Comparison of diagnostic yield of core-needle and fine-needle aspiration biopsies of thyroid lesions: Systematic review and meta-analysis

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Abstract
Objectives Thyroid nodular disease is one of the most commonly observed medical conditions. Cytological evaluation of the specimens obtained with fine-needle aspiration biopsy (FNAB) is the most accurate tool for selecting nodules which should be further surgically removed. A major limitation of this method is the high occurrence of non-diagnostic results. This indicates the need for improvement of the thyroid biopsy technique. The aim of this meta-analysis was to compare the diagnostic value of thyroid core-needle biopsies (CNBs) and FNABs.

Materials and methods PubMed/MEDLINE, Cochrane Library, Scopus, Cinahl, Academic Search Complete, Web of Knowledge, PubMed Central, PubMed Central Canada and Clinical Key databases were searched. Risk ratios (RRs) of non-diagnostic results were meta-analysed using the random-effects model.

Results Eleven studies were included in the quantitative analysis. CNB yielded significantly more diagnostic results – the pooled risk ratio (RR) of gaining a non-diagnostic result was 0.27 (p<0.0001). For lesions with one previous non-diagnostic FNAB, RR was 0.22 (p<0.0001).

Conclusions CNB seems to be a valuable diagnostic technique yielding a higher proportion of diagnostic results than conventional FNAB. It is also significantly more effective in case of nodules with a prior non-diagnostic result of FNAB results than repeated FNABs.

Key Points
• Core-needle biopsy yields a higher proportion of diagnostic results than fine-needle biopsy.
• Core-needle biopsies may decrease the amount of unnecessary thyroidectomies.
• Probability of gaining non-diagnostic result using core-needle biopsy is almost four times lower.

Keywords Fine-needle aspiration biopsy · Core-needle biopsy · Thyroid · Thyroid lesions · Biopsy

Introduction

Thyroid nodular disease (TND) is one of the most commonly observed medical conditions, affecting a large number of individuals, especially women, subpopulations in iodine-deficient regions, elderly people and patients with some specific clinical conditions. The prevalence of TND is high, affecting 10–70% of the general population and malignancies are observed in 3–10% of patients [1–5]. Cytological evaluation of the specimens obtained with fine-needle aspiration biopsy (FNAB) is the most accurate tool for selecting nodules which should be further surgically removed (malignancies, indeterminate follicular lesions) [6]. One of the major limitations of this method is a high occurrence of non-diagnostic results, falling in group I of the Bethesda Classification [7]. According to numerous studies, around 10–20% of FNABs yield non-diagnostic results [8–10]. Most endocrinological societies recommend consideration of total thyroidectomy in cases of repeated FNABs with non-diagnostic results [11]. This may increase the number of unnecessary thyroidectomies and also delay the final diagnosis of thyroid cancer. This
indicates the need for improvement of the thyroid biopsy technique or even searching for new tools which may decrease the prevalence of non-diagnostic results. Biopsy with the use of a core needle (CNB) is believed to be reliable improvement on FNAB, bringing high diagnostic yield [12, 13]. The aim of the current meta-analysis was to compare the diagnostic value of thyroid CNBs and FNABs.

Materials and methods

Study selection

PubMed/MEDLINE, Cochrane Library, Scopus, Cinahl, Academic Search Complete, Web of Knowledge, PubMed Central, PubMed Central Canada and Clinical Key databases from January 2001 up to December 2014 were searched in order to find all relevant, full-text journal articles written in English. We used the search term: ((“core-needle”) or (core and needle)) and thyroid. Articles comparing the percentage of diagnostic results of thyroid FNAB and CNB, performed with sonographic guidance, were included in the meta-analysis. According to the Bethesda System for Reporting Thyroid Cytopathology [14], categories II–VI are interpreted as diagnostic results. Samples classified as Bethesda category III and IV are inconclusive results in the context of differentiation between benign and malignant lesions but assessed as adequate for cytological assessment. We excluded studies about very particular groups of lesions (e.g. hyalinising trabecular tumours, follicular tumours) and studies where FNAB or CNB was performed without ultrasound guidance. Studies without control groups, comparing results of FNAB with FNAB and CNAB performed simultaneously (without distinct data about the FNAB and CNAB results) were systematically reviewed.

Two researchers (K.W. and A.S.) searched all included databases independently and prepared a list of included studies. In case of discrepancies between lists, authors read questionable articles together.

Quality assessment of the studies

All included studies were assessed using the Newcastle-Ottawa Scale [15]. Studies with a result of seven stars or more were included.

Statistical analysis

All calculations were performed using Statistica v.10 with the medical package from Statsoft. Risk ratios (RRs) of non-diagnostic result were meta-analysed using the random-effects model. Publication bias was assessed using Kendall’s tau.

