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Ultrasound Guided Fine-Needle Aspiration Biopsy of Thyroid Nodules: Does Radiologist Assistance Decrease the Rate of Unsatisfactory Biopsies?

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Abstract

Background. Ultrasound guided fine-needle aspiration biopsy (UG-FNAB) is the main presurgical, minimally invasive, accurate and generally safe procedure for the diagnosis of thyroid pathology. At present it is recommended as a valuable diagnostic tool for the management of thyroid nodules.

Objectives. This study aimed to evaluate if a radiologist's assistance in the UG-FNAB procedure decreased the rate of unsatisfactory biopsies.

Material and Methods. Over a 3-year period, 385 (100%) patients were enrolled to the study. All individuals had UG-FNAB performed for the first time due to multiple nodules of the thyroid gland. Patients with a family history of thyroid cancer, receiving radioactive iodine and other predispositions for thyroid malignancy were excluded. 184 (47.79%) patients were examined using UG-FNAB with a radiologist's assistance (group 1) and 201 (52.21%) without such support (group 2). All biopsies were performed by the same surgeon. All specimens obtained were examined by two cytologists experienced in thyroid pathology.

Results. The specimens from the UG-FNAB were more frequently diagnostic when obtained from procedures performed with a radiologist's assistance (77.8% vs. 56.8%, $p < 0.0001$). The cellularity of the specimens obtained from the UG-FNAB performed with a radiologist's assistance was higher than those obtained without such support (66.7% vs. 56.9%, $p < 0.0001$).

Conclusions. UG-FNAB of the thyroid nodules performed with a radiologist's assistance makes it possible to obtain more valuable specimens, which may improve diagnostic accuracy in the preoperative management of thyroid pathology (Adv Clin Exp Med 2016, 25, 1, 93–100).

Key words: thyroid nodules, UG-FNAB, radiologist assistance.

The incidence of thyroid lesions which are undetectable in physical examination, and only detectable using ultrasonographic imaging, accounts for up to 50%. Numerous thyroid nodules can be detected only by high resolution ultrasonography examination [1]. Most of these lesions are benign, however the detection of such tumors involves some concern about possible malignancy [2].

Ultrasonography examination is the main diagnostic tool for the detection and determination of thyroid nodule presence and for describing its clinical characteristics. It is also used for needle guidance during fine-needle aspiration biopsy (FNAB) [3–5].

Nowadays it is advised that the initial preoperative diagnostic evaluation of thyroid nodules

should be based on ultrasonography and ultrasound-guided fine-needle aspiration biopsy (UG-FNAB), which in the opinion of some authors, are the most accurate diagnostic procedures leading to correct presurgical diagnosis [6]. Others add, however, that both of these examinations need to be improved [7]. They have proposed an additional molecular evaluation of the material obtained from UG-FNAB, with regard that the thyroid cells gained in this procedure need to be not only in a very good state but also in a sufficient amount for such testing. Nevertheless, UG-FNAB is considered to be one of the most valuable and accurate diagnostic procedures used in almost every case of thyroid nodule [8, 9], to distinguish benign and malignant lesions [10].

UG-FNAB procedures may be performed by physicians of numerous specializations, e.g. endocrinologists, pathologists, cytologists, oncologists and surgeons, but the assistance of a radiologist is not clearly established. The diagnostic accuracy of UG-FNAB and the adequacy of obtained specimens differ from each other due to various factors. One of the most important is the state of the nodule's area which is undergoing biopsy [11]. Therefore, some authors emphasize the role of a radiologist in the UG-FNAB procedure [6]. They add that the assisting radiologist should have a basic knowledge of thyroid disease, be familiar with specimen processing and recognize the cytology and radiologic appearances of thyroid nodules. Some radiologists have proposed algorithms for the management of a solitary thyroid nodule, multinodular goiter and casually-discovered nodule [6]. In their opinion, this should increase the value of subsequently performed UG-FNAB. Very often this procedure is performed to make a decision for further treatment of thyroid nodules. It is also used in a follow-up of patients who were qualified for surgery due to thyroid nodules but who refused the treatment.

