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ROUTINE LEVEL VI LYMPH NODE DISSECTION FOR PAPILLARY THYROID CANCER: SURGICAL TECHNIQUE

[CLINICAL REVIEW]

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Abbreviations:AES, Australian Endocrine Surgeons; ATA, American Thyroid Association; LND, lymph node dissection; PTC, papillary thyroid cancer; SLNB, sentinel lymph node biopsy.

Abstract

Total thyroidectomy is the treatment of choice for clinically significant papillary thyroid cancer (PTC); **however, 10–15% develop palpable local recurrence in the cervical lymph nodes. Metastases in the cervical lymph nodes account for 75% of loco-regional recurrence and up to 50% of these patients eventually die of their disease. I**t is generally accepted that surgical excision of grossly involved lymph node disease should be carried out. **The role of routine lymph node dissection, however, is greeted with far more controversy. Regional lymph node metastases have been shown to be associated with more frequent tumour recurrence.** Not only is recurrence associated with increased disease-related mortality, but recent data have shown that the presence of involved lymph nodes is associated with adverse survival. Additionally, there have been significant changes to the way patients are managed after treatment for PTC in recent years. **Surveillance previously relied on clinical assessment and radioiodine scans whereas now the use of serum thyroglobulin and high-resolution ultrasound are the standard as evidenced by recommendations by the American Thyroid Association**. These techniques have greater sensitivity and subsequently lymph node metastases are being detected earlier and more frequently. **This has led to a paradigm shift in the aims of treatment of PTC, from a focus on survival data to a focus on disease-free status. Routine central neck lymph node dissection can be carried out with no increased morbidity and**

can achieve lower 6-month stimulated thyroglobulin levels when compared with total thyroidectomy alone. Routine ipsilateral level VI lymph node dissection in addition to total thyroidectomy should be carried out for the management of clinically significant PTC.

Background

Thyroid cancer is the most common endocrine malignancy, accounting for approximately 1% of all human cancers and causing approximately 0.5% of all cancer deaths.[1] Papillary thyroid cancer (PTC) is the most common thyroid malignancy and carries an excellent prognosis with an overall 10-year survival exceeding 90%.[2,3] Lymph node metastases are a common finding in PTC and tend to occur relatively early. **The incidence of lymph node metastases has been reported to be as high as 90% and the incidence of palpable disease up to 40%.[4–8] In addition, 10–15% of patients treated with total thyroidectomy develop palpable local recurrence in the cervical lymph nodes over the subsequent decade.[8,9]** Metastases in the cervical lymph nodes accounts for 75% of loco-regional recurrence [10] and up to 50% of patients who experience recurrent thyroid cancer eventually die of their disease.[11]

Despite this, there are no prospective, randomized data to support any management for PTC. The low prevalence of PTC combined with its relatively indolent nature has meant that ideal treatment research protocols are difficult to undertake. Differences in method, the selection of patients and the duration of follow up make comparison between studies and the interpretation of results problematic; thus we rely on imperfect retrospective analyses to define risk factors. **It is generally accepted that total thyroidectomy is the procedure of choice for all PTC >10 mm in size.[12,13]**

Anatomy and distribution of cervical lymph nodes

There are 500 lymph nodes in the body and **200 of these are in the head and neck region.[14]** The lymph node regions of the neck are divided into levels I–VII: (i) level I nodes are the submental and submandibular nodes; (ii) level II are the upper jugular nodes; (iii) level III are the mid-jugular nodes; (iv) level IV are the lower jugular nodes; (v) level V are the posterior triangle and supraclavicular nodes; (vi) level VI or central compartment nodes incorporate the

Delphian/prelaryngeal, pretracheal and paratracheal lymph nodes; and (vii) level VII nodes are those within the superior mediastinum (Fig. 1).15

