A B S T R A C T

Most patients with newly diagnosed differentiated thyroid carcinoma have tumours with low risk of mortality and recurrence. Standard therapy has been total or near total thyroidectomy followed by post-operative radioiodine remnant ablation (RRA). Although RRA provides benefits, current clinical guidelines do not recommend it universally, since an increase in disease-free survival or a decrease in mortality in low risk patients has not been demonstrated so far. Advancements in our understanding of the biological behaviour of thyroid cancer have been translated into the clinic in a personalised approach to the patients based on their individual risk of recurrence and mortality. Current evidence suggests that RRA is not indicated in most low-risk patients, especially those with papillary carcinomas smaller than 1 cm, without extrathyroidal extension, unfavourable lymph node involvement or distant metastases. Follow-up of these patients with serial measurements of serum thyroglobulin and neck ultrasound is adequate. Careful evaluation of all risk factors of clinical relevance will allow a more realistic assessment of each individual patient.

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Ablación posquirúrgica con radioyodo en pacientes con carcinoma diferenciado de tiroides de bajo riesgo

R E S U M E N

La mayoría de los pacientes con carcinoma diferenciado de tiroides presentan tumores de bajo riesgo de mortalidad y recidiva. El tratamiento estándar de estos tumores ha consistido en la tiroidectomía total o casi total, seguida de la ablación de los restos tiroides con radioyodo (ARI). Aunque la ARI aporta ventajas, las actuales guías clínicas no la recomiendan de forma universal, ya que no se ha demostrado que aumente la supervivencia libre de enfermedad o reduzca la mortalidad en pacientes de bajo riesgo. Los avances en la comprensión del comportamiento biológico del cáncer de tiroides se han traducido en la clínica en una aproximación personalizada al paciente basada en su riesgo particular de recidiva y mortalidad. La evidencia actualmente disponible muestra que la ARI no está indicada en la mayoría de los pacientes de bajo riesgo, especialmente los que presentan carcinomas papilares menores de 1 cm, sin extensión extratiroidea, histología desfavorable, compromiso ganglionar ni metástasis a distancia. El seguimiento de los pacientes de bajo riesgo con determinaciones de tiroglobulina sérica y ecografías seriadas se considera suficiente. La evaluación cuidadosa de todos los factores de riesgo de relevancia clínica nos permitirá una evaluación más realista de cada paciente concreto.

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Introduction

Radioiodine (RI) has been used since the 40s due to the ability of thyroid follicular cells to capture and concentrate this element through the sodium-iodide transporter. RI ablation (RIA) refers to the first administration of this radio drug in a patient with differentiated thyroid carcinoma (DTC) in order to remove the thyroid tissue remnants left after total thyroidectomy. This procedure is generally used 4–8 weeks after surgery and must not be confused with RI treatment, which refers to the administration of therapeutic doses of RI in patients with persistent or recurrent disease after a proper surgical treatment, in order to destroy macroscopic structural disease. Total thyroidectomy followed by RIA and thyroid hormone suppressive treatment improves the overall survival of patients with medium-to-high risk DTC. However, there is an important group of patients with low-risk DTC that have an excellent prognosis, even without RIA, and represent almost 50% of all the thyroid cancer cases currently.

The selection of patients that need not receive RIA and the dosage required are controversial subjects. Clinical guidelines recognise that there are groups of patients in which the indication is mandatory, others in which its use is selective and, finally, others in which it must not be administered. The controversy began when some authors showed that some low-risk patients with theoretically no RIA indication might present lymph node metastases and other characteristics that increase the risk of recurrence during follow-up. This article analyses the basics of RIA, its advantages and disadvantages and, finally, the current criteria for the indication or lack of indication for this procedure in patients with low-risk DTC.

