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Review

Postoperative Use of Radioiodine (131-I): Review of Recommendations and Guidelines

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A B S T R A C T

In the management of large number of patients with differentiated thyroid cancer, the radioactive iodine (131-I) administration plays an important role. The guidelines of numerous international and national medical societies regarding the issue of postoperative 131-I administration have been published and updated in the last few years. The guidelines differ in the shape and content, and contain some specific features. The different methods for evaluation and analysis of clinical evidence level and resulting grades of recommendations have been used in line with the very guidelines. The postoperative 131-I administration refers to the radioiodine ablation as a form of adjuvant treatment and radioiodine therapy in the management of patients with recurrent cancer, persistent disease and regional or distant metastases. According to the indications for the postoperative 131-I administration, the patients could be divided into the three risk groups: the very low risk group in which there is no indication for the postoperative131-I administration, the low risk group in which the indication could be considered, and the high risk group in which there is a clear indication for the131-I administration. The different criteria for distribution of patients into these three groups are expressed in a certain guidelines. There are different opinions about the necessary dosage of 131-I for the efficient ablation in the low risk group. Moreover, the opinions are also divided regarding the conduction of postoperative (preablative or pretherapeutic) scintigraphy with 131-I. As regards the instructions on preparation of patients for the radioiodine ablation and therapy, all the guidelines recommend the low iodine diet and endogenous or exogenous stimulation of TSH. The endogenous stimulation is accomplished by the withdrawal of thyroid hormones, whereas the recombinant human TSH (rhTSH) is used for exogenous stimulation. For conducting the therapy with 131-I the level of TSH has to be >25–30 mU/L.

***Key words**: differentiated thyroid cancer, thyroid remnant ablation, radioiodine therapy, guidelines, recombinant human thyrotropin*

Introduction

The thyroid cancer is subject of interest to many international and national medical societies that are formed out by experts of different clinical specialties. In the last few years the most of societies have published and updated their recommendations (in the form of guidelines; algorithms) regarding the management of patients with differentiated thyroid cancer (DTC)[1–12]. The majority of these recommendations (guidelines) are based on the methods for evaluation of evidence, evaluation and treatment of thyroid nodules, diagnostics, staging of disease, initial treatment and follow-up of patients with DTC. On the grounds that the appliance of the radioactive iodine plays an important role in the treatment of a large number of patients with DTC, this article presents the review of recent guidelines that refer to postoperative radioactive iodine (131-I) administration.

This article presents the differences between the guidelines regarding the indications and procedures in cases the postoperative 131-I is applied, characteristics (specific features) of certain guidelines, the strength of evidence and the grades of recommendations pursuant to different guidelines. The terms that closely describe the postoperative use of 131-I have been defined, and the recommendations regarding the procedures which are to be conducted prior to radioiodine remnant ablation and radioiodine therapy have been analyzed. The Table 1 shows the different society guidelines that contain different recommendations for various aspects of DTC, that is,

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TABLE 1
DIFFERENT SOCIETY GUIDELINES FOR THE TREATMENT OF DIFFERENTIATED THYROID CANCER

AACE/AME (American Association of Clinical Endocrinologists and Italian Associazione for Medici Endocrinologi):2006; Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules
ATA (American Thyroid Association): 2009; Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer
BTA/RCP (British Thyroid Association and Royal College of Physicians): 2007; Guidelines for management of thyroid cancer
Croatian Thyroid Society: 2008; Guidelines for the management of patients with differentiated thyroid cancer
DGE/DGN (German Endocrine and Nuclear Medicine Society): 2007; Procedure guidelines for radioiodine therapy of differentiated thyroid cancer (version 3)
Dutch Endocrine Society and Society of Nuclear Medicine: 2007; Nationwide guideline thyroid carcinoma
EANM (European Association of Nuclear Medicine):2008; Guidelines for radio-iodine therapy of differentiated thyroid cancer
ETA (European Thyroid Association): 2006; European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium
ETA (European Thyroid Association):2005; Post-surgical use of radio-iodine (I-131) in patients with papillary and follicular thyroid cancer and the issue of remnant ablation: a consensus report
ESMO (European Society for Medical Oncology): 2010; Thyroid cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up
NCCN (National Comprehensive Cancer Network): 2011; Version. 1; Practice guidelines in oncology – Thyroid Carcinoma

for the postoperative 131-I administration. All the guidelines are recently published in renowned international journals and are easily available.

