Prognostic Significance of Blood-based Cancer Detection in Plasma Cell-free DNA (cfDNA): Evaluating Risk of Overdiagnosis

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BACKGROUND
- Early detection of cancers can save lives, often cure patients quickly, and improve quality of life.
- Current cancer screening approaches can miss cancers or detect them late when they are harder to treat.
- Blood-based detection of cancer has the potential to identify cancer early in its stages, improving outcomes.

METHODS
- Patients in the Circulating Cell-free Genome Atlas (CCGA) substudy had their blood drawn and underwent genome sequencing with a high specificity to detect cfDNA.
- Participants were categorized into two groups: those with cancer and those without cancer.
- The primary outcome was the ability of cfDNA detection to predict cancer risk.
- Statistical analyses were performed to assess the prognostic significance of cfDNA detection.

RESULTS
- Sensitivity was higher in participants with cancer who died during follow-up (506/20,406, 38%) than those who were alive (1534/20,406, 100%).
- The median follow-up duration was 12.9 months.
- Detection using this methylation assay was more prognostic than detection by screening, and more sensitive in identifying high-risk cancers, than USPSTF-recommended screening.

CONCLUSIONS
- cfDNA-based detection using a methylation assay had a worse prognosis than cancers not detected, indicating the need for additional research.
- Methylation-based cancer detection can improve the sensitivity of cancer detection, reducing the risk of overdiagnosis.
- These findings highlight the potential of cfDNA as a promising tool for early detection and risk assessment.

Figure 1. CCGA Study Design

Figure 2. Methylation Assay Detection in (A) Stage I, (B) Stage II, (C) Stage III, and (D) Stage IV Cancers

Figure 3. Survival by Methylation Assay Detection in (A) Onco-delived Cancers, (B) Onco-detected Cancers, and (C) Symptom-based Clinical Presentation-detected Cancers (cfDNA, WBCs)

Figure 4. Detection by the Methylation Assay Compared to (A) Clinical Presentation-detected Cancers, (B) Symptom-based Clinical Presentation-detected Cancers, and (C) Best-guess Clinical Diagnosis

Figure 5. Follow-up for 5 yrs

Figure 6. Survival by Methylation Assay Detection in (A) Stage I, (B) Stage II, (C) Stage III, and (D) Stage IV Cancers

Figure 7. Prognostic significance of blood-based cancer detection in plasma cell-free DNA (cfDNA): evaluating risk of overdiagnosis.