CLINICAL STUDY

The usefulness of sonographic features in selection of thyroid nodules for biopsy in relation to the nodule's size

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Abstract

Objective: To evaluate the efficacy of selected ultrasound (US) features of thyroid focal lesions useful for establishing indications for fine-needle aspiration biopsy (FNAB) with regard to the lesion's size.

Methods: US imaging features of 1141 thyroid nodules (shape, echogenicity, pattern of blood flow, presence of microcalcifications and the presence of other nodules in the thyroid) and their palpability were compared with the post-operative histopathological outcomes. The efficacy of the selected sets of the features was assessed for small nodules (SN) ≤ 15 mm and large nodules (LN) > 15 mm, as well as separately for nodules ≤ 10 mm.

Results: Logistic regression analysis showed that in SN hypoechogenicity (odds ratios, OR: 3.18), microcalcifications (OR: 19.12), solitary occurrence (OR: 3.29) and height-to-width ratio ≥ 1 (OR: 8.57) were independent risk factors for malignancy. The optimal set of small lesions that should be biopsied includes all lesions presenting at least one of the above-mentioned features (sensitivity 98%, specificity 44%). In the LN group, the selection criteria based on the shape of lesions and hypoechogenicity were less sensitive than in the SN group, but they allowed further reduction in the number of performed FNABs. Large nodules primarily selected for FNAB should be hypoechoic, more tall than wide or contain microcalcifications (sensitivity 84%, specificity 72%).

Conclusions: The obtained results provide rationale for using features from the US examination in selecting both small and large nodules for FNAB. In the case of LN, the usefulness of sonographic features is less sensitive, but more specific than in the case of SN.

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Introduction

In recent years, the spread of thyroidological diagnostics using high-definition ultrasound imaging (US) has resulted in a growing number of patients with revealed small focal lesions in the thyroid. Such lesions are often visualised in examined patients ranging in frequency from 20% to – according to some data – more than 60% (1, 2). Our data are concordant with these observations. At our department, the percentage of patients with thyroid lesions not larger than 15 mm in maximal diameter reaches 67% of all diagnosed with US. In $\sim 30\%$ of examined patients, only nodules not larger than 10 mm are revealed (3).

The clinical significance of small thyroid lesions has not been clarified. At first it was assumed that such lesions could be left cytologically undiagnosed in patients without history positive for the high risk of thyroid carcinoma (as with previous neck irradiation or others; 2, 4). Some recent papers have brought

convincing data on high percentage of carcinomas (some of them with extrathyroidal invasion) in small lesions subjected to fine-needle aspiration biopsy (FNAB; 5–11).

The precise indications for FNAB of small thyroid lesions are still being investigated. The main criteria considered include sonographic features like the size, shape and echogenicity of lesions, the vascular pattern in Doppler imaging, the presence of microcalcifications and appearance of lesion's borders (12–16). There is some discrepancy in available data as it comes to the optimal selection of these criteria, as well as the influence of the proposed criteria on the number of biopsies to be performed.

The problem of proper selection of nodules for FNAB is particularly relevant in countries with high number of patients with multinodular goitre, i.e. in areas of iodine deficiency or areas of recently corrected deficiency like Poland (3, 17, 18). At our department, any focal lesions in the thyroid gland were found in 77% of

the patients subjected to US examination, in the majority of those patients (78%), multiple nodules were revealed (3). In such settings often, even selection between several larger lesions must be made.

The aim of our paper is to evaluate the efficacy of selected US features of thyroid focal lesions useful for establishing indications for FNAB with regard to the lesion's size.

Materials and methods

The study included 1141 nodules diagnosed at our centre between years 2000 and 2005 in 672 patients (mean age $\pm$ s.d.: 49.5 ± 11.4 years) for which there were available US features, data on palpability and post-operative histopathological outcomes. Patients were referred to thyroid surgeons for large multinodular goitre (regardless of benign FNAB – in majority of cases) or because of suspected or malignant lesion diagnosed cytologically. The study included not only biopsied nodules, but also all accompanying lesions described in US examination with known histopathological diagnosis. All the nodules were divided into malignant tumours and benign lesions on the basis of histopathological outcome. No patient included in this series had a history of external or ionising radiation or previous diagnosis of thyroid malignancy.

