



# Continuing controversies on the extent of surgery in papillary thyroid carcinoma

Juan J. Díez<sup>1,2^</sup>

<sup>1</sup>Department of Endocrinology, Hospital Universitario Puerta de Hierro Majadahonda, Instituto de Investigación Sanitaria Puerta de Hierro Segovia de Arana, Majadahonda, Spain; <sup>2</sup>Department of Medicine, Universidad Autónoma de Madrid, Madrid, Spain

*Correspondence to:* Juan J. Díez. Department of Endocrinology, Hospital Universitario Puerta de Hierro Majadahonda, Instituto de Investigación Sanitaria Puerta de Hierro Segovia de Arana, Calle Manuel de Falla, 1, 28222 Majadahonda, Madrid, Spain. Email: juanjose.diez@salud.madrid.org.

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Surgical treatment continues to be the main therapeutic procedure in differentiated thyroid cancer. The long-term prognosis, complications, and quality of life of many patients largely depend on the adequacy of the initial surgery. For many years, total thyroidectomy (TT) with or without radioiodine (RAI) ablation has been the standard initial treatment for most of these patients. However, in patients with low-risk papillary thyroid carcinoma (PTC), who are the majority of thyroid cancer patients in clinical practice (1), several recent studies have shown that less aggressive surgical interventions, such as hemithyroidectomy, may be a valid alternative without having a significant impact on disease-specific or overall survival (2,3).

TT is indicated in tumors larger than 4 cm, with gross extrathyroidal extension (ETE) or with distant metastases (clinical M1). However, the extent of surgery is less rigid in tumors of 1–4 cm that are not associated with risk features. The 2015 American Thyroid Association (ATA) guideline, in its recommendation 35, states that in patients with tumors >1 and <4 cm, without ETE and without clinical evidence of node involvement (cN0), the initial treatment can be either a bilateral procedure (TT or near-total thyroidectomy) or a unilateral procedure (lobectomy) (4). This guideline acknowledges that the treatment team may choose TT to enable RAI therapy or to facilitate follow-up, depending on the characteristics or preferences of the

patient. Prophylactic central compartment lymph node dissection (pCND) is another of the most controversial issues in PTC surgery. The 2015 ATA guideline recommends that this procedure, unilateral or bilateral, should be considered in patients with PTC without clinical evidence of central neck lymph node involvement (cN0) who have advanced tumors (T3 or T4), in patients with clinically demonstrated lateral neck node involvement (cN1b), or in cases where the information obtained is to be used for further treatment planning (4).

Hemithyroidectomy is associated with very few perioperative complications. The preservation of the contralateral lobe and the parathyroid glands is an unquestionable advantage for patients, since it is accompanied by a decrease in the need for thyroid hormone replacement therapy and calcium and vitamin D supplements (5). Hospitalization time and costs associated with hemithyroidectomy are notably lower than those of a TT (6). Hemithyroidectomy has the drawback of the risk of tumor recurrence in the residual lobe, although the proportion of patients in which this occurs is low and easy to detect, as has been reported in a previous study (7). In turn, pCND has been associated with a reduced risk of locoregional recurrence in the central neck compartment, although it has the drawback of a higher rate of perioperative complications, including permanent

<sup>^</sup> ORCID: 0000-0002-2017-0694.

hypoparathyroidism (8).

The debate about the appropriate extent of surgery for PTC has persisted for decades. It is worth noting that although hemithyroidectomy has been shown to be suitable for a large proportion of patients with PTC, especially in patients with tumors up to 4 cm and no evidence of nodal metastases or ETE (9), and despite the extensive experience gained in countries such as Japan and Korea (5,9,10), this surgical procedure has been scarcely used in Western countries (1,7,11). In this issue of *Gland Surgery*, Cheon *et al.* (12) have dealt with analyzing current trends in the use of hemithyroidectomy in various clinical settings. These authors report the results of a survey on surgical procedures used in Korea by specialists with expertise in thyroid cancer. This is an interesting study for several reasons. First, because results reflect real clinical practice in Korea. Second, because it focuses on a subgroup of patients with PTC of an intermediate size (1.5 to 2.5 cm) that are very common in the clinic and whose treatment remains controversial. And, lastly, because it compares the attitudes of specialists who may have a different points of view on patient management, i.e., endocrinologists and head and neck surgeons.

The authors analyze in detail both the extent of thyroidectomy (hemithyroidectomy *vs.* TT) and the use of pCND according to the tumor size and location and the degree of ETE. Even though in the standard case proposed by the researchers (1.5 and 2.5 cm PTC without ETE) the preference for hemithyroidectomy was high and similar between endocrinologists and surgeons, the criteria changed as the burden of disease progressed. In cases of suspected anterior minimal or anterior gross ETE, endocrinologists were more aggressive than surgeons, with less preference for hemithyroidectomy. Furthermore, endocrinologists recommended TT more often than surgeons in isthmic tumors, a location that is usually associated with increased risk of invasion of adjacent tissues, central lymph node metastases, and recurrence (13). These results might be due to the fact that surgeons believe that gross strap muscle invasion does not significantly impact disease-specific survival in tumors <4 cm as it has been shown by several authors (14,15). It is also possible that surgeons are more confident in their abilities to eradicate cancer in larger and more invasive tumors and that endocrinologists prefer a more extensive removal, probably with a view to consolidating treatment with the use of post-surgical RAI. Remnant ablation with RAI allows for patient follow-up with serum thyroglobulin level monitoring, a comfortable

follow-up approach for most endocrinologists.

