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Original article

EFFECT OF ANATOMO-TOPOGRAPHIC AND SONOGRAPHIC POLARITY OF THE THYROID NODULES ON THE THYROID MALIGNANCY BY EVALUATING ITS IMPRESSION ON THE RELATIONSHIP BETWEEN THE BETHESDA SYSTEM, TBSRTC, STRAIN ELASTOGRAPHY SCORE AND THE THYROID HISTOPATHOLOGY

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Abstract: **Background:** The goal is to evaluate the association between the topo-sonographic polarity of the thyroid nodules and the thyroid malignancy by analyzing its effect on The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), score of Strain Elastography (SE) for thyroid as Tsukuba Elasticity Score (TES), and histopathologic assessment.

Material and Methods: A preliminary single-center retrospective study was carried out by including the documents of 641 consecutive eligible patients, possessing 770 thyroid nodules which undergone neck ultrasonography (US), Doppler US, SE, and US-guided-fine needle aspiration (FNA) during April 2011 to April 2017. The stiffness had been measured by TES of SE. The ability of the prediction of the malignancy by the polarity of 770 thyroid nodules considering the association between; i) TBSRTC and histopathology and ii) TES and histopathology had been evaluated.

Results: Of the 770 thyroid nodules evaluated, 408 (53.0%) were located at the superior pole (Pol 1) while 362 (47.0%) were at the inferior pole (Pol 0) with 0.9046 AUC and 0.8171 AUC for the association between TBSRTC and histopathology and 0.9280 AUC and 0.7888 AUC for the association between TES and histopathology, respectively. However, those difference were not significant for Pol 1, topographically.

Conclusion: The topograghic and sonographic polarity of the thyroid nodules may not be useful for estimating the thyroid malignancy by using the association between TBSRTC and histopathology with TES and histopathology. However, the association with Pol 1, the superior thyroid pole, was stronger though the difference was not significant.

Key words: Polarity; Elastography; Fine-needle aspiration; Bethesda; TBSRTC; Thyroidectomy.

INTRODUCTION

Fine-needle aspiration (FNA), performed with or without local anesthesia, is an easy and confidential outpatient procedure. The sampling aspirates are get via 23- to 27-gauge, frequently 25- or 27-gauge, needle through the indicated thyroid nodule by repetitive movings (1). The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), a six-diagnostic-category system, is still currently the utilized and acquiesced worldwide, that offer an important interpretation system for reporting FNA cytology (FNAC). The first edition of TBSRTC was structured through a multidisciplinary concensus that was accepted at the Thyroid Fine Needle Aspiration State of the Art and Science Conference, National Cancer Institute (NCI), held in Bethesda, Maryland in 2007 (2). Nine years later, Ali and Vielh presented 'The Bethesda System for Reporting Thyroid Cytopathology: Past, Present, and Future' at The 19th International Congress of Cytology (ICC) in Pacifico Yokohama, Japan, on 30May, 2016 (3, 4). The related preparations for the symposium began 12

months earlier with the designation of international panel, including 16 cytopathologists (5).

Zhang et al presented a late-breaking abstract (6) in May 16-20- 2018, than reported a study (7) in November 2018 about the location of thyroid nodule in terms of both laterality and polarity as a predictor of malignancy. In the present study, it is purposed to evaluate the association between the polarity of the thyroid nodules and their ultrasonography-guided FNAC and its influence on TBSRTC vs. histopathology and Strain Elastography (SE) Score, Tsukuba Elasticity Score (TES), vs. histopathology.

To our knowledge, it is the first study in the English literature analyzing solely the efficacy of the polarity of the nodules as a topographical anatomic feature, forecasting the thyroid malignancy by investigating its impact on the association between i) TBSRTC and histopathology and ii) TES and histopathology in a large serial with the duration of six year.

