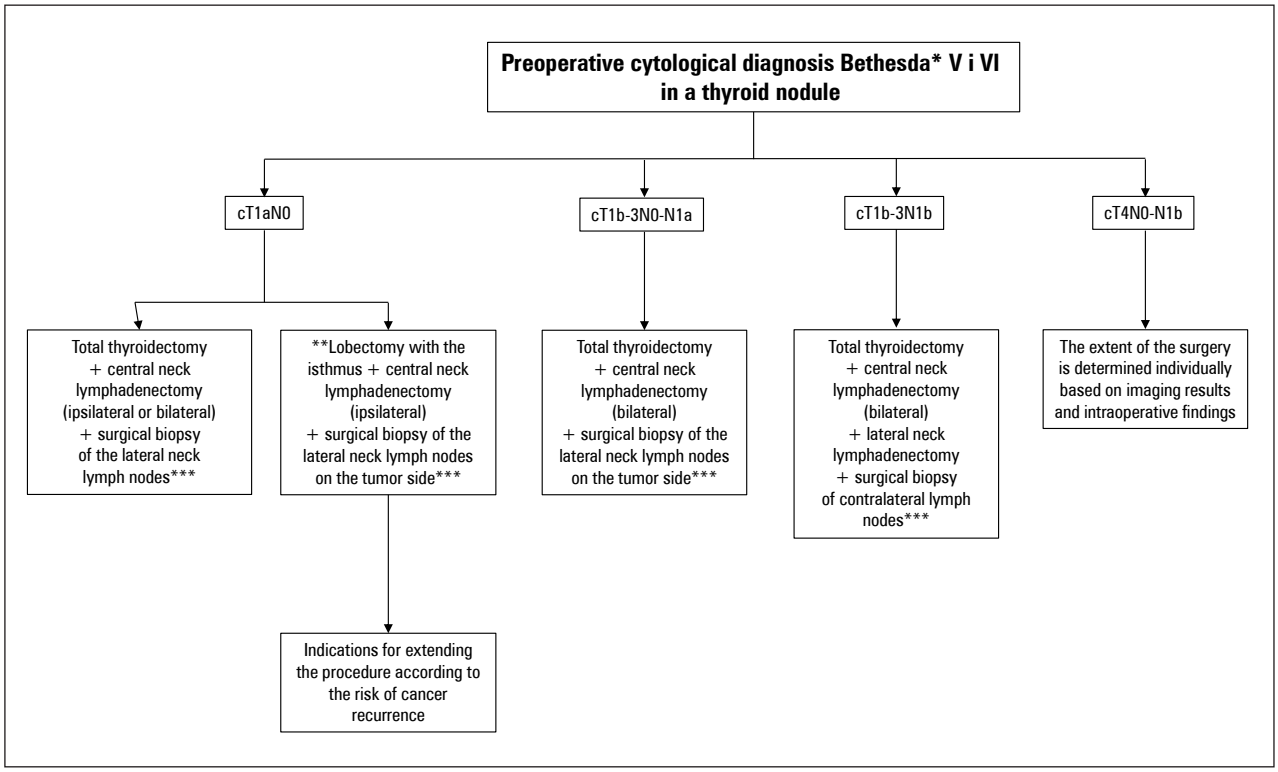

Figure 1. *Surgical treatment of differentiated thyroid cancer in children. *In the case of Bethesda category V, intraoperative examination may be considered to adjust extent of surgery; **To be considered above the age of 14 or after reaching stage 5 on the Tanner scale; ***Lateral neck limphadenectomy if in histopathological examination: micrometastasis in more than one lymph node, or metastasis in a single lymph node exceeding 2 mm*

of thyroid cancer, and upon their acceptance of this approach. However, such a procedure should be reserved for patients with accompanying focal lesions in both thyroid lobes, ensuring that the patient benefits from the total thyroidectomy even if the final diagnosis identifies the changes as benign.
SoR: 2B QoE: V

1.2.2.3. In a cytological diagnosis of Bethesda category V, management should proceed as in thyroid cancer; however, in older children (see section 1.3.1), an approach similar to that for adults may be considered.
SoR: 2A QoE: V

1.3. Surgical management in children preoperatively diagnosed with thyroid cancer [56] (Fig. 1).
1.3.1. In every case, total thyroidectomy. The authors of the recommendations believe that currently there is no clear evidence that lobectomy is sufficient in children/adolescents with unifocal papillary carcinoma at stage cT1a. However, not all authors share this view. Reports are emerging suggesting that, as in the adult population, this approach is safe in post-pubertal children (particularly those over 14 years of age or who have reached stage 5 on the Tanner scale) [57]. However, as with the European recommendations, we believe that prospective clinical trials would be necessary for this purpose.
SoR: 2B QoE: IV

1.3.2. In patients with advanced thyroid cancer (extensive, palpable, poorly mobile lesions in the neck), additional imaging studies should be considered: CT with contrast or MRI to optimally plan surgical treatment.
SoR: 2A QoE: V

1.3.3. Assessment of distant metastases in other imaging studies should only be performed if indicated [58, 59].
SoR: 2A QoE: V

1.3.4. If invasion of adjacent organs (trachea, oesophagus, blood vessels) is detected and there is a possibility of complete tumour removal (R0 resection), a multi-organ surgery should be considered. However, care must be taken to minimise the consequences of the surgery, limit potential postoperative complications, and ensure the patient has the best possible quality of life. Such cases should be evaluated individually within a multidisciplinary team.
SoR: 2A QoE: IV

1.4. The assessment of the radicality of surgical treatment in the context of indications for completion thyroidectomy
1.4.1. The indications for completion thyroidectomy, if a less extensive surgery was performed, should be considered in a multidisciplinary setting based on the results of postoperative histopathological examination, assessment of the disease stage, evaluation of the risk of recurrence, and indications for adjuvant radioiodine (RAI) therapy.
SoR: 2A QoE: V

1.4.2. If the extent of surgery is unclear, the assessment of surgical radicality is based on a combined interpretation of the postoperative histopathological examination, ultrasound imaging, postoperative neck scintigraphy, and measurements of thyroglobulin (Tg) and anti-thyroglobulin antibodies (TgAb). These tests should be performed no earlier than 1–2 months after the surgery; TSH stimulation is necessary for scintigraphic evaluation and Tg level assessment.
SoR: 2A QoE: IV

1.4.3. In cases of low-risk thyroid cancer in a child who has undergone lobectomy, completion thyroidectomy may be avoided after discussing all the pros and cons of this approach with the parents/legal guardians and the patient [60].
SoR: 2A QoE: V

1.5. The following principles must be adhered to during surgery performed for the diagnosis/suspicion of thyroid cancer:
1.5.1. The visualisation of the recurrent laryngeal nerve is recommended. Additionally, efforts should be made to preserve the external branch of the superior laryngeal nerve during tissue dissection near the superior pole of the thyroid.
SoR: 2A QoE: IV

1.5.2. To facilitate the identification and assessment of laryngeal nerve function, intraoperative nerve stimulation (neuromonitoring) should be used whenever possible [61].
SoR: 2A QoE: IV

1.6. Lymphatic surgery in DTC.
1.6.1. The recommended approach is the removal of cervical lymph nodes targeted to the anatomical compartment, known as block/compartmental dissection. The "berry picking" method, which involves attempting to assess whether lymph nodes are metastatic through palpation, is not recommended
SoR: 2A QoE: IV

1.6.2. Central neck lymph node surgery.
1.6.2.1. Surgery of central neck lymph nodes due to thyroid cancer should include lymph nodes of group VI (the central neck compartment encompassing prelaryngeal, pretracheal, paratracheal, and perithyroidal lymph nodes).
SoR: 2A QoE: IV

1.6.2.2. Central neck dissection is an intervention:
1.6.2.2.1. Therapeutic in children with gross extrathyroidal extension and/or lymph node metastases (both central and lateral) found in preoperative diagnostics or intraoperatively.
1.6.2.2.2. Prophylactic, if there are no features of central or lateral neck lymph node involvement.
SoR: 2A QoE: IV

1.6.3. Considering the high risk of lymph node metastases in children with DTC, the authors of these recommendations advise performing central lymphadenectomy in every patient, except in situations described in sections 1.6.3.1–2.
1.6.3.1. The extent of central neck dissection can be limited in children with unifocal papillary thyroid cancer at clinical stage cT1aN0M0; in such cases, unilateral (ipsilateral) central lymphadenectomy on the tumour side may be performed, with potential contralateral lymphadenectomy, based on intraoperative assessment.
1.6.3.2. After the surgeon's intraoperative assessment, unilateral central lymphadenectomy can also be performed during a lobectomy with isthmus removal, conducted due to cytologically indeterminate thyroid lesions (Bethesda category III–V).
1.6.3.3. Central neck dissection is not absolutely necessary in well-differentiated FTC.
SoR: 2A QoE: V