The Structure and Characteristics (Specific Features) of Certain Guidelines

The guidelines, although similar in structure, differ in their shape and content and have certain specific characteristics (features). The guidelines of the American Thyroid Association (ATA) are presented in the form of questions and answers. The answers are given in a form of short discussion with references from the respective literature and the recommendations (together with the level of evidence)[3]. The guidelines of the American Association of the Clinical Endocrinology, which are issued in cooperation with the Italian Associazione for Medici Endocrinologi (AACE/AME), provide us with the detailed recommendations for management of patients with thyroid nodules, but they lack the part that refers to the use of the radioiodine therapy[2]. On the other hand, the use of the radioiodine therapy represents the main part of the European Association of Nuclear Medicine guidelines (EANM)[8] and the Consensus report about postsurgical use of radioiodine and the issue of remnant ablation (ETA/ABL)[10].

The most extensive guidelines are the ones of the Dutch Endocrine Society and Society of Nuclear Medicine (Dutch), that on more than 150 pages give recommendations that are based on 599 references[7]. The guidelines that are mutually brought by the British Thyroid Association and the Royall College of Physicians (BTA) contain the detailed instructions for the general practitioners as well as for the patients who are important participants in the management of DTC. The guidelines are updated every five years (working version of 2002, current version of 2007, which is planned to be revised in the course of the year 2012)[4]. The National Comprehensive Cancer Network (NCCN; USA) presents the guidelines in the form of algorithms, decision pathways and practical clinical guidelines, respectively. The algorithms are followed by the text and the references that contain the discussion about the aspects related to the algorithm. The guidelines are updated on a regular basis, therefore the current version dates from the year 2011 (the previous version is from 2010)[12].

A part of the EANM guidelines describes in detail the dosimetry of the tumor and the dosimetry of the bone marrow. Also, it gives detailed description of the procedures as well as the early and late effects of the radioiodine therapy[8]. The European Consensus for the Management of Patients with Differentiated Thyroid Carcinoma of the Follicular Epithelium (ETA) is adopted in a form of joint statement of the European Thyroid Association experts[9]. The above mentioned ETA/ABL consensus has already been established by the experts of ETA[10]. The European Society for Medical Oncology guidelines (ESMO) are based on ETA and ATA guidelines[11]. Joined guidelines of German Endocrine and Nuclear Medicine Society (DGN) consist of three separate documents: Procedure guidelines for the radioiodine therapy of DTC, the guidelines for the 131-I whole body scintigraphy and the guidelines for the pediatric patients with DTC[6]. The backbone of the Croatian guidelines for the treatment of patient with DTC (CTS) is made of the four detailed algorithms; two of them refer to the diagnostics and the other two on the DTC therapy[5] (Figure 1).

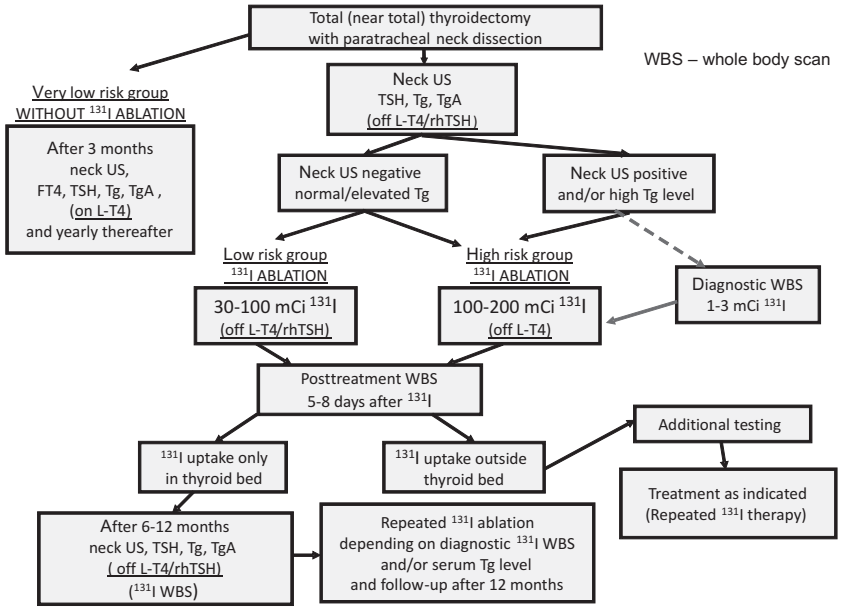

Fig. 1. Example of algorithm: primary treatment of differentiated thyroid carcinoma (Algorithm of treatment and follow up by Croatian Throid Society; Reproduced with permission; Copyright © 2007 Croatian Thyroid Society. All Rights Reserved[5]).