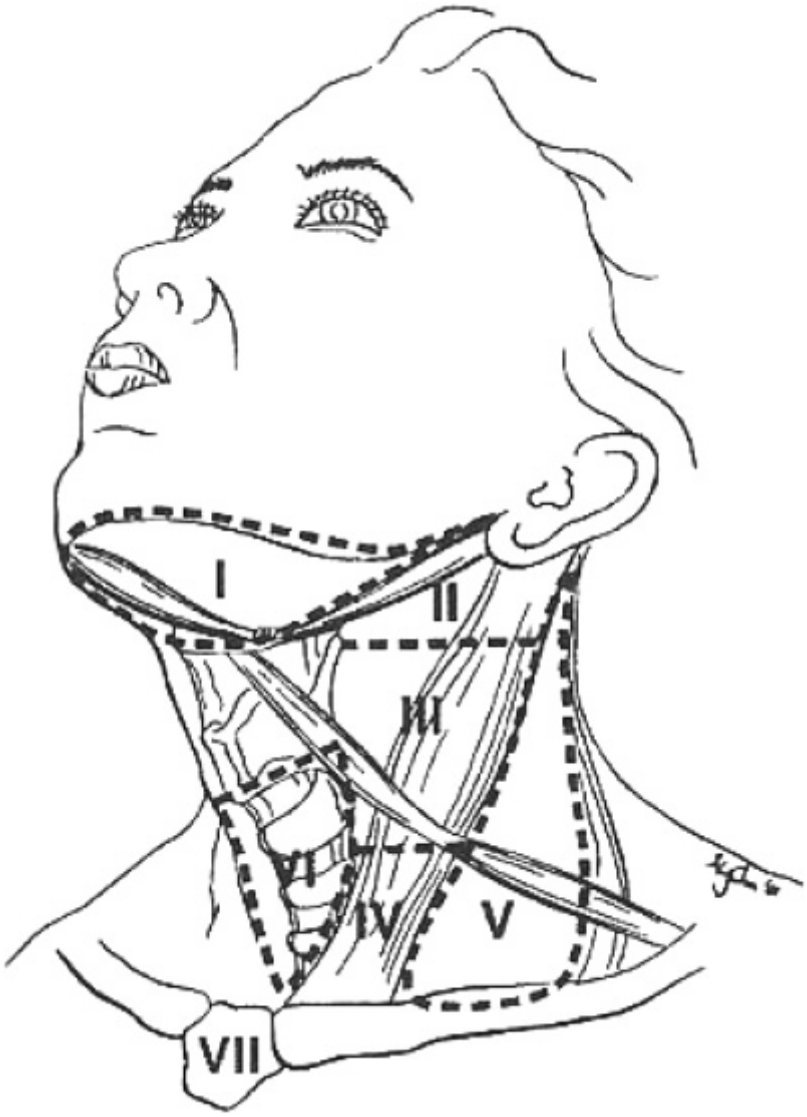

Fig. 1. Schematic diagram indicating the location of the lymph node levels in the neck. (Reproduced from Greene *et al.*55 with permission from Springer-Verlag).

The thyroid gland contains a dense network of intrathyroidal lymphatics with communication across the isthmus. The lymphatics leave the thyroid together with the important thyroid vessels; superiorly with the superior thyroid vessels, inferiorly with the inferior thyroid artery and also with the middle thyroid vein. **Lymphatic flow tends to be to the ipsilateral level VI lymph nodes primarily. The upper poles, along with the pyramid and isthmus also drain superiorly toward lymph node levels II/III while the lateral aspect of each lobe drain towards lymph node levels**

III/IV. The lower pole of the gland drains initially into level VI then goes on to levels IV and VII.