Definition of low-risk patient

It is important not to confuse the risk of mortality with the risk of recurrence of the disease. The TNM staging system is given to patients in 4 stages and is used to assess overall and specific mortality (Table 1). Stage I includes patients <45 years without distant metastases and patients >45 years with tumours <2 cm without lymph node or distant metastases. In patients <45 years, stage I is defined by the presence of distant metastases, while in older patients, stage II includes tumours of up to 4 cm without lymphatic or distant metastases. Low-risk patients are those included in stages I and II of the American Joint Committee on Cancer without distant metastases, since they practically have a 100% survival after 5 years.

However, to estimate the risk of persistence or recurrence of the disease, other clinical and histological parameters are used. The European Consensus defines very low-risk and low-risk patients pursuant to the characteristics shown in Table 1. These patients have a long-term recurrence rate lower than 2%. The American Thyroid Association (ATA) classifies the risk of recurrence as low, intermediate and high. The patients from the first group present a risk of recurrence of 3%. Basics of radioiodine ablation

Objectives

RIA is a form of radioisotope treatment used after a total thyroidectomy, with the objectives included in Table 2. In low-risk patients, the objective of RIA is to remove all the remaining normal thyroid tissue, as well as to destroy possible microscopic tumour remnants not removed during surgery, in order to facilitate the follow-up of the patient with serum thyroglobulin (Tg) determination and full body scans. The Tg is a specific marker of tumour recurrence in patients treated with surgery followed by RIA.

In patients with intermediate or high risk, RIA is a form of adjuvant treatment whose objective is to treat the postoperative or metastatic residual disease, as well as to conduct a full body scan 2–5 days after the RIA for the assessment of the distant disease with a higher sensitivity than scans with diagnostic doses.

Preparation

The preparation of the patient requires a diet low in iodine (<50 μg/day) during the 2–3 weeks prior, no iodine medication, and thyrotropin (TSH) serum levels above 30 mU/L to achieve sufficient RI capture in the healthy or tumour thyroid tissue remnants. An increase in TSH can be achieved by an increase in endogenous TSH through the withdrawal of the treatment with levothyroxine during 4–6 weeks or the administration of recombinant human TSH (rhTSH) (2 injections of 0.9 mg during 2 consecutive days). The advantages of using rhTSH include improvements in the quality of life of patients by avoiding the symptoms of hypothyroidism and a reduced exposure to radiation of the extrathyroidal tissues, since the clearance of RI is quicker than in the case of hypothyroidism. Pregnancy must be avoided during the administration of RIA and during the following 6–12 months.

Dosage and activity

Ablation is generally achieved when the dose absorbed by the thyroid remnant is equal to or higher than 300 Gy. To estimate the activity of RI required by each patient to achieve this dose, two methods are used: the empirical method and the dosimetric method. The first one is based on the experience and the assessment of several factors, such as the patient’s age, the tumour size and histology, the presence of extrathyroidal extension and metastasis. It uses fixed activities ranging from 30 to 200 mCi. The dosimetric method is more complex and involves the calculation, through or of the radiation absorbed by the various organs, in order to administer the highest tumoricidal dose and avoid undesirable doses in critical organs, such as the lungs and bone marrow.

Two recent randomised clinical trials have compared the RIA success rates after the administration of 30 and 100 mCi, with levothyroxine withdrawal and rhTSH stimulation procedures in low and intermediate risk patients. The results, which were very similar, showed that the ablation success rate did not change when using low or high doses of RI, nor when increasing endogenous or exogenous TSH (Table 3). Fewer adverse events were observed after the administration of 30 mCi of RI and after the preparation with rhTSH, As a corroboration of these findings, 2 recent meta-analyses, one with 7 randomised trials including 1772 patients and another one with 9 randomised trials including 2,569 patients, demonstrate that there are no significant differences as to the success of percentages of ablation nor as to the scores of the test on quality of life with activities of 30, 50 and 100 mCi. Moreover, data showed that the lowest dose involved reduced adverse events and admission times.

