

Original Research Article

Thyroid nodule size as an indicator for surgery

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ABSTRACT

Background: Several authors have questioned the accuracy of fine-needle aspiration cytology (FNAC) in large thyroid nodules. It's the current practice to provide thyroidectomy to patient with thyroid nodules 4 cm or larger regardless of the FNAC results. The aim of the study is to answer two questions: is the size of nodule associated with higher risk of malignancy and is the size indication for surgery.

Methods: Authors conducted a retrospective review of 201 patients who underwent thyroidectomy between 2011 and 2017 at Bahrain defense force hospital. Authors compared all thyroid nodules with benign FNAC and their final histopathology reports. Patients were divided into two groups based on the size of the nodule (< 4cm or >4cm) and indication of surgery.

Results: 201 patients with thyroid nodule underwent thyroid surgery. 136 patients had nodule <4cm and 65 patients were ≥4 cm. For patients with nodules <4 cm, 37 patients (18.4%) had a malignancy, and for those with nodules ≥4 cm, 13 patients (6.4%) had a malignancy. comparison between size of the nodule, FNAC result and final histopathology: FNAC diagnosed 55 cases (27.3%) are malignant, final histopathology reported only 50 cases are malignant. But for benign cases FNAC and histopathology reports are showing same results, (p<0.05).

Conclusions: Thyroid nodules ≥4 cm are not risk factor of malignancy. Thyroid nodules ≥4 cm with benign FNAC should not undergo thyroidectomy as false negative rate is low. Therefore, the decision for surgery ought not to be taken based on the size of the nodule.

Keywords: Biopsy, Diagnostic accuracy, Fine-needle, Large nodules, Thyroid neoplasms, Thyroid nodule

INTRODUCTION

Thyroid nodules are common diseases of the endocrine system, with prevalence of 3%–7% by palpation and 19%–67% by high resolution ultrasound.^{1,2} Thyroid cancer accounts for approximately 5% to 15% of thyroid nodules.³ In recent years; the number of thyroid cancer has been on the rise.

Due to early identification of thyroid nodule, diagnosis and management of thyroid cancer have been expanded. History and physical examination, thyroid function test

(TFT), ultrasound of the neck and fine-needle aspiration cytology (FNAC) are all part of initial evaluation of a thyroid nodule.⁴

Fine needle aspiration cytology is gold standard tool to define nature of thyroid nodule.⁵ FNAC was introduced in the 1950s and has become a commonly used procedure, its accuracy improved with ultrasound guided. Sensitivity and specificity >90%. Based on its evaluation surgeon can plan extent of surgery and further treatment. The most valuable information that FNAC provides is whether a nodule has neoplastic potential.^{6,7}

The false negative rate for thyroid FNAC is low. The expected incidence of malignancy in cytological benign nodules is 0% to 3% according to the Bethesda system for reporting thyroid cytopathology.^{2,7}

Skilled FNA technique and the availability of experienced cytologists are vital to achieving high diagnostic accuracy. Several diagnostic pitfalls have been described in the literature, including inadequate sampling, insufficient cellular material from cystic or hemorrhagic lesions, and limited experience of those who perform and interpret FNAC. Additionally, number of punctures and the smear preparation techniques also affect results.²

Number of studies have attempted to associated size of thyroid nodule with accuracy of FNAC. Several studies in the past reported the larger the nodule size the higher false negative rate for FNAC due to sampling error, these studies concluded nodular size 4cm and larger more likely to harbor cancer cell and considered thyroidectomy even when FNAC result is benign.

In other hand other studies showed false negative rate in larger thyroid nodule is not higher than those with small nodule. Therefore, the size of the nodule is not independent risk factor for malignancy, should not take part in therapeutic decision making and it would prevent unnecessary surgery with its possible complications, including injury to the recurrent laryngeal nerve, hypoparathyroidism, and lifelong thyroid hormone.

Other study concludes that male gender, age ≥ 60 years old, microcalcification, cervical lymphadenopathy was risk factor of malignancy.^{4,8-10} Based on benign cytology features and low false negative rate of the FNAC patient's required regular follow up with annual clinical examination and repeat ultrasound. Repeat cytology recommend for patient with abnormal feature in ultrasound and changes in the size of the nodule.^{4,11}

Therefore, the purpose of this study was to investigate the relationship between the size of thyroid nodules and malignancy risk.

