A Retrospective Study to Assess the Role of Using Fine Needle Aspiration Cytology and Frozen Section in the Diagnosis of Thyroid Swelling

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Abstract The most cost-effective test is fine needle aspiration cytology (FNAC). Many surgeons use intraoperative frozen section to confirm the FNAC findings and to guide the extent of thyroid surgery. Though it is a valuable tool in the diagnosis of the thyroid lesion and determining the extent of thyroid surgery, still in certain cases diagnosis can be incorrect or inconclusive, so histopathology of the excised specimen remains the most reliable test. The purpose of this study will be to compare the result attained by FNAC and frozen section of the thyroid to the final histopathological diagnosis, in order to establish their role in thyroid surgery today. A retrospective study with a total of 140 patients who underwent thyroid surgery at the ENT department, of a tertiary hospital in coastal Karnataka. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated for FNAC and frozen section. The sensitivity, specificity, positive predictive rate, and negative predictive rate of frozen section was found to be 66.7%, 88.4%, 76.6%, 82.4% respectively for detecting malignancy. This was found to be higher than the results of FNAC for the same which were 64.4%, 77.8%, 64.4%, 77.8% respectively. As the sensitivity of FNAC is similar to frozen section in detecting malignant cases, FNAC is a good tool for screening the patient for determining malignancy in thyroid, but frozen section is more specific in confirming the malignancy.

Keywords FNAC · Frozen section · Thyroid swelling · Histopathology

Introduction

Thyroid swellings are very common in the general population, affecting women more commonly than men. According to recent population studies conducted in South India, thyroid swellings are so common that they can be clinically detected in 12% of adults [1]. Thyroid glands' superficial location makes it easily amenable to direct physical examination, Fine Needle Aspiration, and surgical biopsy. Thyroid swellings can be attributed to a wide variety of etiologies, most of which may be benign in nature. However, the aim of appropriate investigations and management is not only to evaluate for the cause of the swelling but more importantly, to rule out malignancy of the thyroid gland [2].

The importance of classification of thyroid swellings into benign and malignant swellings is to decide the best approach for management of the patient. Only about 5% of people with thyroid swelling are diagnosed to have malignant nodules [3]. In India, thyroid carcinoma was found to account for 2% of all male carcinoma and about 5–6% of carcinomas in women [4]. Accurate screening and diagnostic tools are needed to correctly diagnose these patients with malignancy. The importance of finding the best suited investigatory methods lies in the fact that not all patients with thyroid swelling require surgery. Among the patients that do require surgery, the results of the investigations play a large role in determining the extent of thyroid removal surgery. Hence, these tests play a large role in deciding the management plan for the patient [2, 5].

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Fine needle aspiration cytology (FNAC) is a useful tool to detect the pathology of the thyroid gland as it is a simple, quick, and affordable procedure that can be done in the outpatient setting. Today, FNAC has become a standard compulsory procedure before any thyroid surgery. The main utility of FNAC is in its ability to distinguish between benign and malignant lesions, as well as classify the swelling in terms of its etiology [2]. FNAC is found to be a highly specific test, but it may not be the most sensitive test as it has a large number of false negatives. A larger number of false negatives can mean that clinicians may miss out on potentially malignant cases leading to higher rates of mortality due to thyroid malignancies. Furthermore, patients who are found to have a false positive result will have unnecessarily undergone extensive surgical procedures associated with an increased risk of complications. Although FNAC is a useful source of identifying the pathology related to a thyroid swelling, on several occasions it may report results which may be indeterminate or suspicious [6, 7]. Shortcomings of FNAC can be frequently noticed in its inability to differentiate follicular lesions into benign and malignant pathology [2, 6]. It is found that Hashimoto thyroiditis is one of the most commonly misdiagnosed swelling in the thyroid, and follicular and hurthle cell adenomas are wrongly classified as papillary carcinomas on numerous occasions [6, 8, 9]. False negative or indeterminate diagnosis can result in incomplete surgery requiring a repeat surgery at a later date. During such occasions, many surgeons use intra-operative frozen section to confirm the FNA diagnosis and to guide the surgeon regarding the extent of thyroid surgery required [2, 10].