Numerous studies have been conducted to assess the ultrasonographic parameters of nodules which, when used during UG-FNAB, should increase its predictive value, but their results are not certain [12]. The authors indicate some ultrasonography-specific areas of thyroid nodules that should be biopsied. Some investigators have proposed ultrasonography feature-oriented criteria to characterize benign thyroid nodules that do not require UG-FNAB [13]. In their opinion, the combination of four ultrasonography (US) features (calcification, no increase in vascularity, well-defined margin and no lymphadenopathy) is highly predictive for a biopsied thyroid tumor to increase its results. A high number of fluid lesions in a multinodular goitre or high vascularization of

biopsied nodules decreases the diagnostic value of UG-FNAB, which sometimes leads to a false negative diagnosis. This then leads to detection of the malignancy only in post-operative histopathological examination. Yoon et al. constructed US nomograms of thyroid nodule areas which should be biopsied during UG-FNAB to increase the accuracy of cytological diagnosis. It may be useful in selecting patients who are at high risk for the malignancy [14]. Notwithstanding, the only ultrasonography area selected for the UG-FNAB procedure, proven to increase the diagnostic value of specimens in the detection of the malignancy, is microcalcification, which was presented in Iannuccilli's study [15]. Urgurlu et al. also showed that a biopsy of an area with microcalcifications increased the prognostic value of specimens and subsequently the detection of malignancy by up to 39 times [16].

As contradictory information is given regarding which of the ultrasonography features should be elaborated on during the UG-FNAB procedure to obtain the most accurate, cellular rich, colloid-poor or blood-ingredient-poor specimen in order to decrease the number of non-diagnostic results of UG-FNAB, it seems appropriate to consider radiologist support to increase the predictive value of this procedure [16].

To the best of our knowledge, no reports on the efficacy of radiologist assistance during UG-FNAB have been published to date. Therefore, we undertook this study to assess the potential benefits of a radiologist's assistance during UG-FNAB.

The aim of the study was to evaluate if a radiologist's assistance in the UG-FNAB procedure decreased the rate of unsatisfactory biopsies.

Material and Methods

The agreement for our study was prepared and approved by the Bioethics Committee of Wrocław Medical University (signature no.: KB-419/2015).

Three hundred eighty five patients (352 females 91.4% and 33 males 8.6%) with thyroid nodules, referred to the General and Endocrine Surgery Outpatients Clinic by the 1st Department and Clinic of General, Gastroenterological and Endocrine Surgery of Wrocław Medical University from 2012 to 2014, were enrolled into the study. One hundred eighty four patients had UG-FNAB performed by one surgeon with a radiologist's assistance (Group 1). Group 2 consisted of 201 patients in whom the UG-FNAB was performed by the same surgeon, however without a radiologist's assistance. The same equipment and ultrasonography set in both groups were used. A 10 MHz linear

ultrasonography probe set was used. The UG-FNAB was performed using 0.5 mm gauge needles and 10 cc syringes for each procedure. When accurate placement of the needle in the targeted area of the nodule was confirmed on the ultrasonography monitor screen by the assisting radiologist in the first group and in the second group by the surgeon performing the procedure, an ultrasound photograph was taken. The ultrasound characteristics of each nodule, such as echogenicity, internal fluid or solid structure, the presence of microcalcifications, irregular margins and intranodular vascularity, were analyzed to indicate the area of the nodule for a biopsy. A sample was taken and the specimen was prepared on glass slides, fixed in 95% ethanol and sent for cytology examination to cooperating cytologists. All specimens obtained in both groups were examined by the two idem cytologists experienced in thyroid pathology. Patients with a family history of thyroid cancer, who had received radioactive iodine or had any other predisposition to thyroid malignancy, such as a history of head or neck irradiation in childhood or the presence of the multiple endocrine neoplasia syndrome in first degree relatives, were excluded from this study.

Statistical Analysis

The statistical analysis was conducted with the use of the STATISTICA data analysis software system, v. 12 (StatSoft, Inc. 2014), based on the license owned by the Wrocław Medical University.

