

# Accuracy of ultrasound-guided fine-needle aspiration cytology for diagnosis of carcinoma in patients with multinodular goiter

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### ABSTRACT

**Background:** Fine-needle aspiration (FNA) is a useful method for evaluating multinodular goiter; however, its role is still controversial. The aim of this study was to assess the utility of ultrasound-guided thyroid FNA in detecting malignancy in patients with multinodular goiter in Oman. **Materials and Methods:** This was a retrospective study where all patients with multinodular goiter seen at the Sultan Qaboos University Hospital endocrinology clinic in Oman in 2005 were evaluated. The thyroid FNA results were grouped into either malignancy (positive result) or others (negative result). They were compared to those of final histopathological examination in order to calculate the value of the test in diagnosing malignancy. Analyses were evaluated using descriptive statistics. **Results:** A total of 272 patients were included in the study. The mean age was 39±13 years with an age range from 5 to 85 years. The majority of the patients were females (n=236; 87%). The results of thyroid FNA revealed that 6% (n=15) of the patients had malignancies while histopathological results showed that the proportion of subjects with malignancies was 18% (n=49). Out of the 15 cases identified to have malignancies by thyroid FNA, only 53% (n=8) of the subjects were confirmed to have malignancy by biopsy. Overall, the results of the tests were poor, revealing a sensitivity of 16%, specificity of 97% and a diagnostic accuracy of 82%, with a positive predictive value of 53% and a negative predictive value of 84%. **Conclusion:** Thyroid FNA is not a useful test in differentiating multinodular goiter from malignancy, as more than 80% of the malignancies go unnoticed.

**Key words:** Fine-needle aspiration, malignancy, multinodular goiter

## INTRODUCTION

Nodularity of thyroid tissue is extremely common. In a large population study in the USA (Framingham, MA), clinically apparent thyroid nodules were present in 6.4% of women and 1.5% of men.<sup>[1]</sup> The process of goitrogenesis is

distinct from true neoplasia.<sup>[2,3]</sup> It is therefore assumed those multinodular goiters are unlikely to contain a carcinoma. However several studies have suggested that the frequency of carcinoma in nodular goiters is about 25-60% of that in solitary nodules.<sup>[4,5]</sup> The incidence of malignancy in multinodular goitre (MNG) ranges from 1% to 10%.<sup>[4-9]</sup> It is therefore difficult to differentiate goiters with a malignant nodule by palpation, ultrasound, or scintigraphy, as no symptom or sign is indicative of malignancy.

A fine-needle aspiration (FNA) biopsy is a well-established procedure in the primary diagnosis of thyroid disorders.<sup>[10]</sup> However, the usefulness of FNA in multinodular goiter is controversial. Recently, Antonio Ríos *et al.* reported that FNA is not useful for differentiating MNG with malignant

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degeneration from benign MNG, as more than 80% of carcinomas go unnoticed,<sup>[11]</sup> whereas Cap and colleagues reported the ability to discriminate 11.7% of patients with a 34% probability of malignancy (suspicious/malignant cytology) from 81.2% of patients (benign cytology) with a probability of only 3%.<sup>[12]</sup>

To our knowledge, no similar studies have yet been conducted in Oman or the Arabian Gulf for that matter. Hence, the aim of this study was to assess the utility of ultrasound (US)-guided thyroid FNA in detecting malignancy in patients with multinodular goiter in Oman.

## MATERIALS AND METHODS

This was a retrospective study where all patients with multinodular goiter seen at the Sultan Qaboos University Hospital (SQUH) endocrinology clinic in Oman in 2005 were evaluated. Patients selected were those who had MNG with prominent nodules who had US-guided FNA and histology report. All FNAs at SQUH are performed by the same radiologist guided by ultrasound. The results of FNA were compared grouped into either malignancy (positive result) or others (negative result) to those of final histopathological examination in order to calculate the value of the test in diagnosing malignancy. True positives (TP) were defined as those having malignancy by both FNA and histopathology; false positives (FP) were those that were returned positive by FNA but not confirmed by histopathology; true negatives (TN) were those confirmed not to have malignancy by both the FNA and histopathology; false negatives (FN) were those that were returned negative by FNA but histopathology confirmed otherwise; sensitivity is a percentage of true positives over a total of true positives and false negatives ( $TP/(TP+FN)$ ); specificity is a percentage of true negatives over a total of true negatives and false positives ( $TN/(TN+FP)$ ); positive predictive value (PPV) is a percentage of patients with true positives against all those confirmed by histopathology ( $PPV=TP/(TP+FP)$ ); negative predictive value (NPV) is a percentage of patients with true negatives against all those confirmed not to have malignancy by histopathology ( $NPV=TN/(TN+FN)$ ); diagnostic accuracy (DA) is a percent of those that were correctly diagnosed by the FNA test ( $DA=(TP+TN)/total$ ).

Descriptive statistics were used to describe the data. For categorical variables, frequencies and percentages were reported. Differences between groups were analyzed using *Pearson's*  $\chi^2$  tests. For continuous variables, means and standard deviations ( $\pm$ SD) were presented. A *priori* two-tailed level of significance was set at the 0.05 level.

## RESULTS

A total of 282 patients were available for the study; however only 272 of them were included into the study. As the inclusion requirement was to keep only those who had both FNA and biopsy performed, 10 patients (3.5%) were excluded due to nonavailability of either FNA or biopsy. The overall mean age of the study cohort (N=272) was  $39\pm 13$  years with an age range from 5 to 85 years. The majority of the patients were females (N=236; 87%). The diagnostic results of FNA of the study cohort are detailed in Table 1. The FNA results indicated malignancy in 15 (5.5%), suspicious of malignancy in 34 (12.5%), and benign in 174 (64.0%). The FNA was inconclusive in 49 (18.0%) of the patients.

