

Surgical management of papillary thyroid carcinoma: an overview

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Abstract The surgical management of papillary thyroid carcinoma remains contentious and the optimal surgical strategy has not been yet established. The extent of thyroid resection has been the nub of this debate. Literature lacks prospective randomized controlled trials that could help put this debate to rest, and these have been labeled as being impractical. Consequently, large retrospective studies and expert opinion have constituted the basis of clinical practice guidelines. Recent American Thyroid Association and National Comprehensive Cancer Network guidelines consider a conservative approach in the form of a thyroid lobectomy sufficient for low-risk disease and that total thyroidectomy remains the standard of care in the presence of high-risk features. Nevertheless, many authorities still advocate more aggressive therapy for low-risk disease. The challenge in standardizing the surgical strategy to papillary thyroid carcinoma is mainly related to a major tumor characteristic: the high frequency of occult cancerous foci whether within the thyroid gland itself or within loco-regional lymph nodes as this tumor characteristic has been incriminated for a higher risk of recurrent disease and its adverse sequelae. The purpose of this article is to provide an overview of the surgical management of papillary thy-

roid carcinoma and the main arguments surrounding this hotly debated topic. All evidences for this review article were drawn from PubMed articles in English language mostly cross-referenced with international guideline statements.

Keywords Papillary thyroid carcinoma · Surgical management · Thyroid lobectomy · Total thyroidectomy

Introduction

Papillary thyroid carcinoma (PTC) is the most common primary thyroid malignancy. It is currently one of the cancers with the most rapid increase in prevalence in most areas of the world and this has been largely but not fully attributed to the increased detection of subclinical lesions [1–3]. As a result, the optimal treatment modality for PTCs, particularly the extent of thyroid resection for low-risk disease has been gaining increasing popularity among endocrinologists and endocrine surgeons. However, to date, this remains an area of ongoing controversy.

The main objectives of initial management of differentiated thyroid cancer (DTC) are to reduce disease/treatment-related morbidity, reduce the risk of persistent/recurrent disease and its associated morbidity, and improve overall and disease-specific survival. Udelsman et al. demonstrated that due to the low recurrence and death rates from DTC, addressing these primary endpoints when evaluating the optimal initial surgical strategy for the management of DTC requires a large, lengthy, and costly prospective randomized controlled trial [4]. Accordingly, conducting sufficiently powered studies in this area could be labeled as impractical and the debate is unlikely to be put to rest any time soon.

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The extent of thyroidectomy for PTC in current clinical practice guidelines

Adequate surgery is the most important prognostic determinant in the management of DTC, while other treatment variables including radioiodine ablation (RIA) and thyroid stimulating hormone (TSH) suppression therapies only serve as adjuncts at least in some patients [5]. Recent American Thyroid Association (ATA) and National Comprehensive Cancer Network (NCCN) guidelines consider thyroid lobectomy as adequate surgery for DTCs up to 4 cm in maximal diameter in the absence of high-risk features with total thyroidectomy remaining the preferred option in their presence [6, 7]. This is mainly attributed to the otherwise indolent nature of these tumors and their favorable prognosis. This paradigm shift in the extent of thyroidectomy for DTC was largely based on a population-level study by Adam et al. in which they analyzed 61,775 patients from the National Cancer Data Base (NCDB) demonstrating that in low-risk patients with low-risk tumors 1–4 cm in size, total thyroidectomy does not offer a survival advantage over lobectomy, and patients are unnecessarily subject to both an increased risk of complications and life-long hormone replacement therapy [8]. By adjusting for several patient, clinical and tumor-related prognostic factors their study weathered the limitations of the study by Bilimoria et al. on the same data that advocated total thyroidectomy for DTCs >1 cm in size [9], and served as the basis for the management recommendations for DTC of the 2009 version of the ATA guidelines [10]. Furthermore, a recent assessment of the impact of the extent of thyroid resection in 43,032 patients under the age of 45 years collected from the two largest oncology databases: the NCDB and the Surveillance Epidemiology and End Results (SEER) database, underscored the prognostic significance of low-risk disease and confirmed the current American Joint Committee on Cancer (AJCC) staging system for DTC in low-risk patients [11]. The AJCC staging system classifies these patients as having only stage I or II disease, based solely on the absence or presence of distant metastasis, respectively, regardless of the size of their tumors or extent of loco-regional disease [12].

Total thyroidectomy vs. thyroid lobectomy: an ongoing debate

Papillary thyroid carcinomas are favorable prognosis cancers. Most patients have an excellent long-term overall survival rate; a 5-year overall survival rate well above 90% [13, 14]. As a result, disease-free survival has replaced overall survival as the main outcome of interest when the

extent of thyroidectomy for these tumors is evaluated. Essential to any assessment of the extent of thyroid resection is the verification of its oncologic rationale and whether or not its benefits outweigh its potential risks.

