AN INDEPENDENT PERFORMANCE COMPARISON OF THE AFIRMA GENOMIC SEQUENCING CLASSIFIER (GSC) AND GENE EXPRESSION CLASSIFIER (GEC) FOR CYTOLOGICALLY INDETERMINATE THYROID NODULES

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For thyroid nodules with indeterminate FNA cytology (Bethesda class III or IV), the Afirma Gene Expression Classifier (GEC) classifies aspirates as benign or suspicious with high negative predictive value and reduces the need for diagnostic thyroid surgery. However, many benign lesions were classified as suspicious, particularly when cytology was characterized by Hurthle cells. The recently developed Afirma Genomic Sequencing Classifier (GSC) showed similar sensitivity with improved specificity, suggesting more nodules would have a benign result. A retrospective analysis of all thyroid nodules ≥1cm with Bethesda III or IV cytology tested with GEC or GSC from 2011-2018 at our institution. Demographic, sonographic and cytologic data were collected. The proportion of results that returned benign (the benign call rate [BCR]) for GEC versus GSC tested nodules was compared and further stratification of BCR was evaluated by Bethesda classifications. We evaluated 583 nodules in 546 patients tested with either GEC (n = 486) or GSC (n = 97). The GEC BCR was 233/486 (47.9%) compared to 63/97 (64.9%) for the GSC BCR (p = 0.003). In Bethesda III nodules characterized by Hurthle cells, the GSC BCR was 100% (5/5) versus 36.8% (14/38) for GEC BCR (p = 0.01), but the BCRs were similar for nodules with cytologic or architectural atypia. In Bethesda IV nodules, the BCR for follicular neoplasm was 63.1% (70/111) for GEC and 68.4% (13/19) for GSC (p = 0.68), but for cytology suspicious for Hurthle cell neoplasm, the GSC BCR was 68.2% (15/22) compared to the GEC BCR of only 16.4% (10/61) (p < 0.0001). Demographic parameters were similar between groups. GSC tested nodules tended to be larger compared to GEC group (2.1 vs. 1.9 cm, p = 0.06), and were less likely to be >50% cystic (3/97[3.1%] vs 56/486 [11.5%], p = 0.009), though the distribution of ATA sonographic risk patterns was similar between groups. The GSC identified a higher percentage of benign results compared to the GEC for indeterminate thyroid nodules, predominantly due to improved BCR among nodules with Hurthle cell cytology. The clinical result is likely further reduction in surgical management.