

# Bilateral central neck dissection in the treatment of early unifocal papillary thyroid carcinomas with poor risk factors

## A mono-institutional experience.



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### Bilateral central neck dissection in the treatment of early unifocal papillary thyroid carcinomas with poor risk factors. A mono-institutional experience.

**INTRODUCTION:** Papillary thyroid carcinoma is the most common type of thyroid cancer worldwide. While total thyroidectomy is widely considered the standard surgical approach for papillary thyroid carcinomas, the role of central lymphadenectomy in early stage poor-risk papillary thyroid tumors is still a matter of debate. This study was designed to assess surgical complications and local disease control rates in patients affected by poor-risk early stage papillary thyroid carcinomas.

**METHODS:** We retrospectively analyze three groups of patients affected by poor-risk early stage papillary thyroid carcinomas treated with three alternative surgical strategies: I) routine total thyroidectomy; II) total thyroidectomy and routine central lymphadenectomy; III) total thyroidectomy and central lymphadenectomy upon positive intraoperative histological evaluation of lymph node involvement.

**RESULTS:** Data from patients treated with routine total thyroidectomy showed 32% of persistence of disease in the central compartment with concurrent positivity in laterocervical compartment in 25% of these cases. By contrast, patients receiving total thyroidectomy and routine central lymphadenectomy showed the involvement of central compartment in 40% of cases, while the remaining 60% of patients were free from lymph node metastases. Finally, patients undergoing total thyroidectomy and central lymphadenectomy upon positive intraoperative lymph node biopsy exhibited lack of persistence of lymph node involvement in central compartment after surgery. Of note, postsurgical complications were lower in patients undergoing conservative surgical approaches.

**CONCLUSIONS:** These data suggest that central lymphadenectomy, performed only in case of positive intraoperative lymph node biopsy, ensures reduced incidence of postoperative complications and optimal loco-regional disease control.

**KEY WORDS:** Bilateral central neck dissection, Intraoperative lymph node biopsy, Papillary thyroid carcinoma, Poor risk factors

### Introduction

Papillary thyroid cancer (PTC) is the most common type of thyroid cancer with an incidence constantly increasing over the years <sup>1</sup>.

Main reasons responsible for its higher incidence are the increased exposure to carcinogens and the improvement of diagnostic techniques. Moreover, the incidence of biologically aggressive forms occurring in young women is also increased <sup>2-4</sup>.

Surgery is the standard of care for localized thyroid carcinomas <sup>5</sup>.

Indications for total thyroidectomy and dissection of the central and laterocervical compartments for PTC have been defined, based on specific criteria, i.e. nodule size, age, sex, lymph node involvement as demonstrated by

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preoperative radiological assessment<sup>6,7</sup>. However, there are specific clinical conditions, such as early stage thyroid nodules classified as malignant upon cytological examination (tir5 according to SIAPEC classification)<sup>8</sup>, less than 1 cm in diameter and occurring in patients below 45 years of age that, classified as low-risk patient, according to guidelines, are not suitable for central lymphadenectomy<sup>9</sup>.

In such a context, it is important to note that, after total thyroidectomy, lymph node involvement may also occur in form of micro metastases (20-50% to 90%) [10] mainly in central compartment and with less extent in laterocervical compartment (45-69%)<sup>11</sup>, and sometimes these metastatic locations are not sensitive to metabolic radioiodine therapy<sup>12-14</sup>. Thus, postoperative positive assessment of lymph node involvement implies a restaging of the disease and a subsequent therapeutic strategy with a reoperation with lymphadenectomy in patients previously treated only with total thyroidectomy<sup>15</sup>.

Based on this background, this study was designed to retrospectively analyze our series of poor-risk patients (female below 45 years of age) and with a malignant thyroid nodule less than 1 cm in diameter to evaluate the impact of postoperative central lymph node involvement leading to a second surgical look.

## Materials and Methods

From January 2006 to today, 1100 surgical interventions for thyroid disease were performed in the Surgical Department of the University of Foggia, 936 patients were treated for benign disease (85.09%) and 164 for malignancy (14.91%). Among the latter subgroup, female patients below 45 years of age and with a nodule of PTC less than 1cm in diameter, classified as Tir5 upon cytology were further evaluate for this study. Overall, 75 patients with this clinic-pathological profile were included.