Results

The search results and steps of selection are shown in the flowchart (Fig. 1). Eleven studies were included to the meta-analysis – the basic data are shown in Table 1 [6, 16–25]. CNB yielded significantly a higher amount of diagnostic results. The forest plot is shown on Fig. 2. The pooled RR of non-diagnostic results was 0.27 with a 95 % confidence interval (CI) 0.16–0.46 (p<0.0001). There is no evidence for publication bias (Kendall’s tau = −0.24, two-tailed p-value = 0.31).

Fig. 1 Flowchart showing the steps included in the literature search and selection
There was evidence of significant heterogeneity ($Q = 85.3$, $df=10$, $\hat{i^2}=88.3 \, \%$, $p<0.0001$). (Table 2)

We have also performed some analyses in subgroups.

Seven studies focused on lesions with one previous non-diagnostic result of FNAB [17–21, 23, 24]. The forest plot is shown on Fig. 3. The pooled RR of gaining a non-diagnostic result was 0.88 (95% CI 0.61–1.33, $p=0.6103$).

![Forest plot showing individual and pooled risk ratios (RRs) of gaining non-diagnostic results with core-needle biopsy in comparison to fine-needle aspiration biopsy; with 95% confidence intervals and p-values given in columns 2–4.](image)
result was 0.22 (95% CI 0.10–0.45, p=0.0001). There is no evidence for publication bias (Kendall’s tau = −0.33, two-tailed p-value = 0.29). There was evidence of significant heterogeneity (Q =47.5, df=6, $\hat{\tau}^2=87.37\%$, p<0.0001).

Four studies from South Korea were performed with very similar methodology [17, 18, 20, 23]. Lesions with one previous non-diagnostic FNAB were included, in all studies the ACECUT system by TSK, Japan was used. For these studies the pooled RR was 0.05 (95% CI 0.02–0.10, p<0.0001). There is no evidence for publication bias (Kendall’s tau = 0.0, two-tailed p-value = 1.0). There was no evidence of significant heterogeneity (Q =1.2, df=3, $\hat{\tau}^2=0.0\%$, p=0.76).

Discussion

CNB yielded a significantly higher percentage of diagnostic results than FNAB in lesions with previous non-diagnostic results with FNAB. RR was 0.27, which means that the probability of gaining a non-diagnostic result was almost four times lower. However, the number of studies comparing the diagnostic efficacy of FNAB was rather low. We found 11 case-control studies on the topic. In addition, these studies differed with regard to the diameters of needles and design of the study (CNB as the first-line procedure or as a procedure performed after one or more non-diagnostic FNABs,

| Author          | Year | Country      | Design                                                                                      | Needles                          | FNAB – diag. | FNAB – ndg. | CNB – diag. | CNB – ndg. |
|-----------------|------|--------------|---------------------------------------------------------------------------------------------|----------------------------------|--------------|-------------|--------------|------------|
| Yeon et al. [26]| 2013 | South Korea  | Retrospective; lesions with previous ndg. FNAB; no control group                           | CN: 18 G; FN: no data; automatic biopsy gun used | No data      | No data     | 135          | 2          |
| Khoo TK [31]    | 2008 | USA          | CNB and FNAB simultaneously compared with lesions that underwent FNAB only                 | No data                          | 296          | 15          | 303*         | 37*        |
| Zhang et al. [32]| 2007 | USA          | Retrospective; CNB and FNAB simultaneously, in most cases after two ndg. FNABs            | CN: 20, 22 G; FN: 25, 23 G       | 409          | 39          | 217*         | 8*         |
| Mehrrota et al. [33]| 2005 | UK           | Retrospective; US-guided CNB and freehand FNAB compared                                  | CN: 20 G, automatic biopsy gun used; FN: 21 or 23 G | 75           | 66          | 102          | 19         |
| Harvey et al. [34]| 2004 | UK           | Retrospective; CNB in random patients; FNAB partially without sonographic guidance      | CN: 18 G; FN: 21–23 G            | 159          | 107         | 69           | 10         |
| Screaton et al. [35]| 2002 | UK           | Retrospective; no control group; CNB – lesions with previous ndg. FNAB and also as first choice | CN: 16–18 G                     | No data      | No data     | 199          | 10         |

*Summary data for simultaneous CNB and FNAB – without distinction of FNAB and CNB component

FN – fine needle, CN core needle, FNAB fine-needle aspiration biopsy, diag. diagnostic results, ndg. non-diagnostic results

Fig. 3 Cumulative forest plot for studies comparing risk ratios (RRs) of gaining non-diagnostic results with core-needle biopsy in comparison to fine-needle aspiration biopsy; with 95% confidence intervals and p-values given in columns 2–4.
The CNB seems to be a valuable diagnostic technique yielding a higher proportion of diagnostic results than conventional FNAB. It is also significantly more effective in cases of nodules with prior non-diagnostic results with FNAB than repeated FNABs. However, further studies on the topic are required.

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One of the authors has significant statistical expertise. Institutional Review Board approval was not required because the study is a meta-analysis. Written informed consent was waived by the Institutional Review Board. Some study subjects or cohorts have not been previously reported.

Methodology: meta-analysis, performed at one institution.

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