Abbrevations: L-T4 – levothyroxine; TSH- thyrostimulating hormone, rhTSH – recombinant human TSH, neck US – ultrasound of the cervical region; WBS – whole body scintigraphy; Tg – thyroglobulin; TgA – antithyroglobulin antibodies.

The Level of Clinical Evidence and Grading of Recommendations Used in the Guidelines

Different methods of evaluation and analysis of the strength of scientific evidence are used in the guidelines[13]. All the listed guidelines are created by expert professional bodies, and in some of the guidelines evidence is evaluated according to strength (Table 2). The ATA guidelines divide the recommendations into seven grades depending on the level of evidence[3,14]. In the NCCN guidelines there are four categories of recommendations. All recommendations are category 2A unless otherwise noted[12]. The BTA guidelines, according to the type of evidence, define six levels of evidence and three grades of recommendation[4]. The Dutch guidelines differ the levels of evidence for the procedures that apply to the intervention or the diagnosis. Resulting level of evidence for recommendation is divided in four categories (1, 2, 3 and 4)[7]. The authors of the EANM guidelines, instead of formally categorizing the level of evidence due to low-level strength of evidence in many aspects of treatment, diagnostic and follow-up of the patients with DTC, have listed the references of the significant trials through which they argu-

TABLE 2
STRENGTH OF RECOMMENDATIONS BASED ON THE AVAILABLE EVIDENCE USED IN VARIOUS GUIDELINES

	ATA	NCCN	Brits*	Dutch**
The recommendation is based on high level of evidence (e.g. meta analysis; randomized control trials)	A – strongly recommends F – strongly recommends against	Category 1	A (Ia, Ib)	A1 A2
The recommendation is based on lower level of evidence (e.g. well-designed controlled study without randomization)	B – recommends E – recommends against	Category 2A	B (IIa, IIb, III)	B C
Evidence obtained from expert committee reports or opinions	C – recommends D – recommends against	Category 2B	C (IV)	D
Disagreement among experts/ Insufficient evidence	I – recommends neither for nor against	Category 3 (major disagreement among experts)		

* Types of evidence that the grades of recommendation are based on, are presented in the brackets
** For procedures regarding intervention and for procedures regarding diagnosis

ment their recommendations[8]. Some other guidelines are also based on the quotations of the »significant« trials and on the »evidence based« medicine, but do not indicate the strength of clinical evidence and grades of recommendations[5,6,9,10].

The Postoperative Radioactive Iodine Administration: Definition

In the postoperative 131-I administration, the terms radioiodine ablation and radioiodine therapy can differ. Certain societies use the term radioiodine ablation for the postoperative 131-I administration in all patients, like ATA, which defines the term radioiodine ablation as the postoperative 131-I administration in patients of all risk groups with appropriate indication[3]. The ETA also considers the postoperative 131-I administration in two risk groups with appropriate indication[9] as radioiodine ablation. The authors of Dutch guidelines define the term ablation in the postoperative 131-I administration by using different activities[7]. The ESMO also states the term ablation of the thyroid remnant, in the low and high risk groups[11]. In the CTS guidelines all terms that refer to the postoperative 131-I administration use the term ablation independently of the risk group[5].

Authors of certain guidelines differentiate radioiodine ablation as a form of adjuvant appliance of the 131-I, whereas radioiodine therapy stands for the appliance of the 131-I in the high risk group of patients. The DGN guidelines differentiate radioiodine therapy used for the adjuvant thyroid remnant ablation from radioiodine therapy in patients with local recurrence, positive lymph nodes and distant metastases[6]. The NCCN guidelines also differentiate adjuvant radioiodine ablation of the thyroid bed with lower activities from radioiodine therapy with higher activities[12]. According to the BTA guidelines radioiodine ablation refers to the 131-I induced destruction of the thyroid remnant, whereas the term radioiodine therapy refers to the 131-I administration in treating loco-regional recurrence or metastatic disease[4]. In the EANM guidelines the administration of 131-I stands for the ablation as a post-surgical adjuvant modality and for the treatment of unresectable or incompletely resectable lesions[8].