In order to improve loco-regional control in patients undergoing total thyroidectomy for the treatment of papillary carcinoma in our Institution, indications to lymphadenectomy of central and laterocervical compartments were modified over the time. Surgical outcome was evaluated in terms of local disease control (as assessed by radioiodine scintigraphy 2-3 months after surgery) and postoperative complications. From 2006 to 2010, a group of 25 patients (Group A) with papillary carcinoma was treated with total thyroidectomy. Postoperative complications and loco-regional disease control, as reported in Results, led to change our therapeutic strategy. Thus, from 2011 to 2018, patients with papillary carcinoma having the same characteristics as the previous study group, excluding those cases with preoperative detection of laterocervical and central lymph node involvement, were divided into 2 subgroups (Groups B and C). Group B patients (25 cases) were

treated with total thyroidectomy and routine central lymphadenectomy, group C patients (25 cases) underwent to intraoperative biopsy and histological examination of upper/lower isthmic and peri-recurrent lymph nodes ipsilateral to the tumor. In the case of positivity to intraoperative histological examination, total thyroidectomy with central linfectomy was performed; in case of negative results, patients received only total thyroidectomy.

The Ethics Committee of the Foggia University Hospital approved the study.

This study was performed in accordance with current international guidelines.

## SURGICAL TECHNIQUE

The surgical technique was the same in all patients. A 15 blade was used to incise through the epidermis and dermis, the platysma was separated with a monopolar cautery and subplatysmal flaps elevated superiorly and inferiorly. In the midline between the strap muscles (sternohyoid and sternothyroid), the cervical *linea alba* was identified and sectioned, this maneuver showing the thyroid gland. After a careful inspection of the gland, some lymph nodes, located above and below the *isthmus* and at the recurrent nerve level, were removed from the site of the neoplasia for intraoperative histological examination. Once the thyroid gland was identified, attention was turned to a single lobe. The next step involved the superior pole section with parathyroid recognition. The superior parathyroid gland was often found cephalad to the *tubercle of Zuckerkandl* and also adjacent to the superior pole. *Recurrent laryngeal nerve* at this side was identified throughout its course. Subsequently, the section of the inferior thyroid pole was performed with parathyroid recognition. The inferior parathyroid gland is usually located in a 1 cm radius around the inferior pole of the thyroid gland and almost always anterior to the plane of the *recurrent laryngeal nerve*. In case of central linfectomy, the limits considered were: medial margin of the common carotid artery, recognition and isolation of *recurrent laryngeal nerve* along its course, preavventional tissue of the anonymous trunk. A valsalva maneuver is performed, before closing the wound, to look for possible sources of bleeding, and the hemostasis control is perfected with the application of collagen patch coated with human fibrinogen and human thrombin (CFTP)<sup>16</sup>.

## Results

Surgical complications and local disease control were analyzed in three subgroups of 25 patients each (Table I):

1. Patients treated with total thyroidectomy without intraoperative assessment of lymph node involvement (Group A);

TABLE I - Surgical complications and local disease control observed in the 3 different groups.

Complications	Groups A (n.25)	Reintervention (n.4)	P value	Group B	Group C	P value A reint. vs C
Permanent-monolateral injury of RLN	–	1 (25%)		1 (4%)	–	
Transient-monolateral injury of RLN	1 (4%)	1 (25%)	0,12	2 (8%)	1 (4%)	0,12
Transient-bilateral injury of RLN	–	1 (25%)		–	–	
Permanent hypoparathyroidism	–	1 (25%)		1 (4%)	–	
Transient hypoparathyroidism	6 (24%)	3 (75%)	0.04	10 (40%)	3 (12%)	0.003
Hemorrhage	1 (4%)	–		1 (4%)	–	
Persistence of disease in CL	6 (24%)	–		–	–	
Persistence of disease in CL and omolateral LCL	2 (8%)	–		–	–	

RLN: Recurrent Laryngeal Nerve; CL: Central Lymph nodes compartment; LCL: Laterocervical lymph nodes compartment.

2. Patients treated with total thyroidectomy and routine central lymphadenectomy (Group B);

3. Patients treated with total thyroidectomy and routine central lymphadenectomy only upon positive intraoperative histological evaluation of lymph node involvement (Group C).