MATERIAL AND METHODS

From April 2011 to April 2017, a retrospective study was designed by enlisting the data and documents of the patientswith the thyroid nodules with FNAC. To rule out the malignant formations in the thyroid nodules, all the cases had undergonetheneck US, Doppler US, SE application, and ultrasound-guided-FNA (US-g-FNA) to exhibit whether prediction with an anatomo-topographic polarity.

The Criteria for Enrolling into the Study

The inclusion criteria for being enrolled into the present study were possession of the thyroid nodules with the performed non-invasive, the neck US, SE, and invasive, US-g-FNA, applications and evaluation of FNACs based on TBSRTC with the histopathologic outcomes of the thyroidectomy procedures which had been performed for the indicated cases. Nevertheless, the exclusion criteria were the cases with the thyroid nodules, but had not indication for performing US-g-FNA and the cases with the purely cystic thyroid nodules.

Figure 1a: *An ovoid hypoechoic solid nodule, 21.1x8.3 mm, with the regular borders, possessing the minimal cystic apertures, located at the thyroid right lobe superior zoneextending along the isthmus, B-Mode US*

Figure 1b: *Some peripheral vascularization of the nodule in Figure 1a, Doppler US*

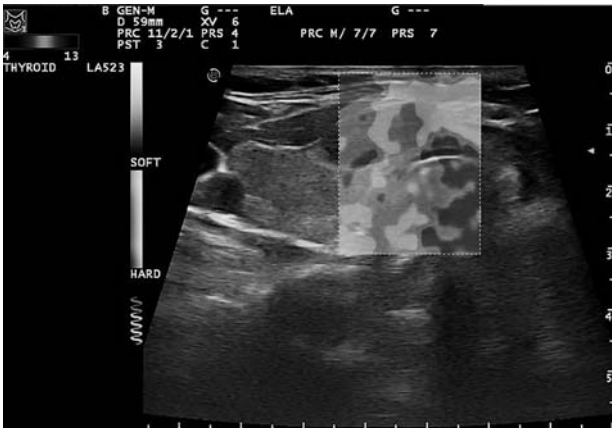

Figure 1c: *The Tsukuba Elasticity Score, TES, 2 of the nodule in Figure 1a, Strain Elastography*

Sonographic evaluation

The sonographic examination and evaluation had performed by using the neck US (Figure 1a), Doppler US (Figure 1b), and SE (Figure 1c) (Esaote MyLab 60, Geneva, Italy) with a linear probe of 4–13 MHz broadband,possessing the mean 12 MHz broadband.

Tsukuba elasticity score and coherent macroscopic/histopathologic characteristics

Sonoelastography of a thyroid nodule is evaluated by a 5-point-strain Itoh-Score or Elasto-Score, TES [8]. TES 1 and 2 (Figure 1c) are evaluated as soft benign nodules. TES 3, the medium consistency, is accepted as usually benign, while TES 4 and 5 are hard nodules and considered as malignant.

US-guided-FNA and FNAC

From each targeted and indicated thyroid nodule, three to eight smears had been prepared byusingthefine needle with 27-gauge (Hayat, 2 ml and 3P with 27G-0.40 x 50 mm, Istanbul, Turkey) by administrating the local anesthesic agent, Prilocaine hydrochloride 2%, i.v. 400 mg/20 ml. The smear materials had been implemented into the 95% alcohol for alcohol fixation and the technique of air fixation performed, then all the prepared materials had submitted to the cytopathologic assessment by haematoxylin-eosin (H&E), PAP, and May-Grünwald-Giemsa (MGG), respectively. Cytopathologic evaluation had been performed considering TBSRTC: (1) non-diagnostic, I (2) benign, II (3) atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), III; (4) follicular neoplasm/suspicious for follicular neoplasm (FN/SFN), IV; (5) suspicious for malignancy (SM), V (6) malignant, VI. Currently, Moss et al (8) reported a systematic review and meta-analysis, exhibitingthe application of FNA should be performed with the smallergaugesof needle (24-27 G). In the present study, all the applications of US-g-FNA had been administrated via the smallest needle with 27 G.

