ABSTRACT

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Circulating Tumor DNA in Adults With Glioma: A Systematic Review and Meta-Analysis of Biomarker Performance.

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BACKGROUND: Circulating tumor DNA (ctDNA) has emerged as a promising noninvasive biomarker to capture tumor genetics in patients with brain tumors. Research into its clinical utility, however, has not been standardized because the sensitivity and specificity of ctDNA remain undefined.

OBJECTIVE: To (1) review the primary literature about ctDNA in adults with glioma to compare the sensitivity and specificity of ctDNA in the cerebrospinal fluid vs the plasma and (2) to evaluate the effect of tumor grade on detection of ctDNA.

METHODS: PRISMA-guided systematic review and meta-analysis was performed using published studies that assessed ctDNA in either plasma or cerebrospinal fluid among adult patients with confirmed glioma. Summary receiver operating characteristic curves were generated using the Rücker-Schumacher method, and area under the curve (AUC) was calculated.

RESULTS: Meta-analysis revealed improved biomarker performance for CSF (AUC = 0.947) vs plasma (AUC = 0.741) ctDNA, although this did not reach statistical significance (P = .141). Qualitative analysis revealed greater sensitivities among single-allele PCR and small, targeted next-generation sequencing panels compared with broader panels. It additionally demonstrated higher sensitivity of ctDNA detection in high-grade vs low-grade gliomas, although these analyses were limited by a lack of specificity reporting in many studies.

CONCLUSION: ctDNA seems to be a highly sensitive and specific noninvasive biomarker among adults with gliomas. To maximize its performance, CSF should be studied with targeted genetic analysis platforms, particularly in high-grade gliomas. Further studies on ctDNA are needed to define its clinical utility in diagnosis, prognostication, glioblastoma pseudoprogression, and other scenarios wherein neoadjuvant therapies may be considered.

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