Lymph node metastases generally occur in a stepwise fashion, to the ipsilateral central neck first and then move on to the ipsilateral lateral neck and subsequently to the contralateral neck although skip metastases do occur. The ipsilateral central neck (level VI) is the most common site of metastatic PTC.**16,17 The ipsilateral level VI lymph nodes are involved in up to 69% of patients and it is the only lymph node compartment involved in 26%.18 The contralateral central neck is involved in approximately 10–20% and the ipsilateral lateral neck (node levels II–V) in 37–54% of patients.18–20**

The history of lymph node surgery for ptc

The treatment of regional lymph nodes in PTC is controversial. **It is generally accepted that surgical excision of grossly involved lymph node disease, either on clinical or ultrasonographical grounds, should be carried out.**6,21–26 Surgical approaches to loco-regional lymph node disease in PTC range from 'berry picking' to selective lymph node dissection (LND) to modified radical neck dissection.27 Formal LND has been shown to be superior to simple 'berry picking' of involved nodes as evidenced by lower recurrence and is generally preferred when managing lymph nodes in thyroid cancer.28

The role of routine LND, however, is greeted with far more controversy.29–32 There have long been geographical variations in practice with Japanese centres carrying out routine central and lateral neck LND in the absence of I^{131} treatment, whereas centres in Australia, USA and Europe have generally avoided such an approach.33

The argument against routine lymph node surgery

The argument for a conservative approach to loco-regional lymph nodes centres around two main concepts. First, in the past lymphatic metastases have not been shown to increase rates of cause-specific mortality and second, more radical surgery carries a greater morbidity. **It is generally accepted that lymph node involvement increases the likelihood of local recurrence**; however, **early evidence suggested there is no adverse relation between lymph node metastases and survival.4,34,35 A 12-year follow-up study of patients at the University of Chicago showed that extrathyroidal invasion, distant metastases, age and tumour size all had predictive value for cause-specific**

mortality unlike cervical lymph nodes, which were associated with increased recurrence but not increased mortality.[34] Grebe and Hay reported on a series of cases spanning 52 years and likewise reported that lymph node metastases at presentation, while increasing the risk of recurrence, did not have an adverse effect on cause-specific mortality.[4] The authors concluded that extensive LND at presentation offers no advantage in the treatment of PTC and may cause increased morbidity. Consequently, lymphatic involvement at presentation did not feature in the **MACIS** (distant metastases, age, completeness of resection, extrathyroidal invasion, size),[35] **AMES** (age, distant metastases, extrathyroidal invasion, size)[36] or many other prognostic systems for the classification of PTC.

The argument for routine lymph node surgery

In contrast to these findings, however, **regional lymph node metastases have been shown to be associated with more frequent tumour recurrence.[9,26,37,38]** Additionally, data showing higher mortality for patients with locally recurrent PTC have led to a renewed interest in routine LND.[39–41] **An age-matched study of patients with differentiated thyroid cancer found that not only were recurrences more common (32 vs. 14%) among patients with nodal involvement, but cause-specific mortality was also higher in these patients (24 vs. 8%).[26]** Noguchi and Murakami also argued for routine LND when they reported a clinical benefit associated with cervical LND, although this must be understood in the context of radioiodine not being used in Japan.[33] Subsequently, more recent publications acknowledge the adverse influence of lymph node metastases.[39,40,42] **The recent findings of a large population-based study has further strengthened the argument of those that believe the presence of lymph node metastases confers an adverse prognosis.[43] This analysis of 5123 patients over a 30-year period showed a significantly higher mortality rate for patients with lymph node involvement, even when corrected for TNM stage. Scheumann *et al.* not only showed greater recurrence and mortality associated with lymph node metastases, but also improved survival when LND was carried out in these patients.[5]**

The importance of lymph node metastases is reflected in the adoption of the TNM staging system (Table 1). TNM is now widely used and its international acceptance allows for comparison of data from different centres. The TNM system takes into account the size and extent of the primary tumour as well as the presence of lymph node and distant metastases.[42] Age at diagnosis also confers prognostic information, with patients under 45 years falling into a lesser stage

than older patients. The TNM system is used to stratify patients into different risk groups, stages I–IV, which allows for prognostic data.