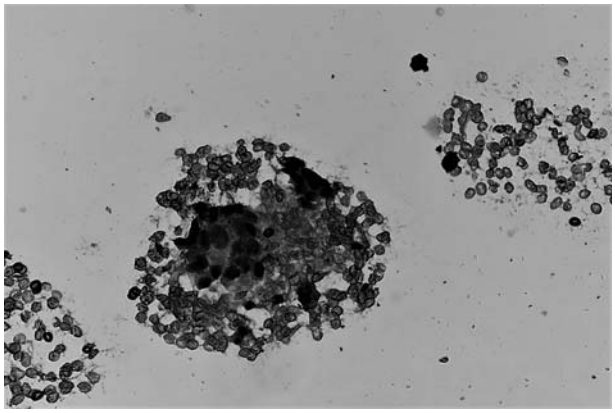

Figure 1d: A photomicrograph, revealing the cytopathology of TBRSTC Category III, (H&E; Original magnification, 20 x 0.40)

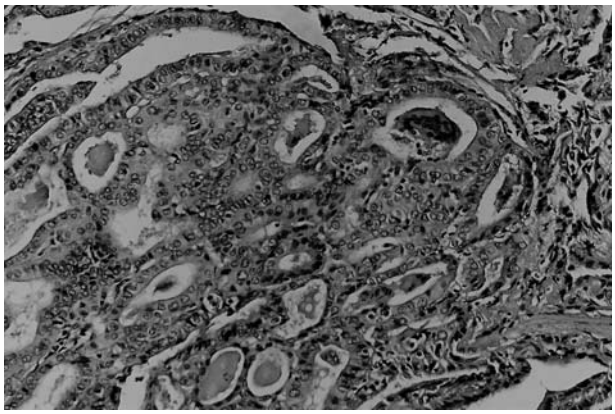

***Figure 2:** A photomicrograph, revealing the histopathology of PTC, (H&E; Original magnification, 20 x 0.40)*

Statistical Analysis

The statistical analyses of the present study were performed by utilizing SPSS 23.0 and NCSS 12.0 computer programs. The descriptive statistics and frequency tables were created to examine the data and variables in the statistical analyses. In addition, the receiver operating characteristic curves (ROC curves) and hyphothesis tests for the diagnostic tests were performed to compare and analyze the diagnostic test performances. ROC curve is a graph showing the performance of a classification model at all classification thresholds. The Z-tests were performed by NCSS 12.0 computer program for comparing the area under the ROC curves (AUCs) for the independent groups. AUC measures the whole two-dimensional area underneath the complete ROC curve, an integral calculus, from (0,0) to (1,1). In addition, AUC provides an aggregate measure of performance across all possible classification thresholds.

RESULTS

An application of US-g-FNA had been performed for a sum of 641 cases with the mean age of 51 ± 2,499 (77.8%) women and 142 (22.2%) men, with 770 indicated thyroid nodules with the mean size of 19 ± 9 mm in diameter which had been exhibited on the sonograghic evaluation during six years. On the basis of polarity, the thyroid nodules located at the superior pole, polarity 1 (Pol 1), and inferior pole, polarity 0 (Pol 0), were detected as 408 (53.0%) and 362 (47.0%), respectively. Cytologically, Bethesda Category I, II, III, IV, V, and VI were detected as 31 (4.0%), 515 (66.9%), 145 (18.9%) (Figure 1d), 41 (5.3%), 37 (4.8%) and 1 (0.1%), respectively. Histopathologically, benign, 191 (85.7%); PTC (Figure 2), 20 (9.0%); FTC, 7 (3.1%); HCC, 5 (2.2%) had been revealed. Of the 770 thyroid nodules examined, 408 (53.0%) were locates at the superior pole while 362 (47.0%) were at the inferior pole. Sonographically, SE Scores, TES 1, 2, 3, 4, and 5, were detected as 187 (24.3%), 368 (47.8%), 164 (21.3%), 39 (5.1%), 12 (1.6%), respectively for 770 thyroid nodules.