All the US examinations were performed by the team of three physicians with at least five years experience, with the same equipment, namely Elegra Advanced (Siemens Medical Systems Inc., Issaquah, WA, USA) with a 7.5 MHz linear transducer and power Doppler capability. Its state-of-the-art technology allows visualisation of tiny lesions within the thyroid (diameter ≥ 1 mm). The following lesion features obtained through the US examination were analysed: shape (categorised by the ratio of anterior-posterior dimension (height) to the transverse dimension (width) of lesion, with values of the ratio ≥ 1 in one category and < 1 in the other); echogenicity (solid hypoechoic versus another appearance); pattern of blood flow in power Doppler imaging (intranodular vascular pattern versus other patterns); the presence of intranodular microcalcifications; and the presence of other lesions in the thyroid (Figs 1–4). Because of a retrospective design of the study in the case of two evaluated features – the pattern of blood flow and the shape of lesion – the analysis included only 316 and 210 lesions respectively. The assessment of pattern of blood flow was not performed from the beginning of the analysed period, and in some cases only single diameter of lesion was examined and it was not possible to calculate the shape index. The lesions margins were not described in a uniform fashion and could not be included in the analysis. Additionally, palpability of examined lesions was also considered.

Figure 1 Hypoechoic nodule.

The efficacy of the above-mentioned features in prediction of malignancy was evaluated separately for small nodules (SNs) – lesions with the maximal diameter not longer than 15 mm and large nodules (LNs) – lesions with the maximal diameter longer than 15 mm. Additionally, in SN group, the lesions with diameters not exceeding 10 mm and lesions with diameters 11–15 mm were distinguished. Moreover, the impact of various criteria based on a combination of the above-mentioned features on the potential efficacy of cytological examination in diagnosing thyroid malignancy and optimisation of number of performed FNAB was evaluated.

The comparison of frequency distributions was performed by χ^2 test. Multivariate (logistic regression analysis) odds ratios (OR), with 95% confidence intervals, were calculated to assess the relevance of the US features and lesion palpability to predict histological outcome. The diagnostic value of selected criteria was also assessed in terms of sensitivity, specificity, positive predictive value and negative predictive value. For the evaluation of the sets of US features, only lesions with data available on all analysed features were included. The value of 0.05 was assumed as the level of significance.

Figure 2 Microcalcifications in thyroid nodule.

Figure 3 Nodule with intranodular vascular pattern.

Results

The analysed lesions according to histopathological examination were non-neoplastic in 881 cases, follicular adenomas in 164 cases and malignant in 96 cases (72 papillary cancers, 11 medullary cancers, five oxyphilic cancers, two follicular cancers, four anaplastic cancers and two metastases). Among 96 cancers, there were 33 nodules with diameters below 10 mm, of which five were found in patients operated because of multinodular goitre with no malignancy suspected. Between analysed lesions, there were 462 (40.5%) LNs and 679 (59.5%) SNs. The mean maximal diameter of nodules in LN group was 32.97 ± 14.31 mm (mean $\pm$ s.d.), median was 28 mm, minimal size 15 mm and maximal size 80 mm. Mean maximal diameter of nodules in SN group was 11.25 ± 2.77 mm (mean $\pm$ s.d.), median 10 mm, minimal size 4 mm and maximal size 15 mm. Size distribution of small lesions was as follows: maximal diameter of 351 lesions did not exceed 10 mm (mean maximal diameter was 8.93 ± 1.24 mm, median 9 mm, minimal size 4 mm and maximal size 10 mm) and there were 328 lesions with maximal diameter in range 11–15 mm (mean maximal diameter was 13.93 ± 1.06 mm, median 14 mm, minimal size 11 mm and maximal size 15 mm). Among lesions not exceeding 10 mm, there were only several nodules with maximal diameter below 5 mm, none of them was malignant.

It was found that the malignant lesions when compared with the benign ones were more frequently hypoechoic (61.5 vs 34.2%; $P < 0.0001$), solitary (35.4 vs 21.1%; $P < 0.005$) and contained small calcifications (26.0 vs 3.1%; $P < 0.0001$). The ratio of height to width ≥ 1 was found among the malignant lesions more frequently than in the case of the benign lesions (45.0 vs 10.0%, $P < 0.0001$). The above-mentioned features (apart from the solitary occurrence of lesions) differentiated the malignant and benign nodules also within separately analysed groups LN and SN (hypoechoicity – $P < 0.0001$, $P < 0.0005$ respectively; microcalcifications – $P < 0.0001$ in both group; height-to-width

ratio ≥ 1 – $P < 0.005$, $P < 0.0001$ respectively; Table 1). The solitary occurrence of lesions differed significantly between the malignant and benign lesions only in the group of SN ($P < 0.001$). The intranodular vascular pattern was observed significantly more frequently in the large malignant nodules than in small ones (75.0 vs 33.3%, $P < 0.05$), but no significant difference was observed between the malignant and benign lesions, irrespective of their size.