Indications for the Postoperative Radioactive Iodine Administration

Indication for the administration of the postoperative radioiodine ablation (therapy) is often considered in some guidelines. Most of the guidelines use the UICC-AJCC--TNM classification to divide the patients into different risk groups[15]. Depending on the indication, patients can be divided into three groups; a group where there is no indication for the 131-I administration, a group where the administration of the 131-I could be considered and a group where there is a clear indication for the 131-I administration. There are some differences in the definition of the group of patients with DTC where there is no indication for the postoperative administration of the 131-I. It is considered that administration of iodine in this group is not indicated due to low risk of recurrence or mortality.

ETA defines this group as one of very low risk, and it includes the patients with complete surgery, favorable histology, unifocal with tumor size ≤1 cm, N0, M0 and without extrathyroid extension[9]. Dutch guidelines recommend unilateral lobectomy for the unifocal papillary carcinomas smaller than <1 cm without positive lymph node or distant metastases, while the 131-I administration is not indicated[7]. The BTA also considers lobectomy as a sufficient surgical procedure in the group of patients with complete surgery, favorable histology, unifocal tumor ≤1 cm in diameter, N0, M0, or minimally invasive follicular thyroid carcinoma, without vascular invasion, smaller than 2 cm in diameter and without extension beyond the thyroid capsule[4]. The DGN guidelines include patients with papillary microcarcinoma (size ≤1 cm) in this group where total or near-total thyroidecomy isn't mandatory[6]. According to the NCCN guidelines there is no indication for radioiodine therapy in patients with limited tumor size (<1 cm), favorable histology, with no local or distant metastasis, thyroglobulin (Tg) level <1 ng/mL with negative antithyroglobulin antibodies (TgA), and negative whole body scintigraphy[12].

The ATA also doesn't recommend radioiodine ablation in patients with solitary and multifocal tumors where all foci are smaller than 1 cm, but with no other high risk features. However, the strength of this recommendation is low, and is based on expert opinion[3]. According to the EANM guidelines radioiodine therapy is not necessary in patients with unifocal papillary carcinoma with ≤1 cm in diameter, without metastasis, thyroid capsule invasion, previous radiation exposure and unfavorable histology[8]. The CTS in the group of very low risk includes the patients with complete surgery, unifocal tumor ≤1 cm, N0, M0, with no thyroid capsule penetration and with favorable histology[5].

Ablation in the Low-risk Group of Patients

The radioiodine ablation in the low-risk group of patients is the subject of many debates. The ablation benefit is not yet confirmed with clear evidence[16–18]. Also, there are different opinions about the optimal activities of the 131-I required for effective ablation of the thyroid residue in this group of patients[19–22]. The ETA introduces probable indication in patients younger than 18 years with tumor T>1 cm; in case of less than total thyroidectomy or no lymph node dissection, with T2, N0, M0 or in case of unfavorable histology, meaning that in some patients from this group the radioiodine administration could be avoided. In the case of application it is advised to use 30 mCi or 100 mCi of 131-I[9]. The ETA/ABL consensus has identical criteria with the difference that patients younger than 16 years are included in this group[10]. The ATA recommends radioiodine ablation in patients with tumor size from 1 to 4 cm, lymph node metastases

and other features which increase the risk of recurrence or death with activities from 30–100 mCi[3]. The ESMO guidelines quote ATA and ETA guidelines in the postablative staging and in the risk evaluation[11].

The probable indication, according to the BTA/RCP guidelines, includes patients with less than total thyroidectomy where status of lymph nodes is not assessed at surgery, with tumor size between >1 cm and <4 cm in diameter, tumors <1 cm in diameter with unfavorable histology and multifocal tumors. In the version from the year 2002, it is advised to use 30–100 mCi, however in the version from the year 2007 the recommendations are for the usage of higher activities (100 mCi) of the 131-I[4]. The Dutch recommend the activities of 50–100 mCi for the thyroid remnant ablation after the thyroidectomy. The ablation is recommended in all patients with DTC, except in those without indications (above mentioned)[7]. In the DGN guidelines the radioiodine ablation is considered as a standard procedure. In microcarcinomas the administration of the radioiodine therapy could be considered depending on the prognostic factors such as closeness to the capsule, family history, previous neck radiation, 5–10 mm tumor diameter. In case of application, the activities from 54 to 100 mCi of 131-I are recommended[6].

