Differentiated thyroid cancer: feasibility of loboisthmectomy in an endemic region

P.G. CALÒ, E. ERDAS, F. MEDAS, L. GORDINI, A. LONGHEU, G. PISANO, A. NICOLOSI

Introduction

Differentiated thyroid cancer (DTC) represents the most frequent thyroid cancer, originating from the follicular epithelium and accounting for 90% of all thyroid carcinomas (1-4). DTC is usually an indolent disease associated with a favorable prognosis for most patients. Some patients, however, exhibit local invasion or extensive metastases, and a small number of patients die of the disease (5-7).

Debate still exists with regard to the optimal surgical approach but trends toward a more conservative approach, such as loboisthmectomy (LI), are being more favored, especially in papillary thyroid cancer, of tumor sizes less than 4 cm, in the absence of other high-risk suggestive features (3, 8). In contrast to Western countries, LI has been the mainstay of primary surgery for DTC in Japan, and total thyroidectomy (TT) is reserved for advanced cases (9, 10).

American Thyroid Association (ATA) revised guidelines recommend TT for DTC > 1 cm, unless there are contraindications to this surgery (11); LI alone may be sufficient treatment for small (< 1 cm) papillary thyroid cancer, of tumor sizes less than 4 cm, in the absence of other high-risk suggestive features (5-7). In contrast to Western countries, LI has been the mainstay of primary surgery for DTC in Japan, and total thyroidectomy (TT) is reserved for advanced cases (9, 10).

Conclusions. Total thyroidectomy remains the safest treatment in differentiated thyroid cancer, especially if performed in high volume centers in which complications can be minimized. Loboisthmectomy is limited in endemic areas by the association with other thyroid diseases. A correct and detailed information of the patient is essential before planning surgery.

KEY WORDS: Differentiated thyroid cancer - Thyroidectomy - Loboisthmectomy.
Patients and methods

Between 2007 and 2014 2504 patients were submitted to TT with or without prophylactic lymphadenectomy in our Department of Surgical Sciences at the University of Cagliari; final diagnosis was DTC in 1154 (46.08%). 241 were male and 913 female; mean age was 51.93±14.57. The clinical records of these patients were retrospectively reviewed to analyze the histopathological features and the results. The data were collected from retrospective chart review. In all cases, surgery was performed by three experienced endocrine surgeons. The preoperative work-up consisted of free thyroid hormone (FT3, FT4), thyrotropin (TSH), Tg and anti-Tg antibody (TgAb) measurements, and high resolution ultrasound (US) of the neck by a skilled sonographer. A pre- and postoperative fibrolaryngoscopy was routinely performed in all patients. In suspected cases, a preoperative US-guided fine-needle aspiration cytology (FNAC) was performed. Patient demographics and postoperative complications were recorded, including neck hematomas requiring reoperation, transient or permanent hypoparathyroidism; transient or permanent vocal cord palsy, and distant and locoregional recurrence detected by postoperative surveillance. Hypoparathyroidism (defined as a parathyroid hormone (PTH) level < 10 pg/ml; normal values range between 10 to 65 pg/ml) was considered permanent when it lasted for more than six months. Permanent recurrent laryngeal nerve injury was defined as vocal fold paralysis, confirmed with laryngoscopic examination persisting for more than six months. Qualitative data were expressed as percentages, while quantitative data were expressed as the mean value ± standard error of the mean (SEM). The study was approved by the Institutional Ethical committee of the University of Cagliari.

Results

In 1044 cases we observed a papillary cancer (90.5%), in 110 a follicular carcinoma (9.5%); microcarcinomas were 399 (34.5%) (Table 1).

Tumor size varied from 0.3 to 70 mm, with an average value of 14.12±12.415. Thyroid weight varied from 5 to 348 g, with a mean value of 35.23±34.72. Multifocality was present in 323 cases (28%), in 142 unilateral (12.3%) and in 181 bilateral (15.7%) (Table 1).

Thyroiditis coexisted in 472 patients (40.9%), Graves’ disease in 48 (4.1%), multinodular toxic goiter in 38 (3.3%), toxic adenoma in 5 (0.4%), and multinodular goiter in 404 (35%) (Table 2).

Complications were: postoperative bleeding in 20 patients (1.7%), in 8 cases conservatively treated (0.7%)...
and in 12 cases surgically treated (1%); a transient unilateral vocal cord paralysis occurred in 20 cases (1.7%) and a definitive one in 10 (0.86%); a transient bilateral paralysis in 1 patient (0.08%) submitted to emergency tracheotomy for acute respiratory failure; a transient hypoparathyroidism was recorded in 351 patients (30.4%), a definitive one in 24 (2.07%); a chylous fistula surgically treated was recorded in one patient (0.08%), a wound infection in 2 (0.17%), and a seroma in 2 (0.17%) (Table 3). We had no definitive bilateral vocal cord paralysis and no mortality.