The rate of long-term recurrence also seems similar when levothyroxine or rhTSH withdrawal is implemented. A recent study examined, during a 10-year follow-up, 159 patients with DTC, most of whom were low or intermediate-risk patients, who received RIA with low activity (30 mCi) and were prepared with rhTSH or withdrawal. The authors found no significant differences among these groups regarding the rates of remission or recurrence.
Ablation benefits

One of the advantages of RIA is that it allows the conduction of a full body scan 2–5 days after the administration of RI, which is a high sensitivity test for the detection of disease sites outside the thyroid bed. Besides, RIA facilitates the patient follow-up and the detection of recurrent disease through the determination of Tg or the conduction of diagnostic scans with RI.\textsuperscript{17} After the thyroidectomy plus RIA, the detectable serum Tg results from tumour cells, which is an unquestionable advantage offered by this procedure.\textsuperscript{12}

It also seems evident that RIA improves survival and reduces the recurrence in high-risk patients, but this is not so evident in low-risk patients. In fact, the initial study conducted by Mazzaferri and Jhiang\textsuperscript{20} showed, in a group of 1,355 patients with DTC, with a follow-up median of 15.7 years, that the rates of recurrence and specific mortality were about 3 times lower in patients who received RI after surgery than those who did not. However, more recent studies have not been able to confirm these initial results, especially when analysed in low or intermediate-risk patients.\textsuperscript{21}

The broad meta-analysis conducted by Sawka et al.,\textsuperscript{22} including 28 observational studies with more than 5,000 patients, could not confirm the efficacy of RI regarding the reduction of the rate of recurrence or specific mortality in low-risk patients. A prospective study conducted by the National Thyroid Cancer Treatment Cooperative Group in 2936 patients in stage I did not show any significant benefit from RIA regarding overall, specific and disease-free survivals.\textsuperscript{23} An extension of this study conducted with 4767 patients concluded that RIA in patients with stage I DTC offered no survival benefits.\textsuperscript{24} These studies are limited by a relatively short follow-up period (5.3 years). However, another recent observational multicentre study including 1,300 low-risk patients, with more than 10 years of follow-up, determined that the use of RI did not extend the overall or the disease-free survival in low-risk patients.\textsuperscript{25}

In conclusion, the evidence available to date, based on observational studies, given that there are no randomised clinical trials, has shown no definite benefits from RIA regarding the reduction of the rate of recurrence or mortality in patients with low-risk DTC.\textsuperscript{22–25}

Ablation risks

RI is considered a safe treatment, though it has adverse events, such as those included in Table 4, most of which are temporary. The risk of leukaemia or other neoplasias increases especially

Table 1
Stratification of the risk of mortality and risk of recurrence or persistence in patients with differentiated thyroid carcinoma.

<table>
<thead>
<tr>
<th>Risk of mortality (AJCC/UICC classification)</th>
<th>( &lt;45 ) years</th>
<th>( \geq 45 ) years</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>M0</td>
<td>T1N0M0</td>
</tr>
<tr>
<td>II</td>
<td>M1</td>
<td>T2N0M0</td>
</tr>
<tr>
<td>III</td>
<td>T1-2, N1a, M0</td>
<td>T3, N0-1a, M0</td>
</tr>
<tr>
<td>IVA</td>
<td>T1-3, N1b,M0</td>
<td>T4a, N0-1b, M0</td>
</tr>
<tr>
<td>IVB</td>
<td>T4b, M0</td>
<td>M1</td>
</tr>
</tbody>
</table>