The ROC curve of Pol 1 for TBSRTC and histopathology was superior to the one of Pol 0 (Figure 3), indicating the association between TBSRTC and histopathology had been stronger in Pol 1, the thyroid nodules located at the superior poles. However, the significancy of that difference was analyzed by using Z-test ($Z = 1.025$) and it was revealed that the association between TBSRTC and histopathology was not significant with regard to the different groups of the polarity, Pol 0

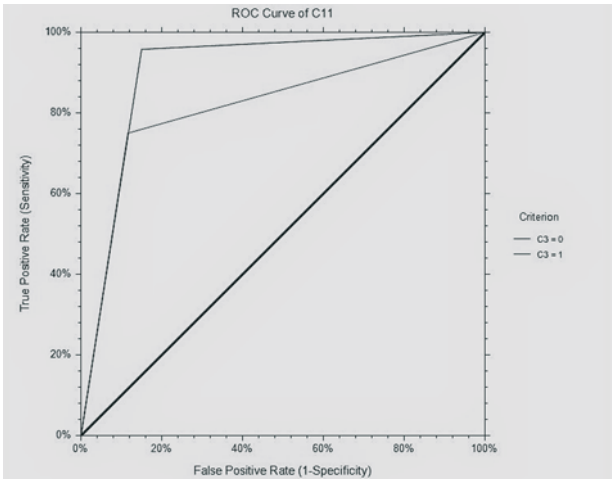

Figure 3: *The Sensitivity, Specificity, TPR, FPR, AUC, and ROC curves of Pol 1 and Pol 0fot comparing the association between TBSRTC and histopathology of the thyroid nodules.*
TPR: True positive rate; FPR: False positive rate; Pol 1: Group of Polarity 1, superior pole; Pol 0: Group of Polarity 0, inferior pole

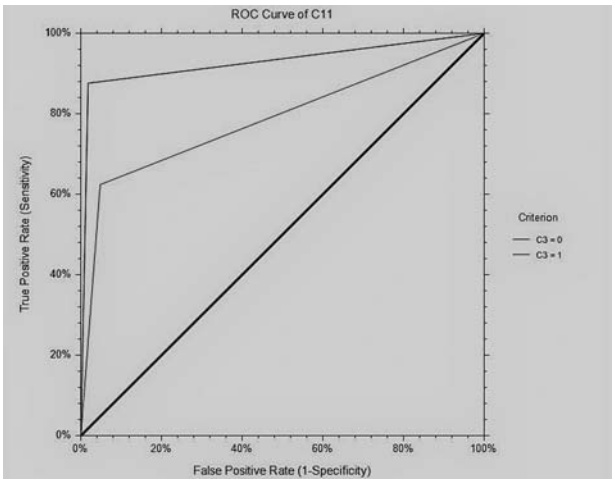

Figure 4: *The Sensitivity, Specificity, TPR, FPR, AUC, and ROC curves of Pol 1 and Pol 0 fot comparing the association between TES and histopathology of the thyroid nodules.*
TPR: True positive rate; FPR: False positive rate; Pol 1: Group of Polarity 1, superior pole; Pol 0: Group of Polarity 0, inferior pole; TES: Tsukuba Elasticity Score

and 1 ($p > 0.05$) (Table 1). Similarly, the ROC curve of Pol 1 for SE score, TES, and histopathology was superior than the one of Pol 0 (Figure 4), indicating the association between TES and histopathology had been stronger in Pol 1, the thyroid nodules in the superior poles. Nevertheless, the significancy of that difference was analyzed by using Z-test ($Z = -1.421$) and it was appeared that the relationship between TES and histopathology was not significant according to the different groups of the polarity, Pol 0 and 1 ($p > 0.05$) (Table 2).

