ONCOLOGÍA roe-solca.ec ORIGINAL ARTICLE

Dynamic risk of recurrence in patients with thyroid microcarcinoma with and without iodine-131 ablation

Mónica Guisellaa Mejía Naranjo [1]*, José Camilo López Estrella [2]

1. Endocrinology Service, Enrique Ortega Moreira General Hospital, Ministry of Public Health, Durán-Ecuador.
2. Endocrinology Service, Hospital de Especialidades Teodoro Maldonado Carbo, Ecuadorian Institute of Social Security, Guayaquil-Ecuador.

***Correspondence:**

dramomena@hotmail.com

Address: Eloy Alfaro Manzana A, Solar 4, Vía Guayas-Durán, kilómetro 2.5. Durán, Guayas.

Conflict of interest: The authors declare that they have no conflicts of interest.

Received: January 30, 2023
Accepted: February 10, 2023
Published: April 12, 2023
Editor: Dr. Lorena Sandoya

Cite:
Mejía M, López J. Dynamic risk of recurrence in patients with thyroid microcarcinoma with and without iodine-131 ablation. Revista Oncología (Ecuador) 2023;33(1):70-80.

ISSN: 2661-6653

DOI: https://doi.org/10.33821/669

SOCIEDAD DE LUCHA CONTRA EL CÁNCER-ECUADOR.

Abstract

Introduction: Differentiated thyroid cancer has increased in incidence in the last three decades due to overdiagnosis of small tumors or microcarcinomas; new trends in its management make surgery and radioactive iodine therapy the treatment of choice for selected cases. The current direction of thyroid microcarcinoma is based on the initial risk of recurrence and its follow-up over time with the dynamic risk of recurrence. Objective: The present work focused on analyzing the risk of dynamic recurrence in patients with thyroid microcarcinoma who received or did not receive ablative therapy with iodine-131 after surgical treatment at the Teodoro Maldonado Carbo Hospital during the years 2016 - 2018.

Methods: An ambispective, nonexperimental, descriptive, analytical, cross-sectional, and correlational study was conducted. Fifty-one patients treated at the endocrinology technical unit were analyzed.

Results: Of 51 cases of microcarcinoma, 60% were treated with ablative therapy, and the initial response was excellent in 53.3% of ablated patients and 66.7% of nonablated patients. The initial recurrence risk was significantly lower in the group not treated by ablation (100%), while in the group treated with ablation, it was low, intermediate, and high in 16 (53.3%), 7 (23.3), and 7 (23.3) patients, respectively.

Conclusions: There is a low risk of dynamic recurrence, regardless of the indication for ablative therapy with I131; recurrence risk stratification is a valuable tool for selecting patients who should receive radioactive iodine.

Keywords:

MESH: Thyroid Neoplasms; Iodine Radioisotopes; Thyroid Carcinoma, Anaplastic; Ablation Techniques

DOI: 10.33821/669

Introduction

Differentiated thyroid cancer is the fifth most common among women, accounting for 3.1% of all new cancers. Since 1990, the incidence of this cancer has increased, but its mortality remains stable at a rate of 0.5 deaths per 100,000 people [1].

It is considered that this increase in incidence is due to early diagnosis of small tumors or microcarcinomas (microcarcinoma being understood as those tumors smaller than 1 cm).

The current worldwide trend in managing these tumors is conservative surgical and ablative treatment with iodine 131, indicated in selected cases that meet specific inclusion criteria [2-4].

After the initial surgical treatment, the risk of recurrence is stratified and defined. Accordingly, the need for ablative treatment with iodine 131 is evaluated, with subsequent follow-up over time with biochemical and imaging data, which is throughout what we call dynamic recurrence risk assessment, which will tell us if there is an excellent, indeterminate, incomplete structural, or insufficient biochemical response [5- 7].

In China, a retrospective study was carried out between 2012 and 2018. They found that the recurrence rate of thyroid cancer after surgery is between 23-30%, generally due to an inadequate presurgical evaluation, which does not detect metastases to lymph nodes appropriately early. Among the risk factors for recurrence are tumor size (microcarcinomas are the ones with the lowest risk of recurrence, being more frequent in tumors with a length between 2-4 cm), those of undifferentiated histological type, and those with lymph node metastases are those with the highest risk of recurrence [8].