1.6.4. Lateral cervical lymph node surgery
1.6.4.1. Unilateral or bilateral surgery of the lateral neck lymph nodes as a modified neck dissection (without removal of the jugular vein, sternocleidomastoid muscle, or cranial nerve XI) is indicated after confirmation of metastasis (in a preoperative FNAB or intraoperative surgical biopsy).
SoR: 2A QoE: IV

1.6.4.2. Intraoperative bilateral surgical biopsy of the lateral neck lymph nodes (performed by the surgeon during the operation) is helpful in excluding or confirming metastases to the lateral cervical lymph nodes. If metastases are diagnosed, it constitutes an indication for modified lateral neck dissection on that side. In such cases, the lymphadenectomy serves as a therapeutic procedure.
SoR: 2A QoE: V

1.6.4.3. A modified lateral neck dissection may be abandoned in cases where a single micrometastasis (< 2 mm) is identified in a lymph node obtained during intraoperative biopsy.
SoR: 2B QoE: IV

1.6.4.4. Intraoperative frozen section analysis is helpful in biopsies of lateral cervical lymph nodes to confirm or exclude the presence of cancer metastases.
SoR: 2A QoE: IV

1.7. General recommendations for surgical treatment and minimising adverse events and complications.
1.7.1. The surgical treatment of the thyroid gland in children should be performed in a specialised centre with a full range of specialised medical care, including endocrinology, radiology (ultrasound and anatomical imaging), nuclear medicine, anaesthesiology, intensive care, and, above all, a surgeon experienced in thyroid surgeries and cervical lymphadenectomy. Alternatively, the centre should collaborate with another facility that ensures comprehensive specialised care for treated patients.
SoR: 2A QoE: V

1.7.2. The surgical treatment of the thyroid gland in children should optimally be performed by a surgeon conducting at least 30 such procedures annually [a quantitative criterion proposed by American Thyroid Association (ATA) recommendations], particularly if compartmental lymph node dissection is indicated.
SoR: 2A QoE: V

1.7.3. The most common complications following surgical treatment include recurrent laryngeal nerve paralysis and hypoparathyroidism. Both complications may be transient or permanent. The frequency of permanent complications is an important measure of the experience of the centre; however, it is also related to the stage of the disease, which is often advanced in children.
SoR: 2A QoE: IV

1.7.4. Early treatment with calcium and alfacalcidol — 1(OH)D3 or calcitriol — $1,25(OH)_2D3$ in patients at high risk of hypoparathyroidism may reduce the risk of developing symptoms of hypocalcaemia.
SoR: 2A QoE: V

1.7.5. Postoperative measurement of intact parathyroid hormone (PTH) can be helpful in predicting which patients may require more intensive monitoring and treatment for postoperative calcium-phosphorus metabolism disorders.
SoR: 2A QoE: V

Table 7a. ***Staging according to the American Joint Committee on Cancer–Union for International Cancer Control (AJCC-UICC) tumour–node–metastasis (TNM) system (8th edition)***

Primary tumour		
T1	T1a	Tumour ≤ 1 cm
	T1b	Tumour > 1 cm but ≤ 2 cm
T2		Tumour > 2 cm but ≤ 4 cm
T3		Tumour > 4 cm or tumour of any size with gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles)
T4	T4a	Tumour of any size with gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, oesophagus, or recurrent laryngeal nerve
	T4b	Tumour of any size with gross extrathyroidal extension invading prevertebral fascia or carotid artery or mediastinal vessels
Lymph nodes		
Nx		Regional lymph nodes were not evaluated
N0		No lymph node metastases
N1	N1a	Metastases to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)
	N1b	Metastases to unilateral, bilateral, or contralateral cervical (levels I, II, III, IV, or V) or retropharyngeal lymph nodes
Distant metastases		
Mx		No evaluation
M0		No distant metastases
M1		Distant metastases present

Table 7b. *Differentiated thyroid carcinoma (DTC) stage in children based on histopathological evaluation*

Stage	T	N	M
Stage I	Any T	Any N	M0
Stage II	Any T	Any N	M1

Table 8. *Postoperative risk classification of differentiated thyroid carcinoma (DTC) according to the American Thyroid Association (ATA) 2015 criteria [62], modified*

Low-risk DTC	PTC with all the following features: • no lymph node and distant metastases • all macroscopic tumour resected • no extrathyroidal invasion • no aggressive histologic subtype (tall-cell, columnar cell, hobnail subtypes) • no RAI uptake in whole-body scintigraphy after postoperative RAI treatment — if it is given • no vascular invasion • lymph nodes — clinically N0 or ≤ 5 lymph node micrometastases (< 0.2 cm in the greatest dimension) • intrathyroidal PTC ≤ 10 mm, uni- or multifocal, also with the presence of the *BRAF*^{V600E} mutation
Intermediate-risk DTC	Microscopic extrathyroidal invasion Aggressive histological subtype Vascular invasion Clinically N1 or > 5 lymph node metastases (diameter of 0.2–3 cm) Multifocal PTC ≤ 10 mm with extrathyroidal extension and the *BRAF*^{V600E} mutation RAI uptake outside the thyroid bed in posttreatment whole-body scintigraphy after postoperative RAI treatment
High-risk DTC	Gross extrathyroidal extension Incomplete tumour resection Distant metastases Increased postoperative serum Tg level suggesting distant metastases Lymph node metastases > 3 cm in the greatest dimension

PTC — papillary thyroid cancer; RAI — radioiodine therapy; Tg — thyroglobulin

2. Postoperative evaluation
2.1. Postoperative assessment is primarily based on the postoperative histopathological examination (Tab. 7), which allows prediction of cancer recurrence risk (Tab. 8). However, it should be complemented by clinical evaluation.
SoR: 2A QoE: V

2.2. Postoperative histopathological examination.
2.2.1. The handling of surgical material during macroscopic and microscopic examination should follow the guidelines for adults. Additionally, thyroid tumours in children are classified similarly to those in adults according to the new WHO 2022 Classification of Thyroid Tumours (Tab. 6).
SoR: 2A QoE: V

2.2.2. Molecular tests are not recommended as routine additional examinations for histopathological analysis of surgical material. However, in specific cases, there are indications for their use (see Part IV, section 3.2.4).
SoR: 2A QoE: V

2.3. Clinical postoperative evaluation should include:
2.3.1. The assessment of disease advancement is based on the TNM staging (Tab. 7) and the evaluation of recurrence risk, also known as risk classification (Tab. 8).
2.3.2. Physical examination, sonographic assessment of the thyroid bed, cervical and supraclavicular lymph nodes, Tg and TgAb measurement, as well as levels of total calcium (corrected), ionised calcium, phosphates, magnesium, and PTH.
2.3.3 Diagnostic whole-body scan (DxWBS) with stimulated Tg and TgAb measurement.
SoR: 2A QoE: V

3. Postoperative management
3.1. Radioiodine (RAI) treatment.

3.1.1. Conditions for RAI treatment in children.
3.1.1.1. Due to the prolonged isolation of the child in a closed ward during RAI therapy, proper preparation of the sick child and their parents or guardians for the planned treatment is very important.
3.1.1.2. A child undergoing RAI therapy should be provided with appropriate psychological comfort, preferably through constant contact with a parent or guardian. The space where the child stays should be properly secured and arranged according to the patient's age.
3.1.1.3. Parents/legal guardians and the patient, if aged 16 years or older, should receive comprehensive information about the purpose of the treatment, its course (including radiation protection principles), potential consequences, and contraindications. Consent to the treatment is required from the child's parents/legal guardians and from the patient if they are 16 years or older.
SoR: 2A QoE: V

3.1.2. Goals of the postoperative RAI treatment:
— destruction of thyroid remnants remaining after surgical treatment (ablation of residual thyroid tissue);
— sterilisation of distant micrometastases (adjuvant treatment).
SoR: 2A QoE: IV

3.1.3. Types of postoperative RAI treatment.
— adjuvant therapy (this category also includes ablative therapy);
— radical treatment;
— palliative treatment.
SoR: 2A QoE: V

3.1.4. In children, RAI treatment is most commonly used as adjuvant therapy or as radical treatment for RAI-avid distant metastases. In selected cases, if the disease is advanced or RAI uptake in metastases is low, the treatment becomes palliative.
In every case, the decision to proceed with RAI therapy should be preceded by a benefit-risk analysis conducted together with the parents or guardians of the child.
SoR: 2A QoE: V