Traditionally, intraoperative frozen sections (FS) were used in clinically suspicious thyroid nodules after an ipsilateral lobectomy to determine the extent of thyroid resection required for the patient. With the advent of FNAC, the use of frozen section is declining; however, its use is still controversial. A frozen section can aid in the differentiation of benign and malignant swellings in situations where FNAC results were found to be inconclusive, hence enabling the surgeon to decide whether to follow through with a complete thyroidectomy or not [10]. This can benefit the patient as it reduces the need for a follow-up surgery if diagnosed as malignant [9, 11]. Though it is a valuable tool in the diagnosis of the thyroid lesion and determining the extent of thyroid surgery, still in certain cases diagnosis can be incorrect or inconclusive, so histopathology of the excised specimen remains the most reliable test.

Histopathology can undoubtedly identify basic tumor features required for staging of thyroid carcinoma. It also gives valuable information regarding the status of the resected lymph node status and can provide definitive proof regarding the type of tumors affecting the gland [11, 12].

The purpose of this study will be to compare the result attained by FNAC and frozen section of the thyroid to the final histopathological diagnosis, in order to establish their role in thyroid surgery today.

Aim of this Study

To study the accuracy of fine needle aspiration cytology and frozen section of thyroid swellings by comparing these reports with the final histopathology findings and to determine the role of using both of these methods as investigatory tools in patient management.

Methodology

Type of study Retrospective study.

Study site The study was conducted in a tertiary hospital of coastal karnataka, with hospital records from the Department of ENT.

Duration of study The study was conducted from March to May 2016.

Inclusion criteria:

1. Patients with thyroid swelling who had undergone FNAC, frozen section and a final histopathological examination as a diagnostic procedure.
2. Patients with euthyroid status.

Exclusion criteria:

1. Patients who had undergone a previous thyroid surgery.
2. Patients with a history of Hypothyroidism or Hyperthyroidism.
3. Patients who were immunocompromised.

Process

The patients who presented to the hospital with a mid-line neck swelling were evaluated with a detailed history and clinical examinations to localize the swelling to the thyroid, which was documented in the patient files.

Investigations done prior to surgery were thyroid function test (TFT), baseline blood investigations, neck ultrasonography and fine needle aspiration cytology.

Frozen section was done intraoperatively, followed by final histopathology of the thyroid gland.

Histopathology results were taken as gold standard.

Data Collection

Data were collected between March to May 2016. Approval was granted by the Institutional Ethical Committee prior to the start of the data collection. The outpatient records were collected from the Medical Records Department, Kasturba Hospital. Data was collected from all existing records from 2004 to June 2016. The data was collected as per the pre-approved proforma. No personal identification details were collected from patient records. There was no interaction between the patients during record collection.

The following data was collected:

- *Demographic details* Age, gender, occupation.
- History of presenting illness, past history, examination of thyroid, diagnosis after examination.
- *Investigation* Blood hemoglobin, PCV, WBC, calcium levels, thyroid function test (T3, T4, TSH).
- Reports of FNAC, frozen section, and histopathology.
- Surgery performed on the patient.

FNAC were classified into 4 categories: [2]

- Benign.
- Malignant.
- Inadequate.
- Indeterminate.

Frozen section was classified into 3 categories: [11]

- Benign.
- Malignant.
- Indeterminate.

The final histopathology samples were classified into 3 categories

- Benign.
- Malignant.
- Benign lesion with micrometastatic areas.

Statistical Analysis

SPSS Version 16.0 was used to calculate all of the statistical parameters.

The measures being assessed are:

1. Sensitivity.
2. Specificity.
3. Positive predictive rate.
4. Negative predictive rate.

Outcome Measures

The outcome was measured by comparing the results of the FNAC and intraoperative frozen section with final histopathological findings. The sensitivity, specificity, positive predictive value, negative predictive value, and accuracy were calculated for FNAC and frozen section. The results of the FNAC and frozen section were also compared to determine the reason behind the discrepancy or incorrect results. In addition, FNAC and frozen section were compared on their basis to differentiate follicular nodule into benign and malignant.