Posteriorly located tumors carry a special risk due to the complexity of posterior anatomical structures. It is known that laryngotracheal structure invasion leads to a higher possibility of incomplete resection and therefore, a higher risk of recurrence and poorer prognosis (14). In this survey, both surgeons and endocrinologists preferred TT with pCND in patients with posterior gross ETE. Both groups of specialists had similar opinion in patients with suspected posterior gross ETE or anterior and posterior gross ETE. This suggests that surgeons and endocrinologists share the same concern about possible invasion of adjacent tissues in unfavorably located tumors. There were few differences in recommendations for pCND, although endocrinologists are generally more prone to pCND than surgeons. Likewise, it appears that endocrinologists are trending toward more extensive surgery, including pCND, with the goal of minimizing the risk of locoregional recurrence (16).

A review of the recent literature shows that preferences for PTC treatment show great variability in different countries. Thus, in a survey conducted in Turkey (17) endocrinologists were more aggressive than surgeons, while the opposite occurred in the USA (18). Interestingly, the professional experience of both surgeons and endocrinologists does not seem to significantly modify preferences for hemithyroidectomy in Korean physicians. These data contrast with those obtained in the survey by McDow *et al.* (19) conducted in the USA. These authors showed that only a minority of surgeons in the USA recommend hemithyroidectomy for patients with low-risk PTC. In addition, high-volume surgeons tended to recommend lobectomy more frequently and low-volume surgeons were less likely to be aware guidelines support lobectomy for low-risk PTC 1–4 cm. Nevertheless, it should be noted that in the USA most thyroidectomies are performed by low-volume surgeons. In Cheon's survey, 58% of the surgeons were considered high-volume, while in the McDow's survey most of the respondents (64.4%) were low-volume surgeons.

The state of the contralateral lobe changed the decision of the specialists in those conditions associated with higher risk or greater size. In this case there were few differences of opinion between surgeons and endocrinologists. There are other variables that have not been considered in this study and that also generate controversy in decision making. It would be interesting for future research in this field to consider patient-dependent factors, such as age, comorbidity, history of previous cervical radiation, or family

history of thyroid cancer.

A message that is clear from Cheon's study is that there are differences in criteria between specialists in endocrinology and surgery and that this, consequently, can generate uncertainty or confusion in the patient. The intermediate clinical situations that frequently appear in certain conditions, such as PTC, are gray areas in the therapeutic decision-making process and are, therefore, the most likely to elicit diverse opinions conditioned by the physician experience, local routines or availability of health resources. In the case of PTC there are no randomized clinical trials comparing the different surgical extents because of the need for a huge sample size and a long follow-up time. Additionally, published retrospective studies may be puzzling, as better recurrence and survival rates have been reported with both hemithyroidectomy in some reports and with TT in others (20,21). On the other hand, it has been shown that there are non-clinical factors that have a significant influence on treatment recommendations, such as the physician's specialty, physician's or patient's personal preferences, or physicians' beliefs about factors influencing patients' treatment choice (18).

Clinical guidelines can help to solve these uncertainties, but they do not always resolve the dilemma presented by a specific patient and there is not always a great adherence of doctors to the recommendations. This is where joint decision-making within a multidisciplinary team acquires its greatest importance. Multidisciplinary approach is an optimal model for the caring of cancer patients, since it offers decisions agreed upon by several expert specialists and allows a holistic view of the patient from diagnosis to long-term follow-up (22). The advantages for the patient of this way of working include an improvement in the choice of diagnostic procedures and treatments, a reduction in clinical variability and an increase in satisfaction (23,24). Professionals also benefit from this teamwork model. Multidisciplinary teams facilitate the adaptation of clinical practice to the recommendations of national and international guidelines, improve the continuing education of professionals and increase the satisfaction of specialists (23).

In recent years, clinicians and surgeons with a special focus on thyroid disease have witnessed a notable change in criteria regarding the extent of initial treatment for patients with differentiated thyroid cancer. Current opinions have strikingly expanded the indications for hemithyroidectomy versus TT in low-risk patients, as evidenced by the survey by Cheon *et al.* In this search for the most appropriate

treatment for each patient with low-risk PTC, other procedures such as minimally invasive thyroid surgery, non-surgical ablative procedures, and even active surveillance also have their place and their long-term results will have to be analyzed in detail in future research. Indications for RAI therapy have become more restricted in last years. Its use is now not recommended in low-risk PTC patients and should be selective in intermediate-risk patients (4).

The current trend of personalized medicine in the field of thyroid cancer advises a careful evaluation and stratification of the risk of each patient and seeks to make possible the individualization of treatment, avoiding both under and overtreatment (25). Cheon's survey shows that this change in mentality has reached the Korean specialists. Hemithyroidectomy is a safe and effective treatment for a large proportion of patients with low-risk PTC. Previous studies reported that only a minority of these patients undergo lobectomy (2,3) and that many surgeons do not offer lobectomy to patients with 2.5 cm PTC (19) or even prefer TT in unilateral papillary microcarcinomas (17). On the contrary, in the standard case raised in this survey, the majority of endocrinologists and surgeons recommend hemithyroidectomy for both 1.5 and 2.5 cm tumors.

This conceptual change has resulted in a search for the adaptation of treatments to the needs of individual patients and, therefore, in the use of less aggressive treatments when this is suitable according to the available evidence and following the lines marked by the personalized and precision medicine. Multidisciplinary team must be a leader in the emerging field of precision medicine and must be able to apply the most appropriate treatment to each patient in the right environment, with the right scope and at the right time.

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