The NCCN indicates the radioiodine ablation where, accordingly to the clinical data and 131-I whole body scintigraphy, there exists a reasonable doubt (based on pathology, postoperative values of Tg and on intraoperative findings) or if the thyroid bed uptake is proven. The recommended activities are 30–100 mCi[12]. The EANM considers radioiodine ablation after the total or near total thyroidectomy as a standard procedure in the patients with DTC (except above mentioned). They discuss about the activities in the range from 1 to 5 GBq (27–135 mCi), but no clear recommendations on optimal 131-I dosage are given[8]. The CTS guidelines include in this group all patients that do not belong in the very low risk, or in the high risk group. In this group of patients (T1>1 cm, T2, N0, M0 and T1 multifocal) the application of low and high activities of 131-I is indicated[5].

Radioiodine Therapy in the High-risk Group of Patients

In the postoperative treatment of the high risk patients, the authors of the guidelines agree that there is a definite indication for the radioiodine therapy administration, and suggest the use of higher therapeutic activities of 131-I. The ETA includes in this group patients with persistent disease or with high risk of persistent or recurrent disease, which includes patients with distant metastases or incomplete tumor resection or with complete tumor resection, but high risk for recurrence or mortality, tumor extension beyond the thyroid capsule (T3 or T4) or lymph node involvement. In this group the recommended postoperative 131-I activities are higher than 100 mCi[9]. Similarly to the the ETA guidelines, BTA guidelines also have definite indication for the 131-I administration in case of patient with distant metastases, incomplete tumor resection, but high risk for recurrence or mortality[4].

The ATA guidelines include radioiodine therapy in all patients with distant metastases and extra-thyroid invasion regardless of tumor size and tumors larger than 4 cm[3]. According to the DGN guidelines this group includes the patients with local recurrence, lymph nodes metastases and distant metastases. The use of high activities of 131-I (up to 200 mCi) is recommended[6]. The authors of the NCCN guidelines recommend the administration of high 131-I activities (100–200 mCi) in case of doubt (based on pathology, postoperative Tg values and intraoperative findings) or proven tumor remnant uptake of 131-I[12]. The EANM recommends multiple administrations of 100–200 mCi 131-I in patients with unresectable or partially resectable tumor (for example, local recurrence, lymph nodes metastases or disseminated lung metastases or any other distant iodine-avid metastases)[8].

The CTS guidelines in the high risk group include patients with incomplete tumor resection, distant or regional metastases (N1, M1), extrathyroidal extension (T3, T4) and with unfavorable histology. The authors suggest the administration of 131-I activities in the range of 100 to 200 mCi[5,23]. In the Dutch guidelines for the patients with positive lymph nodes and distant metastases diagnosed with postoperative scintigraphy as for the patients that haven't undergone through the radical resection of the primary tumor, the recommended 131-I activities are in the rage from 100 to 200 mCi[7].

The Preparations for Radioiodine Ablation and Therapy

TSH level

Preparation of patients for the postoperative 131-I administration includes a certain procedures that apply. The authors of the guidelines agree that certain level of the thyrostimulating hormone (TSH) in the serum needs to be reached. The needed level of TSH is slightly different depending on the guidelines: TSH>25 mU/L[7] TSH> 25–30 mU/L[10]; TSH≥30 mU/L[8]; TSH>30 mU/L[3–6,9]. This TSH level can be accomplished endogenously (by thyroid hormone withdrawal or pausing with thyroid hormone intake) or exogenously (by using recombinant human TSH – rhTSH)[24–27].

Preparation of adequate TSH stimulation

The ATA guidelines recommend withdrawal of the levothyroxine (L-T4) for at least 2–3 three weeks in the preparation of the patient for the ablation. Also, 131-I ablation can be performed following rhTSH stimulation, which was approved in the USA for remnant ablation in year 2007[3,28]. The NCCN recommends the administration of 131-I in the period from 2 to 12 weeks after the thyroidectomy and the use of both methods of TSH stimulation (the thyroid hormone withdrawal or stimulation with rhTSH)[12]. In the ETA guidelines the withdrawal of

the L-T4 is recommended during 4–5 weeks[9]. The use of rhTSH is approved in Europe in low risk patients for the administration of 100 mCi 131-I[29].

