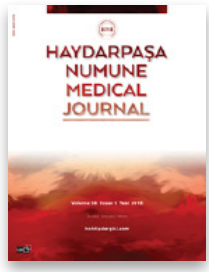
HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2021.83584
Haydarpasa Numune Med J 2023;63(3):241–246



hnhtipdergisi.com

ORIGINAL ARTICLE

Is Lobectomy an Appropriate Surgical Strategy for Nodular Goiter in Endemic Areas?

Nurdan Altan[1], Bahar Canbay Torun[2], Adnan Hut[2], Hüda Ümit Gür[2], Yusuf Yunus Korkmaz[3], Gamze Çıtlak[2]

[1]Department of General Surgery, Sarıkamış State Hospital, Kars, Türkiye
[2]Department of General Surgery, University of Health Sciences, Haseki Training and Research Hospital, Istanbul, Türkiye
[3]Department of General Surgery, Sungurlu State Hospital, Corum, Türkiye

Abstract

Introduction: Thyroid nodules are evaluated by fine-needle aspiration biopsy (FNAB) according to their radiologic characteristics. International guidelines recommend lobectomy according to the size of the nodules and FNAB results. The aim of this study is to assess whether lobectomy is one of the treatment choices in endemic areas.

Methods: Patients who underwent lobectomy between January 2013 and September 2017 were studied retrospectively. Patients' demographic features, thyroid hormone levels, medications, FNAB results before the surgery, lobectomy indications, ultrasonographic features, final pathologies, and secondary surgical interventions were recorded.

Results: Data of 388 patients who underwent lobectomy were examined. As patients were classified according to their FNAB results, all categories had higher malignancy rates than expected in the final pathology results. One hundred and eighteen (30.4%) patients had undergone completion thyroidectomy. The final pathology of the completion thyroidectomy samples showed 24.07% (n=26) malignancy.

Discussion and Conclusion: FNAB is the gold standard for the malignancy risks in thyroid nodules in all guidelines. In endemic areas, this classification system may be inadequate. Two-staged thyroid surgery is becoming more popular. In our series, 30.4% of patients had undergone completion thyroidectomy according to their final pathology results. We need to add newer sights to guidelines for endemic areas.

Keywords: Bethesda classification; completion thyroidectomy; hemithyroidectomy; lobectomy; secondary surgery.

Considering the vital functions of the thyroid gland, surgeons must make surgical decisions carefully. Thyroid nodules are evaluated by the fine-needle aspiration biopsy (FNAB) according to their sonographic features, and the surgical decision is taken according to specific indications[1]. Lobectomy is recommended for subcentimetric papillary carcinoma patients with no poor prognostic factor and those with benign thyroid disorders[2]. Bethesda classification used to assess FNAB is considerably beneficial[3]. Nevertheless, the surgical choice for the multinodular goiter is still controversial. In many studies, bilateral total thyroidectomy is advised for bilateral multinodular goiter; and it is advocated that bilateral total thyroidectomy leads to low complication and recurrence rates when performed by experienced surgeons[4-6]. Nonetheless, the treatment for unilateral disease is still debated. Some authors recommend unilateral lobectomy for its lower complication rates and fewer hormone replacement needs[7-12].

Correspondence: Nurdan Altan, M.D. Department of General Surgery, Sarıkamış State Hospital, Kars, Türkiye
Phone: +90 530 408 40 89 **E-mail:** nurdanbezir@gmail.com
Submitted Date: 21.06.2021 **Revised Date:** 21.06.2021 **Accepted Date:** 12.12.2021

The aim of this study is to evaluate whether lobectomy is a treatment of choice in endemic areas.

Materials and Methods

Patients who had undergone lobectomy between January 2013 and September 2017 in the General Surgery Clinic of the University of Health Sciences Haseki Training and Research Hospital were reviewed retrospectively after approval of the local Ethics Committee (2017–572). Patients who were operated on for toxic adenoma, those accompanying parathyroid gland disorder, unknown FNAB results, and those that were operated on for relapsed disease were excluded from the study. Moreover, patients with terminal pathological diagnoses such as medullary carcinoma, tumor of unknown malignancy potential, and follicular carcinoma were also excluded from the study.

Patients demographic features, the diameter of the radiologically detected nodules, the pre-operative FNAB results, the surgical technique and the surgical indication, the terminal pathological outcomes after the lobectomy, the number and the diameter of the nodule post-operatively, the presence of multicentricity, the tumor size, the presence of lymphovascular and/or capsular invasion, and the evidence of extrathyroidal extension, the presence of lymphocytic thyroiditis, whether the completion thyroidectomy was performed and the final pathological diagnosis of the completion thyroidectomy was recorded.