The risk of recurrence of papillary thyroid cancer (the most common histological type) is influenced by certain clinicopathological factors, such as tumor multifocality, extrathyroidal extension, invasion of lymph nodes in the central region of the neck, and number of lymph nodes invaded [9].

The 2020 NCCN Guidelines indicate that the risk of recurrence in unifocal papillary thyroid microcarcinomas is between 1% and 2% and between 4% and 6% in multifocal microcarcinomas, with approximately 20% metastasizing to cervical lymph nodes. Some investigators report that up to 60% of cervical lymph node metastases in multifocal microcarcinomas are associated with distant metastases [10].

This study aimed to analyze the risk of dynamic recurrence in patients with thyroid microcarcinoma who received or did not receive ablative therapy with iodine-131 after surgical treatment at the Teodoro Maldonado Carbo Hospital.

Materials and methods

Study design

The present study is cross-sectional. The source is retrospective.

Scenery

The study was carried out in the endocrinology service of the Hospital de Especialidades Teodoro Maldonado Carbo of the Ecuadorian Institute of Social Security in Guayaquil-Ecuador. The study period was from January 1, 2016, to December 31, 2018.

Participants

Older patients with a diagnosis of thyroid cancer were included. Clinical records with the ICD-10 code C73 were included. Cases with incomplete data were removed for analysis. Patients without histopathological reports were excluded. Two groups were formed: Group 1 included patients who underwent thyroidectomy and received radioactive iodine 131. Group 2 included patients who underwent thyroidectomy and did not receive radioactive iodine 131.

Variables

The study variables included sociodemographic characteristics, thyroglobulin, TSH, locoregional structural alterations or a. distance, risk of dynamic recurrence (independent variable), and therapeutic response (dependent variable).

Data sources/measurements

The source was indirect; reviews of medical records were carried out in the statistics department and the institutional electronic file AS400. The information was treated confidentially; no personal data were included to allow the identification of the study subjects. The presence of locoregional or distant structural alterations was determined with neck ultrasound, tomography, and scintigraphy.

Biases

To avoid possible interviewer, information, and memory biases, the principal investigator always kept the data with a guide and records approved in the research protocol. Observation and selection bias was avoided by applying the participant selection criteria. All the clinical and paraclinical variables of the period above were recorded. Two researchers independently analyzed each of the records in duplicate, and the variables were recorded in the database once their concordance was verified.

Study size

The sample was nonprobabilistic, census type, where all possible cases of the study period were included.

Quantitative variables

Descriptive and inferential statistics were used. The results were expressed on a scale of means and standard deviation. Categorical data are presented in proportions.

Statistical analysis

Noninferential and inferential statistics are used. For the descriptive analysis, measures of central tendency and dispersion were calculated according to the measurement scale of each variable. Qualitative variables are presented as absolute numbers and percentages; quantitative variables are presented as medians and standard deviations.

Inferential analysis: an analysis of the comparison of proportions between groups with chi-square and comparison of means between groups with t test is presented. The statistical significance level was $P < 0.05$. The statistical package used was SPSS 23.0 (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp).

Results

Participants

Fifty-one patients participated in the study, 30 in group 1 (total thyroidectomy + ablative therapy) and 21 in group 2 (total thyroidectomy without ablative treatment).

General characteristics of the sample

During the study period, a total of fifty-one cases were included, of which 30/51 (60%) received ablative therapy with radioactive iodine (RAI). The median age of the study population was 53 years; 46 (90%) were women, and 49 (96.1%) and 2 (3.9%) were located in stages I and II,

respectively. There was no association between the baseline characteristics of the study population and the indication for ablative therapy. In those who indicated ablative treatment with RAI, an average dose of 50 (30-138) mCi was administered (Table 1).

Table 1. General characteristics of the study population.

