

## LYMPHECTOMY IN THE TREATMENT OF THYROID CANCER IN ADULTS AND CHILDREN.

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Thyroid carcinoma is the most frequent endocrine malignancy in Italy and differs in natural history according to histological type and age of patients. Lymph node metastases are more frequently seen in young patients with papillary carcinoma. However, many clinical series suggested that although the incidence of lymph node invasion in high-risk patients (over-50s) is slightly lower than in low-risk patients, the local recurrence rate is higher than in the former.

From the results of our experience, confirmed by other authors, we retain total thyroidectomy with lymphectomy of the central compartment as the procedure of choice in the treatment of well-differentiated thyroid carcinoma in the under-50s. In the over-50s, functional bilateral lymphectomy improves survival and should be considered mandatory, just as for medullary carcinoma. On the contrary, the prognosis of anaplastic carcinoma is not improved by lymphectomy.

Folia Oncol., 17, 1995

Thyroid carcinoma is the most frequent endocrine malignancy in our country. It affects 18-28/1.000.000 patients every year and is responsible for 0.4% of deaths for malignancies in Italy<sup>1</sup>. In females, the frequency is two-three times higher than that of male patients<sup>2,3</sup>. The rates reported vary significantly if we consider the autopsy data: in such a case, thyroid cancers account 2.8% - 4.5% of malignancies<sup>4</sup>. It is therefore safe to say that most of these neoplasms are not evident during life and do not affect life expectancy. Thyroid cancers, in children and adolescents, are rare and are mostly well-differentiated carcinomas<sup>5</sup>. Papillary carcinoma is the most common thyroid cancer in children<sup>6</sup>.

Thyroid carcinoma differs in natural history according to histological evolution<sup>7</sup>. Generally, papillary and follicular carcinomas are considered to be differentiated cell cancers; although medullary carcinoma is also a differentiated cell carcinoma, it is not usually included in the differentiated group because of its biological behaviour and its origin from the parafollicular cells (C cells) producing calcitonin.

The most common thyroid malignancy is papillary type (58%), followed by follicular (25%), anaplastic (13%) and medullary carcinomas (4%)<sup>8</sup>.

Mortality varies by histological type. It is reported that mortality is about 11% for papillary

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and about 24% for follicular carcinoma 15 years after surgery. Factors significantly influencing the prognosis of patients treated with radical surgery have recently been identified<sup>9-11</sup>. The malignant course may differ not only by histological type but also by age at surgical treatment: patients treated before 50 years of age showed a higher life expectancy. Patients with papillary carcinoma have a significantly better prognosis than those with follicular carcinoma. The evidence of node metastases from a differentiated carcinoma seems not to increase the mortality after 15 years of follow-up<sup>12-14</sup>. Lymph node metastases are more frequent in papillary carcinoma and affect more frequently young patients; 88% of node metastases occur in patients under 18 years of age<sup>5,6</sup>.

The stage of disease at diagnosis does not influence survival in patients under 50 years, but it does in patients over 50 years of age. For this reason, the TNM classification (UICC)<sup>15</sup> provides a different staging by patients age.

Medullary carcinoma is classified among differentiated carcinomas and the anaplastic variety also, due to its biological behaviour. Most of the cases are familial (about 90% of the cases observed), transmitted as an autosomal dominant disease, frequently multifocal and bilateral<sup>16</sup>. Rarely it is sporadic, although it could be the first case recognized in a family. Lymph node metastases are present in half of medullary carcinoma cases on diagnosis<sup>15,20</sup>, but they are not always detected by routine diagnostic procedures. Anaplastic carcinoma shows greater malignancy with rapid and painful local enlargement; local nodes are included in the enlarged neoplastic tissue invading contiguous areas.

The thyroid gland is drained by several lymphatics including the cervical and mediastinal nodes. The main nodes are those along recurrent laryngeal nerve, pretracheal area, inferior thyroid veins, jugular veins, transverse cervical artery, and the spinal accessory nerve<sup>21</sup>. Lymphatic vessels anastomose freely and so radical treatment should include each group of nodes bilaterally (functional bilateral lymphectomy).