Proponents of total thyroidectomy argue that the high frequency of occult disease whether in the thyroid gland itself or in loco-regional lymph nodes is the hallmark of PTC. This feature is a prognosticator and implies an increased risk of recurrence which in turn implies the need for reoperation and decreased overall survival [9, 15–17]. Furthermore, the need for a second operation makes local recurrences a source of additional morbidity and cost [18, 19]. Complete removal of thyroid tissue facilitates the detection and elimination of persistent and/or metastatic disease by radioiodine which would in turn have a favorable reflection on disease-free survival. It also renders serum thyroglobulin a sensitive postoperative marker for persistent and/or recurrent disease improving surveillance accuracy. Following patients after lobectomy may be more challenging. Thyroglobulin levels are easier to interpret after total thyroidectomy than after lobectomy and detecting central nodal recurrence using ultrasound is also more technically challenging with a thyroid lobe left in situ. Using a decision-analytic model developed to assess the extent of thyroid resection in PTC as an outcome determinant, Esnaola et al. demonstrated that compared to thyroid lobectomy; total thyroidectomy maximized disease-free survival, overall survival, and quality-adjusted life expectancy in patients with PTC, irrespective of risk-group classification [20]. A recent meta-analysis confirmed that total thyroidectomy was associated with a significantly lower risk of recurrence. However, this did not translate to a significantly improved overall survival. Nevertheless, total thyroidectomy trended towards improved survival [21]. In a recent retrospective analysis of 8676 patients with classical papillary microcarcinomas, Kim et al. evaluated the extent of thyroid resection in terms of loco-regional recurrence distinguishing between contralateral remnant lobe recurrence and recurrence in thyroid lobe and/or regional nodes [22]. They demonstrated that in the setting of multifocal disease, total thyroidectomy significantly lowered the overall risk of loco-regional recurrence in all of its forms. Advocates of total thyroidectomy also cite that lobectomy is not without consequences. Hirsch et al. demonstrated that the rate of definitive complications following hemithyroidectomy was comparable to that following total thyroidectomy. However, the former represented a significant follow-up burden [23]. Furthermore, hypothyroidism and the requirement for thyroid hormone replacement therapy are considerable after thyroid lobectomy [23–25]. Finally, when high-risk features in the current clinical practice guidelines are considered collectively,

these can be broadly classified into two categories: features determined pre- and intra-operatively prior to histopathological examination of the surgically resected specimen and features determined postoperatively after histopathological examination of the surgically resected specimen. This classification implies that a proportion of patients initially undergoing thyroid lobectomy will be placed in a higher risk category consequently warranting total thyroidectomy; this proportion has been reported as considerably high in the literature [26–29]. Arguments for total thyroidectomy are summarized in Table 1.

The main argument of proponents of thyroid lobectomy is that the higher rate of complications after total thyroidectomy outweighs its potential benefits with respect to disease-free and overall survival in low-risk disease [8, 11, 30–34]. In comparison with total thyroidectomy, thyroid lobectomy is inherently associated with a lower risk of postoperative morbidity particularly postoperative hypoparathyroidism, and is devoid of the risk of bilateral vocal fold palsy. In a recent population-based analysis of 62,722 thyroidectomies performed for benign and malignant disease, Hauch et al. demonstrated that total thyroidectomy, compared to thyroid lobectomy, was significantly associated with a higher risk of complications even in the hands of high-volume surgeons [35]. Therefore, thyroid lobectomy could be viewed as exchanging a relatively low risk of recurrence for half of the complications of total thyroidectomy at a minimum. Kwon et al. demonstrated that the significantly lower risk of loco-regional recurrence following total thyroidectomy in comparison with thyroid lobectomy was attributed to contralateral remnant lobe recurrences rather than the thyroidectomy site and/or nodal recurrences and that the former could be easily managed by completion thyroidectomy without additional morbidity [36]. In a recent retrospective analysis, Kuba et al. compared the extent of thyroidectomy for PTCs up to a size larger than that