In the group A patients, no permanent lesions of *recurrent laryngeal nerve* and *parathyroids* were observed. However, transient hypoparathyroidism occurred in six patients (24%), one-sided and transient lesion of *recurrent laryngeal nerve* in one case (4%) and postoperative hemorrhage in one other case (4%). Persistence of disease in the central compartment was observed in eight patients (32%), as demonstrated by radioiodine scintigraphy control carried out 2-3 months after surgery. Two of these eight patients (8%) had iodine positive uptake also in omolateral laterocervical compartment. In four cases with post-surgery persistence of disease in the central compartment, a reintervention was required for the execution of the central lymphadenectomy, associated in two cases with the omolateral laterocervical linfectomy. Reintervention increased complications at parathyroid and *recurrent laryngeal nerve* level as follows: transient hypoparathyroidism in three cases (75%), transient and monolateral lesion of *recurrent laryngeal nerve* in one case (25%), transient and bilateral lesion of the laryngeal nerve in one case (25%), definitive hypoparathyroidism in one case (25%) and monolateral and definitive laryngeal nerve injury in one case (25%).

The others 4 cases underwent to radioiodine therapy.

In the Group B, transient hypoparathyroidism was observed in 10 (40%) patients, definitive hypoparathyroidism in one (4%) patient, unilateral and transient lesion of the laryngeal nerve in 2 (8%) patients, unilateral and definitive laryngeal nerve lesion only in 1 (4%) patient, postoperative hemorrhage occurred in only 1 (4%) patient. In this group, postoperative histological examination showed the involvement of central lymph nodes in 10 patients (40% of cases). The subsequent radioiodine scintigraphy control showed positive iodine uptake in omolateral laterocervical compartment in additional four cases (16%), that underwent to radioiodine therapy.

In Group C, the intraoperative histological examination of central compartment lymph nodes showed the presence of disease in nine (36%) cases; thus, these patients underwent total thyroidectomy with central linfectomy. In these patients, the incidence of surgical complications was as follow: transient ipoparathyroidism in three patients (12% of cases), transient and monolateral recurrent nerve injury in one case (4%), no cases of definitive hypoparathyroidism and definitive recurrent nerve injury were observed. Postoperative radioiodine scintigraphy showed two cases of positive iodine uptake in the laterocervical compartment, homolateral to the thyroid lesion (8%). In the remaining 16 cases, intraoperative histological examination of the central compartment did not show any lymph node involvement and consequently surgical treatment was limited to total thyroidectomy without surgical complications. Postoperative radiiodine control showed no case of iodine uptake in the neck.

## Discussion

The incidence of PTC appears to have increased in recent years. This datum can be attributed to an increased exposure to risk factors, but above all to a greater diffusion of diagnostic techniques such as fine needle aspiration cytology which is a reliable, safe procedure with few risks<sup>17-18</sup>. To date, international guidelines for the surgical treatment of this disease have been continuously updated in order to fulfill optimal loco-regional disease control with minimal surgical morbidity. While in presence or suspicion of early stage papillary carcinoma, total thyroidectomy is widely considering the standard of care, the issue on whether patients should receive routine central lymphadenectomy is still debated<sup>19</sup>, thinking about the patients undergoing total thyroidectomy with central lymphadenectomy can experience greater overall hypocalcemic morbidity compared to patients subjected only to thyroidectomy<sup>20</sup>. The surgical approach for routine lymphadenectomy of the central compartment depends on clinical data such as age, size of the nodules and lymph node preoperative assessment<sup>21</sup>. By contrast, late-

rocervical lymphadenectomy is considered based only on positivity of preoperative radiological examination and FNAC. However, in some cases, post-operative radioiodine scintigraphy shows positive foci in central lymph nodes, often resistant to radiometabolic therapy, making the clinical and therapeutic management of these patients more difficult. This condition often occurs in papillary thyroid nodules, malignant upon cytological examination, with a diameter less than 1 cm, occurring in patients under the age of 45 years, and treated with total thyroidectomy only. However, it should also be taken in account that the incidence of postoperative complications after total thyroidectomy<sup>22</sup> is lower than those observed after total thyroidectomy with associated central lymphadenectomy<sup>23</sup>. In our initial experience, patients with early stage thyroid carcinoma with poor risk prognostic factors, treated with total thyroidectomy (Group A), showed, at post-surgery radioiodine scintigraphy, 32% of persistence of disease in the central compartment with 25% of these cases exhibiting concurrent positivity in laterocervical compartment, and 5.9% of exclusive laterocervical lymph node involvement. These results were interpreted as insufficient from a therapeutic point of view, since 50% of these patients underwent a re-intervention with further complications. Because of this, we decided to critically analyze the guidelines by searching for a different surgical strategy with the aim to reduce the percentage of post-surgery lymph node involvement upon radioiodine. Two additional strategies were prospectively evaluated: total thyroidectomy with routine central lymphadenectomy (Group B) and total thyroidectomy with central lymphadenectomy only in case of a positive intraoperative biopsy of central lymph nodes (Group C).

