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(SHORT COMMUNICATION)

Are we ready to endorse new multiple cancer early-detection tests?

Felix Wu Shun WONG [1,*] and Bee Luan KHOO [2]

[1] *Women and Babies Clinic, Central Building, Hong Kong, SAR, China.*
[2] *Department of Biomedical Engineering, City University of Hong Kong, Hong Kong, SAR, China.*

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Abstract

Cancer detection tests open a new era of developing cancer markers, allowing early detection and improving cancer treatments. Existing cancer detection technologies, for example, CA125, CA 19.9, CT, MRI, and others, are either not highly sensitive or specific enough for early detection. Recent technological development of "liquid biopsy" research led to more sensitive biomarkers. Newly developed multiple-cancer early-detection tests can screen up to multiple cancers in asymptomatic individuals with one blood draw. These tests, however, might pose significant challenges in our clinical practice. This paper highlights the issues we face and how to solve their problems.

Keywords: Cancer detection test; Biomarkers; MCED tests; NHS-Galleri trial

1. Introduction

Early cancer detection tests might open a new era of cancer detection resulting in a better prognosis for cancer treatment. Not uncommonly, we have been disappointed by various promising discoveries to detect early cancers at their times. Still, they are either not highly sensitive or specific enough for early cancer detection. Examples are CA125, HE4, CA 19.9, CT, MRI, and others. Technology development enables blood "liquid biopsy" research to develop more sensitive biomarkers (1). The challenge of taking blood for early cancer detection may be revisited because new cancer detection tests are available. These new tests might pose considerable challenges to our clinical practice.

Currently, only a few cancers, like the breast, colon/rectum, prostate, and lung, have established screening protocols such as mammograms for breast cancer, stool tests, and colonoscopy for large bowel cancer, the blood PSA for prostate cancer, and low-dose CT scans for lung cancer. However, these screening protocols using existing cancer markers are neither sensitive nor specific for early-stage cancer. Besides, subsequent investigations and invasive procedures might create more harm. Also, many cancers still do not have early-detection tests.

2. Multiple-cancer early-detection tests

On the other hand, a newly developed multiple-cancer early-detection test has emerged that screens up to 50 cancers in asymptomatic individuals with one blood draw (2). This Multiple-Cancer Early Detection (MCED) test can detect fragments of circulating free DNA/RNA shed by cancers and released into the bloodstream. Detecting fragments of DNA/RNA genomic mutations in the circulation might imply the presence of cancer in the body (3). Circulating tumor cells (CTCs) shredded from the primary and secondary tumors can also be detected from liquid blood or urine biopsies (4-7). The cancer cells can be further utilized to generate human-derived tumor models for drug efficacy and high throughput screening assessment(8, 9). In 2004, FDA approved an assay using magnetophoretic separation using ferromagnetic microparticles with antibodies targeting epithelial markers for clinical use (Cellsearch)(10). A positive

* Corresponding author: Felix Wu Shun WONG

test would indicate that an individual has cancer before developing symptoms in all the above circumstances. A multiple-cancer detection blood test (Galleri) has also been commercialized (2). There are also efforts to introduce label-free technologies to identify patients at high cancer risk based on proliferative capabilities (9), biochemical cues (11), and physical attributes (4) to complement conventional screens with automated analysis for robust and high throughput screening (8). However, since its introduction, many cancer specialists warn that we might not be ready to endorse these new cancer detection tests.

2.1. Issues arising from new cancer detection tests

- Cancer specialists to whom patients with positive tests are referred will have problems managing these patients. For them, there is a need for more diagnostic and treatment resources and infrastructures to cope with the rising number of people identified by the tests to have early cancers.
- There should be more guidelines to agree on who will be tested, when, how, and where a test will be carried out, and to anticipate the long-term investigative follow-up and psychological support necessary once there is a positive test.
- The Multiple-Cancer detection tests still do not have high sensitivity and specificity for cancer detection.
- Doctors dealing with patients after a test should need a background in genetic testing to order or interpret the test findings.
- More medico-legal conflicts could arise from having the tests, e.g., failure to investigate adequately, inadequate follow-up, erroneous advice, financial loss, or treatment delay.
- The government has to provide more resources for education forums to clarify any questions or confusion about the tests; doctors must understand the tests before recommending them to their patients.
- Because they are genetic tests, there is an implication that a genetic counselor should be consulted whenever it is necessary for doctors and patients.
- Likely, many insurance companies would not reimburse out-of-pocket bills for a patient's tests and investigations at this stage. A test should not be available only to people who can afford it can get the tests.