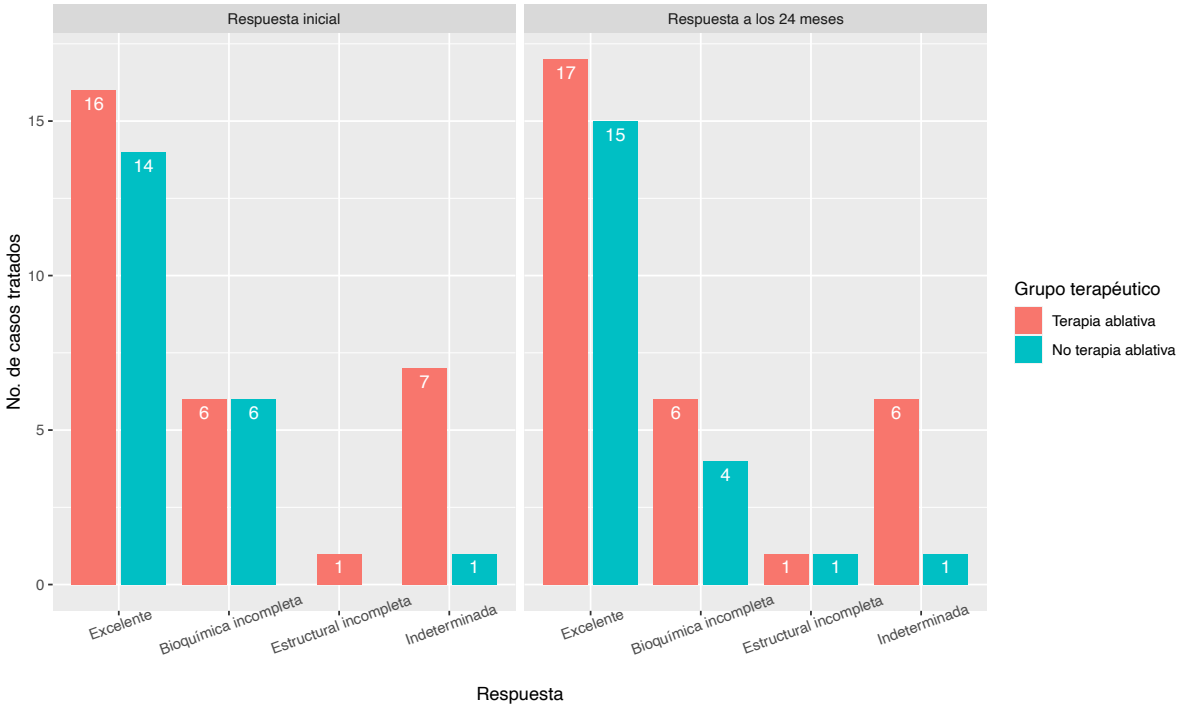
	Group 1 Ablative therapy (n=30)	Group 2 Without ablative therapy (n=21)	*P*
Age (years)*	49.0 (41.0, 58.5)	54.0 (52.0, 61.0)	0.916[a]
Young adult (18-39)	7 (23.3)	4 (19.0)	
Adults (40-64)	20 (66.7)	14 (66.7)	
Older adults (≥65)	3 (10.0)	3 (14.3)	
Sex (female), n (%)	26 (86.7)	20 (95.2)	0.391[a]
Clinical stage (II), n (%)	2 (6.7)	-	0.506[a]
I131 Dose (mCi)	50.0 (30.0, 138)	-	n/a

I131, iodine 131; mCi, millicuries; *Median and IQR, interquartile range.
[a]. Fisher's exact test.

Assessment of risk of recurrence

In group 1, which was treated with I131, complete response to treatment was observed in 16/30 cases, and at 24 months, complete response was observed in 17/30 cases. The biochemical and structural reactions were the same at baseline and 24 months (Figure 1). In group 2, which did not receive therapy with I131, it was evidenced that 2 cases had an incomplete biochemical response; one patient went on to have a complete answer, and another patient had an incomplete structural answer at 24 months; in the indeterminate response, there was no change.

