УДК [61+615.1](06)(043.2)
ББК 5+52.81
А 43
ISBN 978-985-21-1569-8

Upadhyay Aryan, Suresh Aishwarya

ROLE OF MOLECULAR MARKERS IN DIFFERENTIAL DIAGNOSIS OF THYROID NODULES WITH INDETERMINATE CYTOLOGY

Tutor: MD, PhD, associate professor Yakubouski S.U.
Department of Surgery and Transplantology
Belarusian State Medical University, Minsk

Fine-needle aspiration (FNA) biopsy is the gold standard in detecting malignancy of thyroid gland. Up-to 30% cases fall in the category of indeterminate cytology (Bethesda class III and IV) where the morphological features are insufficient to classify the type of neoplasm. This necessitates implementation of new approaches, which can help to stratify patients according to the risk of malignancy in order to avoid overdiagnosis. Recent advances in molecular studies of thyroid cancer have allowed molecular testing as a new approach.

According to PubMed, Cochrane Library, and Scopus databases, up to 60% of adults in the general population harbour one or more thyroid nodules [Guth S, et al., 2009] but the actual prevalence of cancer ranges from 1 to 5% [Grussendorf M et al., 2022]. Examination of patients with thyroid nodules consists of initial evaluation, lab tests, thyroid ultrasound and FNA as a definite diagnostic procedure, which helps to recognize nodule morphology. Nonetheless, FNA in up to 30% of patients may result in false or indeterminate results [Rossi ED et al., 2019]. The term "indeterminate cytology" refers to Bethesda class III or class IV findings, that's associated with an estimated malignancy rate of 10% to 30% and 25% to 40%. The options suggested for identifying these nodules include repeat FNA, but it provides a definitive diagnosis for only 40% of class III nodules [Allen L et al., 2019]. Class IV refers to so-called follicular tumors, which include both benign and malignant lesions, and in this situation cytology can't help. On performing 2nd cytological study; if indeterminate results persists or follicular tumor is found, diagnostic lobectomy is traditionally done to get a confirmatory pathological diagnosis. This procedure is costly and possess certain risks.

Often reoperation (complete thyroidectomy) is done if nodule is found to be malignant. Hence, patients up to 60% that undergo lobectomy for an indeterminate nodule are often under- or overtreated at initial surgery [Stewart R et al., 2020]. Recent advances in molecular studies of thyroid cancer have allowed to use new approach – *molecular testing* - to solve the above problem. It has reduced the number of diagnostic surgeries performed. They are based on three principle molecular approaches:

1. Evaluation of gene expression
2. Somatic mutation testing
3. Classifiers based on microRNA [Labourier E et al., 2015].

Few of them are also currently used in rule- in and rule- out testing as they have enough positive and negative predictive values.

However, the currently available data differs significantly from one another in cohort selection criteria, sample sizes, malignancy rates, study design, and applied reference standards; there are no direct head-to-head comparisons. Nevertheless, major molecular approaches proved to be considerably more cost-effective than diagnostic lobectomy.

It's still debatable if a comprehensive molecular profile of thyroid nodules can provide predictive information and guide the extent of surgery. But, if all clinical, imaging and cytological findings indicates a requirement of diagnostic surgery then molecular testing should be certainly considered.