METHODS

Retrospective review of maintained thyroid database was completed. The case records of 201 patients with thyroid nodule who underwent thyroidectomy between January 2011 and April 2017 was identified and their medical record reviewed. Five surgeons at Bahrain defense force hospital performed all thyroidectomies.

All thyroid nodule $>5\text{mm}$ with abnormal sonographic feature or high-risk history and nodule $>1\text{ cm}$ (the solid and hypoechoic areas) underwent ultrasound guided FNAC. Thyroid nodule FNA cytology was reported using diagnostic group outlined in the Bethesda system for reporting thyroid cytopathology.

Pathology reports were reviewed and nodules with benign FNAC were matched with the histologic results. In addition, physical examination, ultrasound exam and location of the nodule were correlated with size of the nodule in operative and pathology reports. The results of the final pathology were classified as either benign or malignant.

All data were extracted from the hospital's main database and patients' medical records including age, sex, family history of thyroid disease, nodular size, indication of thyroidectomy and final pathology. Patients were divided into two groups based on nodule size: $<4\text{ cm}$ or $\geq 4\text{ cm}$, clinical factors and rate of malignancy were compared.

Statistical Analysis

Statistical analysis was performed by the SPSS program for Windows, version 23.0. Continuous variables were presented as mean \pm SD, and categorical variables as absolute numbers and percentage. Chi-Square test was applied as appropriate for comparison of nominal data. Normally distributed continuous variables were compared using paired T-test. A "p" value of less than 0.05 was considered significant.

RESULTS

Between January 2011 and April 2017, a total of 201 patients were presented with thyroid nodule and they were subsequently underwent thyroid surgery. The average age of the patient population was 45.0 ± 12.31 . Among 201 patients, 161 (80%) were female and 40 (20%) were males. 136 patients had nodules that were $<4\text{ cm}$ and 65 patients had nodules that were $\geq 4\text{ cm}$. 50 patients were diagnosed to have malignancy based on final histopathology report.

Out of 136 patients with nodules $<4\text{ cm}$, 37 patients (18.4%) had a malignancy, and among those 65 patients with nodules $\geq 4\text{ cm}$, 13 patients (6.4%) had a malignancy. There was no significant difference found in the rate of malignancy in these two Groups ($p= 0.27$) (Table 1).

The primary indications for thyroidectomy included compressive symptoms ($n= 25.8\%$), follicular lesion ($n= 8.9\%$), papillary carcinoma ($n= 12.9\%$), thyrotoxicosis ($n= 8.4\%$), Progression in size ($n= 25.8\%$) and patient preference due to neck pain, cosmetic concerns, fear of undiagnosed malignancy and suspicious of papillary carcinoma ($n= 7.4\%$), suspicious feature of malignancy on US ($n= 4.4\%$).

Most of them had multiple indications for surgery. Of these indications, patients with compressive symptoms were equal in number in both the group were observed (Table 1).

Table 1: Demographic and pathologic data.

	Total cohort nodule	Nodule <4 cm	Nodule ≥4 cm	P value
Number of patients	201	136	65	
Mean age ±SD	45.0 ±12.31	45.0 ±12.02	44.8 ±12.98	0.35
Gender (% female)	161	114	47	<0.05*
Gender (% male)	40	22	18	<0.05*
Mean nodule size±SD (cm)	3.2 ±1.62	2.2 ±0.93	4.9 ±1.06	0.46
Malignancy	50	37	13	0.27
Compressive symptoms	52	26	26	<0.05*
Follicular lesion	18	13	5	0.4
Papillary Ca	26	25	1	<0.05*
Preference	12	9	3	0.41
Progression in size	52	28	24	<0.05*
Suspicious of papillary Carcinoma on FNAC	15	13	2	0.08
Suspicious feature of malignancy on US	9	5	4	0.32
Thyrotoxicosis	17	15	2	<0.05*

*significant

Of the total 201 patients, FNAC results were reported as benign in 146 cases (72.6%), malignant in 55 patients (27.4%). FNAC results of total 136 patients with <4cm nodules were reported as benign in 94 cases (69.1), malignant in 42 cases (30.9%). Also, FNAC results of 65 patients with ≥4cm nodules were reported as benign in 52 cases (80.0%) and malignant in 13 cases (20.0%). But this association is statistically not significant (p= 0.07) (Table 2).