Observations and Results

Demographic Details

There was a female preponderance of the disease i.e. 78.5% of the patients with a thyroid nodule were women. About a quarter of the patients were male patients. Majority of the women were housewives. The mean age overall was found to be 43 years with the majority of patients presenting in their 5th decade of life.

Among the male patients, the average age of the patients was 43.3. Out of a total of 30 male patients, half were found to have benign swellings, and the other half of the patients had malignant swellings (Table 1).

In comparison with the female patients, 32.7% of the swellings were malignant i.e. 41 out of 130 patients. Remaining swellings were benign and 5 were found to have micropapillary carcinoma in the background of a benign nodule.

The malignancy rates in the overall sample population were 36.4%. On the whole, the distribution of benign and malignant lesions among the population collected is represented in the Fig. 1. The most common benign pathology was colloid goiter and the most common malignant was papillary carcinoma of the thyroid.

Among the patients with papillary carcinoma, 4 of them had a follicular variant of papillary carcinoma of the thyroid.

Out of the sample size of 140, 67 cases were identified as benign on FNAC, 41 were malignant, 27 cases were inadequate for opinion, and 5 had indeterminate results.

On frozen section, of the of the total sample size of 140, 90 patients were diagnosed as benign, and 44 were diagnosed as malignant. The remaining 6 cases were indeterminate on frozen section.

The sensitivity, specificity, PPR, NPR was calculated according to the formulae described above in the methodology (Table 2).

Table 1 Distribution of final histopathology results

Histopathology	Number of cases
Benign	84
Malignant	51
Benign with microcarcinoma	5

Figure 2 shows all of the benign cases confirmed on final histopathology reports.

On retrospective evaluation, the results of FNAC and frozen section were compared. A total of 47 benign cases detected by FNAC, 43 were diagnosed as benign by frozen section as well. 13 cases were incorrectly diagnosed as malignant on FNAC. Nine of these were detected as benign on FS and subsequently declared benign on histopathology. Similarly, on retrospective analysis of histopathologically confirmed benign swellings, on FNAC, 20 cases were declared inadequate on FNAC. 13 of these cases were picked up as benign on frozen section, 5 were reported as malignant and 2 cases were indeterminate on frozen section.

Similarly, Fig. 3 shows all of the cases which were confirmed as malignant cases. 16 of the patients were diagnosed as having benign lesions on FNAC, of which 6 were diagnosed as malignant on frozen section subsequently. Four of 26 histologically confirmed malignant cases were incorrectly diagnosed as benign on FNAC. Six histologically confirmed malignant cases were reported as inadequate for an opinion on FNAC, of which frozen section was able to catch four cases as malignant; however, two were undetected on both FNAC and frozen section.

Most frequently incorrect diagnosis was seen with follicular lesions. Out of 11 cases of follicular adenoma,

Table 2 Statistical analysis of FNAC and frozen section

	FNAC	Frozen section
Sensitivity	63.6	67.35
Specificity	79.7	87.1
PPR	68.3	75
NPR	77.8	82.4
Accuracy	73.1	79.9

FNAC was able to detect only 6 of them as benign lesions. Of the six cases of malignancy on histopathology, only one was picked up as malignant follicular neoplasm on FNAC. Interestingly, two cases of papillary carcinoma were detected on FNAC but were later proved to be follicular carcinoma on histopathological examination.

On the contrary, frozen section was able to detect seven cases of benign follicular lesions among the 11 cases of histopathologically confirmed benign cases. Among the six malignant nodules, frozen section picked up on three of them, with one case reported as indeterminate between follicular carcinoma or follicular nodule, and the final decision was deferred to the histopathological diagnosis.

There were only two cases where both FNAC and frozen section findings correlated for follicular lesions with the final histopathological report.

Discussion

According to Menon et al thyroid swellings are very common in India, and can be detected as palpable masses in as much as 12% of the population [1]. As stated above, we found that thyroid nodules have a greater

Fig. 1 Most common histopathology lesion

Fig. 2 Comparison of FNAC versus FS in patients with benign swelling on histopathology

Fig. 3 Comparison of FNAC versus FS in patients with malignant swelling on histopathology

preponderance in females, however, the incidence of carcinoma in females are found to be less frequent than in the male population. This can be substantiated by various studies, where the male to female ratio was 1:5 with thyroid swellings [11, 14, 15]. Male patients were found to have malignancy rates ranging from 19 to 26% [11, 13, 15].