In this trial, the following statistical measures were used: arithmetical mean ($\bar{x}$), median and standard deviation (SD), and ranges of the determined parameters in the study groups.

The Shapiro-Wilk test was used to confirm the consistency of the analyzed samples' age distribution within the normal distribution. As the distribution of the analyzed samples was not significantly different from the normal distribution of statistically identical variance, to assess the eventual differences, the t -test was used. An intergroup frequency assessment was performed with the use of a χ^2 test. Yate's correction was applied when the expected frequency was less than 5 or the total count was less than 50. Any difference with a p -value < 0.05 was statistically significant, while a p -value from 0.05 to < 0.10 was considered on the borderline of statistical significance.

Results

Altogether 453 biopsies in 385 patients were performed, 212 (in 184 patients) in group 1 (with a radiologist's assistance) and 241 (in 201 patients)

in group 2 (without a radiologist's assistance). The patients' characteristics are presented in Table 1. The cytological diagnosis was significantly more frequently possible to be obtained in 77.8% of the UG-FNAB with a radiologist's assistance and in 56.8% of UG-FNAB without a radiologist's assistance ($p < 0.0001$). Specimen cellularity obtained during the UG-FNAB performed with a radiologist's assistance was of a more sufficient amount (Fig. 1., 1a., 1b.) compared to those obtained without a radiologist's assistance (Fig. 2., 2a., 2b., 66.7% vs. 56.9%, $p < 0.0001$). There was no statistical significance between gender, age, vascularization, type of biopsied nodule (dominant/not dominant) and the type/number of complications after the UG-FNAB procedures.

Discussion

Many articles, reports and reviews about the techniques of performing FNAB have been written so far. The first description of the use of needle aspiration biopsy as a diagnostic procedure for the evaluation of thyroid nodules was made by Martin and Ellis in 1930 [17]. They used an 18 gauge aspiration technique but in 1960 these investigators presented a new diagnostic tool and introduced fine-needle biopsy as more profitable and friendlier for patients. Some other authors have described a slightly different technique to obtain thyroid cells, which has been called fine-needle non-aspiration biopsy (FNNAB) [18]. In this technique we do not use a syringe or suction, which causes less blood contamination of the specimens. Instead of suction, the physician performing FNNAB moves the needle forward and backward inside the nodule for 5–10 s. Generally, fine-needle aspiration biopsy of the thyroid gland is a safe method and no serious complications like hemorrhage or hematoma have been observed [19]. The implantation of thyroid cell carcinoma in the needle track is extremely rare, poorly documented and is not taken under consideration as essential problem [20].

In our study, UG-FNAB procedures performed with a radiologist's assistance were as safe as those done without such support ($p = 0.37367$). In the first group of patients (with radiologist presence) we did not observe hematoma, but in 4 (1.9%) patients we observed bruising. In 2 (0.83%) patients from the second group (without radiologist's assistance) we observed postaspiration hematoma. Those patients did not require surgical intervention. We repeated the procedure after 6 months because the specimens contained fresh blood with a few scant thyroid follicular cells. The second,

Table 1. Characteristics of patients with UG-FNAB performed with (Group 1) and without (Group 2) radiologist's assistance. Descriptive data are presented as numbers (n) and percent (%) or the mean + standard deviation (+ SD)