DISCUSSION

The incidence of thyroid cancer, the most frequent endocrine cancer, has significantly increased, recently at higher rate than any other cancer and that increase in its detection is estimated mainly due to common use of

Table 1. *The Z-test for comparing the association between TBSRTC and histopathology with regard to the different groups of the Polarity, Pol 0 and 1*

The Test, Comparing Two AUCs (Empirical Estimation)

H0: AUC 0 = AUC 1
H1: AUC 0 ≠ AUC 1
Total Sample Size: 770

Polarity	AUC	(AUC 0-AUC 1)	Std. Error	Z value	p value
0	0,8171	-0,0875	0,0854	1,025	0,3055
1	0,9046				

TBRSTC: Thyroid Bethesda System for Reporting Thyroid Cytology; AUC: Area under the ROC curve

Table 2. *The Z-test for comparing the association between SE score, TES, and histopathology with regard to the different groups of the Polarity, Pol 0 and 1*

The Test, Comparing Two AUCs (Empirical Estimation)

H0: AUC 0 = AUC 1
H1: AUC 0 ≠ AUC 1
Total Sample Size: 770

Polarity	AUC	(AUC 0-AUC 1)	Std. Error	Z value	p value
0	0,7888	-0,1393	0,0980	-1,421	0,1554
1	0,9280				

SE: Strain elastography; TES: Tsukuba Elasticity Score; AUC: Area under the ROC curve

diagnostic methods such as ultrasound worlwide (9–12). The percentage of clinical ascertaining of the thyroid nodules are 5% for females and 1% for males in non-endemic areas, 50% in autopsy series, and 19-68% by using US as a diagnostic tool in a wide range of of the studied populations (13, 14). US-g-FNAC is rapid, reliable, minimally invasive, cost-effective, and out-patient procedure, used in the determining the surgical indication or follow-up procedures for the suspicious thyroid nodules and attenuating the risk of unnecessary surgery, with approximately 62% to 85% diagnostic accuracy (15, 16). Moss et al (9) propunded that FNA should be performed without aspiration and with smaller needle gauges, 24- to 27- Gauge needles. In the present study, all the FNA performed as US-g-FNA via 27 G, to our knowledge.

Considerable investigations, such as clinical parameters, US patterns of the nodules, Doppler US, repeated US-g-FNA practices, US elastography, core-needle biopsy, intraoperative frozen sections, TBSRTC, TBSRTC II, cytological subclassifications, molecular mutational analyses, and diagnostic thyroid lobectomy, have been performed to be able to distinguish the malign thyroid nodules from the benign ones to refrain from an unnecessary surgical procedure and its possible complications. Unfortunately, any diagnostic tool among them or the other diagnostic methods can precisely warrant the malignant formation of a thyroid nodule to date. Therefore, the clinical management of the indeterminate cytology remains challenging and a non-invasive application, i.e. elastography for the mentioned purposes is still debated. SE is a quasi-static strain imaging, working by the policy of Hooke's law of elasticity which was discovered by the Robert Hooke in 1660. It aims to differentiate the tissues in accordance with their stiffness or elasticity as defined in guidelines of EFSUMB (European Federation of Societies for Ultrasound in Medicine and Biology) (17). SE is applied by comparing the stiffness of the thyroid nodule and paranchyma via Hooke's law. Any pathologic processes change the structure of the related tissues, finally their elasticity.The meta-analyses with the mean sensitivities of 82-92% and mean specificities of 67-92%, considering SE in terms of prediction of malignant thyroid nodules were reported (18, 19, 20).