In this study, we found that frozen section was slightly more sensitive than FNAC, but substantially more specific in detecting malignancy in the thyroid gland. The results from the frozen section can help the surgeon avoid unnecessary resection of the thyroid gland, as it can rule out malignancy more accurately than FNAC. However, even though FNAC has its limitations, i.e. the results heavily depend on how the sample has been taken, experience of the clinician taking the FNAC, taking multiple aspirations, and performing the procedure under ultrasonographic guidance can substantially improve capability of the clinician to get an aspirate of the best quality to get a diagnosis. The results also depend on the ability of the pathologist to detect malignancy of the swelling based on the aspirate collected [2, 6]. Nevertheless, as the sensitivity of FNAC and frozen section are similar, FNAC proves to be a more significant tool in screening for malignancy of the thyroid gland [7, 11, 14, 17]. In more recent studies, it has been found that the specificity of FS is lower than expected when the lesions are classified according to the current Bethesda Classification of thyroid nodules [16, 18].

Among the 5 cases which were incorrectly diagnosed as malignant on frozen section, 3 were found to be follicular lesions, in which malignancy can be accurately predicted

based on capsular or vascular invasion. One of the cases among these was found to have colloid lesion with papillary hyperplasia which may have been the reason behind the incorrect diagnosis. Five patients with inconclusive results on FNAC were followed up with frozen section; four out of five were confirmed as malignant on frozen section and histopathology. These 4 cases were treated with total thyroidectomy. The remaining one was detected as benign on both FNAC and frozen section but was a rare tumor of the thyroid which was a hyalinizing trabecular tumor.

Another unexpected finding was that ten cases were diagnosed as benign, on both FNAC and frozen section but were found malignant on final histopathology. On retrospective analysis of the reason as to why there was such a discrepancy, it was found that three of the cases were minimally invasive follicular carcinomas, one was found to be a micropapillary carcinoma in colloid goiter. These findings highlight a fallacy in both tests i.e. both FNAC and FS only get a sample of the thyroid gland from one particular area to evaluate. If the pathology in question is not seen in these areas, there can be an incorrect diagnosis. There was one case of papillary carcinoma of a follicular variant which was undetected both on FNAC and frozen section, later diagnosed on histopathology. Papillary carcinoma was unexpectedly unnoticed in 3 cases by both FNAC and frozen section. As both investigations were reported as benign, most of these patients were treated with hemithyroidectomy necessitating a need for repeat surgery due to malignant pathology found on histopathology.

The diagnoses of follicular lesions can be challenging. According to previous literature, the follicular lesions can only be distinguished as benign or malignant based on the invasion of the capsule. Such findings, especially in minimally invasive follicular carcinoma, are only clearly picked up on histopathological diagnosis [16]. However, as a part of routine investigations, FNAC can be attempted to identify cases of the Follicular lesion which can further be managed based on histopathology findings [18].

Neither FNAC nor frozen section was proficient enough to detect follicular carcinoma correctly. FNAC could only pick up on one case of malignancy, and frozen section picked up three out of six total cases. Two of the remaining cases were incorrectly diagnosed as benign colloid goiter and in one case the decision was deferred to the final histopathological diagnosis. frozen section could detect malignancy in more cases and be more accurate in detecting the correct type of malignant lesion than FNAC. In the cases that FNAC did correctly diagnose as benign, the reports would be in the favor of colloid or adenomatous nodules by the majority.

Conclusion

Our study concludes that fine needle aspiration cytology is a good screening tool to detect malignancy in thyroid carcinoma, as it is sensitive enough to differentiate between the most common benign and malignant swelling. frozen section, as an intraoperative procedure, can be avoided as it may be cumbersome and prolong the duration of the surgery if the FNAC reports are conclusive. However, when FNAC shows an inconclusive result, frozen section can be a valid investigation to find out the pathology and plan the patient management accordingly.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed Consent Retrospective study using hospital records.