The detailed analysis of SN group divided into lesions with diameters ≤ 10 mm and 11–15 mm showed that features like hypoechoicity, solitary occurrence and height-to-width ratio ≥ 1 tended to be more sensitive in smaller nodules; on the contrary, the presence of microcalcifications was less sensitive (Table 2). Considering other parameters, neither palpability nor the size above 10 mm was significantly associated with the histological diagnosis. It was found in the SN group that the limitation of indications for FNAB to palpable lesions only or to the lesions larger than 10 mm, according to some already proposed algorithms, would result in 63.5% of small (< 15 mm) cancers not being examined in each case. Even if all lesions satisfying at least one of those two criteria had been examined, large percentage of small cancers – 48.1%, including many invasive cases, would not have been biopsied.

The most sensitive single feature allowing selection of lesions for FNAB in both groups of nodules (SN and LN) was hypoechoicity (Table 3). The selection of hypoechoic lesions only would have resulted in biopsying of 69.2% of cancers in SN group and 52.2% of cancers in LN. However, the specificity of that criterion was relatively low in SN, significantly lower than in the group of LN (57.9 vs 77.8%, $P < 0.0001$). On the other hand, the most specific criterion in both groups of lesions was the presence of microcalcifications ($> 95\%$), but sensitivity of that feature was very low (29.5% in LN and 23.1% in SN). It was also found that the ratio describing the shape of lesion showed higher sensitivity of revealing cancers in the SN group than in the LN group (55.1 vs 29.0%, $P < 0.02$), but lower

Figure 4 Nodule with anterior-posterior to the transverse dimension ≥ 1 .

Table 1 Frequency analysis of sonographic features of thyroid lesions and their palpability with respect to size of nodules in groups of benign and malignant lesions.

Features of lesions	Histopathological outcome					
	Benign lesions			Malignant lesions		
	All nodules (n=1045)	LN (n=418)	SN (n=627)	All nodules (n=96)	LN (n=44)	SN (n=52)
Hypoechogenicity	357 34.2%	93 22.2%	264 42.1%	59 61.5%	23 52.3%	36 69.2%
Solitary occurrence	221 21.1%	112 26.8%	109 17.4%	34 35.4%	15 34.1%	19 36.5%
Presence of microcalcifications	32 3.1%	18 4.3%	14 2.2%	25 26.0%	13 29.5%	12 23.1%
Intranodular vascular pattern ^a	143/289 49.5%	84/142 59.2%	59/147 40.1%	14/27 51.9%	9/12 75.0%	5/15 33.3%
Height/width $\geq 1^b$	13/130 10.0%	4/76 5.3%	9/54 16.7%	36/80 45.0%	9/31 29.0%	27/49 55.1%
Palpable	591 56.6%	339 81.1%	252 40.2%	54 56.3%	35 79.5%	19 36.5%

^aAnalysis included 316 nodules.^bAnalysis included 210 nodules.

specificity (83.3 vs 94.7%, $P < 0.05$). The solitary occurrence of lesion was the feature more specific in SN group than in LN group (82.6 vs 73.2%, $P < 0.001$). There were no significant differences in the sensitivity or specificity of the other examined features between the SN and LN groups.

The results of multivariate logistic regression analysis of the features suggestive of malignant thyroid nodules are shown in Table 4. The diagnostic efficacy of the various feature combinations in selection of the thyroid lesions for FNAB is shown in Table 5. It was found in the SN group that the limitation of FNAB to the lesions, which showed at least one of the features significantly differentiating malignant and benign nodules, would

have led to aspiration of 98.0% of lesions with cancer while lowering the number of examinations by 24.3%. In the same group (SN), the sensitivity over 90% was also found for the selection including all hypoechoic lesions and those with height-to-width ratio ≥ 1 . With such selection criteria, specificity would be 46.3% and the number of FNABs would be lowered by 28.2%. In the group of nodules with diameters not exceeding 10 mm, such selection criteria (hypoechogenicity and height-to-width ratio ≥ 1) would preserve 90% sensitivity while specificity would be as low as 34.6%, and the number of FNABs would be lowered by 22.1%.