Risk of recurrence or persistence

<table>
<thead>
<tr>
<th>ATA</th>
<th>European Consensus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low risk</td>
<td>Very low risk</td>
</tr>
<tr>
<td>Completely removed primary tumour</td>
<td>Unifocal microcarcinoma (( \leq 1 ) cm)</td>
</tr>
<tr>
<td>No extrathyroidal extension. No lymph node metastases.</td>
<td>No extrathyroidal extension. No lymphatic metastases</td>
</tr>
<tr>
<td>No distant metastases. No vascular invasion</td>
<td>Complete surgery. Favourable histology</td>
</tr>
<tr>
<td>If RIA is conducted: no capture outside the thyroid bed</td>
<td></td>
</tr>
<tr>
<td>Intermediate risk</td>
<td></td>
</tr>
<tr>
<td>Microscopic extrathyroidal extension</td>
<td></td>
</tr>
<tr>
<td>Cervical lymph node metastases</td>
<td></td>
</tr>
<tr>
<td>Aggressive histology\textsuperscript{4}</td>
<td></td>
</tr>
<tr>
<td>Vascular invasion</td>
<td></td>
</tr>
<tr>
<td>Extrathyroidal capture after RIA</td>
<td></td>
</tr>
<tr>
<td>High risk</td>
<td></td>
</tr>
<tr>
<td>Macroscopic extrathyroidal extension</td>
<td></td>
</tr>
<tr>
<td>Incomplete tumoral resection</td>
<td></td>
</tr>
<tr>
<td>Distant metastases</td>
<td></td>
</tr>
<tr>
<td>Inadequately high or increasing thyroglobulin</td>
<td></td>
</tr>
</tbody>
</table>

AJCC/UICC: American Joint Committee on Cancer/Union Internationale Contre le Cancer; RIA: postoperative radioiodine ablation; ATA: American Thyroid Association; MD: no distant metastasis; M1: distant metastasis; N0: no lymph node metastasis; N1a: central cervical lymph node metastasis (level VI); N1b: other lymph node metastasis (levels I–V or VII); T1: tumour \( \leq 2 \) cm; T2: tumour \( >2 \) cm to 4 cm; T3: tumour \( >4 \) cm or minimum extrathyroidal invasion; T4a: macroscopic extrathyroidal invasion; T4b: macroscopic invasion of fascia or prevertebral vessels.\textsuperscript{4} Aggressive histology: variant of tall cells, columnar cells, diffuse sclerosing cells (papillary carcinoma); highly-invasive and poorly differentiated (follicular carcinoma). Summarised and adapted from Pacini et al., Cooper et al.\textsuperscript{1} and American Joint Committee on Cancer.\textsuperscript{2}

Table 2
Objectives of radioiodine ablation in patients with low-risk differentiated thyroid carcinoma.

<table>
<thead>
<tr>
<th>Objective</th>
<th>Additional benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remove any normal thyroid tissue remnants left after the surgery</td>
<td>Increase the specificity of serum Tg (facilitate follow-up)</td>
</tr>
<tr>
<td>Destroy small hidden sites of DTC</td>
<td>Reduce the rate of recurrence (adjuvant treatment)</td>
</tr>
<tr>
<td>Allow the conduction of a full body scan after RIA with high sensitivity</td>
<td>Detect locoregional and distant diseases</td>
</tr>
</tbody>
</table>

RIA: postoperative radioiodine ablation; DTC: differentiated thyroid carcinoma; Tg: thyroglobulin.
with high-accumulation activities. Rubino et al.25 determined that a 100 mCi dose of RI would result in an overall increase of the risk of second neoplasia in 27% and that there was a linear dose-response relationship between RI and the appearance of tumours. In a cohort of 30,278 patients with DTC who participated in the SEER programme, after a 103-month average follow-up, there was a 20% increase of the risk of second neoplasia in patients who had received RI.26 Additionally, the most recent results from the SEER database show that the incidence of second neoplasia due to exposure to RI is increasing slightly in patients with low-risk thyroid cancer.27 Another study, conducted in 895 patients with DTC, showed that the accumulated risk of second neoplasia after 20 years was significantly higher in patients who had received RI compared to those who had not received it (13.5 versus 3.1%).28 These results, combined with the lack of evidence that RI treatment improves survival in low-risk patients, show that the generalised use of RIA leads to overtreatment, followed by problems for the patient and economic costs.

