Detecting thyrotropin receptor mRNA from peripheral blood of patients with differentiated thyroid cancer rules out non-aggressive cases

Abstract

Background

Early diagnosis of thyroid cancer is hampered by the inability of fine-needle aspiration biopsy (FNAB) to accurately classify ~30% of cases while preoperative cancer staging detects lymph nodal involvement in only half of cases. Liquid biopsy may present an accurate, non-invasive alternative for preoperative thyroid nodule assessment. Thyrotropin receptor (TSHR) mRNA, a surrogate marker for circulating cancer cells (CTC), may be an option for early detection of malignancy from peripheral blood, but requires methodological improvements. We aimed to investigate if TSHR mRNA can be detected in low sample volumes by employing an ultrasensitive method – droplet digital PCR (ddPCR).

Methods

Less than 5 mL of blood was collected from 47 patients with thyroid nodules (25 benign and 22 malignant). RNA was isolated from the fraction of mononuclear cells where CTCs segregate. Samples were analysed for the presence of TSHR mRNA by ddPCR.

Results

Thyrotropin receptor mRNA was detectable in 4 mL sample volumes, with the test having good specificity (80%) but modest diagnostic accuracy (68.1%). Combining TSHR mRNA with ultrasound features and FNAB diagnosis, the test reaches high rule-out performances (sensitivity = 90% and NPV = 88.2%). Strikingly, TSHR mRNA correctly classified all samples with thyroid capsule invasion, lymph node metastasis and extrathyroidal extension. If aggressiveness is defined using these parameters, TSHR mRNA test reaches 100% sensitivity and 100% NPV for detecting high-risk cases.

Conclusions

Employing ddPCR for TSHR mRNA improves its measurement by enabling detection in sample volumes common for laboratory testing. The test displays high prognostic performance, showing potential in preoperative risk assessment.

Keywords
Circulating tumour cells, droplet digital PCR, liquid biopsy, thyroid cancer, thyrotropin receptor mRNA

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