Currently, Zhang et al (6) presented their study, as a late-breaking abstract, entitled thyroid nodule location on ultrasonography as a predictor of malignancy at the 27th American Association of Clinical Endocrinologists (AACE) meeting, which was held in Boston, MA, May 16-20, 2018. They presented a retrospective study for the period of July 2016 to June 2017 and analyzed the thyroid nodules from 188 patients who had undergone FNA in terms of the laterality (left versus isthmus versus right), polarity (upper versus middle versus lower), microcalcifications, and multi-nodularity.To our knowledge, Zhang's study (6) was the first of its kind to purpose for demonstrating whether an association between the location of thyroid nodule and the likelihood of the malignancy. Afterwards, Zhang et al (7) reported as a publication, entitled "Thyroid nodule location on ultrasonography as a predictor of malignancy" in 1st of November 2018, very recently. They retrospectively reviewed the data of 219 cases with the thyroid nodules who underwent US-g-FNA during one year. In the mentioned study, the demographic features of the cases as well as the laterality, polarity, morphology and multinodularityof the thyroid nodules were analyzed. Majority of the nodules, 79.3% were in the lower pole, while 9.6% in the upper pole and 6.9% in the middle pole. A significantly higher ratio of the thyroid malignancy was recognized in upper pole, 22.2%, comparing the lower, 4.7% and middle pole,15.4%. In the present study, 53.0% of the nodules were recognized at the superior pole, Pol 1, while 47.0% were at the inferior pole, Pol 0. The association between TBSRTC and histopathology had been stronger for the nodules located at the superior poles, however, that difference was not significant with regard to the different groups of the polarity, Pol 0 and 1, which was the anatomo-topographic situation of the thyroid nodules.

Zhang et al studied the laterality of the nodules for predicting the malignancy with the polarityretrospectively from 219 cases with thyroid nodules who underwent FNA in one year. In the present study, 641 cases with 770 thyroid nodules had been investigated retrospectively for the period of 6 years whether the polarity had effected the association between i) TBSRTC and histopathology and ii) TES and histopathology, separately.

To our knowledge, it is the first study in the English literatute, investigating solely the efficacy of the polarity of the nodules as a topographical anatomic feature, forecasting the thyroid malignancy in terms of having influence upon TBSRTC vs. histopathology and TES vs. histopathology. It is also an extended study with 770 thyroid nodules, had undergone US-g-FNA, with a single-center experience of six years.

CONCLUSION

Of the 770 thyroid nodules evaluated, 408 (53.0%) were Pol 1 while 362 (47.0%) were Pol 0 with 0.9046 AUC and 0.8171 AUC for the association between TBSRTC and histopathology and 0.9280 AUC and 0.7888 AUC for the association between TES and histopathology, respectively. However, those difference were not significant for Pol 1.

In conclusion, the topograghic and sonographic polarity of the thyroid nodules had not been useful for estimating the thyroid malignancy by using the association between TBSRTC and histopathology with TES and histopathology. However, the association with Pol 1, the superior thyroid pole, was stronger though the difference was not significant.

Abbreviations

FNA — Fine-needle aspiration
TBSRTC — The Bethesda System for Reporting Thyroid Cytopathology
FNAC — Fine-needle aspiration cytology
SE — Strain Elastography
TES — Tsukuba Elasticity Score
US — Ultrasound
US-g-FNA — Ultrasound guided fine-needle aspiration
H&E — Haematoxylin-eosin
MGG — May-Grünwald-Giemsa
AUS/FLUS — Atypia of undetermined significance/follicular lesion of undetermined significance
FN/SFN — Follicular neoplasm/suspicious for follicular neoplasm
SM — Suspicious for malignancy
ROC curve — The receiver operating characteristic curve
AUC — Area under the ROC curve
PTC — Papillary thyroid carcinoma
FTC — Follicular thyroid carcinoma
HCC — Hürthle cell carcinoma
US-g-FNAC — Ultrasound guided fine-needle aspiration cytology
EFSUMB — European Federation of Societies for Ultrasound in Medicine and Biology
AACE — American Association of Clinical Endocrinologists

Conflict of interest

No conflict of interest relevant to this article has been declared.