Figure 1 Evaluation of the response to initial treatment and at 24 months in patients who received and did not receive radioactive iodine after surgery



Dynamic risk

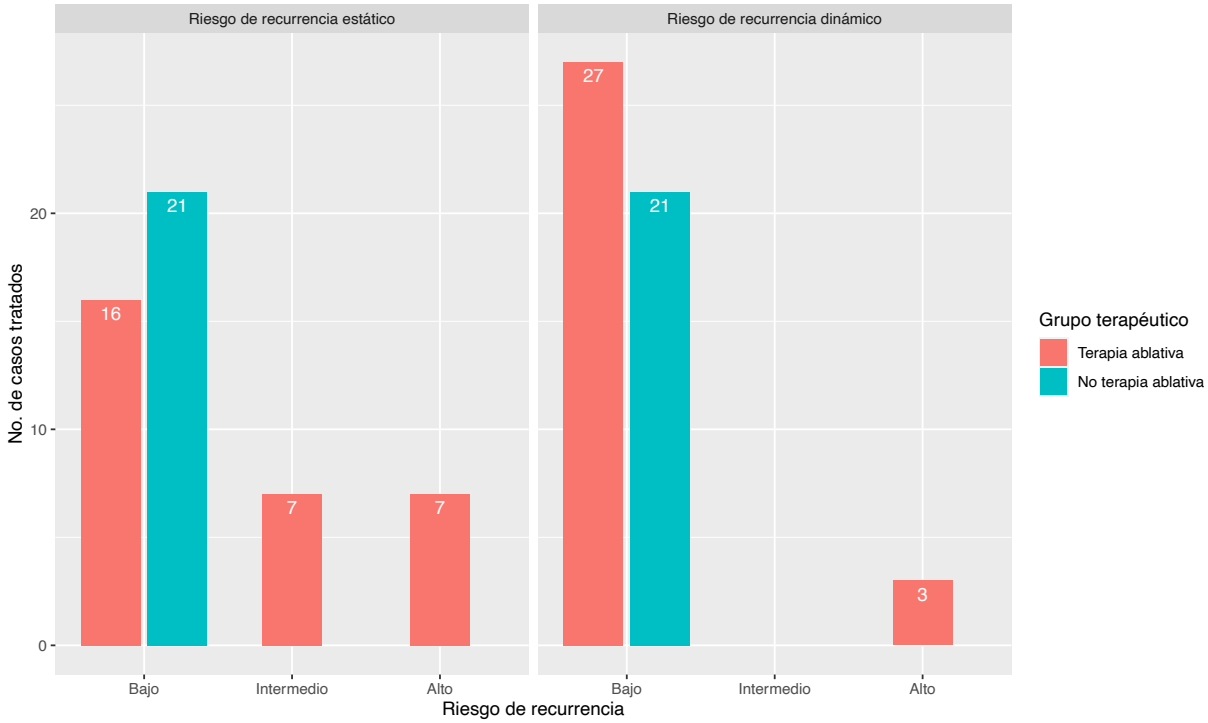
The dynamic risk had a notable increase at the end of follow-up in the group that received I131 ablative therapy compared with the nonablative group that remained stable.

In group 1, there was activity on postiodine scanning in 3/30 (10%) cases, of which one had locoregional metastasis, another patient developed a lung infection by Aspergillus that gave false uptake, and the third had lung metastasis, which offers a recurrence rate of 1.9% (low risk of recurrence).

The initial response to treatment in Group 1 was complete in 53.3% of the cases, and in Group 2, it was complete in 66.7%. The incomplete biochemical response was 20% in group 1 and 28.6% in group 2. The incomplete structural response was 3.3% in Group 1 and none in Group 2. The indeterminate response was 23.3% in Group 1 and 4.8% in Group 2 (Figure 2).

The patients in group 1 at follow-up had a complete response of 56.7%; in group 2, it was 71.4% (P=0.49). The incomplete biochemical response was 20% in group 1 and 19% in group 2. The incomplete structural response was 3.3%, and the indeterminate response was 20% in Group 1; in Group 2, the incomplete structural response was 4.8%, and the indeterminate response was 4.8%. When comparing the initial response between both groups, there was no statistically significant difference, nor when comparing the response at the end of the follow-up.

Figure 2 Static and dynamic recurrence risk assessment.



The risk of initial recurrence in the group that received I131 was low in 53.3% of the cases, intermediate in 23.3%, and high in 23.3%. In comparison, the group that did not receive I131 had a low initial risk of recurrence. When comparing the initial risk of recurrence, a statistically significant difference (*P <0.001a)* was found in the group that did not receive I131 since all were at low risk, but not the group that received I131, which also presented an intermediate risk of recurrence and high risk.