On the other hand, if the selection criteria included all lesions that were solitary or with microcalcifications or with shape ratio ≥ 1 , with hypoechogenicity taken away, the number of performed biopsies would fall by 49.5% (49.2 in nodules ≤ 10 mm), specificity would rise to 77.8% (76.9 in nodules ≤ 10 mm) with the sensitivity at the level of 81.6% (81.8% in nodules ≤ 10 mm). However, hypoechogenicity was the only feature (among analysed ones), which significantly differed between invasive cancers (with extracapsular growth or nodal involvement) and those limited to the thyroid gland. The invasive malignant lesions were hypoechoic in US examination more frequently than other cancers – 75.8 vs 47.6%; $P < 0.05$. These differences were even more noticeable in the SN group; all small invasive cancers were hypoechoic. In the whole analysed material, extrathyroidal growth was observed in 34.4% of the malignant lesions (48.6% in the LN group and 24.5% in the SN group, $P < 0.05$) and in 28.6% of the cancers not exceeding 10 mm.

In the LN group, the selection criteria based on the shape of lesions and hypoechogenicity were less sensitive than in the SN group, but they allowed further reduction in the number of performed FNABs. The most sensitive criteria in the group LN appeared to be those

Table 2 The frequency of selected sonographic features and palpability of small benign and malignant thyroid lesions with respect to their size (above 10 mm in diameter or not exceeding 10 mm).

Features of lesions	Histopathological outcome			
	Benign lesions		Malignant lesions	
	11–15 mm (n=309)	≤ 10 mm (n=318)	11–15 mm (n=19)	≤ 10 mm (n=33)
Hypoechogenicity	117 37.9%	147 46.2%	12 63.2%	24 72.7%
Solitary occurrence	58 18.8%	51 16.0%	6 31.6%	13 39.4%
Presence of microcalcifications	9 2.9%	5 1.6%	7 36.8%	5 15.2%
Intranodular vascular pattern ^a	32/83 38.6%	27/64 42.2%	3/6 50.0%	2/9 22.2%
Height/width $\geq 1^b$	5/28 17.9%	4/26 15.4%	7/16 43.8%	20/33 60.6%
Palpable	163 52.8%	89 28.0%	11 57.9%	8 24.2%

^aAnalysis included 125 nodules.^bAnalysis included 103 nodules.

including echogenicity, the shape of lesion and the presence of calcifications. The examination of all hypoechoic lesions or those containing calcifications or with height to width ratio ≥ 1 would lead to a drop in numbers of FNABs by 56.1% while keeping high sensitivity and specificity (83.9 and 72.4% respectively).

Discussion

Our analysis of the usefulness of the US examination and palpation in selection of thyroid lesions for FNAB was limited to the cases verified by post-operative histopathological examination to assure higher reliability of the results. It should be kept in mind that in cases of FNAB outcomes verified against clinical follow-up only, some false negative results of FNAB may be undiscovered. On the other hand, our data were not significantly biased by possible exclusion of clinically benign nodules in that way as the predominating indication for surgical treatment was multinodular goitre. Clinically benign lesions accompanying suspected nodules were also analysed.

That analysis showed the hypoechoogenicity, the presence of microcalcifications and the shape with height-to-width ratio ≥ 1 to be independent features suggesting malignant lesions, irrespective of their size. The significance of hypoechoogenicity was repeatedly reported already (6, 8, 10, 19–27). Similarly, many authors confirmed the role of microcalcifications in the selection of nodules for FNAB (5, 6, 10, 11, 20–25, 27–29). The shape of lesions has not been much analysed so far. Some authors evaluated the ratio of the long to short axis of a lesion (15, 30), others the

anterior–posterior dimension-to-width ratio (6, 20, 22). These reports showed that malignant nodules are more spherical, with the height-to-width ratio ≥ 1 . The shape indicators can possibly reflect the differences in the stiffness between thyroid cancers and benign thyroid lesions (31).

In our material, the solitary occurrence was also indicative of the necessity of FNAB in the case of small lesions. Others questioned the usefulness of this feature (10, 11), but it has been confirmed in some reports (15, 25) that malignant nodules turn out to be more frequently solitary than benign ones.

