Frozen-section diagnosis of follicular thyroid nodules may have higher specificity and positive predictive value than fine-needle aspiration biopsy, but is not sensitive enough for routine clinical use in most hospitals

Peng Y, Wang HH. A meta-analysis of comparing fine-needle aspiration and frozen section for evaluating thyroid nodules. Diagn Cytopathol 2008;36:916-20.

SUMMARY

BACKGROUND The treatment of patients who have a thyroid nodule that yields indeterminate follicular cytology on fine-needle aspiration biopsy (FNAB) is under debate. Among the options is to perform a frozen-section diagnosis (FSD) at the time of thyroid lobectomy, which might avoid an unnecessary second operation in the 20% of patients with indeterminate cytology that have malignant nodules. These authors performed a meta-analysis of the literature related to this problem.

METHODS A PubMed search was performed to identify English-language articles published from January 1982 through April 2007 that permitted comparisons of the diagnostic accuracy of FNAB and FSD specimens in the same study. Only publications providing sufficient information to determine the number of true positive and true negative tests and false positive and false negative tests were included in the study. FNAB diagnoses were stratified into three FNAB diagnostic categories: (1) follicular lesion/neoplasms and intermediate cytology with special findings such as follicular proliferation with atypia; (2) nonfollicular lesions (predominantly papillary thyroid cancer); and (3) thyroid carcinoma not otherwise specified (NOS). All three FNAB cytology terms were considered positive tests. Accuracy of FNAB and FSD were based on findings in the thyroidectomy specimen.

RESULTS The literature yielded 62 publications, 52 of which met the study criteria. There were 29 studies with 3027 cases with FNAB cytology in the group designated as a follicular lesion/neoplasm that were compared with 23 FSD studies with 2531 cases. In this group, the mean (±SD) sensitivity for FNAB as compared with FSD was 69±32 and 21±23 (P<0.0001), specificity 60±32 and 99±2.4 (P = 0.004), positive predictive value (PPV) 35±28 and 86±26 (P = 0.002), and negative predictive value (NPV) 84±19 and 83±16% (P = 0.03), comparing FNA and FSD, respectively (Figure 1).

In the follicular-lesion category there were only 4 studies and 646 cases in which the FNA cytology was categorized as intermediate. As compared with the 23 FSD studies, there were no statistically significant differences between FNAB and FSD. In the nonfollicular-lesion category there were 20 studies with 2307 cases and 20 FSD studies with 3533 cases. In this group, the mean (±SD) sensitivity of FNAB vs. FSD was 67±25 vs. 66±22, specificity 95±5.1 vs. 98±5.3, PPV 94±7.9 vs. 96±11, and NPV 79±16 vs. 84±13%, comparing FNAB with FSD; all comparisons in this group were statistically nonsignificant. In the nonfollicular-lesion category, there were 12 studies with 941 cases in which FNAB cytology was designated as suspicious. In this group, the FNAB and FSD sensitivity was 83±19 vs. 66±22 (P = 0.0003), specificity 67±23 vs. 98±5.3 (P = 0.005), PPV 81±16 vs. 96±11 (P = 0.0003), and NPV 85±17 vs. 84±13% (P = 0.67) (Figure 2).

In the thyroid cancer lesion termed NOS, there were 21 FNAB studies with 4704 cases compared with 21 FSD studies with 4970 cases. In this category, the sensitivity of FNAB and FSD was 54±19 vs. 71±13 (P = 0.0004), specificity 96±7.2 vs. 99±1.2 (P = 0.08), PPV 88±19 vs. 98±3.5 (P = 0.001), and NPV 87±8.5 vs. 92±6.4% (P = 0.002) comparing FNAB with FSD (Figure 3). In the thyroid cancer group designated only as suspicious, the

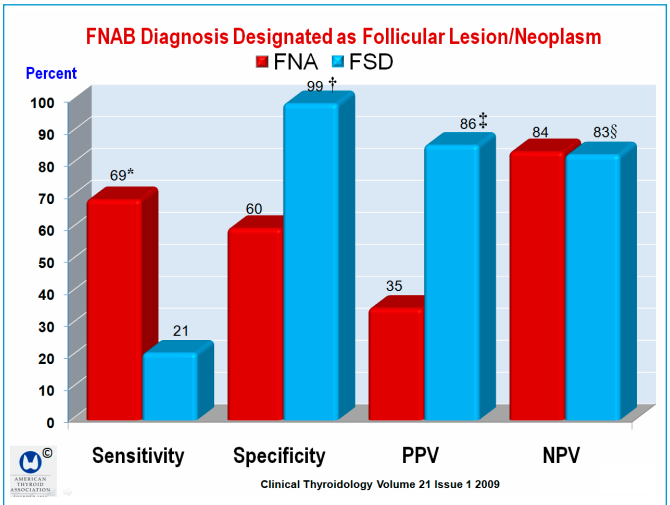

Figure 1. The diagnostic accuracy of fine-needle aspiration biopsy (FNAB) cytologic diagnosis of follicular lesion vs. frozen-section diagnosis (FSD). *P<0.0001., †P = 0.004. ‡P = 0.002.§Negative predictive value (NPV) = 0.03. Here and in the other figures, all comparisons are FNAB vs. FSD. The data in this figure are derived from Table 1 in Peng et al.