The Dutch consider the thyroid hormone withdrawal as a »gold standard« procedure, and as an alternative, the rhTSH can be used in the low risk patients for activities of 100 mCi[7]. Unlike the Dutch guidelines, the EANM gives the advantage to the rhTSH (if it is economically justified) as a method of TSH stimulation in moderate or high ablation activities (50–100 mCi 131-I) and in patients which are unable to tolerate the symptoms of hypothyroidism or in which the acceptable level of the TSH couldn't be reached endogenously. The endogenous rise of the TSH is accomplished by not administering L-T4 replacement therapy for at least 3 weeks after the thyroidectomy in recently operated patients or for 4–5 weeks after the withdrawal of the LT4 in patients on L-T4 replacement therapy. For the ablation with the smaller activities both methods of preparation are recommended, while the endogenous stimulation has the advantage when treating the metastatic disease[8]. The authors of the DGN guidelines recommend the radioiodine therapy 3–5 weeks after the thyroidectomy or 4–5 weeks after the withdrawal of the LT4. After stimulation with the rhTSH, high ablation effectiveness can be noted[6].

For the rise of TSH according to the CTS guidelines the recommendation is the withdrawal of L-T4 suppression therapy during four weeks or performing 131-I administration 4 weeks after the thyroidectomy. The use of rhTSH is approved in 2007 for the ablation of thyroid tissue in low risk patients with 100 mCi 131-I. The rhTSH can be used in metastatic disease when the endogenous rise of serum TSH is insufficient, when prolonged L-T4 withdrawal is contraindicated, when the withdrawal is poorly tolerated or when the delay in therapy might be deleterious[5]. In the BTA guidelines the period of 3–4 weeks after the thyroidectomy and without the L-T4 is considered to be enough time for the rise of TSH on satisfying level[4]. In the endogenous method of stimulation, especially when there is longer period between the operation and planned ablation, as an alternative to the L-T4 withdrawal, many guidelines state the use of triiodothyronine (L-T3) and its withdrawal two weeks before the planned administration of 131-I[3–6,8,9].

A low iodine diet

A low iodine diet is used during the preparation of patients for radioiodine ablation/therapy and it is indispensable part in the most of guidelines. This diet is especially recommended to patients with high iodine intake. The most extensive instructions about the low iodine diet and the groceries that should be avoided are listed in the Dutch guidelines. Its implementation is recommended in patients with low thyroid remnant 131-I uptake or with metastatic disease before the therapy[7]. The stands about duration of the low iodine diet are not reconciled; some authors recommend its implementation during 3 weeks[5,9], 2 weeks[4,6]; that is 1–2 weeks[3,8] before the 131-I administration. The Dutch guidelines recommend the diet implementation 1 week before the hospital admittance and few days during of stay[7]. Except of low iodine diet, it is often recommended to avoid iodine contrast agents, antiseptics, eye drops, amiodarone, multivitamin and mineral supplements that contain iodine and sea food 4–6 weeks before the radioiodine therapy[6,8]. Most of guidelines recommend the measurement of urine iodine excretion[5,6,9] to exclude iodine excess, especially when there is doubt[8], and, if it is possible, even routinely. In the case of iodine contamination it is recommended to postpone radioiodine therapy[6].

Postoperative Preablative Radioiodine Scintigraphy

The opinions about the postoperative (preablative, pretherapeutic) 131-I scintigraphy are divided. Some guidelines indicate its use in almost every patient while the others recommend it only in certain patients and even avoiding it if possible. The main reason for avoidance of preablative scintigraphy the authors find in the »stunning« phenomenon, that is, negative effect of diagnostic use of 131-I on later therapy with 131-I[30].