	Overall	Group 1	Group 2	p
No. of patients	385	184 (47.8%)	201 (52.2%)	p = 0.7741
No. of biopsies	453	212 (46.8%)	241 (53.2%)	
Gender:				p = 0.79059
male	33 (8.6%)	17 (9.2%)	16 (8.0%)	
female	352 (91.4%)	167 (90.8%)	185 (92.0%)	
Age	60.9 ± 14.1	61.3 ± 14.1	60.6 ± 14.1	p = 0.629062
Age:				p = 0.24035
< 45 years	47 (12.2%)	24 (11.9%)	23 (12.5)	
≥ 45 years	182 (47.2%)	103 (51.2%)	79 (42.9%)	
≥ 65 years	156 (40.5%)	74 (36.8%)	82 (44.6%)	
Biopsy:				p < 0.0001*
diagnostic	302 (66.7%)	165 (77.8%)	137 (56.8%)	
non-diagnostic	151 (33.3%)	47 (22.2%)	104 (43.2%)	
Cellularity:				p < 0.0001*
none	151 (33.3%)	47 (22.2%)	104 (43.1%)	
few	269 (59.4%)	138 (65.1%)	131 (54.4%)	
patches	33 (7.3%)	27 (12.7%)	6 (2.5%)	
Vascularization:				p = 0.10391
peripheral	277 (61.1%)	127 (59.9%)	150 (62.2%)	
central	105 (23.2%)	44 (20.8%)	61 (25.3%)	
mixed	71 (15.7%)	41 (19.3%)	30 (12.5%)	
Nodule:				p = 0.05600
dominant in MNG	320 (70.6%)	159 (75.0%)	161 (66.8%)	
MNG	133 (29.4%)	53 (25.0%)	80 (33.2%)	
Complications:				p = 0.37367
none	441 (97.4%)	208 (98.1%)	233 (96.7%)	
bruising	10 (2.2%)	4 (1.9%)	6 (2.5%)	
hematoma	2 (0.4%)	0 (0.0%)	2 (0.83%)	

* – statistically significant.

repeated UG-FNAB procedures were not included in our analysis.

To our knowledge, there are no recommendations on the team performing UG-FNAB: how many physicians and with what specialization. The recommendations of numerous authors focus on the quality of the sample. Some authors suggest taking at least 6 aspirations in order to increase the quality of thyroid samples [21]. They also recommend avoiding a central puncture of a bigger nodule because of the high probability of fluid or degenerated tissue presence. Other investigators also agree about the great importance of the biopsied area which should be carefully selected for UG-FNAB. To emphasize the role of US in this procedure, they concluded that UG-FNAB provides a better representative sample and has a higher diagnostic value than free-hand FNAB in the evaluation of thyroid lesions [22]. Therefore, in our

opinion, the assistance of a radiologist may be helpful while performing UG-FNAB, to localize the most accurate area of the thyroid nodule to obtain diagnostic samples rich in thyroid cells.

Papini et al. say that ultrasonography guidance in the hands of an experienced radiologist makes possible the correct and safe sampling of even small and deeply-located thyroid nodules [23]. What is more, some cases may benefit from ultrasonography-guided minimally-invasive procedures as an alternative to surgery. The cost-effectiveness and relatively high safety of the fine-needle aspiration biopsy of the thyroid nodule has made this procedure the standard, initial and main test in the evaluation of this pathology [24].

Inadequate specimens are treated as non-diagnostic or unsatisfactory and account for 2–20% of all specimens obtained during UG-FNAB procedures [8, 25]. The authors do not say if there

Fig. 1a. UG-FNAB in a 54-year-old woman. Procedure performed with radiologist's assistance. Transverse sonogram of the right lobe of the thyroid demonstrates a solid nodule with a hypoechoic, colloid foci

Fig. 1b. UG-FNAB in a 54-year-old woman. Procedure performed with radiologist's assistance. Photomicrograph (original magnification, $\times 400$; hematoxylin-eosin stain) shows four well-preserved clusters of monomorphic thyrocytes in colloid background and scant of blood

is any correlation between inadequate specimens and the type of specialist performing it or the number of physicians doing this procedure. In our study we observed 22.2% of non-diagnostic specimens in the group where UG-FNAB procedures were performed with a radiologist's assistance (group 1) and approximately two times more (44.6%) in the group without a radiologist's assistance (group 2). This difference was statistically significant ($p < 0.0001$).

Some authors have tried to explain the relatively high amount of non-diagnostic results. They have noticed some especially important factors that influence the non-diagnostic number of FNAB results. They pointed to the skill of the physician performing the procedure, thyroid nodule vascularity, criteria for qualification of the specimen as suitable for cytologic examination and the

fluid component of the nodule [26]. In our study, the types of vascularization in both groups did not differ from each other and did not have any influence on the quality of specimens ($p = 0.10391$).