The patients were divided into two groups according to their surgical indications. Group 1 included patients who chose surgery and had the indication for stage 2–3 goiter with the FNAB results are Bethesda 1 or 2. Group 2 included patients with the recurrent FNAB results of Bethesda 3 and those with clinical suspicion and patients with FNAB results of Bethesda 4 or higher. Lobectomy was performed in all patients. The groups were compared according to their nodule sizes and diameters, the rate of the lymphocytic thyroiditis final pathology results, the tumor size, and the rate of completion of thyroidectomy.

FNAB results according to the Bethesda classification were compared to the final pathology results. The study was conducted in accordance with the Declaration of Helsinki.

Statistical Analysis

IBM SPSS Statistics 20.0 program was used for statistical analysis. Descriptive statistics: mean numeric variables, standard deviation, and minimum and maximum categorical variables are given with both numbers and percentages. Numeric variables comparison between the two independent groups was made by Mann–Whitney U test because normal distribution condition was not provided. A comparison of rates between the independent groups was made using Chi-square analysis. The statistical alpha significance level was accepted as $p<0.05$.

Results

Lobectomy was performed in 461 patients between 2013 and 2017. Sixty-one patients were excluded due to inadequate data, three patients due to accompanying parathyroid gland disorder followed by secondary lobectomy, seven patients with toxic adenoma, and two patients due to a relapsed disease were excluded from the study. Ten patients with final pathological diagnoses such as medullary carcinoma, tumor of unknown malignant potential, and follicular carcinoma were also excluded from the study. Three hundred seventy-eight patients were examined; 313 females and 65 males constituted the study group. The cytological results of pre-operative FNABs showed Bethesda 1 in 54 (14.3%) patients, Bethesda 2 in 165 (43.7%), Bethesda 3 in 96 (25.4%), Bethesda 4 in 50 (13.2%), Bethesda 5 in 12 (3.2%), and Bethesda 6 in 1 (0.3%) patients (Table 1).

When the final pathological results were analyzed, there were 255 patients with benign results, 50 patients with papillary microcarcinoma (PMC), 73 with thyroid papillary carcinoma (TPC), and ten patients with medullary carcinoma, tumor of unknown malignancy potential, the tumor that was suspicious for papillary carcinoma and follicular carcinoma (Table 1). Multicentricity was present in 16.2% (n=20) of malign cases. The lymphocytic thyroiditis rate was 20.6% in all series. The malignancy rate in the final pathology results showed 25.9% (n=14) in Bethesda 1 group, 27.8% (n=46) in Bethesda 2 group, 28.1% (n=27) in Bethesda 3 group, 48% in Bethesda 4 group 91.6% (n=11) in Bethesda 5 and 100% (n=1) in Bethesda 6 groups (Table 1).

Completion thyroidectomy was performed on all 73 patients with TPC and 35 out of 50 patients with PMC. Twenty-nine of 50 patients with PMC were found to be operated on before 2016, and 26 of these patients with PMC had undergone the completion thyroidectomy. Twenty-one of these patients were operated on after 2016, and only 9 of them had completion thyroidectomy for having histologically high suspicious variant or having lymphovascular/capsular extension. Twelve of these patients did not have such features; hence secondary surgical intervention was not performed (Table 2).

The mean diameter of the FNAB-performed nodules was

Table 1. Distribution of pathology results of lobectomies according to FNAB results

FNAB Results	Pathology Results of Lobectomies				Total (%)
	Papillary Carcinoma TPC (n)	Papillary Micro-carcinoma PMK (n)	Benign Disease (n)	Other (n)	
Bethesda					
1	10	4	40	0	54 (13.9)
2	21	25	119	2	167 (43.0)
3	17	10	69	3	99 (25.5)
4	19	5	26	5	55 (14.2)
5	5	6	1	0	12 (3.1)
6	1	0	0	0	1 (0.3)
Total (%)	73 (18.8)	50 (12.9)	255 (65.7)	10 (2.6)	388 (100)

Table 2. Yearly distribution of papillary microcarcinoma cases with or without complementary thyroidectomy

Papillary Microcarcinoma Cases With or Without Complementary Thyroidectomy	Years				
	2013 n	2014 n	2015 n	2016 n	2017 n
With	6	5	15	5	4
Without	2	1	0	9	3
Total	8	6	15	14	7

29.5 mm±12.9 mm. The size of the nodules in 22.2% (n=84) patients was 4 cm and above. By ultrasonography, 72.8% (n=275) of patients had simple nodules, 6.9% (n=26) had 2 nodules, 20.3% (n=77) had 3 or more nodules. According to the histopathological examination, 64% (n=242) of patients had a single nodule, 12.4% (n=47) had 2 nodules, and 22.3% (84) had 3 or more nodules. Five patients did not have any nodules, according to the final pathological assessment. The number of nodules that were examined histopathologically was significantly higher than the number of nodules that were found by ultrasonography ($p<0.001$).