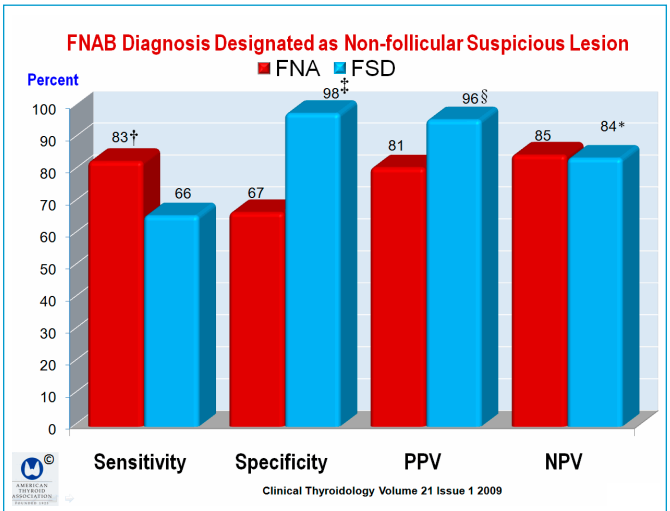

Figure 2. Diagnostic accuracy of FNAB and FSD.*P<0.0003, †P = 0.005, ‡P = 0.003, §P = 0.67. The data in this figure are derived from Table 2 in Peng et al.

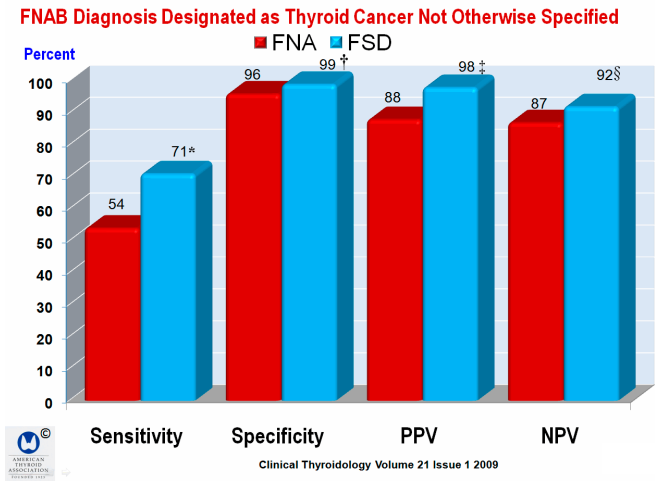

Figure 3. *P = 0.002, †P=0.0004, ‡P = 0.08, §P = 0.001. The data in this figure are derived from Table 3 in Peng et al.

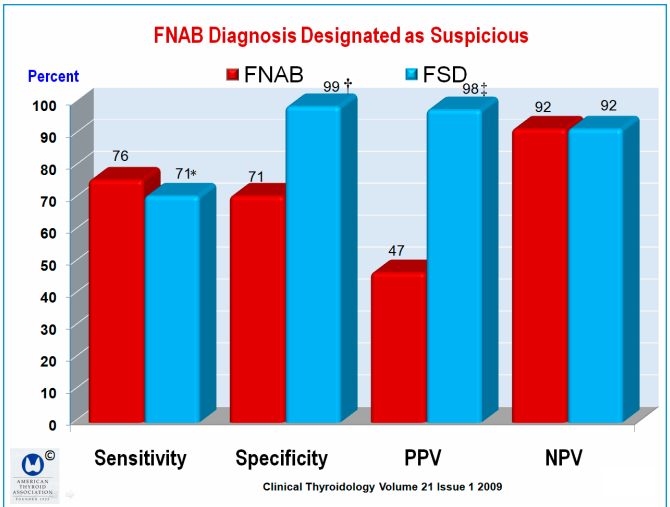

Figure 4. †P=0.0004, ‡P = 0.004 §0.002, *P = 0.002. The data in this figure are derived from Table 3 in Peng et al.

sensitivity of FNAB and FSD was 76±23 vs. 71±13 (P<0.001), specificity 71±21 vs. 99±1.2 (P = 0.004), PPV 47±19 vs. 98±3.5 (P = 0.002), and NPV 92±6.4 vs. 92±6.4% (P = 0.03), comparing FNAB with FSD (Figure 4).

CONCLUSION This meta-analysis fails to demonstrate superiority of FNAB over FSD. Although FSD appears to have a higher specificity and positive predictive value than fine-needle aspiration biopsy, its low sensitivity significantly limits its applicability in practice in most hospitals.

COMMENTARY

The only reason to raise the question asked in this study is how can one gauge the accuracy of identifying follicular thyroid cancer at the time of thyroid lobectomy in order to avoid patients undergoing needless completion thyroidectomy? What is the magnitude of this problem? Indeterminate cytology, often reported as “follicular neoplasm” or “Hürthle-cell neoplasm” can be found in approximately 15 to 30% of FNAB specimens, only 20% of which turn out to be malignant (1). While certain FNA and clinical features such as male sex, nodule size > 4 cm, older age, and cytologic features such as cellular atypia may improve the FNAB diagnostic accuracy for malignancy, the overall predictive values are low (2;3).

Peng et al. found that the specificity and positive predictive value of FSD is significantly higher than that of FNAB; however, the diagnostic sensitivity of FNAB, which ranges from 71 to 21 % (Figures 1 and 4) is generally higher than that of FSD, depending on exactly how the FNAB features are described by the cytopathologist. Although the diagnostic sensitivity of FSD is slightly greater than that of FNAB in some cases (Figure 3), there is a much more fundamental issue: FSD has a major advantage over FNAB because vascular or thyroid invasion is not apparent on FNAB, making it virtually impossible to meaningfully compare the two diagnostic approaches. In the final analysis, this study fails to demonstrate the superiority of FSD over FNAB, if for no other reason than that 1 to 2% of patients would still undergo unnecessary total thyroidectomy using FSD (Figures 1 to 4). It is doubtful that many patients would opt for this choice. Furthermore, there are widely divergent opinions in various centers concerning the use of FSD for thyroid nodules, which is likely to reflect the frequency with which FSD is practiced for thyroid nodules (4-10).

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