In group B patients, the definitive histological examination showed the involvement of central compartment in 40% of cases, while the remaining 60% of patients were free from lymph node disease and thus the lymphadenectomy was potentially "unnecessary". In patients in Group C, a complete correspondence was observed between positivity to the intraoperative histological examination and the consequent execution of the central lymphadenectomy, as further confirmed upon post-surgery iodine scintigraphy which did not show persistence of lymph node involvement in central compartment.

In addition to this the study shows the reduction of postoperative complications compared patients reoperated of group A and patients of group C (p value 0,003 according to the  $\chi^2$  test).

Postoperative complications reported in our study are conform to data of literature<sup>24</sup>.

## Conclusion

In poor risk early stage papillary carcinomas (with a nodule size less than 1 cm in diameter and below 45 years of age, at the time of diagnosis) there is a lymph

node involvement in the central compartment in 32-40%, and to a lesser extent in laterocervical compartment (16-25%), also as single site affected by the disease (5.9-13.3%). Frequently radioiodine post-surgical therapy fails to provide optimal healing results, and in such cases surgery is needed again to treat the central compartment with an increase in the incidence of surgical complications. Therefore, in these patients, it is of primary importance to perform a surgical treatment that guarantees a complete control of the neoplastic disease, with acceptable complications and without operatory overtreatment in order to avoid a reintervention, that can lead to dangerous complications<sup>25</sup>. The results of our study suggest that central lymphadenectomy, performed only in case of positive intraoperative biopsy on upper/lower isthmic and peri-recurrent lymph nodes, is a rationale surgical strategy, ensuring a reduced incidence of postoperative complications and optimal oncological loco-regional disease control. Finally, this surgical strategy may also deserve to be evaluated for the treatment of Tir4 thyroid nodules upon cytological examination.

## Riassunto

Il carcinoma papillare della tiroide è il tipo più comune di tumore alla tiroide in tutto il mondo. Mentre la tiroidectomia totale è ampiamente considerata l'approccio chirurgico standard per i carcinomi papillari della tiroide, il ruolo della linfoadenectomia centrale nei tumori della tiroide papillare a stadio precoce a basso rischio è ancora oggetto di discussione. Questo studio è stato progettato per valutare le complicanze chirurgiche e i tassi di controllo delle malattie locali nei pazienti affetti da carcinomi della tiroide papillari in stadio precoce a basso rischio.

Analizziamo retrospettivamente tre gruppi di pazienti affetti da carcinomi papillari della fase iniziale a basso rischio trattati con tre strategie chirurgiche alternative: i) tiroidectomia totale di routine; ii) tiroidectomia totale e linfoadenectomia centrale di routine; iii) tiroidectomia totale e linfoadenectomia centrale su valutazione istologica intraoperatoria positiva del coinvolgimento dei linfonodi.

I dati provenienti da pazienti trattati con tiroidectomia totale di routine hanno mostrato il 32% di persistenza della malattia nel compartimento centrale con positività concomitante nel compartimento laterocervicale nel 25% di questi casi. Al contrario, i pazienti sottoposti a tiroidectomia totale e linfoadenectomia centrale di routine hanno mostrato il coinvolgimento del compartimento centrale nel 40% dei casi, mentre il restante 60% dei pazienti era privo di metastasi linfonodali. Infine, i pazienti sottoposti a tiroidectomia totale e linfoadenectomia centrale in seguito a biopsia linfonodale intraoperatoria positiva hanno mostrato mancanza di persistenza del coinvolgimento dei linfonodi nel compartimento cen-

trale dopo l'intervento chirurgico. Da notare che le complicanze post-chirurgiche erano più basse nei pazienti sottoposti a approcci chirurgici conservativi.

In conclusione questi dati suggeriscono che la linfonodectomia centrale, eseguita solo in caso di biopsia linfonodale intraoperatoria positiva, garantisce una ridotta incidenza di complicanze postoperatorie e un controllo ottimale della malattia loco-regionale.

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