Group 1 and Group 2 were compared according to their nodule sizes, lymphocytic thyroiditis rates, tumor diameter, and completion thyroidectomy rates. Nodules' diameters found by sonography and pathology were 34±11.7 mm and 32±13 mm, respectively, in Group 1; and 23.3±12 mm and 23.3±13 mm in Group 2. The difference was statistically significant ($p<0.001$). In addition, lymphocytic thyroiditis rates determined in group 2 higher than in group 1 ($p<0.001$). Other parameters showed no statistical significance (Table 3).

Twenty-six patients (24.07%) who had undergone completion thyroidectomy had malignancy in their final pathology even though the pre-operative assessments showed no apparent nodular formation. Twenty-one of these patients had PMC, and the other 5 had TPC.

Table 3. Comparing Group 1 and Group 2 according to their nodule sizes, lymphocytic thyroiditis rates, tumor diameter and completion thyroidectomy rates

	Group 1	Group 2	p
Sonographic Nodule sizes	34±11.7 mm	23.3±12 mm	<0.001
Pathologic Nodule sizes	32±13 mm	23.3±13 mm	<0.001
Lymphocytic thyroiditis rates (%)	14.1	29.5	<0.001
Tumor diameter	19.58±19.2 mm	17.86±12.8 mm	ns
Completion thyroidectomy rates (%)	8.3	15.8	ns

Discussion

There is a lifelong hormone replacement therapy need for patients who have undergone bilateral total thyroidectomy, which reduces the quality of life for those operated on for benign reasons[13]. The patients who only have lobectomy could take lower doses of hormone replacement, and some even become euthyroid without any replacement[13]. Moreover, untreated patients with hypothyroidism or those without adequate hormone replacement have been shown to have a higher risk for cardiovascular diseases and bone fractures[14]. Some patients may still present with tiredness, weakness, cognitive dissonance, and mood disorders even when they become euthyroid by hormone replacement therapy[15].

Lobectomy is a relatively low-morbidity approach compared to total thyroidectomy. Hypocalcemia, hypoparathyroidism, hypothyroidism, and recurrent nerve injury are all seen less in lobectomy[16]. In our series, 71.4% of patients did not need a completion thyroidectomy following lobectomy, ensuring a lower morbidity rate.

No extra invasion was needed following lobectomy for some patients with benign diseases, and PMC made lobectomy a treatment choice[2]. The cost of a lifelong hormonal therapy after bilateral total thyroidectomy is considered to be higher than the total cost of the clinic and radiologic follow-up and even the FNAB, if needed, of the remaining lobe after lobectomy. However, there is often more than one nodule present in endemic areas like our country; therefore, the diagnostic cost could get higher in the follow-up of these nodules.

In the histopathological examination of our series, 12.4% (n=47) cases had two nodules and 22.5% (n=84) cases had three or more nodules. The patient group that had a single nodule in radiological examination and was a candidate for lobectomy, 36% of them had, in fact, multiple nodules by the final pathological results. It should not be forgotten that pathological examination of the nodule number is always higher than the number of the nodules found by ultrasound pre-operatively. In addition, there is no data on when to end the follow-up of patients with more than one nodule, those who would need further radiologic and cytopathologic follow-up plans. In a multicentric retrospective study by Shrime et al.,[17] total thyroidectomy is more cost-effective than lobectomy; however, they determined that this could be only hospital-based due to the heterogeneity of its long-term follow-up results, so they decided that there is a need for more prospective studies.