**Follow-up of no ablation patients**

The follow-up of low-risk patients may be conducted through serial determinations of Tg during the treatment with levothyroxine and cervical scans. In a group of 290 low-risk patients who did not receive RIA, 60% of them had undetectable Tg during the first year of thyroidectomy. In the rest of the patients, Tg was detectable during the first year, but it progressively and spontaneously decreased later on, so, after 5 years, 79% of the patients had undetectable Tg and 95% of them had Tg under 1 ng/ml.30 Only one of 290 patients had recurrence, which was associated with a gradual increase of Tg levels.

The specificity of Tg in RIA patients is reduced during the first year, but its level increases as the follow-up continues. Residual normal thyroid cells usually stabilise or reduce Tg production, unlike neoplastic cells. Therefore, the increasing or decreasing tendency of its levels is essential.31,32

The scan is important for patients both with and without RIA and it provides valuable information about the location of the disease. Several studies have demonstrated that cervical scans are more sensitive to the detection of lymphatic metastases than stimulated Tg or RI scans.32 Besides, they have an excellent predictive value, especially in low-risk cases. Therefore, their use is particularly useful during the first months of follow-up in low-risk patients without RIA, when serum Tg results are more difficult to interpret. A negative scan during the first months indicates an almost 100% chance of having a favourable long-term result, regardless of serum Tg.33 The specificity of this test may increase by conducting puncture-aspiration cytology of suspicious nodes according to the scan34 and Tg measurement in needle washout fluids.9

In patients with anti-Tg antibodies, follow-up must be carried out through cervical scans and diagnostic scans. However, serial antibody titres may be used as a surrogate marker of thyroid or tumour remnants. In these patients, the decrease in antibody titres is considered an indicator of recovery from the disease.33 Logically, diagnostic full body scans are more sensitive in patients who have received RIA. However, after a thyroidectomy conducted by expert surgeons, capture within the thyroid bed is generally low, and this level of capture does not usually prevent the visualisation of distant metastasis, if a diagnostic scan is conducted.34

### Risk stratification

Most DTC classified as low-risk carcinomas are not very aggressive. Some retrospective studies have demonstrated that there are, however, thyroid papillary microcarcinomas (TPMC) that may be accompanied by lymphatic metastases8 or other characteristics that worsen prognosis, such as extrathyroidal extension and multifocality.4,35,36 In spite of that, specific mortality in these patients is still very low, with a survival rate higher than 99% after 10 and 15 years.37 Therefore, when deciding whether or not to use RIA in specific patients, it is essential to assess their risk of recurrence, which may be based on various variables, including the characteristics of the tumour and the host.

Unlike what happens with papillary carcinomas larger than 1 cm, the age ≤45 years was a negative prognostic factor in patients with TPMC in one study,9 given that it was more commonly associated with other risk factors. Younger patients commonly have

### Table 3

Success of postoperative radiiodine ablation in patients with differentiated thyroid carcinoma according to the results of 2 recently published randomised, Phase III clinical trials.

<table>
<thead>
<tr>
<th></th>
<th>Estimab13</th>
<th>HiLo24</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (total/assessable)</td>
<td>752/684</td>
<td>438/421</td>
</tr>
<tr>
<td>Characteristics of the patients</td>
<td>≥18 years old; 78% female patients; 9.4% lymph node metastases</td>
<td>16–80 years old; 74% female patients; 16% lymph node metastases</td>
</tr>
<tr>
<td>Characteristics of the tumour</td>
<td>T1/any N or T2N0; no metastasis</td>
<td>T1 to T3/any N/M0</td>
</tr>
<tr>
<td>Ablation assessment (months)</td>
<td>6–10</td>
<td>6–9</td>
</tr>
<tr>
<td>Definition of ablation success</td>
<td>Normal cervical scan and Tg stimulated with rhTSH ≤1 ng/ml (or negative scan in patients with anti-Tg antibodies)</td>
<td>Tg &lt;2 ng/ml and negative scan</td>
</tr>
</tbody>
</table>

rhTSH: recombinant human thyrotropin; Tg: serum thyroglobulin.