A nodal recurrence occurred in 25 patients (2.16%) while no patient developed distant recurrence during follow-up. An ipsilateral III-IV level node recurrence was found in 24 cases, a VI level node recurrence in 1 case. 20 patients were female and 5 male; 10 patients had been submitted to TT with central neck dissection, 15 patients to TT without it. Histology was papillary cancer in 24 cases (in 2 cases tall cell variant) and follicular in 1. In 9 cases a thyroiditis was present at first intervention; in 7 cases there were nodal metastases, in 9 the tumor was multicentric, and in 8 there was extrathyroidal invasion (Table 4). Mean size of recurrence was 21.18 mm. No patient died during follow-up. No data reached statistical significance.

**Discussion**

Treatment guidelines published in Western countries basically recommend TT as the initial surgery for DTC, and although they allow LI for limited “low-risk cases”, the definitions of “low-risk” are not consistent (9). The controversy regarding the extent of thyroidectomy required persists, mainly because little is known about the long-term outcomes of DTC patients who have been treated by LI (9). Bilimoria et al. (16) reported that TT had improved the survival rate of patients with tumors larger than 1 cm supporting TT as the initial surgery for DTC patients. For DTC < 1 cm there is no difference in outcomes between TT and LI (16). They reported increased recurrence rates in LI patients for all size of tumors compared to TT patients. Based on this evidence the ATA guidelines now recommend TT for all lesions over 1 cm and LI only for lesions under 1 cm in low risk patients (recommendation 26) (11), which is also the recommendation of the consensus statement from the European Thyroid Cancer Taskforce (27). Loh et al. (28) found that LI resulted in increased rates of both recurrence and deaths compared with TT.

Nixon et al. (14) report that for intraglandular cancers, the rates of death due to disease are below 1% over a period of 10 years in patients treated with either LI or TT. Although for overall survival, advanced age and
male gender were predictors of poor outcome in this group of patients, neither T stage, nor surgical procedure was significant on multivariate analysis (14) showing that the extent of surgical resection did not have any impact on overall or disease specific survival. In addition, there was no difference in either local or regional recurrence in patients with intraglandular cancer under 4 cm in size.

Indeed several groups have demonstrated that TT does not improve survival, even among high-risk patients (9, 12, 15). Matsuzu et al. (9), in their study of 1088 cases and a follow-up of 17.6 year demonstrated that age 45 years or older, tumor larger than 40 mm, extrathyroidal invasion, and clinical lymph node metastasis were significant risk factors for a poor outcome, concluding that LI (without RAI therapy) represents a valid alternative to TT for selected patients (younger than 45 years, tumor diameter of 40 mm or less, and without clinical lymph node metastasis or extrathyroidal invasion).

Our experience is based only on TTs and one of the reasons that led us to opt for this choice is the extreme difficulty in identifying low-risk patients preoperatively. For example, the presence of an aggressive variant (e.g tall cell) and of multifocality are not identifiable preoperatively. Our incidence of recurrence was very low: a nodal recurrence occurred in 2.16% of patients while no patient developed distant recurrence during follow-up. Even if the incidence of recurrence was very low, it is also true that our data confirm the difficulty of predicting preoperatively the cases at high risk. However, some elements appear important as the multicentricity, the extrathyroid invasion and the presence of lymph node metastases at the time of thyroideectomy.

Another reason for performing TT as the initial treatment for DTC is the possibility of intrathyroidal metastasis in the contralateral lobe, because bilateral cancers have been reported in 30-85% of DTC patients (9, 15, 29). However the recurrence rate in the remnant thyroid gland at 25 years in the study of Matsuzu (9) was just 6.5%, and it was almost the same as the rates in previous reports (17, 22, 30, 31). Thus, the possibility of intrathyroidal metastasis in the contralateral lobe should not be the only one sufficient reason to justify routine TT in all DTC cases (9).

In our experience multifocality was present in 28% of patients, in 12.3% unilateral and in 15.7% bilateral. These rates are lower than those reported in the literature; the significance of this finding is not clear. Perhaps the high incidence of micrometastases associated to other thyroid diseases such as Hahimoto’s thyroiditis or nontoxic goitre could explain these low rates of bilateral cancer.

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Conclusions

TT remains the safest treatment in DTC, especially if performed in high volume centers in which complications can be minimized. LI can be a viable and safe alternative in small (<1 cm) unifocal tumors in patients at low risk. LI in tumors larger than 1 cm should be validated by further studies and cannot be currently considered a standard of care. The use of LI is limited in endemic areas by the association with other thyroid diseases. A correct and detailed information of the patient is essential before planning surgery.

References