The dynamic risk in the group ablated with I131 at the end of follow-up was low in 90% and high in 10% of the cases. The group that did not receive I131 at the end of the follow-up had a low dynamic risk similar to the initial risk.

When comparing the dynamic risk in both groups, it was evident that there was an increase in patients with low dynamic risk at the end of follow-up in the group ablated with radioactive iodine I131 (from 53.3% to 90%) compared to the group that did not receive ablative therapy in the two groups, in which the low risk was maintained until the end of follow-up. Based on the results found in dynamic risk, it can be deduced that ablative therapy with radioactive iodine 131 improves the effectiveness of treatment in patients with thyroid microcarcinoma who have a higher probability of disease recurrence (Table 2).

Table 2. Objective evaluation of the oncological response based on the dynamic risk.

	Group 1 Therapy ablative (n=30)	Group 2 Without ablative therapy (n=21)	P
Initial response , n (%)			
Complete	16 (53.3%)	14 (66.7%)	1,000[a]
Incomplete biochemistry	6 (20.0%)	6 (28.6%)	
Incomplete structural.	1 (3.3%)	0 (0%)	
Indeterminate.	7 (23.3%)	1 (4.8%)	
Initial recurrence risk, n (%)			
Low	16 (53.3%)	21 (100%)	<0.001 [a]
Intermediate	7 (23.3%)	-	
High	7 (23.3%)	-	
Response at 24-month follow-up, n (%)			
Excellent	17 (56.7%)	15 (71.4%)	0.490[a]
Incomplete biochemistry	6 (20.0%)	4 (19.0%)	
incomplete structural	1 (3.3%)	1 (4.8%)	
indeterminate	6 (20.0%)	1 (4.8%)	
Dynamic risk of recurrence, n (%)			
Low	27 (90.0%)	21 (100%)	0.258[a]
Intermediate	-	-	
High	3 (10.0%)	-	

a. Fisher's exact test

Discussion

There have been different opinions regarding the therapeutic benefit of radioactive iodine administration in patients with thyroid microcarcinoma, given the well-known high frequency of excellent response to treatment, low recurrence, and remarkable survival in this population.

The results found in this study showed that 53.3% of patients treated with total thyroidectomy and radioactive iodine 131 (I131) had an excellent initial response to treatment and were stratified with a low initial recurrence risk. The other patients presented an incomplete biochemical response in 20%, an incomplete structural response in 3%, and an indeterminate response in 23.3%. This group of patients was stratified with an intermediate and high initial risk of recurrence in equal proportions (23.3%). At the end of the follow-up, it was found that the incomplete biochemical and incomplete structural responses remained the same, but not the indeterminate response, which decreased, and the excellent response increased. These findings are similar to two studies by Abelleira et al. (2017 and 2019) [2]. However, they found a more significant incomplete structural response related to including patients with a higher probability of recurrence. In the study, the greatest indeterminate

response was associated with a high level of antithyroglobulin antibodies (TgAb), which remained stable in most patients until the end of follow-up.

In the group of thyroidectomized patients not ablated with I131, it was shown that patients with a low risk of initial recurrence presented an excellent initial response of 66.7%, with an increase to 71.4% at the end of follow-up and without evidence of recurrent disease (0%), if we compare this work with a multicenter analysis carried out by MOMESSO (2016) [11] in which a total of 507 patients were included, of whom 63.1% (n= 320) underwent thyroidectomy without ablation, during their follow-up disease was a recurrent diagnosed in 1.9% of the population studied, so we can indicate that the results of this study are similar to those reported in the universal literature. Therefore, the modified 2015 ATA risk stratification system helps guide the initial management of this group.

What was striking about this group was finding a patient who initially presented an incomplete biochemical response and a low risk of initial recurrence, who went on to have an insufficient structural response, evidenced in the dynamic risk, hence the importance of carrying out an adequate dynamic risk assessment in the patient follow-up.