Summarised and adapted from Schlumberger et al.13 and Mallick et al.14

### Table 4

Advantages and disadvantages of postoperative radiiodine ablation.

<table>
<thead>
<tr>
<th>Advantages</th>
<th>Risks or disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Possibility of scan after the ablation</td>
<td>Sialadenitis, keratoma, dental caries</td>
</tr>
<tr>
<td>Facilitation of follow-up and detection of recurrence or persistence</td>
<td>Nasolacrimal obstruction, epiphora</td>
</tr>
<tr>
<td>Improvements in survival of high-risk patients</td>
<td>Radiation thyroiditis</td>
</tr>
<tr>
<td>Possible reduction of the risk of recurrence</td>
<td>Gonadal dysfunction</td>
</tr>
<tr>
<td></td>
<td>Risk of second neoplasia</td>
</tr>
</tbody>
</table>
larger TPMC, extrathyroidal extension and lymphatic metastases, as well as a greater chance of recurrence in the future. 38 The male sex has also been associated with a higher risk of recurrence of tumours 39 and lymphatic metastases. 40

Some authors believe that the 1 cm limit size is arbitrary and that other sizes may better show if RIA is needed or not. Lee et al. 41 showed that TPMCs ≤7 mm had a lower chance of central lymph node metastases (30.6%) than 7–10 mm carcinomas (47.8%). Extrathyroidal extension 35 and multifocality, 4 as well as the presence of lymphatic metastases, 35,40 are also more common in 7–10 mm TPMCs.

Multifocality has also been observed in about one third of the patients with TPMC. 3,4,8,35,36,42 It is associated with larger tumours, lymphatic metastases and extrathyroidal histology. However, when all sites are <1 cm, current data shows that multifocality does not increase the risk of recurrence, 38 and that RIA provides no benefits regarding the prevention of recurrence. 42 Therefore, multifocality by itself should not be considered a risk factor for RIA, provided that all sites are no larger than 10 mm. 42

The compromise of lymph nodes has been estimated in 27–42% of TPMC cases in more recent studies, 4,35,36,40 but this figure may be underestimated, since lymphadenectomy is not generally conducted when an incidental microcarcinoma is found. Lymphatic metastases are more common in male patients, in young patients (<45 years) and in multifocal TPMC cases, with extrathyroidal extension and larger than 6 mm. 40 The presence of lymph node metastases upon diagnosis has also been associated with the recurrence of the disease during follow-up in a study including 445 patients with TPMC, with a 5.3-year average follow-up, 35 and in another study involving 231 patients with TPMC, with a 12-year follow-up. 38

The histological variants that are considered to be high risk are tall cells, columnar cells, and diffuse scirrhous cells for papillary carcinoma, and highly invasive cells and poorly differentiated cells for follicular carcinoma. Some studies, 43 though not all of them, 40 have demonstrated that the follicular variant of papillary carcinoma is less associated with lymphatic metastases.

Recently, studies have demonstrated that the BRAFV600E mutation is a marker that could improve the prognostic stratification in patients with papillary carcinoma. Some studies, 44,45 though not all of them, 46,47 have associated the presence of the BRAFV600E mutation with lymphatic metastases, extrathyroidal extension and recurrence of the disease and, in general terms, with a more aggressive biological behaviour, even in low-risk patients.

According to some authors, in patients with this mutation, RIA seems advisable to increase the reliability of serum Tg during follow-up, while mutation negativity would render the RIA unnecessary in these low-risk patients, given their high negative predictive level. 45,46 However, the BRAFV600E mutation has been observed in 24–63% of patients with TPMC, and it is unlikely that all of them have aggressive behaviour, so the presence of this mutation is not an absolute predictive agent; instead, it should be assessed together with other histopathologic and clinical characteristics for the stratification of risk. 45

Current indications of ablation

Unfortunately, there are no homogeneous indications in the clinical practice guidelines currently en force. In general, these guidelines distinguish between 3 groups of patients: a group where there is no RIA indication, another where its administration is clearly indicated and, finally, a last group where administration of RIA should be considered or conducted in a selective manner (Table 5).

