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Role Of Core Needle Biopsy in The Diagnosis of Thyroid Nodules: A Systematic Literature Review

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IMPORTANCE With the rapidly increasing number of nodular goiter cases, advances are being made in diagnostic modalities. One of these is the Core Needle Biopsy (CNB) which gives a larger tissue specimen for diagnosis. This technique has its merits as well as demerits. The current article elaborates the characteristics of Core needle biopsy in comparison with the gold standard Fine Needle Aspiration Cytology (FNAC), as a diagnostic tool for thyroid nodules.

OBJECTIVE: This systematic review article aims to find out the role of Core needle biopsy in the diagnosis of thyroid nodules, both as a first-line technique and as a complementary method to fine-needle aspiration cytology (FNAC).

METHODS: A systematic review of full-text articles from the last 5 years, retrieved from PubMed, ProQuest, and Google Scholar, was performed. Out of 1032 articles retrieved, a detailed thematic analysis of records was used for screening out 12 relevant articles for final review.

RESULTS: It is argued that core needle or Tru-Cut biopsy (CNB/TCB) leads to a lower proportion of undiagnosed biopsy results because of adequate tissue sampling, at the cost of increased diagnoses of atypia of undetermined significance, and hence, leading to more diagnostic surgeries. Therefore, FNAC remains the first-line investigation in the majority of medical centers all over the world due to its higher negative predictive value, ease of use, lower pooled proportion of serious complications, and equal diagnostic surgeries performed in comparison with CNB.

CONCLUSION: CNB leads to a lower pooled population of nondiagnostic results as it provides a larger sample size with the availability of immunohistochemistry and histological architecture studies. Some disadvantages also need to be kept in mind such as the risk of more serious complications as it is a more invasive technique in comparison to FNAC.

KEYWORDS Core needle biopsy, Tru-Cut biopsy, Biopsy, Fine-Needle Aspiration cytology, Thyroid nodules

HOW TO CITE Imtiaz I, Kaleem A. Role Of Core Needle Biopsy in The Diagnosis of Thyroid Nodules: A Systematic Literature Review. *Archives of Surgical Research*. 2021, 2 (4):48-52. <https://doi.org/10.48111/2021.04.09>

Original Research

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The thyroid gland lies in the neck in the infrahyoid visceral space. It produces Tri(T3) and tetraiodothyronine(T4) hormones which regulate growth and metabolism¹. The most presented abnormality of the endocrine system is the presence of thyroid nodules². They are clinically palpable in about 5% of the general population, whereas they can be found in up to 70% of the population with the help of diagnostic imaging techniques such as ultrasonography³. They are seen as lesions on ultrasonography that show differences from the surrounding parenchyma⁴. Approximately 10% of the thyroid nodules are at risk of being malignant⁵. The gold standard for evaluation of a thyroid nodule is ultrasonography-guided fine-needle aspiration (FNAC)⁶. FNAC specimens yield more inconclusive and indeterminate results as compared to core needle biopsies⁷. On the other hand, a drawback of core needle biopsy is that it has a higher rate of serious complications⁸.

This review aims to determine the importance of Core needle biopsy for the assessment of thyroid nodules, as compared to more commonly used tools, and whether it can replace FNAC in becoming the first-line diagnostic tool in thyroid nodules.

METHODS:

This article has been designed according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to analyze the evidence available for comparing core needle biopsy with FNAC in diagnosing Thyroid nodules.

Search Strategy, Data Extraction, and Inclusion Criteria

A systematic review of full-text articles, published around the last 5 years retrieved from PubMed, ProQuest, and Google Scholar was performed. We searched the PubMed database using the terms: ((thyroid nodules) AND (core

needle biopsy)). A total of 125 records were identified. The ProQuest database was also searched to identify high-quality systematic reviews, studies, and meta-analyses, clinical trials, and reviews using the terms "Thyroid Nodules and core needle biopsy" that revealed 801 articles. In addition, Google Scholar search using the terms 'thyroid nodules and Tru cut biopsy' to retrieve 148 articles.

Pertinent articles were selected with an inclination toward recent publications, publications in the English language, and studies done on humans only. Detailed scrutiny was carried out by screening for records and thematic analysis to yield 12 articles for final review.

Exclusion Criteria: Exclusion criteria included duplicate papers, irrelevant titles, abstracts, themes, and papers not available in English.

