Underweight, underdetected: does cachexia reduce liquid biopsy positivity in cancer?

Abstract Submitter: Fouad Attieh, Lebanon*

Co-Authors: Marc Boutros, Hampig Raphaël Kourie

*Hôtel-Dieu de France

Abstract

Background: Liquid biopsy is an emerging biomarker increasingly utilized across various malignancies. The detection of circulating tumor DNA (ctDNA) in blood samples aids in cancer diagnosis, prognosis, and clinical monitoring. However, 10–50% of cancer patients are underweight (BMI <18.5), yet no studies have explored the potential impact of low BMI on liquid biopsy detection rates.

Objective: The aim of this study is to determine whether liquid biopsy results are influenced by cachexia and low BMI, in terms of positivity, ctDNA load and sequenced mutations.

Methods: This study analyzed liquid biopsy results from the Discovery, Validation and Generalizability MSK-ACCESS ctDNA sequencing cohort. Patients with available ctDNA status, Variant Allele Frequency (VAF) concentration, and BMI data were included. They were categorized into two groups: underweight (BMI <18.5) and normal weight (BMI 18.5–24.9). The analysis compared ctDNA positivity rates, mean VAF concentration, and conducted a sub-analysis based on cancer type.

Results:

The MSK-ACCESS ctDNA sequencing cohort includes 5,928 patients, of whom 4,650 have available ctDNA, variant allele frequency (VAF), and BMI data. These patients were categorized into underweight (N=430) and normal weight (N=1,846) groups. The underweight group exhibited a lower ctDNA positivity rate compared to the normal weight group (49% vs. 63%, $p<0.0001$). Additionally, the mean log10(max VAF) was significantly lower in the underweight group (-3.343 vs. -2.862, $p<0.001$). A heatmap sub-analysis further revealed that specitic mutation detection rates within the same cancer type are influenced by weight category.

Conclusion:

These findings underscore the importance of considering cachexia when performing liquid biopsy testing in cancer patients. Underweight individuals are more likely to have negative ctDNA results, lower VAF concentrations, and potentially distinct mutation profiles compared to normal weight patients.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.