Table 2: Association of size of nodule and FNAC results.

Size	FNAC2 results		Total
	Benign	Malignant	
<4cm	94 (69.1%)	42 (30.9%)	136
≥4cm	52 (80.0%)	13 (20.0%)	65
Total	146	55	201

P= 0.07 (not significant)

According to postoperative pathologic survey of the nodules that underwent FNAC; 37 patients (22.3%) with <4 cm nodules and 13 patients (20.0%) with ≥4 cm

nodules were diagnosed having thyroid cancer on FNAB (Table 3).

Of total 201 cases FNAC diagnosed, 55 cases (27.3%) as Malignant, final histopathology reports declared only 50 cases having malignancy. But for benign cases FNAC and histopathology reports are showing same results. This relation is statistically significant (p<0.05). This proves that for surgical removal one can rely on the FNAC results than nodule size (Table 4).

Table 3: Association of size of nodule and histopathology results.

Size	Histopathology result		P value
	Malignant	Benign	
≥4cm	13 (20.0%)	52 (80.0%)	65
<4cm	37 (22.3%)	99 (72.7%)	136
Total	50	151	

P= 0.27 (not significant)

Table 4: Comparison between histopathology and FNAC outcome.

FNAC result	Histopathology result		TOTAL
	Malignant	Benign	
Malignant	50 (90.9%)	5 (9.1%)	55
Benign	0 (0.0%)	146 (100%)	146
Total	50	151	201

P<0.05* (significant)

DISCUSSION

Some studies have concluded that thyroid nodule size can be considered as an independent indication to predict the risk of malignancy in people with thyroid nodules, but other studies did not support these data and even reported against their results.¹²⁻¹⁵ Furthermore, diagnostic accuracy of FNAC in large thyroid nodules is still controversial.^{13, 16-19} Therefore, this study is designed to investigate the relationship between the size of thyroid nodules and malignancy risk.

Authors found in present study that, nodule size did not show any association with risk of malignancy in nodules ≥4 cm. Present findings are similar to those of several other studies. Raj et al evaluated the prevalence of thyroid cancer in 223 patients who underwent thyroidectomy for thyroid nodules 4 cm or larger. Sixteen patients (7.2%) had malignancy on final pathology. There was no association between nodule size and malignancy rate.²⁰

Kamran et al. reported that increasing thyroid nodule size had an influence on cancer risk in a nonlinear fashion, and there was no increase in the risk beyond the 2cm threshold.¹⁸ While, Berker et al. reported no significant difference between 1 cm nodules and >1cm in malignancy risk.²¹ Some studies have shown higher

prevalence of thyroid carcinoma in ≥ 4 cm nodules.^{13,22} Conversely, Rausei et al and Mc Henry et al reported higher prevalence of thyroid carcinoma in smaller nodules.^{17,23} In this study, there was no statistically significant ($p= 0.27$) difference between malignant and benign nodules size. These contradictory results show that the size of the nodule is not reliable at predicting malignancy and should not be applied for medical decision making.^{15,17,23-25}

Shrestha et al performed a retrospective study of 540 patients with 695 nodules, who underwent FNAB and subsequent thyroid surgery. There was no set size criterion for surgical referral. The overall malignancy rate was 18.6% and did not vary significantly based on size. The overall false negative rate was 7% and did not differ significantly according to size. The authors noted that the accuracy of FNAC increased with increasing nodule size.²⁶ Similarly, Magister et al performed a retrospective study of 297 patients with 326 thyroid nodules, who underwent FNAB and subsequent thyroidectomy. The overall rate of malignancy on final pathology was 43.9%. The false negative rate was 6% for all nodules combined, and 3.8% for nodules 3 cm or greater. Higher probability of malignancy was found in smaller nodules.²⁷ In these studies finding of increased risk of malignancy and decreased diagnostic accuracy in smaller nodules could be due to selection bias. The smaller nodules included in the study may have undergone thyroidectomy due to the presence of unmeasured risk factors for malignancy.