The European Consensus 5 considers that there is no need for ablation in cases with low risk of recurrence and specific mortality, as with unifocal tumours ≤1 cm, without lymph node metastases or extrathyroidal extension, with favourable histology and complete surgery. Probable indication cases include those with any of the following characteristics: less than total thyroidectomy, no lymphatic dissection, age <18 years, T1 tumours >1 cm or T2 tumours (N0M0), or unfavourable histology.

The ATA does not recommend the administration of RIA to patients with tumours of 1 cm or less, intrathyroidal or microscopic
multifocal tumours without documented lymphatic metastases and complete surgery. Selective use is for intrathyroidal tumours of 1–2 cm, intrathyroidal T2 tumours (>2–4 cm), T3 tumours of any size with minimal extrathyroidal extension and also, for N1 cases. The guidelines of the National Comprehensive Cancer Network do not recommend RIA for unifocal or multifocal microcarcinomas in the thyroid gland and recommend a selective use in patients with tumours of 1–4 cm in the thyroid gland, with a high-risk histology, vascular invasion or cervical lymph node metastases when the combination of clinical factors indicates a significant risk of recurrence or specific mortality. Other guidelines provide recommendations very similar to those mentioned above.

All experts recommend RIA in patients with tumours of any size, with macroscopic extrathyroidal extension and distant metastasis. The European Consensus also recommends RIA in cases of incomplete tumoral resection, tumours with extrathyroidal extension (T3 or T4) and in the presence of lymph node metastases.

The lowest necessary dose must be used to achieve ablation, especially in low-risk cases. The Estimabi and HiLo studies have shown the equivalence of 30 and 100 mCi doses of RI in low-risk patients, so we should increasingly tend to administer low doses in patients of this group who require RIA (tumours of 1–2 cm). It has also been suggested that these low doses should be selectively used in moderate-risk patients (T2, N1) and traditional doses should be used in high-risk patients (T3, T4, M1). It has been shown that the use of rTSH increases the quality of life of patients and reduces exposure to radiation in non-thyroidal tissues, compared to the stimulation of endogenous TSH with T4 withdrawal.

Conclusion and future perspective

RIA is necessary in patients with progressed, aggressive or metastatic disease, but these patients are a minority in current medical consultations. The most common are patients with small DTC and low risk of recurrence, for whom RIA should be limited. The final decision regarding the administration of RIA to low-risk patients may be complex and delicate. General practitioners must avoid unnecessary treatments in most cases, but have to indicate these for a minority of patients who really need them. In our opinion, clinical, radiologic, histologic, molecular and biochemical data must be carefully assessed before making a decision. It is advisable that physicians clearly and objectively explain to patients the advantages and disadvantages of RIA, make sure that patients understand these and take into account their preferences when making a decision.

It is true that some physicians recommend RIA in low-risk patients in order to facilitate their follow-up and that some patients may feel comfortable with this approach. In these cases, the 30 mCi dose may be appropriate, since it has an effectiveness rate similar to that achieved by higher doses. The use of rTSH prevents the occurrence of adverse events resulting from hypothyroidism, which leads to the withdrawal of levothyroxine, which increases the quality of life of patients.

Future research must provide data from clinical trials that compare the long-term results of ablation with no ablation in a population with a considerable number of patients and appropriate follow-up in order to achieve an acceptable statistical power.

In the near future, we will also have data showing if the so-called mini-activities (20 mCi) can be as effective as higher activities and if levothyroxine micro-withdrawal techniques, together with a unique injection of rTSH, could lead to an attractive alternative to ablation. Computer systems that help decision makers could be useful in clinical practice. Finally, molecular biology developments will make it possible to define, with greater safety, the biological behaviour of tumours.

Conflict of interest

The authors affirm that they have no conflicts of interest regarding this article.

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