Metastatic lymph nodes were observed by Frazell and Foote<sup>18</sup> in 61% of cases, by Attie et al.<sup>21</sup>, Tubiana et al.<sup>22</sup> in 71%, and by Noguchi et al.<sup>23</sup> in 76% of patients. These results show that micrometastases occur in only a small percentage of pa-

tients. In fact, compared to the expected frequency of lymph node metastases of over 50%, they were observed as recurrence only in 17% of patients who did not undergo elective lymphectomy; furthermore, Mazzaferri et al.<sup>24</sup> and Wanebo et al.<sup>25</sup> reported that most differentiated carcinoma metastases were located in lymph nodes, respectively in 84% and 56% of patients.

In our opinion, the presence of subclinical metastases does not seem to carry a poor prognosis in the under-50s, although it does in the over-50s, especially in males. Although the rate of lymph node invasion in the high-risk patients (age) is slightly lower than in low-risk patients, the local recurrence rate is higher than in the former.

Cady et al.<sup>26</sup> reported 50% mortality among the over-50s who presented lymph node metastases from papillary carcinoma and only 12% among the under-50s. Morone et al.<sup>27</sup> retained that thyroid cancer surgery must be extensive enough to minimize the chances of recurrence and death. He performed the cervical lymph node dissection in 55 out of 159 patients with thyroid cancer. The 10-years postoperative survival rate was 70,59% with lymphectomy and 65,71% without lymphectomy<sup>27</sup>.

"Regional" micrometastases show greater malignancy in older than in younger patients. Good results were obtained in the patients who underwent mandatory "functional" lymphectomy subsequently, thanks to earlier total thyroidectomy.

Some patients may present lymph node metastases a long time after the intervention and confirm the validity of radioiodine therapy<sup>28</sup> which control 80% of cases. The percentage is higher than that reported by other authors; our opinion is that they performed subtotal thyroidectomy. We do not favor such a limited treatment because the neoplastic lesion is often multifocal, so subtotal thyroidectomy fails to prevent possible lymph node metastases. In fact, their "activation" is not allowed for the higher control of the thyroid residue on the TSH increase; the RAI uptake of normal parenchyma is higher than that of the neoplastic tissue and does not allow the identification of any relapses. The thyroid stump takes up a very high dose of radioiodine without exerting cytolytic activity on neoplastic tissue. Excision of lymph node metastases from follicular carcinoma proved to be a

sufficient local treatment although lymph node metastases from such a tumor have bad prognosis<sup>4</sup>.

In medullary carcinoma, we are convinced of the benefit of elective lymphadenectomy in preventing recurrence. Our opinion is supported by others<sup>29</sup> who report a decrease in the recurrence rate (from 38% to 28%) when lymphectomy is done. Steinfeld<sup>30</sup> and Gottlieb et al.<sup>19</sup> both report good results in their cases.

The prognosis of anaplastic carcinoma is not improved by lymphectomy or by radiotherapy, which are merely palliative in such cases. Some authors<sup>30</sup> favoured radical surgery to prevent the suffocating effects of tumor enlargement.

In conclusion we believe that total thyroidectomy with lymphadenectomy of the central compartment (recurrent laryngeal lymph nodes) is the procedure of choice in the treatment of this disease in the under-50s. In patients over 50 years of age, we find that functional bilateral lymphadenectomy improves survival and should be considered mandatory, just as we always perform lymphadenectomy for medullary carcinoma.

#### RIASSUNTO

#### LA LINFECTOMIA NEL TRATTAMENTO DEL CANCRO DELLA TIROIDE NEGLI ADULTI E NEI BAMBINI

Il carcinoma della tiroide è la neoplasia endocrina maligna più frequente in Italia ed il suo decorso naturale è in rapporto al tipo istologico del tumore e all'età dei pazienti. Le metastasi linfonodali sono più frequenti nei pazienti con carcinoma papillifero ed età inferiore ai 50 anni. Nonostante l'incidenza di metastasi linfonodali sia minore nei pazienti di età superiore ai 50 anni rispetto ai pazienti più giovani, comunque, è nel primo gruppo che si registra il tasso di recidiva locale maggiore. Dai risultati della nostra esperienza, confermati anche da altri autori, riteniamo che la tiroidectomia totale associata a linfadenectomia del compartimento centrale è il trattamento di scelta nei pazienti con carcinoma differenziato della tiroide ed età inferiore ai 50 anni. Nei pazienti di età superiore ai 50 anni ed in quelli con carcinoma midollare è, invece, indicata la linfettomia funzionale bilaterale. Al contrario, l'escissione linfonodale non sembra in grado di migliorare la prognosi del carcinoma anaplastico della tiroide.

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