Like some other authors, we have found that the most sensitive feature of malignancy is hypoechoogenicity, both for small and large lesions. Interestingly, in our material, all invasive microcarcinomas (with the signs of extrathyroidal growth or with spread to lymph nodes) were hypoechoic in the US examination. The role of hypoechoogenicity, in revealing aggressive variants of microcarcinomas, was also indicated by Barbaro *et al.* 2005 (19). Unfortunately, the specificity of this feature is low, especially in SN. The most specific single feature is the presence of microcalcifications in the lesion (6, 10, 11, 20, 24, 27). It increases tenfold the risk of cancer. However, in nodules not exceeding 10 mm, the sensitivity of microcalcifications tended to be lower than in larger lesions. Similar results were obtained by Moon *et al.* 2008 (20). Less but still significantly predictive is the shape index. Our analysis shows that the features describing the shape of lesion are useful mainly in the diagnostics of SNs. Similar results with respect to the ratio of long to short axis of a lesion reported Berker *et al.* 2008 (30). The shape of larger lesions is a less sensitive feature probably because

Table 3 Indices of efficiency of features useful in the selection of nodules for fine-needle aspiration biopsy (FNAB) with respect to the size of lesions.

Features of lesions	Index (%)	Size of lesions		
		LN	All SN	Only nodules ≤ 10 mm
Hypoechoogenicity	Sensitivity	52.3	69.2	72.7
	Specificity	77.8	57.9	53.8
	PPV	19.8	12.0	14.0
	NPV	93.9	95.8	95.0
	Percentage of FNAB performed	25.1	44.2	48.7
Presence of microcalcifications	Sensitivity	29.5	23.1	15.2
	Specificity	95.7	97.8	98.4
	PPV	41.9	46.2	50.0
	NPV	92.8	93.9	91.8
	Percentage of FNAB performed	6.7	3.8	2.8
Height/width ≥ 1	Sensitivity	29.0	55.1	60.6
	Specificity	94.7	83.3	84.6
	PPV	69.2	75.0	83.3
	NPV	76.6	67.2	62.9
	Percentage of FNAB performed	12.1	35.0	40.7
Solitary occurrence	Sensitivity	34.1	36.5	39.4
	Specificity	73.2	82.6	84.0
	PPV	11.8	14.8	20.3
	NPV	91.3	94.0	93.4
	Percentage of FNAB performed	27.5	18.9	27.6

Table 4 The results of multivariate logistic regression analysis of the features suggestive of malignant thyroid nodules. The models were analysed separately for large (LN) and small (SN) lesions. Only features statistically significant in univariate analysis were included in the models of logistic regression.

Size of lesions	Feature of lesions	Odds ratio	95% CI	P value	β -Coefficient and S.E.M.
LN	Hypoechogenicity	4.02	1.29–12.55	<0.02	1.39 $\pm$ 0.57
	Presence of microcalcifications	13.10	3.49–68.76	<0.005	2.57 $\pm$ 0.83
	Height/width ≥ 1	8.55	1.82–40.06	<0.01	2.14 $\pm$ 0.78
SN	Hypoechogenicity	3.18	1.02–9.89	<0.05	1.15 $\pm$ 0.57
	Presence of microcalcifications	19.12	5.27–69.35	<0.005	3.28 $\pm$ 1.12
	Height/width ≥ 1	8.57	2.77–26.53	<0.0005	2.15 $\pm$ 0.57
	Solitary occurrence	3.29	1.69–6.39	<0.05	1.27 $\pm$ 0.66

CI, confidence interval.

such lesions are more frequently partially cystic, and as such are more spherical even if benign.

Our data did not show usefulness of the assessment of blood flow pattern for the selection of small lesions for FNAB. With respect to this feature, the published opinions are contradictory with some reporting that Doppler US is helpful (11, 20, 21, 23, 26, 32), and others reporting that Doppler US did not satisfactorily improve diagnostic accuracy (10, 28, 33, 34). Even though the logistic analysis of regression allows classification of intranodular vascular pattern as an independent feature suggesting malignancy, the OR is several times lower than for other features (21).