The application of the dynamic risk of recurrence was a valuable tool in the follow-up of patients, as demonstrated by Abelleira et al. (2019) [2] and Ruíz-Pardo José (2020) [12], since it made it possible to predict the probability of excellent response at the end of follow-up when compared with the initial risk of recurrence. Thus, in this study, an increase in low dynamic risk was found to be 90%, and a decrease in high dynamic risk was found to be 10% in patients who received ablative therapy with I131. In patients who did not receive I131 treatment, the dynamic risk remained stable without modification. These findings support the evidence found by Ting Yang (2019) [1 3] that patients with thyroid microcarcinoma would benefit from ablative therapy with I131 after surgery by decreasing the chances of disease recurrence.

Initial recurrence risk stratification made it possible to carefully select those patients who should or should not receive ablative therapy with I131, receiving those who were stratified as intermediate and high risk. During follow-up, dynamic risk demonstrated the effectiveness of I131 treatment in this group of patients, evidencing an increase in low dynamic risk at the end of the study. In the group not ablated with I131, the dynamic risk remained low, which validates that patients with a low risk of initial recurrence do not require ablative therapy.

The present study validates the treatment used in patients with thyroid microcarcinoma and sees dynamic risk stratification as an effective tool in follow-up over time; new randomized studies should be carried out in the future.

Conclusions

The initial response was excellent in most cases, as well as the low rate of incomplete structural or biochemical response found in both groups, demonstrating that initial recurrence risk stratification is a valuable tool for selecting those patients who should receive radioactive iodine. The dynamic risk had a notable increase at the end of the follow-up in the group that received ablative therapy with I131 compared to the nonablative group that remained stable, which makes it possible to identify complications and improve their treatment. Adjuvant therapy with radioactive iodine 131 in patients with an intermediate and high risk of recurrence was effective, decreasing their dynamic risk during follow-up and confirming the clinical utility of the ATA risk stratification system as an initial predictor of recurrent disease.

Editor's note
The journal Oncología (Ecuador) remains neutral regarding jurisdictional claims in published maps and institutional affiliations.

Abbreviations

ATA: American Thyroid Association.
RAI: radioactive iodine.

Administrative information

Additional Files

None declared by the authors.

Acknowledgments

Not applicable.

Author contributions

Mónica Guisellaa Mejía Naranjo: Conceptualization, formal analysis, research, project administration, writing of the original draft.
José Camilo López Estrella: Conceptualization, methodology, validation, visualization, writing - review and edition.
All authors read and approved the final version of the manuscript.

Financing

The studies, images, radiotherapy, and surgeries constituted the regular activity of the service and were not an additional cost for the patients. The authors financed the administrative costs of the research.

Availability of data and materials

Data are available upon request to the corresponding author. No other materials are reported.

Statements

Ethics committee approval

Not required for observational studies.

Consent for publication

It is not required when images, resonances, or tomographic studies of specific patients are not published.

Conflicts of interest

The authors declare that they have no conflicts of competence or interest.

References

1.Cabanillas ME, McFadden DG, During C. Thyroid cancer. Lancet. 2016 Dec 3;388(10061):2783-2795. doi: 10.1016/S0140-6736(16)30172-6. Epub 2016 May 27. PMID: 27240885.
https://doi.org/10.1016/S0140-6736(16)30172-6

2. Abelleira E, Peñaloza MA, Jerkovich F, Bueno F, Pitoia F. Dynamic risk allows us to adequately select patients with differentiated thyroid cancer who do not require radioiodine treatment. Arch Endocrinol Metab. 2021 Nov 3;65(3):315-321. doi: 10.20945/2359-3997000000374. PMID: 34731559; PMCID: PMC10065346.
https://doi.org/10.20945/2359-3997000000374

3. Estorch M, Mitjavila M, Muros MA, Caballero E; on behalf of the SEMNIM Endocrinology Working Group. Radioiodine treatment of differentiated thyroid cancer related to guidelines and scientific literature. Rev Esp Med Nucl Image Mol (Engl Ed). 2019 May-Jun;38(3):195-203. English Spanish. doi : 10.1016/j.remn.2018.12.008. Epub 2019 Feb 8. PMID: 30745131.
https://doi.org/10.1016/j.remn.2018.12.008