Table 1. The TNM staging system for papillary thyroid cancer is used internationally and patients can be stratified into prognostic groups based on the stage of the disease

Stage	Age	
	<45 years	>45 years
I	Any T, any N, M0	T1, N0, M0
II	Any T, any N, M1	T2, N0, M0
III	NA	T3, N0, M0 T1–3, N1a, M0
IV	NA	T1–3, N1b, M0 T4, any N, M0 Any T, any N, M1

Stages: T1, primary tumour <2 cm; T2, primary tumour 2–4 cm; T3, primary tumour >4 cm; T4, primary tumour locally invasive; N0, no nodal involvement; N1a, nodal involvement in the ipsilateral level VI; N1b, nodal involvement in the ipsilateral lateral neck or contralateral neck; M0, no distant metastases; M1, distant metastases; NA, not applicable.

Table 1. The TNM staging system for papillary thyroid cancer is used internationally and patients can be stratified into prognostic groups based on the stage of the disease

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The changing goal posts

In years gone by surveillance after treatment for PTC was largely based on clinical assessment and radioiodine scans whereas **now the use of serum thyroglobulin and high-resolution ultrasound are the standard.[13] These techniques have greater sensitivity and subsequently lymph node metastases are being detected earlier and more frequently. This has led to a paradigm shift in the aims of treatment of PTC, from a focus on survival data to a focus on disease-free status.**

Young patients with papillary cancer are no longer prepared to simply accept that any residual disease has a less than 5% chance of leading to their death in the next 20 years. **Rather the aim of treatment should be to render patients disease-free as assessed by undetectable thyroglobulin levels and absence of metastatic disease on imaging, provided that such an approach does not lead to increased morbidity.** Surgeons are under more scrutiny than ever before from our endocrinologist colleagues and the patients themselves. **The American Thyroid Association (ATA) now recommends 6- to 12-monthly thyroglobulin assessment as well as normal ultrasound both preoperatively and postoperatively, with the aim of achieving athyroglobulinaemia.[13] Unfortunately, preoperative**

assessment of the central compartment lymph nodes with ultrasound is unreliable with a sensitivity as low as 10%, as opposed to the lateral compartment where ultrasound is highly sensitive.[44]

What is the role of sentinel lymph node biopsy?

The use of sentinel lymph node biopsy (SLNB) has been popularized for the treatment of melanoma and breast cancer since it was first introduced in 1990.[45] The technique finds its place where formal LND is associated with significant morbidity, such as in the groin or axilla. **SLNB for PTC has been shown to be technically feasible using both vital dye or radiotracer techniques with accuracy as high as 90%**.[46,47] In recent times the benefit of SLNB has been questioned when non-invasive imaging with high-resolution ultrasound can produce similar results.[48] The same argument applies to thyroid cancer where the use of ultrasound is being increasingly used for assessment of the lateral neck.[49] This fact together with the **low morbidity of routine central compartment LND, which is carried out through the same incision, makes many ask 'Why bother?'.**[50]

Routine central compartment lymph node dissection

For routine central neck LND to be a viable treatment option, it needs to be both safe and efficacious. Pereira *et al.* showed decreased local recurrence after carrying out routine bilateral central neck LND, but cautioned against adoption of this technique because of excessive morbidity.[32] Others have also reported increased morbidity with bilateral central neck LND.[31,51] **An alternative option is unilateral level VI LND. University of Sydney data on 56 patients undergoing routine ipsilateral level VI LND showed an increased incidence of temporary hypocalcaemia but no increase in permanent hypoparathyroidism or recurrent laryngeal nerve injury.[52]** Although no differences in recurrence or survival could be shown because of the relatively short follow up in this study, we were able to show significantly lower levels of stimulated thyroglobulin at 6 months and a greater number of patients achieving athyroglobulinaemia. **Others have also published acceptable morbidity figures when carrying out level VI LND for thyroid cancer.[15]**

Although athyroglobulinaemia is only a surrogate marker for tumour recurrence and possible increased mortality it is now the goal of treatment for many endocrinologists as reflected by the importance placed on this tumour marker in the latest guidelines published by

the ATA.[13] With increased surveillance and improved imaging, particularly high-resolution ultrasound, more patients can be identified with local recurrence in the neck. **Reoperative cervical surgery, particularly in the tracheo-oesophageal groove for local recurrence in the level VI lymph nodes is associated with significantly increased morbidity.[53]**