Earlier opinions expressed in some reports (11, 22, 24, 27) have been substantiated as we did not find any single criterion of selecting lesions for FNAB to be satisfactory. The analysis of usefulness of feature combinations showed that in the group of small lesions, high sensitivity (>90%) could be achieved through selecting for FNAB hypoechoic nodules or those with the height-to-width ratio ≥ 1 . Such selection could lower the number of performed biopsies by 28%.

The addition of all solitary nodules and all nodules with microcalcifications would not increase the number of examinations significantly, but would allow for biopsying 98% of malignant lesions. Similar results were reported by other authors who used the selection criteria as the shape of lesions (evaluated as in our study) jointly with other features from the US examination. Cappelli *et al.* 2006 showed that 99% sensitivity can be achieved by aspiration of lesions more tall than wide and possessing at least two of the following features: hypoechogenicity, blurred margins and calcifications (22). The authors claimed that by applying such criteria, the number of performed FNABs could be lowered by 28%. However, in endemic or post-endemic region, with high number of patients with multinodular goitre more rigorous criteria for selection of small lesions for FNAB are needed, which would allow for more significant restriction of the number of performed biopsies (3). Kim *et al.* 2002 reported that reduction number of performed FNABs by 47%, with 94% sensitivity and 66% specificity, could be achieved by selecting lesions fulfilling the above-mentioned shape

Table 5 Efficiency of sets of examined features in the selection of nodules for fine-needle aspiration biopsy (FNAB) with respect to the size of lesions.

Criteria of selection for FNAB	Percentage of FNAB performed			Sensitivity (%)			Specificity (%)		
	LN	All SN	Only nodules ≤ 10 mm	LN	All SN	Only nodules ≤ 10 mm	LN	All SN	Only nodules ≤ 10 mm
Hypoechoic or solitary	43.9	66.0	69.5	58.1	85.7	84.8	61.8	51.8	42.3
Hypoechoic or microcalcifications	38.3	61.1	66.1	71.0	81.6	81.8	75.0	57.4	46.2
Hypoechoic or height/width ≥ 1	38.3	71.8	77.9	67.7	91.8	90.9	73.7	46.3	34.6
Solitary or microcalcifications	32.7	31.1	30.5	54.8	53.1	48.5	76.3	88.9	88.5
Solitary or height/width ≥ 1	31.7	41.7	42.4	51.6	59.2	63.6	76.3	74.1	76.9
Microcalcifications or height/width ≥ 1	18.7	40.8	44.1	51.6	75.5	78.8	94.7	90.7	84.6
Hypoechoic or solitary or microcalcifications	50.5	67.0	71.2	74.2	89.8	87.9	59.2	53.7	42.3
Solitary or microcalcifications or height/width ≥ 1	39.3	50.5	50.8	67.7	81.6	81.8	72.4	77.8	76.9
Hypoechoic or microcalcifications or height/width ≥ 1	43.9	72.8	77.9	83.9	93.9	93.9	72.4	46.3	34.6
Hypoechoic or solitary or height/width ≥ 1	48.6	74.8	77.9	67.7	93.9	90.9	59.2	42.6	30.8
Solitary or hypoechoic or microcalcifications or height/width ≥ 1	55.1	75.7	79.6	83.9	98.0	97.0	56.6	44.4	30.8

criterion or those with microcalcifications, irregular or microlobulated margins or marked hypoechogenicity (relative to the strap muscles in the neck) (6). Those data come from areas of high-iodine supply and low incidence of multinodular goitre. In our epidemiologic situation, similar reduction in the number of performed FNABs is possible on the condition of exclusion of hypoechogenicity from the set of selection criteria. Examination of lesions with height-to-width ratio ≥ 1 only, or those with microcalcification or solitary ones, would allow limitation of the number of biopsies by 50% while keeping sensitivity above 80%. However, it would increase the risk of misdiagnosing small invasive thyroid cancers. It is possible that application of 'marked hypoechogenicity' feature would allow avoidance of that risk. In the present study, as the data on the type of margin were not available in many cases, margins of lesions were not analysed. However, it should be stressed that there are significant differences in the definition of suspected appearance of borders. Some researchers, such as Nam-Gong *et al.* 2004, suggested that ill-defined nodules were important for predicting malignancies, while others (Kim *et al.* 2002, Cappelli *et al.* 2006, 2007 and Kang *et al.* 2004; 5, 6, 10, 21, 22) suggested that irregular margins were important. Moreover, some authors reported that the presence of blurred margins was not significantly linked to malignancy of lesions (8, 25, 28), or that well-defined margins were a common sonographic feature in papillary carcinomas (23).