According to the American Thyroid Association (ATA) 2015 guideline, lobectomy is the ideal treatment of choice for patients with FNAB results of Bethesda 3 and 4. This is because the FNAB cytopathological results of Bethesda 3 and 4 nodules have 7–15% and 15–30% risk of malignancy, respectively[2]. Therefore, if total thyroidectomy is performed on such patients, 70–93% of these patients will be overtreated. In our country, malignancy risk for sonographically suspicious nodules is evaluated according to the Bethesda classification, a recommended evaluation parameter in most guidelines. However, in our series, patients with FNAB results of Bethesda 3 and 4 had 28.1% and 48% of malignancy rates, respectively, according to their final pathological results. In addition, the terminal pathology results revealed malignancy in 25.9% of Bethesda 1 and 27.8% of Bethesda 2. Considering our results, we found a higher malignancy rate than expected in all four categories. The results were related to the fact that the median diameter of nodules in Bethesda 1 and 2 was 34 mm, which could affect the FNAB reliability, as well as the fact that goiter is endemic in our country and that 20% of patients had accompanying lymphocytic thyroiditis which could affect the radiological and cytological results. Outcomes for the Bethesda 3 group in our series were found to be in accordance with the malignancy prediction rates in Bethesda 2017 update[3].

Contrastingly, we found higher malignancy rates for Bethesda 4 group than the predicted values. The malignancy rates for Bethesda 1 and 2 groups were 25.9% (n=14) and 27.8% (n=46), respectively, which were considerably higher than the malignancy prediction rate. Malignancy rates for Bethesda 5 and 6 were 91.6% (n=11) and 100% (n=1), respectively; however, the number of patients in both groups is limited to draw a conclusion.

We divided the patients into two groups according to their surgical indications. Group 1 was low-risk for malignancy according to the FNAB results of Bethesda 1 and 2, and Group 2 was high-risk for malignancy according to the FNAB results of Bethesda 3 and higher. In our series, the nodule diameters in the two groups were significantly larger in group 1. Notwithstanding, malignancy rates showed no significance in the two groups. These findings prove the other studies in demonstrating the weak reliability of the FNAB when the nodule diameter was larger[18,19].

2009 ATA Guidelines suggested completion of thyroidectomy for all the tumors except those smaller than 1 cm, intrathyroidal, nodal negative, and low-risk tumors[20]. Therefore, the completion thyroidectomy rate for PMC performed before 2016 was higher than after 2016 in our clinic.

In our series, malignancy was determined in 26 out of 108 patients (24.07%) who had completion thyroidectomy. Of those patients, 21 were found to have PMC and 5 TPC. During the initial surgery, pre-operative evaluation of the patients showed no apparent nodule on the contralateral lobe, so the surgical technique was chosen to be lobectomy. Lv et al.[21] found that 47% of 1442 patients with unilateral PTC and no radiologically suspicious nodule on the contralateral lob had occult malignancy. In our series, no nodular formation on the contralateral lobe was found by sonographic examination. Turanli et al.[22] showed 20.6% of occult malignancy in completion thyroidectomy material, similar to our findings.

Conclusion

Two-stage thyroid surgery is becoming highly popular. A unilateral lobectomy is a safe approach, especially for benign diseases or low-risk groups for malignancy, for a secondary intervention is usually unnecessary. Patients should be informed about the possibility of secondary surgery, the need to be under close follow-up routine, and the compliance with the treatment. The clinicians and the patients should choose a safe treatment strategy together. The results of our series have shown that 71.7% of cases did not require an extra surgical invasion. We consider the two-staged surgery safe and effective until safer parameters and classifications in malignancy research are described. However, even though 71.7% of patients had lobectomy as a curative surgery and all the benefits with it, 24.08% of 108 patients who had undergone completion surgery had incidental cancer even without an apparent radiologic sign. This may indicate that lobectomy might be inadequate, and a more extensive surgery should be kept in mind for such patients in endemic places. There is a need for more prospective studies in this field.