The discrepancy in the risk of malignancy and accuracy of FNAC reported in the literature for large thyroid nodules may be due to variability in sampling and interpretation of cytopathological findings. The accuracy of FNAC depends on adequate sampling and correct interpretation. Furthermore, the post- test probability of malignancy is significantly influenced by the overall prevalence of malignancy in the population, which varies among institutions. These factors need to be accounted for when counseling patients about the need for thyroidectomy for large nodules.

CONCLUSION

Risk of malignancy was not associated with nodule size. Patients with thyroid nodules ≥ 4 cm and benign FNAC should not automatically undergo thyroidectomy. FNAC as well as the presence of symptoms are important factors to consider when recommending thyroidectomy for these patients. Selection of the appropriate treatment option (thyroidectomy versus observation) should involve shared decision making between the patient and the healthcare provider. The overall accuracy of FNAC and the prevalence of malignancy in the population need to be considered.

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REFERENCES

1. Jiang H, Tian Y, Yan W, Kong Y, Wang H, Wang A, et al. The prevalence of thyroid nodules and an analysis of related lifestyle factors in Beijing communities. *Int J Environmental Research Public Health.* 2016 Apr 22;13(4):442.
2. Jammah A. Evaluation of the accuracy of fine-needle aspiration cytology in the diagnosis of thyroid nodules: a retrospective analysis of data from a tertiary care hospital in Saudi Arabia/ Tiroid Nodullerinin Tanisinda Ince Igne Aspirasyon Sitolojisinin Dogrulugunun Degerlendirilmesi: Suudi Arabistan'da Ucuncu Basamak Bir Hastanenin Verilerinin Retrospektif Analizi. *Turkish J Endocrinol Metabol.* 2012 Jun 1;16(2):30-4.
3. Tan GH, Gharib H. Thyroid incidentalomas: management approaches to nonpalpable nodules discovered incidentally on thyroid imaging. *Annals Internal Med.* 1997 Feb 1;126(3):226-31.
4. Shi H, Bobanga I, McHenry CR. Are large thyroid nodules classified as benign on fine needle aspiration more likely to harbor cancer?. *The Am J Surgery.* 2017 Mar 1;213(3):464-6.
5. Khalife S, Bouhabel S, Forest VI, Hier MP, Rochon L, Tamilia M, et al. The McGill Thyroid Nodule Score's (MTNS+) role in the investigation of thyroid nodules with benign ultrasound guided fine needle aspiration biopsies: a retrospective review. *J Otolaryngol- Head Neck Surgery.* 2016 Dec;45(1):29.
6. Koo DH, Song K, Kwon H, Bae DS, Kim JH, Min HS, et al. Does tumor size influence the diagnostic accuracy of ultrasound-guided fine-needle aspiration cytology for thyroid nodules?. *Int J Endocrinol.* 2016;2016.
7. Kaliszewski K, Diakowska D, Wojtczak B, Strutyńska-Karpińska M, Domosławski P, Sutkowski K, et al. Fine-needle aspiration biopsy as a preoperative procedure in patients with malignancy in solitary and multiple thyroid nodules. *PloS one.* 2016 Jan;11(1):e0146883.
8. Megwalu UC. Risk of malignancy in thyroid nodules 4 cm or larger. *Endocrinol Metabol.* 2017 Mar 1;32(1):77-82.
9. Godazandeh G, Kashi Z, Zargarnataj S, Fazli M, Ebadi R, Kerdabadi EH. Evaluation the relationship between thyroid nodule size with malignancy and accuracy of fine needle aspiration biopsy (FNAB). *Acta Informatica Medica.* 2016 Oct;24(5):347.
10. Tai JD, Yang JL, Wu SC, Wang BW, Chang CJ. Risk factors for malignancy in patients with solitary thyroid nodules and their impact on the management. *J Cancer Research Therapeutics.* 2012 Jul 1;8(3):379.