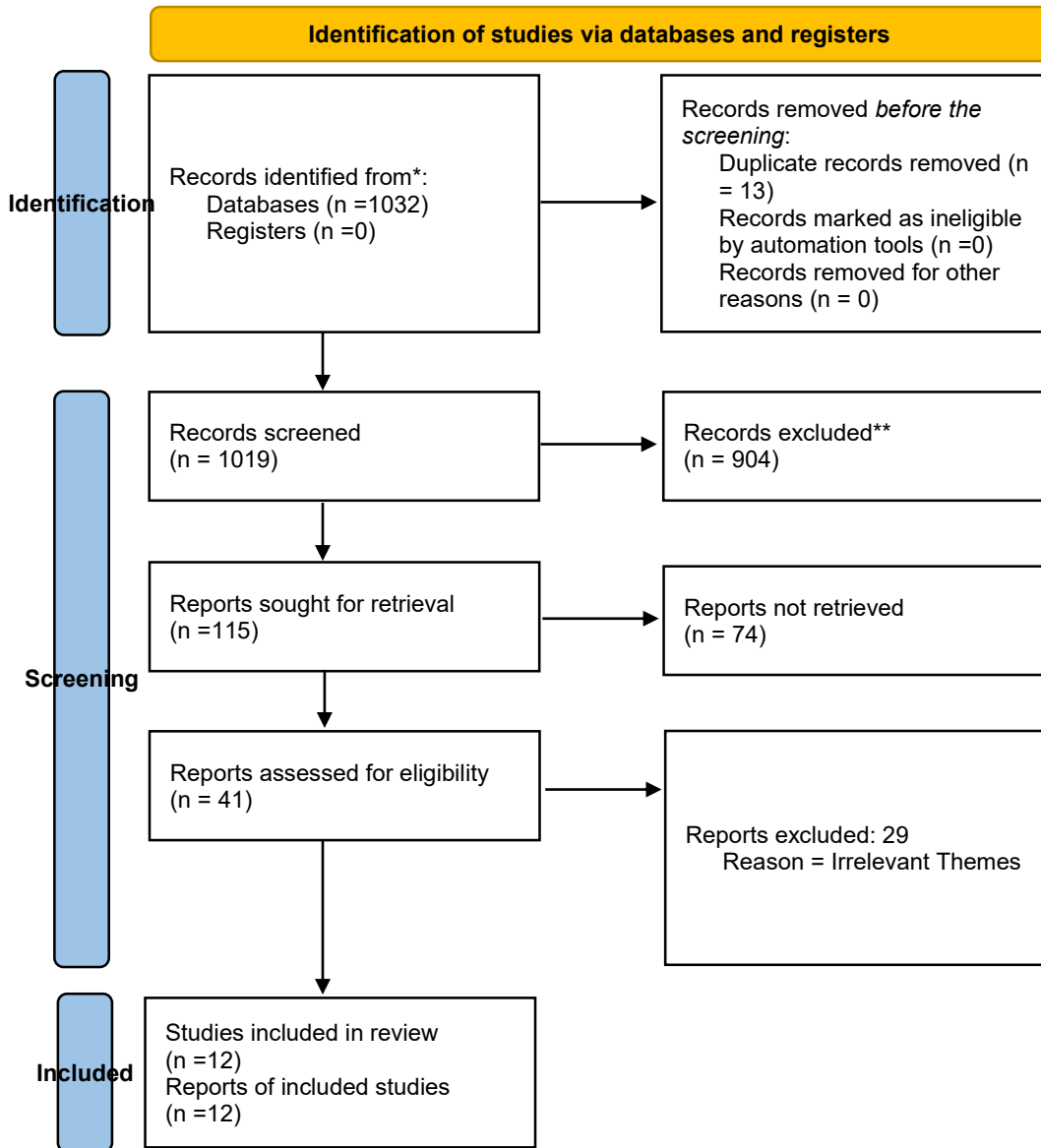


Diagram: Article selection process through computer literature search

Year	Author	Country	Research Method	Themes Identified
2021	Dupain (Dupain et al., 2021)	France	Biopsy samples were taken from the tumors of all enrolled patients in this study and compared	Both the biopsy methods show no significant differences in molecular profiling; core needle biopsy samples can be saved for further investigation
2021	Soon- Hyun Ahn (2021)	Korea	A meta-analysis of published data in Korea retrieved from Embase database	Although CNB has an advantage of reduced inconclusive results, it comes with the disadvantages of increased results of cellular atypia and follicular neoplasia
2020	Pantanowit (Pantanowitz et al., 2020)	USA	Review article comparing FNAC to TCB	Both FNAC and CNB have their own set of advantages and disadvantages, serving each other as complementary methods for thyroid nodule diagnosis.
2020	Reyaz (Reyaz et al., 2020)	Pakistan	Smears were made from aspirates of thyroid nodules using fine-needle cytology and studied	FNAC is an effective, cheap, and gold-standard biopsy method for thyroid nodules
2020	Hahn (Hahn et al., 2020)	Korea	Samples of patients who underwent either CNB or FNAC were studied retrospectively and compared to ultrasonographic findings	Non-diagnostic results were reduced whereas the conclusive rates increased with the use of CNB, the diagnostic performances were comparable for both methods.
2020	Lan (Lan, et al., 2020)	China	Data were retrieved from PubMed, Cochrane Library, and Embase databases and studied	CNB and FNAC show comparable results and are complementary to each other.
2019	Paja (Paja et al., 2019)	Spain	A retrospective study was done on all the CNB procedures done in the authors' institute in the last 11 years, in terms of performance, accuracy, and complications	CNB has a low proportion of non-diagnostic and inconclusive results and is an able replacement in situations where FNAC has a poor performance.
2018	Gupta (Gupta et al., 2018)	India	Overview of some of the already published data relating to biopsy methods of thyroid nodules as well as salivary glands	TCB is not the first-line investigation for biopsy of thyroid nodules; it is a complementary method to FNAC.
2018	Ha (Ha et al., 2018)	Korea	Major and minor complications were studied after CNB in patients.	Some complications did occur but none of them was serious enough to warrant CNB as an unsafe procedure.
2017	Rahman, (Rahman et al., 2017)	USA	A retrospective study was done of all thyroid TCBS and FNACs done in the authors' institute.	FNAC and CNB are valuable tools in diagnosing thyroid neoplasia and metastases, eradicating the need for invasive surgeries for such purposes.