Ethics Committee Approval: Ministry of Health University Haseki Research and Training Hospital Clinical Research Ethics Committee. Date: 18.10.2017. Approval Number: 572.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: N.A., B.C.T., A.H., H.Ü.G., Y.Y.K., G.Ç.; Design: N.A., B.C.T., A.H., H.Ü.G., Y.Y.K., G.Ç.; Supervision: N.A., B.C.T., A.H., H.Ü.G., Y.Y.K., G.Ç.; Fundings: A.H., H.Ü.G., G.Ç.; Materials: N.A., B.C.T., Y.Y.K.; Data Collection or Processing: N.A., B.C.T., Y.Y.K., H.Ü.G., G.Ç.; Analysis or Interpretation: N.A., B.C.T., Y.Y.K., G.Ç.; Literature Search: N.A., B.C.T., Y.Y.K., A.H., G.Ç.; Writing: N.A., B.C.T., A.H., H.Ü.G., Y.Y.K., G.Ç.; Critical Review: N.A., B.C.T., A.H., H.Ü.G., Y.Y.K., G.Ç.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Cibas ES, Ali SZ. The bethesda system for reporting thyroid cytopathology. Thyroid 2009;19:1159–65.
2. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2006;16:109–42.
3. Cibas ES, Ali SZ. The 2017 bethesda system for reporting thyroid cytopathology. Thyroid 2017;27:1341–6.
4. Barczyński M, Konturek A, Hubalewska-Dydejczyk A, Gołkowski F, Nowak W. Ten-year follow-up of a randomized clinical trial of total thyroidectomy versus dunhill operation versus bilateral subtotal thyroidectomy for multinodular nontoxic goiter. World J Surg 2018;42:384–92.
5. Agarwal G, Aggarwal V. Is total thyroidectomy the surgical procedure of choice for benign multinodular goiter? An evidence-based review. World J Surg 2008;32:1313–24.
6. Pappalardo G, Guadalaxara A, Frattaroli FM, Illomei G, Falaschi P. Total compared with subtotal thyroidectomy in benign nodular disease: Personal series and review of published reports. Eur J Surg 1998;164:501–6.
7. Ergul Z, Akinci M, Kulacoglu H. Hemithyroidectomy for unilateral thyroid disease. Chirurgia (Bucur) 2014;109:613–9.
8. Attaallah W, Erel S, Canturk NZ, Erbil Y, Gorgulu S, Kulacoglu H, et al. Is hemithyroidectomy a rational management for benign nodular goitre? A multicentre retrospective single group study. Neth J Med 2015;73:17–22.
9. Olson SE, Starling J, Chen H. Symptomatic benign multinodular goiter: Unilateral or bilateral thyroidectomy? Surgery 2007;142:458–62.
10. Bellantone R, Lombardi CP, Boscherini M, Raffaelli M, Tondolo V, Alesina PF, et al. Predictive factors for recurrence after thyroid lobectomy for unilateral non-toxic goiter in an endemic area: Results of a multivariate analysis. Surgery 2004;136:1247–51.
11. Phitayakorn R, Narendra D, Bell S, McHenry CR. What constitutes adequate surgical therapy for benign nodular goiter? J Surg Res 2009;154:51–5.
12. Barczyński M, Konturek A, Gołkowski F, Hubalewska-Dydejczyk A, Cichoń S, Nowak W. Five-year follow-up of a randomized clinical trial of unilateral thyroid lobectomy with or without postoperative levothyroxine treatment. World J Surg 2010;34:1232–8.
13. Stoll SJ, Pitt SC, Liu J, Schaefer S, Sippel RS, Chen H. Thyroid hormone replacement after thyroid lobectomy. Surgery 2009;146:554–60.
14. Flynn RW, Bonellie SR, Jung RT, MacDonald TM, Morris AD, Leese GP. Serum thyroid-stimulating hormone concentration and morbidity from cardiovascular disease and fractures in patients on long-term thyroxine therapy. J Clin Endocrinol Metab 2010;95:186–93.
15. Wiersinga WM. Thyroid hormone replacement therapy. Horm

Res 2001;56(Suppl 1):74–81.
16. Kandil E, Krishnan B, Noureldine SI, Yao L, Tufano RP. Hemithyroidectomy: A meta-analysis of postoperative need for hormone replacement and complications. ORL J Otorhinolaryngol Relat Spec 2013;75:6–17.
17. Shrime MG, Goldstein DP, Seaberg RM, Sawka AM, Rotstein L, Freeman JL, et al. Cost-effective management of low-risk papillary thyroid carcinoma. Arch Otolaryngol–Head Neck Surg 2007;133:1245–53.
18. Kuru B, Gulcelik NE, Gulcelik MA, Dincer H. The false-negative rate of fine-needle aspiration cytology for diagnosing thyroid carcinoma in thyroid nodules. Langenbecks Arch Surg 2010;395:127–32.
19. Pinchot SN, Al-Wagih H, Schaefer S, Sippel R, Chen H. Accuracy of fine-needle aspiration biopsy for predicting neoplasm or carcinoma in thyroid nodules 4 cm or larger. Arch Surg 2009;144:649–55.
20. American Thyroid Association (ATA) Guidelines Taskforce on Thyroid Nodules and Differentiated Thyroid Cancer; Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009;19:1167–214.
21. Lv T, Zhu C, Di Z. Risk factors stratifying malignancy of nodules in contralateral thyroid lobe in patients with pre-operative ultrasound indicated unilateral papillary thyroid carcinoma: A retrospective analysis from single centre. Clin Endocrinol (Oxf) 2018;88:279–84.
22. Turanli S, Aslan S, Cetin A. Clinical significance of residual occult malignancy in thyroid carcinoma. Am J Otolaryngol 2011;32:398–401.