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It has not been used any funding for the present work. IS and DS had contributed in constituting the notion and hypothesis, intellectual planning and management of the study, writing the whole manuscript, its linguistic and academical revisions. Besides, DS had contributed in collecting the data, performing the statistical analysis. IS had contributed in examining each patient in the outpatient clinic and performing US-guided-FNA for each indicated thyroid nodule. All the authors finally approved the submitted and proof versions without any conflict of interest.

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Sažetak

EFEKAT ANATOMSKO-TOPOGRAFSKOG I SONOGRAFSKOG POLOŽAJA TIROIDNIH ČVOROVA NA MALIGNITET TIROIDNE ŽLEZDE EVALUACIJOM IMPRESIJE NA ODNOS IZMEĐU BETESDA SISTEMA, TBSRTC, REZULTATA ELASTOGRAFIJE I HISTOPATOLOGIJE

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Uvod: Cilj je da se proceni povezanost između topo-sonografskog polariteta tiroidnih čvorova i maligniteta tiroidne žlezde analizom njihovih efekata na Betesda sistem za izveštavanje o tiroidnoj citopatologiji (TBSRTC), rezultate elastografije (SE), rezultate Tsukuba elasticiteta (TES skor) kao i histopatološke procene.

Materijal i metode: Preliminarna unicentralna retrospektivna studija je sprovedena analizom medicinske dokumentacije 641 pacijenta koji ispunjavaju uslove, koji imaju 770 čvorova tiroidne žlezde, a kojima je urađen ultrazvuk vrata, dopler, SE, kao i aspiraciju finom iglom pod kontrolom ultrazvuka, u periodu od aprila 2011. do aprila 2017. Krutost je merena pomoću TES i SE. Sposobnost predviđanja maligniteta polaritetom 770 tiroidnih čvorova, je evaluirana, obzirom na povezanost između: i) TBSRTC i histopatologijei ii) TES i histopatologije.

Rezultati: Od 770 evaluiranih tiroidnih čvorova, 408 (53,0%) je bilo locirano u gornjem polu (Pol 1), dok je 362 (47,0%) bilo u donjem polu (Pol 0) sa 0.9046 AUC i 0.8171 AUC za vezu između TBSRTC i histopatologije i 0.9280 AUCi0. 7888 AUC za povezanost između TES i histopatologije. Međutim, te razlike nisu bile značajne za Pol 1, topografski.

Zaključak: Topografski i sonografski polaritet tiroidnih čvorova možda nije koristan za procenu malignosti štitne žlezde analizom povezanosti između TBSRTC i histopatologije sa TES i histopatologijom. Međutim, povezanost sa Polom 1, gornjim tiroidnim polom, bila je evidentna iako razlika nije bila značajna.

Ključne reči: polaritet, elastografija, aspiracij afinom iglom, Betesda, TBSRTC, tiroidektomija.

REFERENCES

1. Gursoy A, Ertugrul DT, Sahin M, Tutuncu NB, Demirer AN, Demirag NG. Needle-free delivery of lidocaine for reducing the pain associated with the fine-needle aspiration biopsy of thyroid nodules: time-saving and efficacious procedure. Thyroid. 2007; 17(4): 317-21.

2. Cibas ES, Ali SZ. The Bethesda system for reporting thyroid cytopathology. Thyroid. 2009; 19(11): 1159-65.

3. Ali SZ, Vielh P, Pusztaszeri M, Rossi D, Faquin WC, Bishop JA, et al. The Bethesda System for reporting thyroid cytopathology: past, present, future at The 19th International Congress of Cytology in Pacifico Yokohama, Japan, on 28 May–01 June, 2016, Symposiunm 12.

4. Ali SZ, Cibas ES. The Bethesda System for reporting thyroid cytopathology II. Acta Cytol. 2016; 60(5): 397-8.

5. Ali SZ, Cibas SE. The Bethesda System for Reporting Thyroid Cytopathology: Definitions, Criteria, and Explanatory Notes. 2nd ed. Cham: Springer Nature; 2018.

