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Reassessing Combining Real-time Elastography with Fine-needle Aspiration Biopsy to Identify Malignant Thyroid Nodules

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Abstract Debate is still ongoing in the thyroid gland with indeterminate cytology w/wo suspicious clinics and sonographic features, besides their size selection criteria, in Endocrine Pathology, Endocrine Surgery, and Thyroidology, till today. Real-time elastography (RTE) still have been utilized for this purpose though it remains a controversial determinant. We postulate that the so-called RTE diagnostic tool selectively is enriched by considering nondiagnostic, Category I, and indeterminate cytology, Category III, IV, and V, of The Bethesda System for Reporting Thyroid Cytopathology, TBSRTC, 2nd ed., individually and separately, regarding noninvasive follicular thyroid neoplasm with papillary-like nuclear features, NIFTP, all of which a wide range of implied risk of malignancies.

Keywords: *thyroid gland, nondiagnostic cytology, indeterminate cytology, elastography, real-time elastography, Endocrine Surgery, Endocrine Pathology, Thyroidology*

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Dear Editor,

Gland surgery is still in debate for nodules in the thyroid gland with indeterminate cytology w/wo suspicious clinics and sonographic features, till today, besides their size selection criteria. We currently have purposed to emphasize the essentiality of a closer look at the nodule size below 10 mm in a vignette interpretation, published in Volume 9, *American Journal of Medical Case Reports* [1]. We read with a great deal and respect the research article, entitled: 'Combining real-time elastography with fine-needle aspiration biopsy to identify malignant thyroid nodules [2].' This research purposed to cast light on evaluating the diagnostic performance of real-time elastography (RTE) combined with fine-needle aspiration (FNA) in order to rule out malignant thyroid nodules. For this purpose, Zhu and colleagues [2] declared to compare RTE and FNA based on elastography scores of 1-2 as benign and 3-4 as malignant for the former and Bethesda I-II as benign, III-IV as intermediate, and V-VI as malignant for the latter. Finally, the authors proclaimed the combination of RTE imaging with FNA evaluation was being contributed to improving diagnostic performance in the thyroid nodules.

The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), 1st edition (ed), had been utilized widely, in order for evaluating and reporting cytopathology of thyroid FNA applications, worldwide. Recently, TBSRTC, 2nd ed. has been using and Category III, atypia of undetermined significance or follicular lesion of undetermined significance (AUS/FLUS); IV, follicular neoplasm (FN) or suspicious for a follicular neoplasm (SFN); and V, suspicious for malignancy (SM) have been accepted as constituting *indeterminate cytology of thyroid nodules*. The risk of malignancies (ROMs) for indeterminate cytology are declared as 5-15%, 15-30%, and 60-75% in TBSRTC 1st ed. while 10-30%, 25-40%, and 50-75% in 2nd ed. for Category III, IV, and V, respectively, reflecting a wide range of ROM. The 2016 Royal College of Pathologists, United Kingdom (RCPath, UK) reported indeterminate cytology as Thy 3a, neoplasm possible, atypia/non-diagnostic and Thy 3f, neoplasm possible, suggesting FN, with the ROMs of 20-31% and 24-39%, respectively. In addition, the 2016 RCPath, UK declared Thy 4, SM with the ROM of 70-87%. The 2014 Italian Consensus for the Classification and Reporting of Thyroid Cytology (ICCRTC) divided diagnostic category TIR3, indeterminate cytology, into two subcategories, TIR3A (low-risk indeterminate lesion) and TIR3B (high-risk indeterminate lesion), with different expected ROMs and discrete clinical manners as <10% and 15-30%, respectively. The 2014 ICCRTC also harbors TIR4, SM with an expected ROM of 60-80%. The 2014 Royal College of Pathologists of Australasia (RCPA) and the Australian Society of Cytology (ASC) propounded: i) 3,

Indeterminate (AUS/FLUS) with low ROM, 5-13%; ii) 4, Suggestive of an FN (FN/SFN) with moderate ROM, 21-26%; and iii) 5, SM with high ROM, 85-90%. The 2013 Japan Thyroid Association (JTA) Guideline for the Management of Thyroid Nodules declared: i) 3, Indeterminate, 3B, others; Indeterminate, ii) 3A, FNs, 3A-1, favor benign, 3A-2, borderline, 3A-3, favor malignant; iii) 4, Malignancy suspected, respectively. Hereinbefore, Zhu et al. [2] designated Category V, TBSRTC as malignant, Nevertheless, it has been involved in indeterminate cytology and has a considerably different ROM, 50-75%, as SM rather than Category VI with a ROM of 97-99% as Malignant; TBSRTC, 2nd ed. [3-8]

Furthermore, a challenging cytologic category of Non-diagnostic or Unsatisfactory, TBSRTC, 1st and 2nd ed.s still remains being involved in the 2016 RCPath, UK as Thy1, Nondiagnostic for cytological diagnosis, Thy1c, Nondiagnostic for cytological diagnosis–cystic lesion; the 2014 ICCRTC/the Italian Society for Anatomic Pathology and Cytology-the Italian Thyroid Association (SIAPEC-ITA 2013) as TIR1, Nondiagnostic, TIR1c, Nondiagnostic cystic; the 2014 RCPA/ASC as 1, Nondiagnostic; and the 2013 JTA as 1, Inadequate in management of suspicious nodules. Hereinabove, Zhu et al. [2] determined Category I, TBSRTC as benign. Nevertheless, it has been classified as Non-diagnostic or Unsatisfactory cytology and has a different ROM, 5-10%, rather than Category II with a ROM of 0-3% as benign; TBSRTC, 2nd ed. [3-8] Last but not least, Baloch et al. [9] emphasized that the ROM varies with the type/structure of the nodule, i.e. solid vs. complex vs. ≥50% cystic in Category I and nondiagnostic aspirates from solid nodules are interrelated with a higher ROM, regarding those exhibiting ≥50% cystic change and low-risk sonographic features (TBSRTC, 2nd ed.).

As such, each diagnostic category of the last TBSRTC, 2nd ed., with noninvasive follicular thyroid neoplasm with papillary-like nuclear features, NIFTP, harbor a wide range of implied ROMs. Herewith, might the course of the study of Zhu et al. [2] was affected by designating thyroid nodules with Category I in the benign group and V in the malignant one? Therefore, could it change the mentioned study design and the relevant possible outcomes? As a matter of fact that this issue merits further investigation. We thank Zhu et al. [2] for their valued study.

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