3.1.5. Complementary/adjuvant RAI treatment.
3.1.5.1. In adjuvant RAI therapy in DTC children and adolescents, the treatment has been proven to reduce the risk of disease recurrence. However, its effect on overall survival has not been demonstrated.
3.1.5.2. Adjuvant RAI treatment may be omitted in children with low-risk thyroid cancer, provided that a prior DxWBS does not show any uptake outside the thyroid bed and the stimulated Tg concentration is lower than 10 ng/mL.
3.1.5.3. In low-risk children with thyroid cancer, the interpretation of a stimulated Tg > 10 ng/mL should take into account the size of the thyroid remnants.
3.1.5.4 In patients with intermediate- and high-risk thyroid cancer, RAI treatment should always be considered, especially in children within the high-risk group.
SoR: 2A QoE: V

3.1.6. Radical RAI treatment.
Radical RAI treatment is indicated for treating RAI-avid, non-operable, locoregional disease and distant metastases. The decision regarding subsequent RAI treatments should be individualised based on the assessment of the effects of prior RAI therapy (biochemical and imaging studies).
SoR: 2A QoE: IV

3.1.7. Qualification for postoperative RAI therapy.
3.1.7.1. Before RAI therapy for thyroid cancer, qualifying examinations must be performed to determine the patient's eligibility for the treatment and to define its objectives. In every case, the following must be conducted:
— medical history and physical examination;
— neck ultrasound;
— TSH, Tg, and TgAb evaluation;
— haematology, total or ionised calcium and creatinine concentration.
3.1.7.2. In the case of suspected distant metastases, consideration should be given to performing a CT or MRI. However, it should be noted that in children, distant metastases often manifest as lung micrometastases, which are visible only in whole-body scintigraphy (WBS) after RAI administration. A minimum interval of 6 weeks, optimally 12 weeks, should be maintained between a contrast-enhanced CT scan and RAI administration.
3.1.7.3. 18-fluorodexyglucose positron emission tomography-CT (^{18}FDG PET-CT) examination cannot be routinely recommended due to the lack of published data on its sensitivity and specificity in DTC children/adolescents.
3.1.7.4. The optimal time for RAI treatment is between 4 and 12 weeks after surgery, once the wound has healed, postoperative swelling has subsided, and Tg levels have decreased.
SoR: 2A QoE: IV

3.1.8. Preparation for RAI treatment.
3.1.8.1. To enable RAI uptake by residual thyroid cancer tissue, the TSH concentration should exceed 30 mIU/L.

This can be achieved in most children by discontinuing LT4 for approximately 4 weeks (according to American data, in some patients this occurs after just 2 weeks).
3.1.8.2. In patients unable to achieve an appropriate rise in endogenous TSH (due to endogenous TSH deficiency or a large mass of hormone-producing tumour), those who cannot tolerate severe hypothyroidism, or those at increased risk of side effects from the aforementioned conditions, administration of recombinant human thyrotropin (thyrotropin alfa; rhTSH) should be considered. The rhTSH dosing schedule should follow that used in adults: 0.9 mg of rhTSH intramuscularly for 2 consecutive days, with RAI administered on the third day.
3.1.8.3. Published data indicate that adjuvant RAI therapy, following rhTSH stimulation, is as effective in children as in adults. Therefore, such treatment can also be considered for children who do not meet the criteria outlined in section 3.1.8.2.
SoR: 2A QoE: IV

3.1.8.4. The above procedures, described in sections 3.1.8.1–3, also apply to performing DxWBS.
3.1.8.5. RAI treatment should be carried out in centres with appropriate experience and capabilities for monitoring the patient.
3.1.8.6. In the case of menstruating girls, a pregnancy test should be performed before treatment, and if sexual activity has been initiated, they should be informed about the necessity of contraception for at least 6 months after RAI treatment.
SoR: 2A QoE: V

3.1.9. RAI activities used in DTC treatment.
3.1.9.1. Due to the lack of data comparing empirical treatment and treatment preceded by dosimetry, neither of these methods of RAI treatment can be recommended.
3.1.9.2. In adjuvant therapy, the RAI activities most commonly range from 37 to 74 MBq/kg of body weight.
3.1.9.3. When using high RAI activities in the treatment of metastases, dosimetric evaluation should be pursued to minimise the risk of radiotoxicity. The absorbed dose of ionising radiation in the blood should not exceed 2 Gy, and the RAI activity retained in the patient's body 48 hours after administration should not exceed 4.44 GBq (120 mCi) or, in cases of massive diffuse lung metastases, 2.96 GBq (80 mCi).
3.1.9.4. In children with macrometastases to the lungs, early experiences with RAI treatment indicated a significant risk of pulmonary fibrosis. In such cases, special caution is advised when selecting the therapeutic activity. Particular risk applies to children previously treated with pneumotoxic drugs, such as bleomycin, lomustine, etc. In these cases, performing spirometry before subsequent RAI treatments is recommended.
SoR: 2A QoE: V

3.1.10. Post-therapeutic WBS
RAI treatment should be concluded with whole body scintigraphy to assess RAI-avid foci in the patient's body.
3.1.10.1. Post-therapeutic WBS is recommended for all children within 3–7 days of RAI treatment.
3.1.10.2. In cases of suspected metastases, performing an additional single-photon emission computed tomography (SPECT)/CT scan may enable the anatomical localisation of the RAI uptake.
SoR: 2A QoE: IV

3.2. L-thyroxine therapy.
3.2.1. L-thyroxine therapy should be introduced immediately after DTC surgery.
3.2.1.2. Initiation of L-thyroxine therapy in the postoperative period (Fig. 2).
3.2.1.2.1. In the postoperative period, suppressive L-thyroxine therapy should be initiated in patients who do not require adjuvant RAI treatment as well as in those patients for whom adjuvant RAI treatment is planned following rhTSH stimulation.
3.2.1.2.2. The postoperative management of patients scheduled for adjuvant RAI therapy following stimulation with endogenous TSH may exclude the initiation of L-thyroxine therapy (to achieve an appropriate TSH level — at least 30 mU/L before RAI therapy). However, this approach is suboptimal due to the risk of delaying RAI treatment and exposing the child to prolonged hypothyroidism. If RAI therapy is to be implemented later than 1–2 months after thyroid cancer surgery, L-thyroxine therapy should be introduced shortly after surgery and then discontinued approximately 4 weeks prior to the planned adjuvant RAI treatment. For this group of patients, suppressive L-thyroxine therapy should be initiated immediately after the adjuvant RAI treatment.
SoR: 2A QoE: IV

3.2.2. When planning L-thyroxine therapy for children after DTC surgery, the risk of cancer recurrence should be considered in accordance with the principles of postoperative ATA risk stratification (Tab. 8) [62]. Following the principle of dynamic risk stratification (see Part III, Section 7), the following approach is recommended (Fig. 2):

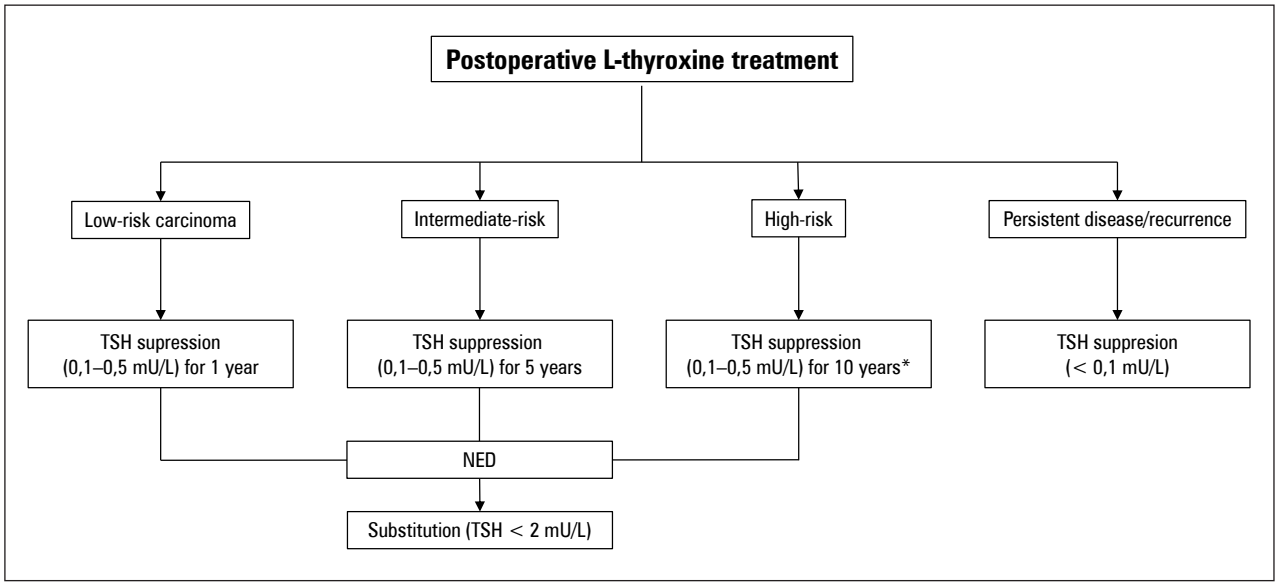

Figure 2. *Postoperative treatment with L-thyroxine in differentiated thyroid cancer in children. TSH — thyroid-stimulating hormone. *Shortening this period is possible according to dynamic risk stratification. NED — no evidence of disease*