Local attitudes towards lymph node dissection

We conducted a survey of all members (*n* = 41) of the Australian Endocrine Surgeons (AES) with regard to their attitudes towards lymph node surgery in papillary thyroid cancer. In total, five scenarios were posed to each surgeon and we had an 85% response rate. Three scenarios dealt with involved lymph nodes in the lateral neck detected clinically or by ultrasound and with recurrent disease in the lateral neck after previous thyroidectomy. All but one surgeon recommended either modified radical neck dissection or selective neck LND in equal proportions. One surgeon preferred a berry-picking procedure in each scenario and one surgeon suggested ^{131}I treatment as the initial course in the scenario of recurrent PTC in the lateral neck after previous thyroidectomy.

Two scenarios dealt with attitudes towards lymph node surgery in the central neck. The first scenario asked about treatment for patients with PTC and involved lymph nodes in the ipsilateral central neck. **Sixty-six per cent of the respondents recommended bilateral central neck LND, 20% an ipsilateral level VI LND, 9% a selective neck LND (presumably equivalent to an ipsilateral level VI LND in this scenario) and 6% a modified radical neck dissection.** The second scenario involved **a diagnosis of PTC with no evidence of involved lymph nodes preoperatively. Forty-three per cent of respondents suggested a bilateral central neck LND, 31% an ipsilateral level VI LND, 14% would rely on radioiodine ablation, 3% would recommend no treatment of the lymph nodes and 9% would recommend berry picking of macroscopically involved nodes only**.

This survey shows that AES members as a group have a progressive attitude towards lymph node surgery for PTC. There seems to be a readiness to carry out modified radical neck dissection or selective neck LND for disease in the lateral neck with only one member recommending a berry-picking procedure. In a review of lymph node surgery form the University of Sydney Endocrine Surgical Unit from 1958 to 2002 the incidence of lymph node surgery has increased from 21.4 to 48.1%.[27] The use of selective neck LND has risen sharply, accounting for 84.1% of procedures in the period 1998–

2002. Over the study period, the use of berry-picking procedures has fallen from almost 50% of lymph node procedures to an insignificant level in the most recent 5-year period.

With regard to attitudes towards central neck LND, bilateral central neck LND is preferred by most respondents when there are involved lymph nodes in the central neck and all surgeons would carry out some form of lymph node surgery in this scenario. In the scenario of routine lymph node surgery, most of the surgeons (74%) would recommend some form of central neck LND. Bilateral central neck LND was marginally preferred over ipsilateral level VI LND.

Surgical technique

In our unit, an ipsilateral level VI LND is carried out at the time of thyroidectomy for known PTC. The prelaryngeal lymph node, sitting directly anterior to the cricothyroid membrane between the cricothyroid muscles, is dissected at the time of mobilization of the thyroid pyramid and isthmus. Thyroidectomy is then completed using the technique described previously.[54] Once the gland is removed, attention is turned to the remaining level VI lymph nodes in the paratracheal and pretracheal spaces.

The field is inspected to identify any macroscopic disease before dissection. Medial and lateral dissection margins are defined using diathermy and surgical clips. The fibrofatty tissue in the midline is incised to expose the trachea down to the level of the brachiocephalic vessels inferiorly and the medial border of the carotid artery is dissected down to the prevertebral fascia. The superior limit of dissection is at the level of the cricoid cartilage (Fig. 2).[55]