2017	Chae (Chae et al., 2019)	Republic of Korea	Association between hematoma formation and clinical /ultrasonographic features was studied following biopsies	Hematoma formation and bleeding were more common after CNB as compared to FNAC.
2016	Wolinski (Wolinski et al., 2016)	Poland	Several databases were searched and retrieved, data were studied to compare FNAC and TCB.	CNB yielded a more pooled proportion of diagnostic results as compared to FNAC and more conclusive results after equivocal FNAC.

Table: Year of publication, author name, country, research method and Themes identified through analysis of 12 included papers. **Important Terms:** CNB: Core needle biopsy; Tru-cut biopsy. FNAC: Fine needle aspiration cytology

RESULTS

CNB and FNAC both have an important place in the diagnosis of thyroid nodules. FNAC is the investigation of choice, whereas CNB plays a complementary role. CNB also lacks a biopsy reporting system¹¹. Data shows an equal number of diagnostic/therapeutic surgeries with CNB as compared to FNAC.

Current Noninvasive Biopsy Method For Thyroid Nodules -FNAC

It is a quick, simple, safe, tolerable, and specific method for obtaining a specimen for cytology^{7,29}. Lower rates of inconclusive and false-negative results have been reported in retrospective studies as compared to clinical examination only. FNAC is also used to evaluate a breast lump; it is a part of the triple assessment. However, it fails to show important data such as the histopathology, grade, and receptors of the tumor²².

Core Needle Biopsy/Tru-Cut Biopsy: This biopsy method yields tissue fragments by using larger bore needles and is based on the histological study²². It has been suggested as

a complementary method to FNAC to overcome inconclusive results⁷. Some of the literature has established Tru-Cut biopsy as a safe, tolerable, and efficient method of obtaining a thyroid nodule specimen⁶.

Advantages: An advantage of CNB is that it can sample greater amounts of tissue which leads to increased ease in assessing histological architecture and performing immunohistochemistry when required²³. Immunohistochemical stains such as cytokeratin-19, galectin-3, BRAFV600E, or HBME-1 are used to diagnose thyroid malignancy in such cases²⁰. However, the Tru-Cut biopsy technique is still not as popular as FNAC, one of the reasons being safety concerns¹⁷.

Disadvantages: Two of the major complications of CNB include bleeding and recurrent laryngeal nerve injury³². Other common complications are hematoma, hemoptysis, parenchymal edema, infection, hoarseness, and dysphagia¹⁸. A rare complication of this biopsy technique is the development of a vasovagal reaction²⁵. Nodules with heavy calcification may not be punctured²¹. Other limitations include relatively higher cost, technical requirements, and increased time consumption¹⁶. There are also no guidelines

on the potential use of Tru-cut biopsy as a first-line biopsy method¹⁹.