3.2.2.1. In low-risk thyroid cancer, L-thyroxine therapy in a suppressive dose should be administered from the postoperative period for 12 months. If there is no suspicion of recurrence after this period (low Tg levels with low TgAb levels), L-thyroxine therapy should be continued in a replacement dose, maintaining TSH levels in the lower range of normal (< 2.0 mU/L).
3.2.2.2. In intermediate-risk thyroid cancer, L-thyroxine therapy in a suppressive dose should be administered starting from the postoperative period for 5 years. If there is no suspicion of recurrence after this observation period (low Tg levels with low TgAb levels), L-thyroxine therapy should be continued in a replacement dose, maintaining TSH levels in the lower range of normal (< 2.0 mU/L).
3.2.2.3. In high-risk thyroid cancer, L-thyroxine therapy in a suppressive dose should be administered starting from the postoperative period for at least 10 years. The principle of dynamic risk stratification (Tab. 8) should be applied. If there is no suspicion of recurrence after an adequate follow-up period (persistently low Tg levels with low TgAb levels), L-thyroxine therapy should be continued in a replacement dose, maintaining TSH levels in the lower range of normal (< 2.0 mU/L).
3.2.2.4. Control TSH and fT4, and fT3 if indicated, should be conducted every 3–6 months.
SoR: 2A QoE: IV

3.3. By the term "suppressive dose" we mean the lowest dose of L-thyroxine that maintains TSH levels within the range 0.1–0.5 mU/L.

3.3.1. The replacement L-thyroxine dose refers to the dosage of the drug that prevents the development of hypothyroidism. However, in the case of thyroid cancer, it is recommended that during substitution therapy TSH levels should not exceed 2 mU/L, to reduce the risk of recurrence.
SoR: 2A QoE: IV

3.4. Follow-up of DTC children who are on a suppressive L-thyroxine dose after surgery.
3.4.1. Children undergoing suppressive treatment for more than 12 months should have an echocardiographic examination every 12–24 months to assess left ventricular systolic and diastolic function, as well as a densitometry to evaluate bone mineral density.
SoR: 2A QoE: V

3.4.2. In the case of detecting myocardial contractility disorders, a cardiology consultation should be conducted, and the L-thyroxine dose should be safely adjusted.
SoR: 2A QoE: V

3.4.3. In the case of detecting reduced bone mineral density, appropriate treatment should be initiated, and, depending on the indications and risk stratification, it should be considered whether lowering the thyroxine dose is feasible and adjusting the L-thyroxine dosage accordingly [63].
SoR: 2A QoE: V

Part III. Monitoring of DTC in children

1. Monitoring of patients after surgical treatment requires appropriate surgical follow-up and further disease surveillance through biochemical and imaging studies.
SoR: 2A QoE: IV

2. Biochemical monitoring with Tg measurements
2.1. Serum Tg concentration is a sensitive marker for evaluating the effects of treatment and for long-term monitoring of children and adolescents after DTC surgery.
2.2. Simultaneously with the determination of serum Tg concentration, the level of TgAb should be measured, because the presence of TgAb complicates the interpretation of the Tg result.
2.3. The Tg concentration can be determined under baseline conditions (during L-thyroxine treatment) or after stimulation with exogenous or endogenous TSH.
2.4. The trend in serial Tg and TgAb results is much more helpful/informative regarding the assessment of disease status than a single measurement of these parameters.
SoR: 2A QoE: IV

2.5. The interpretation of Tg/TgAb test results.
2.5.1. During suppressive therapy with L-thyroxine, Tg levels should remain stable, below 1 ng/mL. However, an increasing Tg level, especially above 1 ng/mL, may indicate disease recurrence.
2.5.2. A serum Tg concentration below 2 ng/mL (in the absence of TgAb) under TSH stimulation identifies patients in remission, with a very high probability of remaining completely disease-free during surveillance. For these patients, intensive oncological monitoring is not necessary, and the degree of TSH suppression can be alleviated.
2.5.3. Rising or significantly elevated Tg levels (> 10 ng/mL) under TSH stimulation require further investigations to localise the source of the elevated Tg concentration.
2.5.4. Detection of a slightly elevated Tg level (between 2 and 10 ng/mL) under TSH stimulation in a patient who underwent surgery and received RAI treatment may indicate persistent disease. However, this value may decrease over time with ongoing L-thyroxine therapy without the need for additional treatment.
SoR: 2A QoE: IV

2.6. The frequency of Tg and TgAb measurements.
2.6.1. The levels of Tg and TgAb should be measured initially during the postoperative period and subsequently based on the risk of thyroid cancer recurrence.
2.6.1.1. In low-risk thyroid cancer cases, Tg and TgAb levels should be measured every 6 months during the first 2 years post-surgery. If results during this time suggest the patient is disease-free, the interval between measurements can be extended to 12 months, and after 5 years, these intervals can be further lengthened or individualised based on the clinical situation and patient needs.
2.6.1.2. In intermediate- and high-risk thyroid cancer cases, Tg and TgAb levels should be measured every 3–6 months during the recommended period of L-thyroxine suppression therapy. If results during this time suggest that the patient is disease-free, the interval between measurements can be extended to every 12 months.
SoR: 2A QoE: IV

3. Monitoring through imaging studies.
3.1. Periodic neck ultrasound is recommended for monitoring DTC children/adolescents.
3.2. Neck ultrasound should be performed at intervals of 6 to 12 months for patients in the intermediate- and high-risk groups, and once a year for patients in the low-risk group.
3.3. Further monitoring beyond 5 years should be individualised based on the risk of recurrence and dynamic risk stratification. It should be noted, however, that the risk of DTC recurrence persists for much longer (even after several decades).
SoR: 2A QoE: IV

4. Monitoring with DxWBS after RAI administration.
4.1. During the monitoring of DTC children/adolescents with suspicion of residual disease, DxWBS may be used to decide on RAI treatment.
4.2. If DxWBS does not show pathological RAI uptake and the stimulated Tg level is below 2 ng/mL, there is no expectation of benefit from further serial diagnostic RAI DxWBS, as long as the patient remains free of clinical evidence of disease recurrence.
SoR: 2A QoE: IV

5. Monitoring of children with elevated thyroglobulin levels without evidence of disease in neck ultrasound or DxWBS.
5.1. In a child with detectable, increasing Tg levels under TSH suppression but with normal findings on neck ultrasound and DxWBS, it is necessary to rule out iodine excess as a cause of a false-negative result. This is particularly important in children who underwent computed tomography with iodine contrast before scintigraphy.

6. Monitoring of low-risk thyroid cancer.

We recall the abbreviated definition of low-risk thyroid cancer: papillary cancer, intrathyroidal, without lymph node metastases, considered cured (see also Tab. 8). Disease monitoring is conducted according to the following principles:

6.1. TSH suppression in accordance with the principles described in Part II, Section 3.2.2.1.

6.2. Neck ultrasound initially every 12 months with a gradual increase in intervals.

6.3. Monitoring of Tg and TgAb levels every 3–6 months for 2 years, and then annually.

6.4. Endocrinological care should be continued in the place of residence, while monitoring should be conducted at a referral centre.

6.5. Before transferring the patient to further monitoring in an adult care centre, a complete medical history, discharge summary, and the results of the latest examinations should be provided.

SoR: 2A QoE: V

7. Dynamic risk stratification.

Dynamic risk stratification of thyroid cancer in children should be conducted according to the criteria proposed by ATA 2015 and reiterated in the 2022 Polish recommendations for adults (Tab. 8 and 9) [3, 64–69].