4. Tarasova VD, Tuttle RM. Current Management of Low Risk Differentiated Thyroid Cancer and Papillary Microcarcinoma. Clin Oncol (R Coll Radiol). 2017 May;29(5):290-297. doi : 10.1016/j.clon.2016.12.009. Epub 2017 Jan 10. PMID: 28087101.
https://doi.org/10.1016/j.clon.2016.12.009

5. McDow AD, Pitt SC. Extent of Surgery for Low-Risk Differentiated Thyroid Cancer. Surg Clin North Am. 2019 Aug;99(4):599-610. doi : 10.1016/j.suc.2019.04.003. Epub 2019 May 13. PMID: 31255194.
https://doi.org/10.1016/j.suc.2019.04.003

6. Nasef HO, Nixon IJ, Wreesmann VB. Optimization of the risk-benefit ratio of differentiated thyroid cancer treatment. Eur J Surg Oncol. 2018 Mar;44(3):276-285. doi: 10.1016/j.ejso.2018.01.077. Epub 2018 Jan 31. PMID: 29402557.
https://doi.org/10.1016/j.ejso.2018.01.077

7. Zerdoud S, Giraudet AL, Leboulleux S , Leenhardt L, Bardet S, Clerc J, Toubert ME, Al Ghuzlan A, Lamy PJ, Bournaud C, Keller I, Sebag F , Garrel R, Mirallié E, Groussin L, Hindié E , Taïeb D. Radioactive iodine therapy, molecular imaging and serum biomarkers for differentiated thyroid cancer: 2017 guidelines of the French Societies of Nuclear Medicine, Endocrinology, Pathology, Biology, Endocrine Surgery and Head and Neck Surgery. Ann Endocrinol (Paris). 2017 Jul;78(3):162-175. doi: 10.1016/j.ando.2017.04.023. Epub 2017 Jun 1. PMID: 28578852.
https://doi.org/10.1016/j.ando.2017.04.023

8. Luo X, Wu ACYZYJBZJ. Analysis of risk factors for postoperative recurrence of thyroid cancer. J BUON. 2019 Mar-Apr;24(2):813-818. PMID: 31128040.

9. Kim Y, Roh JL, Gong G, Cho KJ, Choi SH, Nam SY, Kim SY. Risk Factors for Lateral Neck Recurrence of N0/N1a Papillary Thyroid Cancer. Ann Surg Oncol. 2017 Nov;24(12):3609-3616. doi : 10.1245/s10434-017-6057-2. Epub 2017 Aug 18. PMID: 28822118.
https://doi.org/10.1245/s10434-017-6057-2

10. Yang X, Liang ZY, Meng C, Liang J, Yu Z, Lin YS. [Invasiveness of papillary thyroid microcarcinoma with BRAF mutation]. Zhongguo Yi Xue ke Xue Yuan Xue Bao. 2013 Aug;35(4):398-403. Chinese. doi : 10.3881/j.issn.1000-503X.2013.04.008. PMID: 23987486.
https://doi.org/10.3881/j.issn.1000-503X.2013.04.008 _

11. Momesso DP, Tuttle RM. Update on differentiated thyroid cancer staging. Endocrinol Metab Clin North Am. 2014 Jun;43(2):401-21. doi : 10.1016/j.ecl.2014.02.010. PMID: 24891169.
https://doi.org/10.1016/j.ecl.2014.02.010

12. Ruiz-Pardo J, Ríos-Zambudio A, Rodríguez-González J, Paredes-Quiles M, Soriano-Giménez V, Oviedo-Ramírez I. The results of treatment of papillary thyroid microcarcinoma adapted to the risk of recurrence. cir. cir. [magazine on the Internet]. 2020 Oct [cited 2023 Apr 13] ; 88(5): 576-583.
https://doi.org/10.24875/CIRU.20001560

13. Yang T, Zheng SY, Jiao J, Zou Q, Zhang Y. Radioiodine remnant ablation in papillary thyroid microcarcinoma: a meta-analysis. Nucl Med Commun . 2019 Jul;40(7):711-719. doi : 10.1097/MNM.0000000000001018. PMID: 31095043.
https://doi.org/10.1097/MNM.0000000000001018