11. Iqbal A, Ismail M, Israr M, Ali N, Zaman J. Management of solitary thyroid nodule. *J Postgraduate Med Institute (Peshawar-Pakistan)*. 2011 Jun 10;19(1).
12. Alexopoulou O, Beguin C, Buyschaert M, Squifflet JP, De Burbure C, De Nayer P, et al. Predictive factors of thyroid carcinoma in non-toxic multinodular goitre. *Acta Clinica Belgica*. 2004 Apr 1;59(2):84-9.
13. McCoy KL, Jabbour N, Ogilvie JB, Otori NP, Carty SE, Yim JH. The incidence of cancer and rate of false-negative cytology in thyroid nodules greater than or equal to 4 cm in size. *Surgery*. 2007; 142(6): 837-44.
14. Cappelli C, Castellano M, Pirola I, Gandossi E, De Martino E, Cumetti D, et al. Thyroid nodule shape suggests malignancy. *European journal of endocrinology*. 2006; 155(1): 27-31.
15. Sahin M, Gursoy A, Tutuncu N, Guvener D. Prevalence and prediction of malignancy in cytologically indeterminate thyroid nodules. *Clinical Endocrinol*. 2006; 65(4): 514-8.
16. 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(7): 649-55.
17. McHenry CR, Huh ES, Machekano RN. Is nodule size an independent predictor of thyroid malignancy? *Surgery*. 2008; 144(6): 1062-9.
18. Kamran SC, Marqusee E, Kim MI, Frates MC, Ritner J, Peters H, et al. Thyroid nodule size and prediction of cancer. *The J Clinical Endocrinol Metabol*. 2012; 98(2): 564-70.
19. Kuru B, Gulcelik NE, Gulcelik MA, Dincer H. The false-negative rate of fine-needle aspiration cytology for diagnosing thyroid carcinoma in thyroid nodules. *Langenbeck's Archives Surgery*. 2010; 395(2): 127-32.
20. Raj MD, Grodski S, Woodruff S, Yeung M, Paul E, Serpell JW. Diagnostic lobectomy is not routinely required to exclude malignancy in thyroid nodules greater than four centimetres. *ANZ J Surg*. 2012;82:73-7.
21. Berker D, Aydin Y, Ustun I, Gul K, Tutuncu Y, Isik S, et al. The value of fine-needle aspiration biopsy in subcentimeter thyroid nodules. *Thyroid*. 2008; 18(6): 603-8.
22. Carrillo JF, Frias-Mendivil M, Ochoa-Carrillo FJ, Ibarra M. Accuracy of fine-needle aspiration biopsy of the thyroid combined with an evaluation of clinical and radiologic factors. *Otolaryngol- Head Neck Surgery*. 2000; 122(6): 917-21.
23. Rausei S, Dionigi G, Frattini F, Castano P, Leotta A, Rovera F, et al. Nodule size and fine-needle aspiration biopsy: diagnostic challenges for thyroid malignancy. *The Am J Surgery*. 2011; 201(4): 525-30.
24. Brito JP, Gionfriddo MR, Al Nofal A, Boehmer KR, Leppin AL, Reading C, et al. The accuracy of thyroid nodule ultrasound to predict thyroid cancer: systematic review and meta-analysis. *The J Clinical Endocrinol Metabol*. 2013; 99(4):1253-63.
25. Bestepe N, Ozdemir D, Tam AA, Dellal FD, Kilicarslan A, Parlak O, et al. Malignancy risk and false-negative rate of fine needle aspiration cytology in thyroid nodules ≥ 4.0 cm. *Surgery*. 2016.
26. Shrestha M, Crothers BA, Burch HB. The impact of thyroid nodule size on the risk of malignancy and accuracy of fine-needle aspiration: a 10-year study from a single institution. *Thyroid*. 2012;22:1251-6.
27. Magister MJ, Chaikhoutdinov I, Schaefer E, Williams N, Saunders B, Goldenberg D. Association of thyroid nodule size and Bethesda class with rate of malignant disease. *JAMA Otolaryngol- Head Neck Surgery*. 2015 Dec 1;141(12):1089-95.

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