7.1. In the dynamic risk assessment, based on the obtained results, the response to the initial treatment can be classified as excellent, biochemically incomplete, structurally incomplete, or indeterminate (Tab. 9).

7.2. The effectiveness data of dynamic risk stratification of thyroid cancer have only been published for adults. There are no available data on the effectiveness

Table 9. *Dynamic risk stratification in differentiated thyroid cancer (DTC) [1, 62, 71, 90], modified*

	Total thyroidectomy and RAI treatment	Total thyroidectomy	Lobectomy
Excellent treatment response	Normal imaging results *and* Non-stimulated Tg ≤ 1 ng/mL *or* Stimulated Tg ≤ 2 ng/mL *and* Undetectable TgAb	Normal imaging results *and* Non-stimulated Tg ≤ 1 ng/mL *or* Stimulated Tg ≤ 2 ng/mL *and* Undetectable TgAb	Normal imaging results *and* Stable non-stimulated Tg < 30 ng/mL *and* Undetectable TgAb
Incomplete biochemical resposne	Normal imaging results *and* Non-stimulated Tg > 1 ng/mL *or* Stimulated Tg >10 ng/mL *or* Rising TgAb	Normal imaging results *and* Non-stimulated Tg > 5 ng/mL *or* Stimulated Tg > 10 ng/mL *or* Increasing Tg levels over time at comparable TSH levels *or* Rising TgAb	Normal imaging results *and* Non-stimulated Tg >30 ng/mL *or* Increasing Tg levels over time at comparable TSH levels *or* Rising TgAb
Incomplete structural response	Persistent structural disease in imaging studies, regardless of Tg and TgAb levels		
Indeterminate response	Inconclusive imaging studies *or* Minimal RAI uptake in the thyroid bed *or* Stimulated Tg detectable, but ≤ 10 ng/mL *or* Stable or decreasing TgAb levels in the absence of persistent disease on imaging studies	Inconclusive imaging studies *or* Minimal RAI uptake in the thyroid bed *or* Non-stimulated Tg 1–5 ng/mL *or* Stimulated Tg 2–10 ng/mL *or* Stable or decreasing TgAb levels in the absence of persistent disease on imaging studies	Inconclusive imaging studies *or* Stable or decreasing TgAb levels in the absence of persistent disease on imaging studies

RAI — radioiodine; Tg — thyroglobulin; TgAb — antithyroglobulin antibodies; TSH — thyroid-stimulating hormone

of this stratification in children. An excellent response to initial treatment is achieved in 74–94.5% of patients diagnosed with low-risk cancer, 36–61% of patients with intermediate-risk cancer, and 0–21% of patients with high-risk cancer. Biochemical incomplete response is observed in 3–11% of low-risk patients, 16–22% of intermediate-risk patients, and 18–24% of high-risk patients. Structural incomplete response is noted in 1–2% of low-risk patients, 3.5–19% of intermediate-risk patients, and 24–67% of high-risk patients. Progression to structural disease occurs in 8–17% of patients with a biochemical incomplete response. Ultimately, 56–68% of patients with a biochemical incomplete response show no evidence of disease (NED), while 19–27% present with persistent elevated Tg levels without structural abnormalities, and only 8–17% develop structural disease within 5–10 years of follow-up. An indeterminate response occurs in 12–29% of low-risk patients, 8–23% of intermediate-risk patients, and 0–4% of high-risk patients [70].

7.3. In patients who do not exhibit an increase in Tg levels during L-thyroxine treatment, the assessment of the effectiveness of anti-cancer therapy should be performed 6–18 months after postoperative RAI treatment. The physician can determine whether hospitalisation is required for this purpose or if the evaluation can be conducted on an outpatient basis.

7.4. DTC remission can be stated if a patient, following total thyroidectomy and postoperative RAI treatment (if administered), shows an excellent response to treatment. It is defined as the absence of disease in imaging studies and no increase in Tg levels > 2 ng/mL during TSH stimulation, with the test being fully reliable due to the absence of TgAb [64].

SoR: 2A QoE: IV

7.5. Minimal RAI uptake in the thyroid bed does not necessarily indicate ineffective ablation or constitute an indication for additional RAI therapy if:

— other examinations do not indicate persistent neoplastic disease;
— stimulated Tg level does not exceed 2 ng/mL;
— there is no clear evidence of thyroid remnants in the ultrasound examination.

7.6. Monitoring of patients who have achieved an excellent treatment response.

The criterion for remission after the completion of primary treatment includes the combined finding of a negative neck ultrasound and stimulated Tg levels ≤ 2 ng/mL in the absence of TgAb, alongside no other signs of persistent or recurrent cancer (Tab. 9). Alternatively, an excellent response to treatment can be confirmed by sustained Tg levels < 1 ng/mL during L-thyroxine therapy without other features of persistent or recurrent disease (Tab. 9) [71].

SoR: 2A QoE: IV

7.6.1. The frequency of examinations is specified below; however, at least one confirmatory examination should be conducted within 3–5 years after the first confirmation of remission.

7.6.2. DxWBS is not routinely performed to monitor the further course of disease in paediatric patients with an excellent response to treatment.

SoR: 2A QoE: V

7.6.3. In a patient who was found to have an excellent treatment response during the first assessment after completing therapy and whose subsequent disease course was asymptomatic, thus qualifying them for the low-risk group, monitoring of Tg levels does not require TSH stimulation.

SoR: 2A QoE: IV

7.6.5. There is a lack of evidence confirming the safety of the above-described protocol in high-risk patients who have achieved an excellent treatment response.

SoR: 2A QoE: V

7.7. Monitoring of patients with incomplete biochemical response.

7.7.1. Assessment of Tg levels dynamics at 6-month intervals.

7.7.2. Neck ultrasound at 6-month intervals.

7.7.3. In the case of an increase in Tg levels, imaging studies (primarily neck ultrasound and chest CT, possibly whole-body diagnostic scintigraphy).

7.8. Interpretation of serum Tg concentration in DTC patients.

7.8.1. Because the decisive criterion for detecting recurrence during DTC monitoring is an increasing Tg level over time, efforts should be made to conduct these tests in one centre using the same method.

SoR: 2B QoE: IV

7.8.2. Optimally, standardised methods against the international standard CRM 457 should be used. Each laboratory should also characterise the functional sensitivity of the Tg assay method. Available ultrasensitive methods for Tg measurement are preferred.

SoR: 2A QoE: IV

7.8.3. Monitoring of Tg levels should be accompanied by testing for TgAb, which should be performed no less than once a year.

SoR: 2B QoE: V

7.8.4. In the presence of TgAb, low Tg levels cannot be considered a fully reliable criterion for treatment response.
SoR: 2A QoE: III

7.8.5. The interpretation of Tg levels should consider previous Tg and TgAb levels, current and prior TSH levels, as well as the scope of previous surgery and RAI treatment.
SoR: 2A QoE: V

7.8.6. Ultrasensitive methods for determining Tg (functional sensitivity 0.1 ng/mL) are recommended.
SoR: 2A QoE: III

7.8.7. In the first 5 years after the completion of primary treatment, in patients with an excellent treatment response and no other risk factors, Tg levels should be tested every 12 months. In subsequent years, the intervals between tests may be extended.
SoR: 2A QoE: IV

7.8.8. In a patient who has not undergone complete thyroidectomy and/or RAI therapy, Tg levels may exceed 1 ng/mL (see Tab. 9), and only a rising Tg level may suggest cancer progression. These tests should be performed at intervals, at least as in section 7.8.7, or more frequently if indicated.
SoR: 2A QoE: V

7.8.9. Tg levels cannot be the sole test for monitoring remission in thyroid cancer patients. In addition to medical history and physical examination, it should be accompanied by at least neck ultrasound, performed at similar time intervals [64].
SoR: 2A QoE: IV

7.9. Principles of monitoring a DTC patient in whom TgAb are present.
7.9.1. Neck ultrasound is the primary examination for thyroid cancer patients after radical surgery, where the presence of TgAb prevents reliable reliance on Tg levels. However, it should be remembered that the patient's history and physical examination determine indications for other imaging studies.
SoR: 2A QoE: IV

7.9.2. Neck ultrasound in evaluating the effectiveness of DTC treatment and monitoring.
Neck ultrasound should be performed every 6–12 months for the first 5 years, with intervals potentially being extended thereafter. In cases of suspected recurrence, intervals should be shortened. Detection of focal changes in the thyroid bed and/or lymph node enlargement is an indication for FNAB, especially when cervical lymph nodes exhibit features suggesting metastasis (round shape, absence of a hilum, heterogeneity, cystic degeneration, presence of calcifications).
SoR: 2A QoE: IV