2.2. Validation is necessary

Taking the blood from patients for the tests is easy, but these tests are so new that most hospitals and doctors need medical guidelines about investigating a positive test and whether or not to have more tests. At this stage, to promote cancer detection tests, they need to be validated by large and randomized studies. As expected, there are at least 17 clinical trials on the clinical utility of these commercialized MCED tests. The National Health Service (NHS)-*Galleri* trial is the largest randomized, controlled clinical trial conducted in England to validate the usefulness of the MCED tests. The trial includes 140,000 participants receiving the MCED Galleri from NHS, United Kingdom, where participants will be followed for three years with annual visits at 12 and 24 months (12).

3. Conclusion

Although we are not ready to endorse the MCED tests to replace traditional cancer screening, it might supplement current screening tests to help find other cancers for which no proven screening tests exist. Understandably, more new tests are coming because of rapid technological developments. In many big places, a working group should be set up to prepare themselves and make ready to validate and manage these new tests, the patient's anxiety, and all the social complexities that arise with them.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors declare no conflict of interest.

References

[1] Klein E, Richards D, Cohn A, Tummala M, Lapham R, Cosgrove D, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Annals of Oncology. 2021; 32(9):1167-77.

[2] Grail. Galleri - GRAIL's multi-cancer early detection test. https://wwwgallericom. 2021.

[3] Bredno J, Venn O, Chen X, Freese P, Ofman JJ. Circulating Tumor DNA Allele Fraction: A Candidate Biological Signal for Multi-Cancer Early Detection Tests to Assess the Clinical Significance of Cancers. The American Journal of Pathology. 2022; 192(10).

[4] Khoo BL, Bouquerel C, Durai P, Anil S, Goh B, Wu B, et al. Detection of Clinical Mesenchymal Cancer Cells from Bladder Wash Urine for Real-Time Detection and Prognosis. Cancers (Basel). 2019; 11(9).

[5] Warkiani ME, Khoo BL, Wu L, Tay AK, Bhagat AA, Han J, et al. Ultra-fast, label-free isolation of circulating tumor cells from blood using spiral microfluidics. Nat Protoc. 2016; 11(1):134-48.

[6] Haber DA, Velculescu VE. Blood-based analyses of cancer: circulating tumor cells and circulating tumor DNA. Cancer Discov. 2014; 4(6):650-61.

[7] Yu M, Bardia A, Aceto N, Bersani F, Madden MW, Donaldson MC, et al. Cancer therapy. Ex vivo culture of circulating breast tumor cells for individualized testing of drug susceptibility. Science. 2014; 345(6193):216-20.

[8] Li W, Zhou Y, Deng Y, Khoo BL. Early Predictor Tool of Disease Using Label-Free Liquid Biopsy-Based Platforms for Patient-Centric Healthcare. Cancers (Basel). 2022; 14(3).

[9] Khoo BL, Grenci G, Jing T, Lim YB, Lee SC, Thiery JP, et al. Liquid biopsy and therapeutic response: Circulating tumor cell cultures for evaluation of anticancer treatment. Sci Adv. 2016; 2(7):e1600274.

[10] Riethdorf S, Fritsche H, Muller V, Rau T, Schindlbeck C, Rack B, et al. detection of circulating tumor cells in peripheral blood of patients with metastatic breast cancer: a validation study of the CellSearch system. Clin Cancer Res. 2007; 13(3):920-8.

[11] Zhang J, Chua SL, Khoo BL. Worm-Based Microfluidic Biosensor for Real-Time Assessment of the Metastatic Status. Cancers (Basel). 2021; 13(4).

[12] GRAIL. GRAIL and UK Government to Make Galleri Multi-Cancer Early Detection Blood Test Available to Patients. https://grailcom/press-releases/grail-and-uk-government-to-make-galleri-multi-cancer-early-detection-blood-test-available-to-patients/. 2020.