It is estimated that the diagnostic smear should include at least 6 clusters of well-preserved cells with each group containing at least 10–15 cells. In our study the assistance of a radiologist during the UG-FNAB procedures (group 1) significantly increased the cellularity in this group (66.7% vs. 56.9%, $p < 0.0001$). The percentage of specimens which did not contain any thyroid cells was two times higher in the group of patients in whom UG-FNAB procedures were performed without a radiologist's assistance. It is worth noticing that non-diagnostic smears may be a significant problem in the

aspect of thyroid carcinoma prevalence, as a malignancy rate up to 7% was reported in patients with initial unsatisfactory or non-diagnostic smears [27].

In 2006, the American Association of Clinical Endocrinologist (AACE) and *Associazione Medici Endocrinologi (AME)* published the guidelines for performing FNAB to improve the adequacy and accuracy of cytologic specimens [8]. They suggest that FNAB should be performed by a physician trained in both thyroid gland examination and biopsy. The material should be obtained from various parts of the nodule and especially peripheral areas of low vascularity should be biopsied. The histopathologist who interprets the specimens should be experienced in thyroid gland cytology. A number of studies have suggested some following steps to reduce the number of non-diagnostic results of UG-FNAB [8, 19, 21]. For example, they recommend

Fig. 2a. UG-FNAB in a 55-year-old woman. Procedure performed without radiologist's assistance. Transverse sonogram of the left lobe of the thyroid demonstrates a partially cystic tumor with solid internal projections

Fig. 2b. UG-FNAB in a 55-year-old woman. Procedure performed without radiologist's assistance. Photomicrograph (original magnification, $\times 100$; hematoxylin-eosin stain) shows one small cluster of thyrocytes and abundance of blood

rebiopsy if the cytology is non-diagnostic and have 2–4 aspirates going from one nodule.

UG-FNAB cannot be treated as a screening test for all thyroid nodules in the population, but should be used as an initial diagnostic tool for all patients with palpable nodule or with suspicion of malignancy. Several ultrasonographic characteristics should be taken into consideration while choosing the area of the nodule for biopsy, to receive a higher diagnostic value of UG-FNAB, including: microcalcifications, hypoechogenicity, irregular margins and low intranodule vascularity. It is confirmed that ultrasonography used as guidance for FNAB significantly increases the sensitivity, positive predictive value and negative predictive value [15], however, no information regarding if a radiologist's assistance in the UG-FNAB procedure increases the value of the examination was given. In our opinion, this information is especially

interesting considering the fact that UG-FNAB results are operator-dependent [8, 26].

As sufficient experience is recommended to carry out the procedure, some authors suggest that at least 1 to 5 aspirations per month should be done by a UG-FNAB-performing, “dedicated”, physician [29]. However, FNAB does not have to be confined only to large medical centers. Good results of this procedure might also be obtained in community and rural hospitals, if the number of aspirators and cytopathologists in one center is not large [30].

The other argument for the presence of the radiologist during the UG-FNAB procedure may be safety. Although FNAB is a minimally invasive procedure, some complications may occur, fortunate-

ly rarely. Bleeding or hematoma are almost always self-limiting, when gentle but firm pressure is applied to the aspiration site. During our study, hematoma developed in only two patients, and both were in the group where the UG-FNAB procedure was performed without a radiologist's assistance. Those hematomas did not lead to tracheal compression. Those unfortunate incidences happened in the very beginning of our study, pointing out once again the importance of the UG-FNAB team's experience. We cannot be sure, however, if the presence of a radiologist would have prevented those complications.

It appears that radiologists can point to some areas for FNAB which in their opinion are more suitable for obtaining diagnostic material and in some cases are more suspected for malignancy. In our study, the radiologist's assistance during UG-FNAB performed by a surgeon led to the identification of unique and ultrasonography-specific

areas of the thyroid nodules which caused a better quality of the specimens for further cytologic examination.

UG-FNAB of thyroid nodules performed with a radiologist's assistance makes it possible to

obtain more valuable specimens, which may improve the diagnostic accuracy in the preoperative management of thyroid pathology. UG-FNAB performed with a radiologist's assistance may increase the safety of this procedure.

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