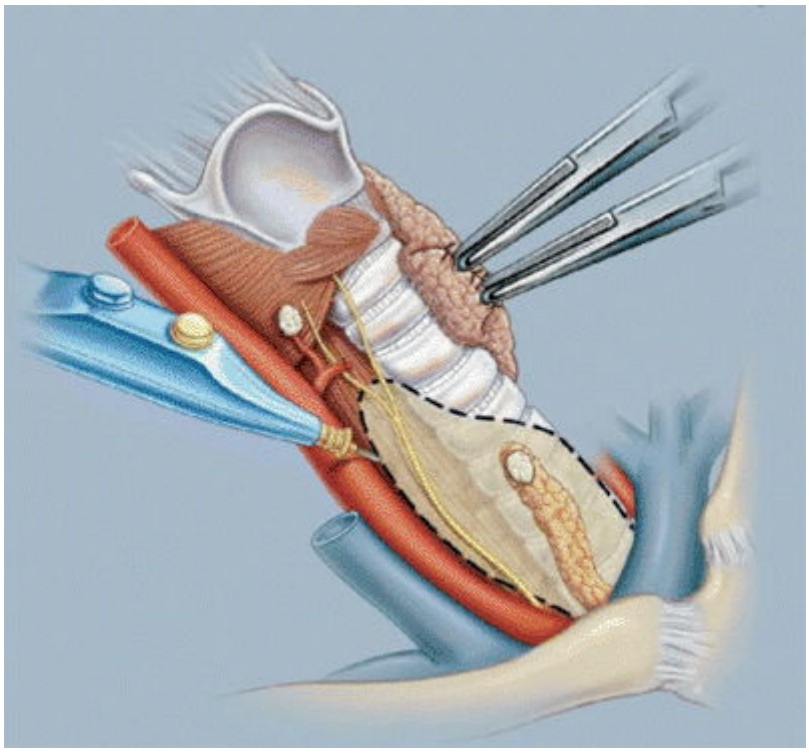

Fig. 2. With the thyroid lobe removed, margins of dissection are defined using diathermy: medial, the midline of the trachea; lateral, the carotid artery; inferior, the brachiocephalic vessels; superior, the cricoid cartilage. The prevertebral fascia forms the floor of the dissection bed.

The plane on the recurrent laryngeal nerve is developed using a right-angled forceps and a combination of surgical clips and sharp dissection (Fig. 3). The nerve is freed from the fibrofatty tissue of the paratracheal space allowing for lateral retraction of the recurrent laryngeal nerve away from the level VI lymph nodes (Fig. 4). **Care is taken to preserve the superior parathyroid on a vascularized pedicle, the inferior parathyroid gland is typically devascularized and removed for autotransplantation by injection technique as previously described (Fig. 5).56**

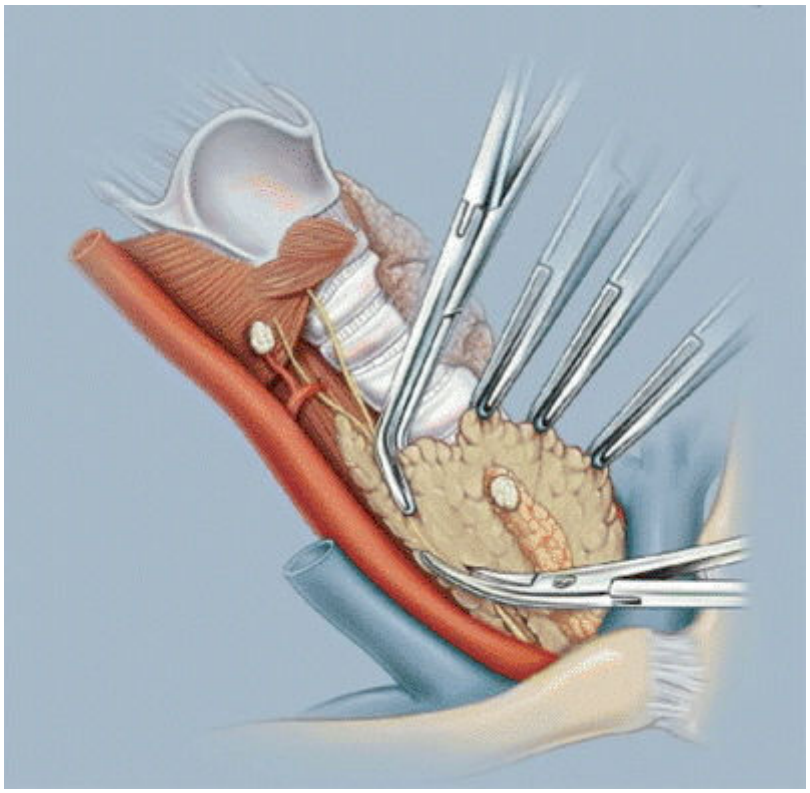

Fig. 3. The recurrent laryngeal nerve is dissected free from the fibrofatty tissue of the level VI lymph node compartment through the length of its course in the neck. A right-angled forceps is used with a combination of sharp dissection and surgical clips.