CNB demonstrated a lower percentage of non-diagnostic and inconclusive results as compared to FNAC in two studies, one of them related to breast nodules^{19,33}. It has been shown to decrease inconclusive results at the cost of increased results of cellular atypia, and in return increased diagnostic surgeries in nodular goiter⁸. In another study using core needle biopsy for diagnosis of breast lump, researchers have found that the results of CNB correlated with gold standard evaluation (1.9% error) whereas the post-surgical diagnosis following FNAC changed in up to 37% of the nodules. This study showed that FNAC led to more inadequate results as compared to TCB. In another study, the sensitivity and specificity of FNAC were 100% and 73.7%, whereas they were 100% and 94.7% for TCB. These data agree with the literature about female breast lesions²⁶.

However, one study has found that the negative predictive value was worse for TCB than FNAC when applying Criteria 1 and 2. The positive predictive value and specificity of FNAC when applying Criteria 3 were also higher than that of TCB irrespective of the size of the nodule. The diagnostic performance, when applying Criteria 4 and 5 (for nodule size > 2cm), did not vary in value. TCB did not demonstrate superior diagnostic performance to FNAC for thyroid nodule diagnosis in this study⁶. Conversely, in another study's results, in nodules categorized as intermediate in suspicion, the superiority of TCB was evident in nodules greater than 2 cm⁷. Some studies show that FNA and CNB are similar in terms of results and that FNAC is better as a first-line investigation in thyroid nodules^{27,28,33}.

The complication rates of FNAC and CNB are similar, although CNB has a greater proportion of major complications, which include bleeding and hematoma formation¹⁹.

DISCUSSION

The Core needle biopsy is being used in many nodular diseases including breast cancer in men and women⁹. It provides tissue within the pathology, the nodule margin, and the normal thyroid tissue¹⁰.

The investigation of choice for thyroid nodules is fine-needle aspiration cytology due to its low cost, minimal invasiveness, and ease of use⁴. The key limitations of this biopsy method are inconclusive results and non-diagnostic samples¹¹. This is because of the monotonous cytological sample and scanty

colloid¹². These results are reported to be between 20 to 46%¹³. To combat these results, FNAC is repeated according to authority guidelines, although in as many as half of the cases, the results will be nondiagnostic again¹¹. These results are generally followed by surveillance or diagnostic surgery, according to risk factors, ultrasound findings, and the choice of the patient. The false-negative rate of FNAC varies from 13.6 to 56.6¹⁴.

On the other hand, even when CNB is used as a primary investigation, the results are good¹³. A major advantage of CNB is that its specificity according to a study is 96-100%^{15,16}. The rate of nondiagnostic and inconclusive results is minimized with CNB¹⁷. There are rarely, if any, false-positive results with CNB¹⁴. The false-negative rates are higher in small nodules (less than 2 cm) whereas they are lower in larger nodules¹⁶. There are no remarkable differences in pain, minor complications, or tolerability between TCB and FNAC¹⁸. It allows the clinician to look for nuclear change, relationship to the adjacent healthy tissue as well as alterations in the follicular structure, important data which the FNAC technique simply does not provide²⁰. It also differentiates between the follicular neoplasm and the nodule without neoplasia¹⁰. However, there are yet no definite authoritative guidelines on the use of TCB¹⁹. TCB is still not routinely used even though it has all these advantages because of limited data on efficacy and safety¹⁵. TCB is also not always feasible, especially when the nodule is present posteriorly or near the major vessels of the neck²¹.

CONCLUSION

Hence, it is proven that both FNAC and CNB play an indispensable role in the diagnosis of thyroid nodules with the advent of technological advances in ultrasonography.³¹ FNAC is the traditional investigation of choice and has made its place as a first-line biopsy method owing to the advantages of being fast, cheap, and readily available. As medical techniques have continued to get better and more sophisticated, Tru-cut biopsy has also emerged as another very important biopsy method due to the advantage of a greater tissue sample size that allows histological studies and immunohistochemistry as more tumor markers are being identified.

More studies need to be done to consider core needle biopsy as a first-line investigation as it yields less nondiagnostic or inconclusive results at the price of a greater pooled proportion of serious complications and an equal number of diagnostic surgeries.

Financial Support and Sponsorship: Nil.

Conflicts of Interest: There are no conflicts of interest

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