The Dutch guidelines recommend the preablative scintigraphy because of the easier monitoring of all patients, except those with unifocal carcinoma <1 cm, without proven metastatic disease[7]. On the contrary, the ETA guidelines question the use of diagnostic scintigraphy for its little clinical benefit and possible stunning. In the case of questionable extent of operation procedure a scintigraphy with 123-I or with low 131-I activities (1 mCi) can be used[9]. The authors of the BTA guidelines haven't found the indication for routine use of preablative scintigraphy. It can be used for the thyroid remnant evaluation, but even in that case it is recommended to use the 123-I or 99mTc-pertechnetate[4].

The DGN guidelines recommend the use of 123-I in the scintigraphy of neck region after the ablation, that is, the whole body scintigraphy after the radioiodine therapy of metastatic disease. Instead of 123-I, the low activities (1–10 mCi) of 131-I can also be used[6]. The recommendation for postoperative scintigraphy according to the NCCN is marked as the 2B category of recommendation, which means there is no unique stand about it. In the decision making the possibility of stunning should be considered, and in any case it is recommended to reduce the period between the diagnostic and therapeutic use of 131-I[12].

The authors of ATA guidelines state the significance of preablative scintigraphy in the thyroid remnant size evaluation, when it is impossible to determine it from ultrasound and surgical findings. In the case of indication for this test the small activities of 131-I (1-3 mCi) are recommended[3]. The EANM guidelines do not recommend the use of pretherapeutic scintigraphy when there is indication for the 131-I therapy. If the scintigraphy is performed, it is recommended to use 123-I or low activities 131-I[8]. In CTS guidelines the preablative scinti-

graphy is often avoided and it is used only when the results of scintigraphy are necessary for the decision on therapy or therapeutic activity of 131-I[5].

Conclusion

The indications and procedures for implementing ablation, that is, radioiodine therapy, significantly differ according to certain guidelines. The biggest disagreements exist between the criteria for setting up indications for use of 131-I and determining the optimal ablative activity in the low risk group of patients, that is, regarding the conductance of postoperative 131-I diagnostic scintigraphy. The guidelines differ in their shape and the methodology for evidence – based recommendations. Most of the guidelines suggest use of low iodine diet. Also, the sufficient level of TSH is not very different among certain guidelines. All the guidelines need to be updated with high level of evidences on a regular basis in order the recommendations could have higher clinical significance.

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POSTOPERATIVNA PRIMJENA RADIOAKTIVNOG JODA (131-I): PREGLED SMJERNICA I PREPORUKA

SAŽETAK

Važnu ulogu u liječenju velikog broja bolesnika s diferenciranim karcinomom štitnjače čini primjena radioaktivnog joda (131-I). U prethodnih nekoliko godina objavljene su i obnovljene smjernice mnogih međunarodnih i nacionalnih

liječničkih društava koje se odnose na postoperativnu primjenu 131-I. Smjernice se međusobno razlikuju u svom obliku i u sadržaju te sadrže neke posebnosti. U smjernicama se koriste različiti sustavi vrednovanja i analiziranja jačine kliničkog dokaza i stupnjeva preporuke koje iz toga proizlaze. Postoperativna primjena 131-I označava radiojodnu ablaciju, kao oblik adjuvantnog liječenja te radiojodnu terapiju u liječenju bolesnika s recidivom, perzistentnom bolesti te regionalnim ili udaljenim metastazama. Prema indikaciji za postoperativnu primjenu 131-I bolesnici se mogu podijeliti u tri rizične skupine: skupinu vrlo niskog rizika u kojoj ne postoji indikacija za postoperativnu primjenu 131-I, skupinu niskog rizika u kojoj se indikacija može razmotriti te skupinu visokog rizika kod koje postoji jasna indikaciju za primjenu 131-I. U pojedinim smjernicama se navode različiti kriteriji za podjelu bolesnika u ove tri skupine. Mišljenja se razlikuju o dozi 131-I potrebnoj za efikasnu ablaciju u skupini bolesnika niskog rizika. Mišljenja o provođenju postoperativne (preablacijske odnosno preterapijske) scintigrafije s 131-I su podijeljena. U pripremi bolesnika za radiojodnu ablaciju i terapiju u svim smjernicama se savjetuje primjena dijete s malo joda te endogena ili egzogena stimulacija TSH. Endogena stimulacija se postiže povlačenjem hormona štitnjače, dok se rekombinantni humani TSH (rhTSH) koristi u egzogenoj stimulaciji. Dostatna razina TSH u serumu potrebna za provođenje terapije s 131-I iznosi >25–30 mU/L.