6. Zhang F, Oluwo O, Castillo F, Gangula P, Castillo M, Farag F, et al. Thyroid nodule location on ultrasonography as a predictor of malignancy. Late-breaking abstract #1204. AACE, American Association of Clinical Endocrinologists 2018, Boston, MA, USA.

7. Zhang F, Oluwo O, Castillo FB, Gangula, Castillo M, Farag F, et al. Thyroid nodule location on ultrasonography as a predictor of malignancy. Endocr Pract. 2019; 25(2): 131-7. doi: 10.4158/EP-2018-0361. [Epub 2018, Nov 1].

8. Itoh A, Ueno E, Tohno E, Kamma H, Takahashi H, Shiina T, et al. Breast disease: clinical application of US elastography for diagnosis. Radiology. 2006; 239(2) 341-50.

9. Moss WJ, Finegersh A, Pang J, Califano JA, Coffey CS, Orosco RK, et al. Needle biopsy of routine thyroid nodules should be performed using a capillary action technique with 24- to 27-gauge needles: a systematic review and meta-analysis. Thyroid. 2018; 28(7): 857-63.

10. La Vecchia C, Malvezzi M, Bosetti C, Garavello W, Bertuccio P, Levi F, et al. Thyroid cancer mortality and incidence: a global overview. Int J Cancer. 2015; 136(9): 2187-95.

11. Rahib L, Smith BD, Aizenberg R, Rosenzweig AB, Fleshman JM, Matrisian LM. Projecting cancer incidence and deaths to 2030: the unexpected burden of thyroid, liver, and pancreas Ccncers in the United States. Cancer Res. 2014: 74(11): 2913-21.

12. Welch HG, Black WC. Overdiagnosis in Cancer. J Nat Cancer Inst. 2010; 102(9): 605-13.

13. Haugen BR, Alexander EK, Bible KC, Doherty GM, Mandel SJ, Nikiforov YE, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid. 2016; 26(1): 1-133.

14. Dean DS, Gharib H. Epidemiology of thyroid nodules. Best Pract Res Clin Endocrinol Metab. 2008; 22(6): 901-11.

15. Machała E, Sopiński J, Iavorska I, Kołomecki K. Correlation of fine needle aspiration cytology of thyroid hland with Histopathological results. Pol Przegl Chir. 2018; 21; 90(6):1-5.

16. Zhao CK, Xu HX, Xu JM, Sun CY, Chen W, Liu BJ, et al. Risk stratification of thyroid nodules with Bethesda category III results on fine-needle aspiration cytology: The additional value of acoustic radiation force impulse elastography. Oncotarget. 2017; 8(1): 1580-92.

17. Cosgrove D, Piscaglia F, Bamber J, Bojunga J, Correas JM, Gilja OH, et al. EFSUMB guidelines and recommendations on the clinical use of ultrasound elastography. Part 2: Clinical applications. Ultraschall Med. 2013; 34(3): 238-53.

18. Bojunga J, Herrmann E, Meyer G, Weber S, Zeuzem S, Friedrich-Rust M. Real-time elastography for the differentiation of benign and malignant thyroid nodules: a meta-analysis.Thyroid. 2010; 20(10): 1145-50.

19. Ghajarzadeh M, Sodagari F, Shakiba M. Diagnostic accuracy of sonoelastography in detecting malignant thyroid nodules: a systematic review and meta-analysis. Am J Roentgenol. 2014; 202(4): W379-89.

20. Razavi SA, Hadduck TA, Sadigh G, Dwamena BA. Comparative effectiveness of elastographic and B-mode ultrasound criteria for diagnostic discrimination of thyroid nodules: a meta-analysis. Am J Roentgenol. 2013; 200(6): 1317-26.

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