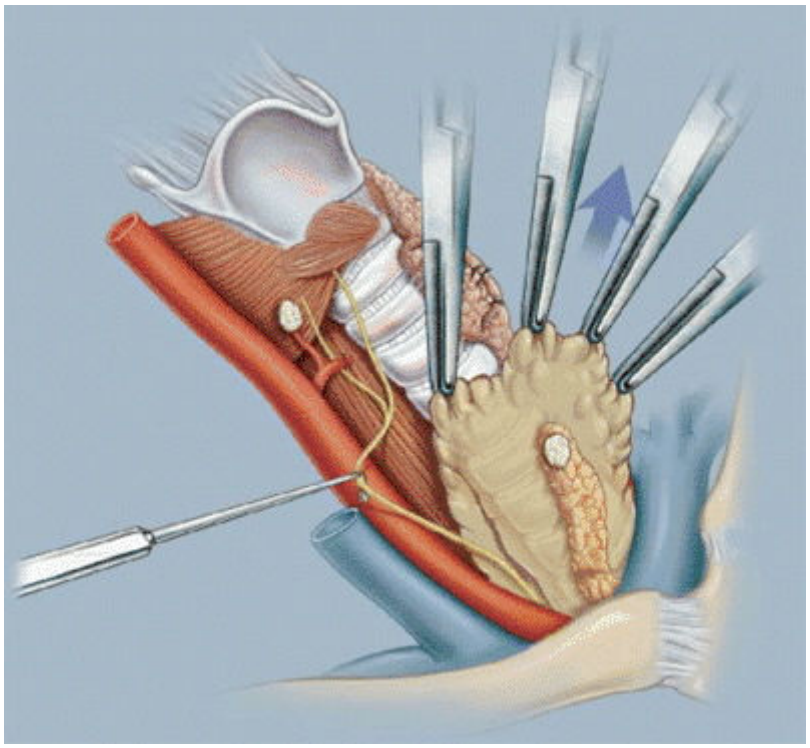

Fig. 4. The recurrent laryngeal nerve is retracted laterally, free from

the level VI lymph nodes. The envelope of fibrofatty tissue containing the level VI lymph nodes is retracted medially and dissected free from the prevertebral fascia, oesophagus and trachea.