Most diagnostic algorithms suggest performing FNAB for all lesions with diameters over 15 mm, even in the absence of any features suggesting the increased risk of cancer (12–14). But in the case of large multinodular goitre, it is necessary to select large lesions for biopsy as well. The present study showed that in the case of large nodules, the usefulness of sonographic features in selecting lesions for FNAB was less satisfactory than in the case of SN. The sensitivity of selection of nearly 84% could be achieved by biopsying all hypoechoic or containing microcalcifications lesions or with the shape index ≥ 1 , which would lower the number of FNAB by more than 55%.

It is also worth mentioning that in the majority of the reports, the influence of nodule's size on the optimal set of features for selecting lesions for FNAB was not investigated. Only Cappelli *et al.* (2006) observed that the associations of US features with malignancy were similar in groups of large and small lesions (22). On the other hand, Lyshchik *et al.* 2005 and Berker *et al.* 2008 found that the usefulness of sonographic features in selecting lesions for FNAB in the group of larger nodules was lower than in the group of smaller ones, and that for thyroid nodules larger than 15 mm (Lyshchik) or than 10 mm (Berker) the only reliable criterion of cancer was hypoechogenicity (26, 30). Moon *et al.* 2008 reported that a set of US features suggestive for malignancy (i.e. the presence of at least one of the

findings including taller than wide shape, spiculated margin, hypoechogenicity and the presence of calcifications) showed lower sensitivity and higher specificity for nodules > 10 mm than for smaller nodules, which is in concordance with our data (20).

In conclusion, the obtained results provide rationale for using features from the US examination, such as the shape of lesion (with height-to-width ratio ≥ 1), hypoechogenicity, the presence of microcalcifications and solitary occurrence in selecting nodules for FNAB. However, it should be considered that these features have different predictive value in diagnosing malignancy and different sensitivity and specificity in respect of nodule size. If keeping high sensitivity of preoperative diagnostic is a primary consideration, the optimal set of small lesions that should be biopsied includes all lesions presenting at least one of the above-mentioned features. In the case of large nodules, the sonographic features are less sensitive in selecting lesions for FNAB than in the case of SN, but they still can be applied for a reduction in the number of performed FNABs in endemic or post-endemic areas. Between large nodules, those primarily selected for FNAB should include hypoechoic, containing microcalcifications or more tall than wide lesions. However, one should remember that epidemiological situation (i.e. iodine supply) may significantly affect the specificity and sensitivity of these features.

It should be stressed that although the set of US features proposed in this study for small lesions is wider than that for larger lesions, it does not mean that in our opinion FNAB of small lesions (of several mm in diameter) should be performed more frequently than in the case of large nodules. It only shows what US features should be considered to obtain the maximal sensitivity of the diagnostics. Small lesions presenting with such features should be biopsied or followed by repeated US examinations. That was discussed by Mazzaferri & Sipos 2008 who indicated that US examinations are a better strategy than FNAB in the follow-up of small lesions not exceeding 5 mm, because US features suggesting necessity of FNAB produce high rates of false positive results, and cytologic specimens are frequently inadequate in the case of such small lesions (35). The results of our earlier studies show that it is particularly indicated to follow up small thyroid lesions by repeated US examination in endemic or post-endemic areas. In such areas, the efficiency of FNAB is lower in the case of small lesions (5–10 mm) than in the case of larger ones. One of the reasons is higher rate of multiple nodules in a goitre that makes the proper selection of lesions more difficult (3). It is reasonable to follow up small suspected lesions by repeated US examinations also because of the increased chances of early detection of small invasive cancers, on account of examination of lesion's relation to the thyroid capsule and evaluation of lymph nodes in the neck (36, 37). Some investigators suggest that such data from US examination may be useful in the selection of optimal

treatment strategy, and according to Ito *et al.* 2003 careful US examinations may even allow refraining from surgical treatment in some cases of papillary microcancers (36).

An important limitation of our study is its retrospective design. Thus, it was not possible to extract information on all analysed US features in some cases. The images from US examinations had not been archived and it was not possible to re-evaluate them. On the other hand, the retrospective design excluded any influence of histopathological diagnosis on interpretation of US images.

Declaration of interest

There is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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