7.9.3. If a suspicious lymph node measures less than 1 cm in its short axis, a watchful waiting strategy can be adopted, and FNAB can be performed only if it shows further growth.
SoR: 2A QoE: V

7.9.3.1. Testing for Tg in FNAB washouts can be helpful in diagnosing lymph node metastasis.
SoR: 2A QoE: IV

7.9.3.2. Normal serum Tg levels do not exclude lymph node metastasis.
SoR: 2A QoE: IV

7.10. RAI studies (particularly neck and whole-body scintigraphy) are useful for the initial evaluation of the effectiveness of RAI treatment but are not mandatory.
SoR: 2A QoE: IV

7.10.1. They can be omitted if studies performed during RAI treatment indicate a very low risk of recurrence in a patient with a low cancer stage who underwent radical surgery.
7.10.2. In case of an increase in Tg levels (measured during L-thyroxine treatment or under TSH stimulation), RAI scintigraphy of the neck and whole body may be useful for detecting and localising RAI-avid lesions and determining indications for RAI treatment.
7.10.3. Routine periodic DxWBS for further monitoring of patients in remission is not necessary because the risk of detecting RAI-avid recurrence without a prior increase in Tg levels is minimal.
SoR: 2A QoE: IV

7.11. Functional and imaging studies.
7.11.1. CT and/or MRI are performed if recurrence is suspected due to increased Tg levels or other indications. However, it should be noted that performing a contrast-enhanced CT scan impairs the RAI uptake of cancer foci for approximately 6–8 weeks.
SoR: 2A QoE: V

7.11.2. When Tg levels increase, a chest CT scan is performed first.
SoR: 2A QoE: IV

8. Monitoring of tumours of uncertain malignant potential.

In thyroid tumours of uncertain malignant potential, there are no data on the optimal monitoring, and the recommendations should be considered as expert opinions.
8.1. Maintain TSH within the lower normal range of 0.5–2.0 mU/L.
8.2. In monitoring (regardless of the extent of surgery), an ultrasound examination of the thyroid and cervical lymph nodes is recommended approximately once a year.
8.3. In monitoring, the evaluation of Tg and TgAb levels may be useful, following different principles for patients after total thyroidectomy and those after hemithyroidectomy.
SoR: 2A QoE: V

Part IV. Treatment of a patient with persistent/recurrent disease

1. Persistent/recurrent disease in the neck
1.1. Surgical treatment should be preferred for disease localised to the neck/mediastinum, as long as surgery is feasible, especially for radioiodine-refractory foci.
SoR: 2A QoE: IV

1.2. A RAI-avid lesion in the neck (visualised on DxWBS) can be treated with RAI in cases of high risk of postoperative complications. In every case, the decision should be individualised.
SoR: 2A QoE: V

2. Distant metastases.
2.1. Most distant metastases in the DTC course in children occur in the lungs, are micrometastases, and exhibit RAI avidity. In this case, the treatment of choice is RAI therapy conducted according to the principles described in Part II, Section 3.1.
SoR: 2A QoE: IV

2.2. Subsequent treatment of RAI-avid lung metastases should be individualised, considering the unique clinical course in a child, the side effect profile, tolerance risk, and the cumulative activity/dose of RAI administered. The intervals between treatment cycles should range from 6 to 12 months.
SoR: 2A QoE: V

3. Treatment of advanced, unresectable, radioiodine-refractory DTC (RR-DTC) in children and adolescents.
3.1. External beam radiotherapy may be considered:
3.1.1. In children with progressive or symptomatic disease.
3.1.2. In children with unresectable/RR-DTC, for whom no other therapeutic options are available, and as palliative treatment.
SoR: 2A QoE: IV

3.2. Molecularly targeted systemic treatment can be considered:
3.2.1. In children with unresectable/RR-DTC, for whom no other therapeutic options are available, and as palliative treatment.
SoR: 2A QoE: V

3.2.2. In children with disease progression during L-thyroxine suppression therapy.
3.2.3. The presence of radioiodine-refractory disease must be confirmed before considering targeted therapy; watchful waiting may be an appropriate approach.
SoR: 2A QoE: V

3.2.4. In children with RR-DTC, molecular testing of tumour tissue should be performed to assess indications for treatment with selective kinase inhibitors [72].
SoR: 2A QoE: IV

3.2.5. Molecularly targeted therapy does not lead to a cure of the disease.
SoR: 2A QoE: IV

3.2.6. None of the multikinase inhibitors (MKI) used in first-line treatment (sorafenib, lenvatinib) are approved for the treatment of RR-DTC in individuals under 18 years of age. Cabozantinib, used in second-line treatment, is approved for patients aged ≥ 16 years. Clinical trials with these drugs have not been conducted in children, and the available data are limited to individual cases. These drugs are currently not reimbursed for children by the National Health Fund.
3.2.7. In children with an identified *NTRK* fusion gene who have exhausted therapeutic options, the use of a selective NTRK inhibitor is recommended: larotrectinib (in all children regardless of age) or entrectinib (in children aged ≥ 12 years). Larotrectinib is reimbursed under the drug program.
SoR: 2A QoE: IV

3.2.8. In children aged 12 and older who have been diagnosed with the *RET* fusion gene, the use of the selective RET inhibitor selpercatinib may be considered. However, this medication is not reimbursed by the National Health Fund.
SoR: 2A QoE: IV

3.2.9. The decision to initiate MKI treatment (sorafenib, lenvatinib, or cabozantinib) or selective inhibitors (larotrectinib, selpercatinib) should be made individually by a multidisciplinary team, considering the potential benefits and risks associated with the treatment.
SoR: 2A QoE: V
3.2.10. Targeted molecular therapy should be continued as long as the patient benefits from the treatment and no unacceptable adverse effects occur. Disease progression during treatment is not an unequivocal indication for treatment discontinuation.
SoR: 2A QoE: IV

3.2.11. Targeted molecular therapy should be conducted in specialised centres with experience in treating thyroid cancer in children, using tyrosine kinase inhibitors, and managing complications associated with this therapy.
SoR: 2A QoE: V

Part V. Management of medullary thyroid carcinoma

1. The management of medullary thyroid carcinoma (MTC) is discussed in the current Polish recommendations for adult thyroid cancer [1]. In these recommendations for children, the key information is reiterated, and detailed guidelines for systemic treatment in children with unresectable locoregional disease and/or distant metastases are discussed.
2. The MTC management exhibits many distinctions compared to differentiated thyroid cancers [73–75] due to the following:
2.1. A significant hereditary component and the possibility of DNA diagnostics, including the detection of hereditary predispositions in family members and the associated need for performing prophylactic surgeries.
2.2. The high specificity and sensitivity of calcitonin measurement allow this test to be used for detecting cancer, precisely determining the extent of necessary surgical treatment, early detection of recurrence/progression of cancer, as well as prognosis of its course.
2.3. The broader use of elective lymphadenectomy than in DTC and the reliance on calcitonin levels when determining indications for its use.
2.4. A high risk of coexistence of pheochromocytoma in patients with the hereditary disease.
SoR: 2A QoE: IV

3. MTC diagnostics.
3.1. The MTC diagnosis in FNAB is complicated due to the requirement for immunocytochemical staining with anti-calcitonin antibodies or confirmation of elevated serum calcitonin levels.
3.2. The MTC diagnosis can be based on the measurement of serum calcitonin levels, and it is very probable if the calcitonin level exceeds 100 ng/L.
3.3. Calcitonin stimulation test allows for the differentiation of ambiguous cases and increases the effectiveness of preoperative MTC diagnosis and its monitoring.
3.4. Measuring calcitonin levels in washings from the biopsy needle supports the MTC diagnosis.
SoR: 2A QoE: IV

4. DNA diagnostics in MTC.
4.1. Every MTC patient should undergo DNA testing, even in the absence of any data from the medical history and physical examination indicating the presence of hereditary cancer.
SoR: 2A QoE: IV

4.2. Scope of testing and the risk of revealing gene mutation carrier status.
4.2.1. The examination involves analysing mutations in the *RET* proto-oncogene in the patient's germline DNA (the test material is peripheral blood) and should be conducted in an accredited centre. In centres equipped with next-generation sequencing (NGS), this method is optimal for detecting *RET* mutations.
4.2.2. A negative result of a full DNA test excludes the hereditary form with approximately 95% probability.
4.2.3. A positive DNA test result warrants screening of family members.
4.2.4. Both the detection of an asymptomatic mutation carrier and a negative result in a patient's family member should be confirmed in a subsequent blood sample taken independently.
4.2.5. In patients with a negative family history of hereditary forms, there is approximately a 10% probability that the result of genetic predisposition testing will be positive [76].
SoR: 2A QoE: IV

