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RISK FACTORS FOR INTRACRANIAL HEMORRHAGE: AN UMBRELLA REVIEW TO INFORM MACHINE LEARNING PREDICTION MODELS IN GLIOMA PATIENTS RECEIVING ANTICOAGULATION

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Introduction. People with glioma (PwG) requiring anticoagulation face high intracranial haemorrhage (ICH) risk due to tumour neovascularity and blood–brain barrier disruption. Current anticoagulation decisions rely largely on risk models derived from non-cancer populations, with limited validation in brain tumour cohorts.

Aim. To synthesise ICH risk factors across clinical populations, identify cancer-specific evidence gaps, and establish a framework to support algorithm development for predicting haemorrhage risk in anticoagulated PwG.

Methods. Systematic searches of Embase, MEDLINE, and the Cochrane Central Library were conducted to November 2024 to identify systematic reviews reporting quantified associations between risk factors and intracranial haemorrhage. Following quality assessment using AMSTAR2, extracted associations were classified into nine clinical domains to support structured candidate predictor selection for subsequent validation in glioma populations.

Results. Seventy-nine reviews reporting 324 unique associations were synthesised. Anticoagulant class showed the strongest and most consistent influence on haemorrhage risk. Direct oral anticoagulants were associated with substantially lower intracranial haemorrhage risk than vitamin K antagonists and low-molecular-weight heparin across multiple populations, including brain tumour cohorts. Vitamin K antagonists markedly increased risk in patients with cerebral microbleeds. Dual antiplatelet therapy and polypharmacy further amplified haemorrhagic risk. Several commonly used co-medications were associated with increased risk, including selective serotonin reuptake inhibitors and statins in acute stroke populations, with genetic modifiers such as APOE variants strongly influencing statin-related haemorrhage risk.

Conclusions. Medication-related factors dominate intracranial haemorrhage risk profiles, with anticoagulant class and drug interactions exerting major effects. These findings support the prioritisation of anticoagulant selection and medication burden as core features in future prediction models for anticoagulated glioma patients. Prospective validation in brain tumour cohorts remains essential.Keywords: Intracranial haemorrhage, glioma, anticoagulation, direct oral anticoagulants, bleeding risk, drug interactions