proposed by current guidelines (5 cm) in terms of prognosis (recurrence free and overall survival) and adverse events. They demonstrated that after adjusting for baseline clinicopathologic factors using a propensity score matching thyroid lobectomy and total thyroidectomy was comparable in terms of prognosis. However, adverse events were less frequent with the former [37]. Another point in favor of thyroid lobectomy is that the majority of patients are spared life-long hormone replacement therapy when TSH suppression therapy is not required and this has a favorable impact on the quality of life [38]. Advocates of thyroid lobectomy also argue that if the need for completion thyroidectomy emerges based on high-risk postoperative findings, its morbidity is comparable to that of upfront total thyroidectomy [39]. They also consider labeling total thyroidectomy as being more cost-effective than thyroid lobectomy an inaccurate description of reality; a valid cost analysis comparing thyroid lobectomy and total thyroidectomy should account for the rate of complications associated with the individual procedures. They cite the fact that thyroid lobectomy becomes or trends towards becoming more cost-effective with increasing rates of complications associated with total thyroidectomy [40, 41]. On the matters of adjuvant radioiodine ablation therapy and adequate disease surveillance, advocates of conservative therapy argue that radioiodine ablation therapy is not only of no clear benefit in low-risk disease, but is also associated with the risk of unacceptable sequelae. These could be immediate from salivary and lacrimal side effects, and post treatment dysphagia and/or delayed from increased rates of second primary malignancies [42, 43]. Furthermore, the role of iodine scans as a surveillance modality is no longer significant. The evolution in sonographic imaging and the sensitivity of thyroglobulin measurements have made them the standard of care for surveillance [44]. Arguments for thyroid lobectomy are summarized in Table 2.

Table 1 Arguments for total thyroidectomy

Multicentricity (bilaterality) is the hallmark of PTC and this translates into a significantly increased risk of persistent/recurrent disease
Total thyroidectomy is associated with a significantly improved disease-free survival, and at a minimum, a trend towards significantly improved overall survival
Local recurrences are associated with reoperative complications and decreased survival
Total thyroidectomy allows for the optimal use of radioiodine as both a diagnostic and therapeutic means (it facilitates the detection and elimination of persistent and/or metastatic disease)
Total thyroidectomy is a forward step towards achieving athyroglobulinemia and improving surveillance accuracy (it renders thyroglobulin a sensitive postoperative marker for persistent and/or recurrent disease)
In experienced hands, morbidity from total thyroidectomy is comparable to that from thyroid lobectomy. However, the latter is associated with a follow-up burden
A considerable proportion of patients initially labeled as having low-risk disease and eligible for thyroid lobectomy will be condemned to completion thyroidectomy based on postoperatively determined high-risk features

Table 2 Arguments against total thyroidectomy

Based on biologic behavior, occult cancerous foci whether in the thyroid gland itself or regional lymph nodes are considered clinically irrelevant (non-progressive and without implications on morbidity or survival)
Loco-regional recurrences are low mostly involving the contralateral remnant lobe. These can be successfully managed surgically and a secondary procedure does not imply an increased risk of morbidity compared to a primary one
Total thyroidectomy is associated with a significantly increased risk of complications regardless of the surgeon's experience
Adequate follow-up could be easily and accurately achieved by serial thyroglobulin measurements and an annual cervical ultrasound
The empiric use of radioiodine ablation therapy is of no proven benefit and is not without consequence. Therefore, it is only advocated in selected patients with intermediate- or high-risk disease
With proper risk analysis, the need for completion thyroidectomy is consistently low and does not necessarily imply additional morbidity or cost

Management of nodal disease in PTC

Therapeutic comprehensive compartment-oriented neck dissection in PTC is widely accepted to be associated with improved outcomes both in terms of recurrence and survival. However, the role of prophylactic neck dissection in the management of PTC remains controversial regarding its benefits and risks [45–48]. Current clinical practice guidelines have adopted a risk-adapted approach in recommending prophylactic surgery for occult nodal disease with such recommendation being considered as weak. This is mainly based on the finding that occult node positivity while being quite common in PTC (even in subcentimetric cancers) rarely demonstrates prognostic parameters of recurrence and/or a possibly worse disease-specific survival and is associated with an increased risk of morbidity; occult metastases usually tend to be small in size and number, with no extranodal extension, and a median risk of recurrence of only 2% [49]. Nevertheless, the debate regarding the role of prophylactic neck dissection in PTC is likely to continue as conclusive studies in this area have been labeled as “readily not feasible” [50].

Conclusion

A definitive correlation between the extent of thyroid resection and long-term survival has not yet been established. Nevertheless, unlike most malignancies where the main focus is survival, the primary endpoint in PTC is recurrence. In light of the current literature, no one surgical strategy fits all. Careful decision making regarding the extent of thyroid resection should be based on pre, intra, and postoperative prognostic features as well as risk-group analysis to maintain an acceptably low risk of recurrence. This should also be balanced with the risk of surgical morbidity which is directly proportional to the extent of resection and inversely related to surgeon's experience, cost, and patients' desire after being actively involved in decision making regarding their clinical condition.

Compliance with ethical standards

Conflict of interest The authors have no conflicts of interest or financial ties to disclose.

Research involving human participants and/or animals All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethic committee approval was waived because of the type of this study.

Informed consent Informed consent was waived because of the type of this study.

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