5. Management in families of *RET* mutation carriers
5.1. Hereditary MTC occurs as a symptom of multiple endocrine neoplasia syndrome (MEN 2). This name should be considered official in the Polish language. Previously used names (e.g. multiple endocrine adenomatosis) are no longer applicable. In typical MEN 2A and MEN 2B, MTC coexists with pheochromocytoma, which manifests within the family, with a risk of up to 50%.
5.2. In a family with a MTC hereditary form, the risk of the disease in first-degree relatives is 50%.
5.3. In families with MEN2A, carrier testing for *RET* mutations should be conducted among relatives,

Table 10. *Diagnostic and therapeutic procedure depending on the location of the germline mutation in the RET proto-oncogene. Based on Diagnosis and treatment of thyroid cancer in adult patients — Recommendations of Polish Scientific Societies and the National Oncological Strategy [1, 91]*

	ATA-HST (*RET 918*)	**ATA-H (*RET 634, 883*)**	**ATA-MOD (other *RET* mutations)**
DNA test	Immediately after birth	2–3 years of age	5th year of age
Basal serum calcitonin	In all family members and tested patients parallel to DNA test, in non-operated *RET* mutation carriers every 6–12 months		
Calcitonin stimulation test	For the first time — immediately after the detection of the *RET* mutation, then every 6–12 months		
Thyroid ultrasound	For the first time — immediately after the detection of the *RET* mutation, then every 6–12 months		
Prophylactic thyroidectomy	In the first year of age	In the 5th year of age	In the 5th year of age or depending on calcitonin level
Biochemical screening for pheochromocytoma	From the age of 11 years, on average once a year	From the age of 11 years, on average once a year	From the age of 16 years, on average once a year
Adrenal imaging	Only in the case of abnormal biochemical tests		
Serum calcium measurement	(–)	From the age of 11 years Once a year	From the age of 16 years Once a year

ATA — American Thyroid Association; HST — highest; H — high; M — moderate

particularly in children, starting at the age of 2–3 years, and necessarily before the age of 5.

5.4. In families with MEN2B, carrier testing for mutations should be conducted in children as soon as possible, optimally before the age of one year.

5.5. Depending on the location of the *RET* mutation and the associated risk of aggressive MTC, ATA recommendations advise classifying patients into one of 3 risk groups: HST (highest) — highest risk, H (high) — high risk, or MOD (moderate) — moderate risk (Tab. 10).

SoR: 2A QoE: IV

5.6. Diagnostic management in *RET* mutation carriers. In RET mutation carriers, comprehensive examinations should be conducted to assess the current stage of the disease:

— basal and stimulated serum calcitonin levels;
— neck ultrasound;
— FNAB in the case of thyroid lesions;
— abdominal ultrasound;
— biochemical diagnosis for pheochromocytoma;
— serum calcium and PTH testing.

SoR: 2A QoE: IV

5.7. Prophylactic thyroidectomy in *RET* mutation carriers.

5.7.1. In asymptomatic *RET* mutation carriers, prophylactic total thyroidectomy should be considered. It is accepted that prophylactic surgery in *RET* mutation carriers provides better protection against cancer development than continuous monitoring of serum calcitonin levels.

5.7.2. Prophylactic total thyroid surgery is indicated:

5.7.2.1. In the first year of life or immediately after detecting a mutation in MEN 2B (in this syndrome, DNA testing is required within the first year of life, HST group according to ATA).

5.7.2.2. Before the age of 5 years or during the fifth year of life in MEN 2A syndrome (H group according to ATA).

SoR: 2A QoE: IV

5.7.2.3. In patients with *RET* mutations causing a later MTC onset (MOD group according to ATA), it is possible to delay prophylactic surgery beyond the age of 5 years, provided that the patient or the patient's parents are fully informed of the risks associated with such a delay and have accepted them. In addition, the baseline calcitonin level must be normal, there must be no focal lesions in thyroid ultrasound, and the family history should indicate a relatively mild course of the disease.

NOTE! Due to the lack of conclusive evidence indicating the familial occurrence of medullary thyroid cancer in *RET* mutation carriers at codon 791 and its pathogenic nature [77], the indications for prophylactic thyroidectomy in this group should be considered very cautiously.

SoR: 2A QoE: IV

5.8. In *RET* mutation carriers who have not yet undergone prophylactic thyroidectomy, annual testing of stimulated calcitonin (in Poland, the test involves intravenous administration of calcium salts) provides earlier information about disease development than testing the baseline calcitonin level.

5.8.1. Normally, the increase in serum calcitonin levels after intravenous calcium administration does not exceed 30 ng/L.
5.8.2. An increase in calcitonin levels to values > 100 ng/L after calcium stimulation is interpreted as a positive result; however, it is not definitive for the diagnosis of medullary thyroid cancer (it may result from C-cell hyperplasia). Nevertheless, in *RET* mutation carriers, it constitutes a clear indication for thyroid surgery.
5.8.3. Intravenous administration of calcium salts is an alternative to the pentagastrin test.
SoR: 2A QoE: IV

5.9. Detection and treatment of pheochromocytoma in MEN2 syndrome.
5.9.1. Indications for testing for pheochromocytoma depend on the type of *RET* mutation identified.
5.9.2. The detection of pheochromocytomas is based on biochemical testing. It is recommended that these tests be performed annually starting at the age of 11 years for MEN2B and MEN2A *RET* 634 and *RET* 883, and at the age of 16 years for carriers of other mutations.
5.9.3. A screening CT scan of the abdomen is not necessary in a MTC patient if there are no symptoms of pheochromocytoma and the results of biochemical tests are negative. However, in a patient with an unknown genetic background being prepared for MTC surgery, the usefulness of such an examination should be considered.
5.9.4. If pheochromocytoma and medullary thyroid cancer coexist, adrenal surgery should be performed first to avoid exacerbation of pheochromocytoma symptoms.
SoR: 2A QoE: IV

5.9.6. Surgical treatment of pheochromocytoma.
Surgery for pheochromocytoma should be preceded by at least 2 weeks of pharmacological pretreatment.
5.9.6.1. When resecting pheochromocytoma, efforts should be made to perform adrenal-sparing surgery, particularly if the second adrenal gland is being operated on in a patient who has previously undergone resection of the contralateral adrenal gland.
SoR: 2A QoE: IV

5.9.6.2. If bilateral adrenalectomy is necessary, the patient should be thoroughly informed about the principles of substitution therapy. It should be remembered that in hereditary MTC occurring as part of MEN 2 syndrome, a significant percentage of deaths are associated with adrenal complications — hypertensive crisis or adrenal insufficiency.
SoR: 2A QoE: V

5.10. Detection and treatment of hyperparathyroidism in MEN2 syndrome.
5.10.1. Indications for testing for hyperparathyroidism depend on the type of *RET* mutation identified. It should be noted that hyperparathyroidism tends to manifest late, usually in adult patients.
5.10.2. In MEN2A, annual serum calcium level testing is primarily justified for carriers of *RET* 634 and *RET* 630 mutations, while for carriers of other mutations, it can be performed less frequently.
5.10.3. The treatment of hyperparathyroidism in MEN 2A follows generally accepted rules.
5.10.4. However, it should be noted that the cause is often parathyroid hyperplasia, and the risk of surgical treatment failure is higher than in the case of surgery for a single adenoma.
SoR: 2A QoE: IV

6. Surgical treatment of clinically evident MTC.
6.1. If MTC is clinically evident (thyroid nodule with positive FNAB), thyroid surgery should always be a total thyroidectomy accompanied by central lymphadenectomy, both in hereditary and sporadic cases.
6.2. The performance of lateral lymphadenectomy depends on the presence of metastases and/or serum calcitonin level.
6.3. There are no clear indications for lateral lymphadenectomy if there are no enlarged lateral cervical lymph nodes and the preoperative calcitonin level is less than 200 ng/L.
6.4. When planning the extent of local surgery, the surgeon should have an abdominal CT scan to assess distant metastases if the calcitonin level exceeds 400 ng/L.
6.5. It should be noted that the ATA recommendations specify these indications depending on the threshold calcitonin level of 150 ng/L.
SoR: 2A QoE: IV

7. Prophylactic surgery in *RET* mutation carriers.
7.1 Indications for prophylactic thyroidectomy, described in section 5.7, should consider the combined interpretation of DNA testing (type of *RET* mutation), current calcitonin levels, the patient's current age, and the family medical history. For this reason, surgical treatment, which in the case of thyroid cancer should generally be performed in specialised centres, should, specifically in this indication, be conducted in centres with extensive experience in this area.
7.2. Prophylactic total thyroidectomy performed at the appropriate time (see section 5.7) can be carried out without central lymphadenectomy if the baseline calcitonin level is normal and there are no signs of lymph node involvement.