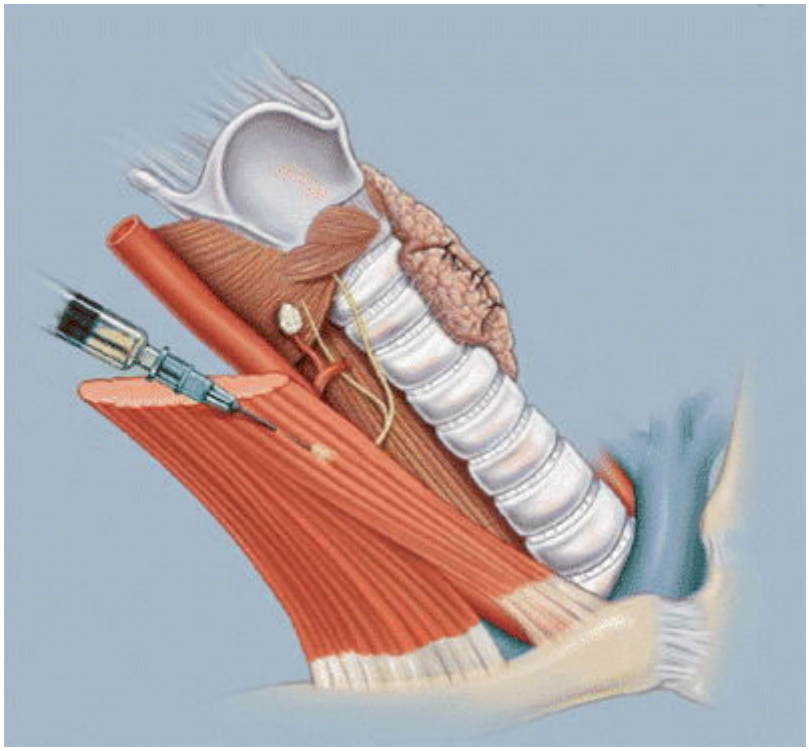

Fig. 5. The inferior parathyroid, devascularized during the dissection, is retrieved, chopped into fine pieces and injected into the sternomastoid muscle.

The envelope of tissue containing the level VI lymph nodes are then retracted medially and excised en bloc using a combination of diathermy and surgical clips to free it from the prevertebral fascia, oesophagus and trachea. The thymus is transected at the level of the brachiocephalic vessels and the specimen is removed. The final surgical field should be clear of all fibrofatty and lymphatic tissue (Fig. 6).

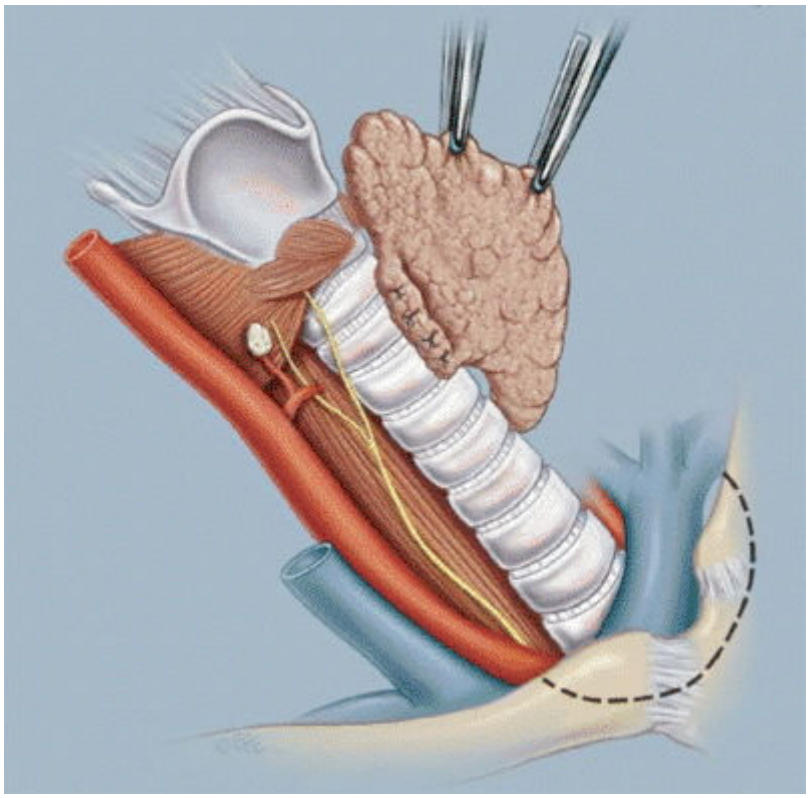

Fig. 6. The final operative field after removal of the specimen should be devoid of all tissue within the dissection field. Note the superior parathyroid maintained *in situ* on a vascular pedicle.

Conclusion

The central compartment/Level VI lymph nodes are at greater risk of harbouring metastasis from PTC than any other LN level. It makes sense to target this area as a routine part of the surgical approach assuming this can be carried out without increased morbidity. Carrying out routine LND appears to decrease the thyroglobulin levels thereby simplifying postoperative care and potentially reducing local recurrence. **We suggest carrying out routine ipsilateral level VI LND in addition to total thyroidectomy for the management of clinically significant PTC.**

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