References

1. Usha Menon V, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H (2009) High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. *J Indian Med Assoc* 107:72–77
2. Yeung MJ, Serpell JW (2008) Management of the solitary thyroid nodule. *Oncologist* 13(2):105–112
3. Belfiore A, La Rosa GL, La Porta GA, Giuffrida D, Milazzo G, Lupo L, Regalbuto C, Vigneri R (1992) Cancer risk in patients with cold thyroid nodules: relevance of iodine intake, sex, age, and multinodularity. *Am J Med* 93(4):363–369
4. Unnikrishnan AG, Menon UV (2011) Thyroid disorders in India: an epidemiological perspective. *Indian J Endocr Metab* 15:S78–S81
5. Dean DS, Gharib H (2000) Fine-needle aspiration biopsy of the thyroid gland (updated 2015 Apr 26). In: De Groot LJ, Chrousos G, Dungan K, et al (eds) *Endotext*. South Dartmouth (MA): MDText.com, Inc. <https://www.ncbi.nlm.nih.gov/books/NBK285544/>
6. Liu F-H, Liou M-J, Hsueh C, Chao T-C (2010) Thyroid follicular neoplasm: analysis by fine needle aspiration cytology, frozen section, and histopathology. *Diagn Cytopathol* 38(11):801–805
7. Mateša N, Tabain I, Dabellæ N, Petric V, Kusia Z (2002) Diagnostic relevance of fine needle aspiration cytology for follicular lesions of the thyroid: retrospective study. *Croat Med J* 43(5):606–609
8. Almeida JPA et al (2009) The role of intraoperative frozen sections for thyroid nodules. *Rev Bras Otorrinolaringol* 75(2):256–260
9. Lumachi F, Borsato S, Tregnaighi A, Marino F, Polistina F, Basso SMM, Koussis H, Basso U, Fassina A (2009) FNA cytology and frozen section examination in patients with follicular lesions of the thyroid gland. *Anticancer Res* 29:5255–5258
10. Cetin B, Aslan S, Hatiboglu C, Babacan B, Onder A, Celik A, Cetin A (2004) Frozen section in thyroid surgery: is it a necessity? *Can J Surg* 47(1):29–33
11. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, Pacini F, Randolph GW, Sawka AM, Schlumberger M, Schuff KG, Sherman SI, Sosa JA, Steward DL, Tuttle RM, Wartofsky L (2015) American thyroid association management guidelines for adult patients with thyroid nodules and differentiated thyroid cancer. *Thyroid* 26(1)
12. Mayoaran N, Waters PS, Kaim Khani TY, Kerin MJ, Quill D (2016) FNAC and frozen section correlations with definitive histology in thyroid diseases. *Eur Arch Otorhinolaryngol* 273(8):2181–2184
13. Chang HY, Lin J-D, Chen J-F, Huang B-Y, Hsueh C, Jeng L-B, Tsai J-SH (1997) Correlation of fine needle aspiration cytology and frozen section biopsies in the diagnosis of thyroid nodules. *J Clin Pathol* 50:1005–1009
14. Gerhard F, Huber F, Dziegielewski P, Matthews TW, Warshawski SJ, Kmet LM, Faris P, Khalil M, Dort JC (2007) Intraoperative frozen-section analysis for thyroid nodules—a step toward clarity or confusion? *Arch Otolaryngol Head Neck Surg* 133(9):874–881
15. Batra C, Singh S, Katra R, Marwah N, Atreja A (2010) Role of fine needle aspiration and frozen section in the diagnosis of thyroid lesions. *Internet J Pathol* 11(1)
16. Kahmke R, Lee WT, Puscas L, Scher RL, Shealy MJ, Burch WM, Esclamado RM (2013) Utility of intraoperative frozen section during thyroid surgery. *Int J Otolaryngol* 2013 Article ID 496138
17. Sengupta A, Pal R, Kar S, Zaman FA, Sengupta S, Pal S (2011) Fine needle aspiration cytology as the primary diagnostic tool in thyroid enlargement. *J Nat Sci Biol Med* 2(1):113–118
18. McHenry RC, Phitayakorn R (2011) Follicular adenoma and carcinoma of the thyroid gland. *Oncologist* 16(5):585–593