7.3. If a carrier of a gene mutation predisposing to MEN2A does not show an increase in baseline calcitonin levels at the age of 5 years, performing a calcium stimulation test is useful for determining whether surgery can be postponed. However, the decision should also consider the type of *RET* mutation.
7.4. If a prophylactic surgery was not performed at the optimal age specified in section 5.7 and the baseline calcitonin level is normal, annual repetition of the calcium stimulation test reduces the risk of missing the optimal time for surgery.
SoR: 2A QoE: V

8. Postoperative evaluation and follow-up of MTC patients.
8.1. Postoperative calcitonin evaluation.
8.1.1. The normalisation or undetectable postoperative calcitonin level is the best evidence of the radicality of the performed surgery and a favourable prognostic factor.
SoR: 2A QoE: IV

8.1.2. Although the authors of the recommendations are aware that some American specialists consider the calcium stimulation test unnecessary, the experience of many European centres supports its use in patients with normal baseline calcitonin levels. A negative test result (some authors believe that no increase in calcitonin should be observed) is a good prognostic factor.
SoR: 2A QoE: V

8.1.3. It should be noted that in some assays for measuring calcitonin, serum dilution is required for reliable measurement when the calcitonin level exceeds 300–500 ng/L.
8.1.4. Efforts should be made to determine the doubling time of serum calcitonin levels because it has very good prognostic and predictive value [78].
SoR: 2A QoE: IV

8.2. Further monitoring includes the folowing:
— calcitonin assessment;
— neck ultrasound;
— serum carcinoembryonic antigen (CEA) assessment.
Imaging studies only if serum calcitonin level rises above 150 ng/L or preferably above 400 ng/L.
SoR: 2A QoE: IV

9. Management of asymptomatic serum calcitonin increase.
9.1. If calcitonin levels do not exceed 150 ng/L, there is no justification for performing CT, MRI, or PET scans because they cannot detect cancer foci.
9.2. With an increase in calcitonin levels above 400–1000 ng/L, the likelihood of localising the cancer focus increases.
9.3. Even at calcitonin levels of 150–1000 ng/L, there is a risk of a false-negative result when trying to locate cancer foci [79].
9.4. In the case of asymptomatic elevation of serum calcitonin levels, central neck lymphadenectomy (if not previously performed) and/or elective lateral lymphadenectomy may be considered.
9.5. However, it should be noted that the most common cause of elevated serum calcitonin levels are liver micrometastases.
SoR: 2A QoE: IV

10. Management of recurrent MTC.
10.1. Surgery is a basic treatment method for local and locoregional recurrence.
10.2. If distant metastases accompany local/locoregional recurrence, the indications for neck/mediastinal surgery are relative.
10.3. The MTC spread very rarely involves isolated metastases, and surgical treatment of metastases (especially liver metastases) is generally not justified.
SoR: 2A QoE: V

10.4. Systemic treatment can be considered in children with unresectable locoregional disease and/or the presence of distant metastases if it meets Response Evaluation Criteria in Solid Tumours (RECIST) criteria for measurable disease and progression and local treatment is not available.
SoR: 2A QoE: V

10.4.1. Before qualifying for systemic treatment, a molecular analysis of the tumour should be performed to identify molecular targets that allow the use of selective inhibitors. This examination is funded by the National Health Fund.
SoR: 2A QoE: IV

10.4.2. MKI therapy does not lead to a cure of the disease.
SoR: 2A QoE: IV

10.4.3. None of the MKIs used in first-line treatment (vandetanib, cabozantinib) are approved for MTC treatment in individuals under 18 years of age. Phase II studies have been published confirming the safety of vandetanib use in children with medullary thyroid cancer in the course of MEN 2B syndrome. Reports on cabozantinib come only from descriptions of individual cases. These drugs are not currently reimbursed for children by the National Health Fund. When using

vandetanib, it should be noted that in individuals without *RET* mutations in tumour cells, the drug may exhibit weaker efficacy.
SoR: 2A QoE: IV

10.4.4. In children aged ≥ 12 years with a detected *RET* mutation in cancer cells, the use of selpercatinib, the selective RET inhibitor, can be considered as a first- or second-line treatment [80]. Currently, this drug is reimbursed under the drug program only for individuals > 18 years of age. In children, selpercatinib can be used under the Emergency Access to Drug Technologies (RDTL).
SoR: 2A QoE: IV

10.4.5. The decision to initiate MKI (vandetanib or cabozantinib) or the selective inhibitor (selpercatinib) should be made individually by a multidisciplinary team, taking into account the potential treatment-associated benefits and risks.
SoR: 2A QoE: IV

10.4.6. Targeted molecular therapy should be continued as long as the patient benefits from the treatment and no unacceptable side effects occur. Disease progression during treatment is not an absolute indication to discontinue therapy.
SoR: 2A QoE: IV

10.4.7. Targeted molecular therapy should be conducted in specialised centres with experience in treating thyroid cancer in children, using tyrosine kinase inhibitors, and managing complications associated with this therapy.
SoR: 2A QoE: V

Part VI. Consequences of thyroid cancer treatment in children

1. Monitoring the sequelae of thyroid cancer treatment in children.
1.1. Total thyroidectomy with central lymphadenectomy is associated with an increased risk of postoperative complications, particularly damage to the recurrent laryngeal nerve and hypoparathyroidism. Therefore, intraoperative monitoring of the nerve (neuromonitoring) and identification and preservation of the parathyroid glands (including the use of autofluorescence, if available) are recommended.
1.2. Laryngeal recurrent nerve function should be evaluated postoperatively in all children with thyroid carcinoma.
1.3. Parathyroid function should be evaluated postoperatively in all children with thyroid carcinoma.
SoR: 2A QoE: IV

1.4. RAI use is associated with the risk of complications such as transient reduced fertility in males, bone marrow function impairment, dysfunction of the salivary and lacrimal glands (most commonly), and secondary cancers [81, 82].
1.5. All male patients with differentiated thyroid cancer, diagnosed and treated after puberty, should be informed about the risk of reduced fertility and the possibility of sperm banking, and they should consult with a specialist in this field.
SoR: 2A QoE: IV

1.7. The use of L-thyroxine in doses causing TSH suppression may be associated with symptoms of thyrotoxicosis and a chronic adverse impact, primarily on the cardiovascular system, especially on the diastolic function of the myocardium.
SoR: 2A QoE: IV

1.8. Assessment of calcium-phosphate metabolism with its periodic monitoring and vitamin D3 supplementation may be beneficial for optimal bone mineralisation in children after thyroid cancer treatment. Calcium supplementation is recommended in cases of reduced serum calcium levels. In cases of low PTH levels, additional administration of 1[OH]D3 or 1,25$[OH]_2$D3 is advised.
1.9. The use of MKIs in children with advanced or treatment-resistant disease may be associated with numerous side effects. Patients should be informed about the potential side effects (hypertension, gastrointestinal symptoms, skin changes).
1.10. The use of external beam radiation therapy in the treatment of thyroid cancer may be associated with numerous early and late consequences, including not only hypothyroidism but also hypoparathyroidism and secondary malignant tumours.
SoR: 2A QoE: IV

2. Assessment of the quality of life in children after thyroid cancer treatment [83–85].
2.1. Studies have not shown significant differences in the quality of life of survivors compared to the control group (at a single point), but more health problems limiting functionality, including chronic fatigue, were observed in those who were treated.
2.2. Quality of life (QoL) is assessed using dedicated and linguistically validated questionnaires designed to evaluate QoL in patients with thyroid diseases or specifically thyroid cancer.
2.3. Due to the risk of long-term consequences affecting various systems, comprehensive care should be provided for survivors of thyroid cancer treatment (involving specialists such as oncologists, endocrinologists,

cardiologists, psychiatrists, laryngologists, and others as needed), as well as psychosocial support.
SoR: 2A QoE: IV

2.4. Due to the risk of late recurrence (5–10 years), patient follow-up should be conducted for a minimum of 10 years after diagnosis. For patients treated in paediatric centres, it is necessary to ensure continuity of care upon reaching adulthood by individually transferring the patient to a centre that will continue the follow-up [86].
SoR: 2A QoE: V

Conflict of interest

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