The biopsy results are found in Table 2. The final histopathological diagnosis was malignancy in 49 (18.0%) of the patients. Forty-seven of these had malignant epithelial tumor while two of the patients had lymphoma. Among the rest, 209 (76.8%) had either benign lesion or tumor, 11 (4.0%) had thyroiditis, and 3 (1.1%) of the patients had biopsies that were nonidentifiable.

Table 3 demonstrates that there was a good correlation between FNA and final histopathology results ( $P=0.003$ ). However, this statistical significance did not translate into clinical significance as indicated in Table 4. The results of thyroid FNA revealed that 6% (n=15) of the patients had malignancies while histopathological results showed that the proportion of subjects with malignancies was 18%

**Table 1: Diagnostic results according to fine-needle aspiration cytology (N=272)**

FNA result diagnosis	Frequency	Percent
Inconclusive	49	18
Benign	174	64
Suspicious	34	12
Malignant	15	6
Total	272	100

FNA: Fine-needle aspiration

**Table 2: Final histopathological test results according to biopsies (N=272)**

Biopsy test diagnosis	Frequency	Percent
Thyroiditis	11	4
Benign lesion	176	65
Benign tumor	33	12
Epithelial tumor	47	17
Lymphoma	2	1
Other (non-identifiable)	3	1
Total	272	100

**Table 3: Correlation between fine-needle aspiration and final histopathology (N=272)**

FNA results	Final histopathology results		Total
	No cancer	Cancer	
Inconclusive	43	6	49
Benign	145	29	174
Suspicious	28	6	34
Malignant	7	8	15
Total	223	49	272

Analysis was conducted using Pearson's Chi-squared ( $P=0.003$ ), FNA: Fine-needle aspiration

**Table 4: Final thyroid fine-needle aspiration results for the diagnosis of carcinoma in patients with multinodular goitre (N=272)**

Result	Frequency
True positives	8 cases
False positives	7 cases
True negatives	216 cases
False negatives	41 cases
Sensitivity	16%
Specificity	97%
Positive predictive value	53%
Negative predictive value	84%
Diagnostic accuracy	82%

( $n=49$ ). Out of the 15 cases identified to have malignancies by thyroid FNA, only 53% ( $n=8$ ) of the subjects were confirmed to have malignancy by biopsy. Overall, the results of the tests were poor, revealing a sensitivity of 16%, specificity of 97% and a diagnostic accuracy of 82%, with a positive predictive value of 53% and a negative predictive value of 84%.

## DISCUSSION

In this study we compared the usefulness of FNA to histology results in the management of MNG with prominent nodules. In our study the indication to perform FNA was clinical by biopsying the prominent nodules. Over the study period, there were a total of 272 patients who had both FNA and histology results. In our series we had 15 prominent nodules associated with cancer while Antonio Ríos *et al.* reported 42 MNG associated with cancer in prominent nodules out of 423 patients with MNG.<sup>[11]</sup> Tollin *et al.* in a study on 61 MNGs proposed FNA only in selected nodules, although unlike the results in our series, they obtained good results with this technique.<sup>[13]</sup>

In our study, the FNA sensitivity and specificity was 16% and 97%, respectively. This coincides with the results reported by Antonio Ríos *et al.*<sup>[11]</sup> Our series is one of the

few that analyze MNGs exclusively; others are Mandreker *et al.*<sup>[14]</sup> and Franklyn *et al.*<sup>[15]</sup> The positive predictive value was 53%, while the negative predictive value was 84%. These results are consistent with those reported by Antonio *et al.* who stated a positive predictive value of 32% and a negative predictive value of 92%.<sup>[11]</sup>

As a triage tool, the FNA biopsy can be used to distinguish thyroid nodules that might have a higher risk of malignancy (i.e., neoplasm), and would thus require surgical excision, from goitrous nodules or thyroiditis, which can be managed medically. It has been thought that the risk of cancer in a multinodular goiter is much less than that in a solitary nodule. The incidence of malignancy in multinodular goiter ranges from 1% to 10%.<sup>[4-9]</sup> However, recent literature indicates that if a nodule in a multinodular goitre has grown steadily, become distinctly dominant or changed in consistency, its risk of malignancy is the same as that of a solitary nodule.<sup>[14,16-18]</sup>

One of the most important issues with MNG is which nodule is to be aspirated. Some claim that it is not practical to puncture all palpable nodules when the clinical suspicion of malignancy is low and propose aspiration of one or two of the more prominent thyroid nodules of each thyroid lobe and those with suspected malignancy.<sup>[6]</sup> We again demonstrate that puncturing only the prominent nodule is more predictive for cancer rather than puncturing all palpable nodules; these results were also replicated by Hurley and colleagues<sup>[6]</sup> and Antonio *et al.*<sup>[11]</sup> studies. No other factors may favor diagnosis of malignancy by FNA like size or multifocality.

FNA has two major limitations: inadequate results and suspicious or indeterminate results. Inadequate or unsatisfactory results are obtained when lesions are cystic or vascular, yielding a dilute specimen and few follicular cells. In our case, the level of non-conclusive FNA was only 18%, possibly because an experienced radiologist carried out the process, from exploration, through puncture, guided by ultrasound. Suspicious or indeterminate FNA (10–30%), suggesting follicular or Hürthle proliferation, is the major limitation of this technique, as between 10% and 50% show malignancy, whereas a final diagnosis can only be established by histological criteria.<sup>[14,18-24]</sup>

This is one of the few studies involved with the use of US-guided FNA in MNG in an effort to improve the diagnostic yield. However, in spite of using this technique, our results were poor. In conclusion, FNA cannot be used as a differentiating tool between a malignant MNG from a benign one.

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