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Glioblastoma treatment, end-of-life resource utilization, and outcomes in Ontario

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Background: The end-of-life (EoL) phase of care is pivotal for glioblastoma (GBM) patients. While early integration of palliative care has shown benefits in various cancer types, its role in GBM care remains underexplored. This study aims to characterize EoL care patterns in GBM patients, assessing their temporal evolution, regional disparities, and socioeconomic influences. Methods: This is retrospective study of all patients with GBM treated in Ontario between 1994 and 2018 using the ICES data repository. Variables analyzed included patient demographics, comorbidities, palliative care utilization, and aggressive/supportive care components. Results: We identified 9,013 GBM patients within the study period. There was a gradual increase in palliative care utilization over time, accompanied by a decrease in in-hospital deaths. However, the proportion of patients receiving chemotherapy in the last 14 days of life increased. Multivariate logistic regression found socioeconomic status influenced palliative care access and rural patients also had a higher rate of in-hospital deaths, possibly due to limitations in outpatient palliative care services. Conclusions: The findings in this study clarify the status of EoL care for GBM patients within Ontario, and demonstrates key areas for future research, underscoring the need for standardized EoL care practices to enhance the quality of care for GBM patients.

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Transfer RNA fragments in patient plasma extracellular vesicles as biomarkers of high grade glioma

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Background: High-grade gliomas (HGG) present challenges with short post-surgery survival and high progression rates. Extracellular vesicles (EVs) in the tumor microenvironment (TME) contribute to a pro-tumorigenic setting. Investigating Transfer RNA fragments (TfRNA) in HGG patient plasma EVs reveals potential biomarkers and therapeutic targets, shedding light on the molecular landscape for enhanced diagnostic and therapeutic strategies. This study examines TfRNA in 10 HGG patients at diagnosis, offering insights into the molecular landscape for improved management strategies. Methods: The study involved the collection of plasma samples from HGG patients and controls. EVs were isolated from these samples and subsequently analyzed for tfRNA. Results: Analysis of plasma EVs highlighted distinct differences in TfRNA fragments between High-Grade Glioma (HGG) and control samples. HGG EVs showed a global reduction in tRNA content, higher 5' tfRNA proportions, and increased nuclear tfrna compared to controls. A notable biological marker, elevated in HGG, holds potential as a diagnostic indicator. Conclusions: Our study concludes that High-Grade Gliomas (HGG) demonstrate a global reduction in tfRNA content in plasma extracellular vesicles compared to non-cancer controls, echoing findings in other cancers. Despite this, specific tfRNA molecules in HGG show significant differential expression or sorting into EVs, indicating their potential as future biomarkers or therapeutic targets.

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Plasma extracellular vesicle sampling from high grade gliomas demonstrates a small RNA signature indicative of disease and identifies lncRNA RPPH1 as a novel biomarker

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Background: High grade gliomas (HGGs) and cells of the tumour microenvironment secrete extracellular vesicles (EVs) into the plasma that contain genetic and protein cargo which function in paracrine signalling. Isolation of these EVs and their cargo could lead to an important tool that can inform on diagnosis and disease-course of HGGs. Methods: EVs were isolated using Vn96 capture from plasma obtained longitudinally from HGG patients. sRNA was enriched from the EVs, followed by next-generation sequencing, multidimensional scaling, differential expression, and *in silico* functional enrichment analyses. Results: Over 750 differentially expressed sRNA were identified between HGG and controls. Pathway analysis revealed miRNA highly enriched in both EV and HGG pathways demonstrating the validity of results in capturing a signal from HGG. Other sRNA included several novel HGG plasma-EV biomarkers including lncRNA *RPPH1*, *RNY4,* and *RNY5*. Furthermore, in paired longitudinal patient sampling, *RPPH1* informed on surgical resection (decreased on resection) and importantly increased again with clinically defined progression. TCGA analysis demonstrated increased expression of *RPPH1* in HGG tissue and additionally, higher expression of *RPPH1* was associated with a worse disease-specific prognosis. Conclusions: The present study supports the role of plasma-EV sRNA sampling (and particularly *RPPH1*) as part of a multi-pronged approach to HGG disease course surveillance.

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Integration of Ultrasensitive electroluminescent immunoassay and cell-free DNA methylation analysis for the non-invasive discrimination of adult diffuse gliomas

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Background: Gliomas are highly aggressive brain tumors with nearly universal recurrence rate. Despite this, the ability to accurately predict tumor recurrence relies solely on serial MRI imaging, highlighting the need for prognostic biomarkers. Due to