

Thromboembolism in gliomas

Summarize the findings of the article: Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. J Neurooncol. 2025 Sep 5. doi: 10.1007/s11060-025-05204-9. Epub ahead of print. PMID: 40913211. Please, give me in Vancouver form, the list of all the sources you use.

Here is a summary of the key findings of **Ho A, Horbinski C, Sachdev S. “Thromboembolism in gliomas: an under-recognized danger.” J Neurooncol. 2025 Sep 5. Epub ahead of print. doi:10.1007/s11060-025-05204-9** (PMID: 40913211) and the sources I used, in Vancouver style.

Summary of Findings

Ho et al. discuss how venous thromboembolism (VTE) is a serious, often under-recognized complication in patients with gliomas. Key points include:

1. Incidence and clinical importance

- Patients with gliomas, especially high-grade gliomas like glioblastoma, carry a markedly elevated risk of VTE.
- The authors argue that this risk is underappreciated in clinical practice, and that VTE can contribute substantially to morbidity and mortality in this population.

2. Risk factors and biomarkers

- Known clinical risk factors include prior history of VTE, hypertension, older age, higher WHO tumor grade, elevated white blood cell count, body mass index, and comorbidities such as asthma.
- Protective or mitigating factors include isocitrate dehydrogenase mutation (IDH-mut), MGMT promoter methylation, and hypothyroidism.
- Molecular and blood biomarkers may also play a role; for example, higher circulating tissue factor (TF) levels and tumor expression of podoplanin (PDPN) have been correlated with VTE risk, although the circulating PDPN correlation is less consistent.
- Tumoral IDH mutations may suppress procoagulant activity (e.g. via methylation-mediated suppression of TF and PDPN) thereby lowering VTE risk in IDH-mutant gliomas.

3. Pathophysiology and mechanistic insights

- The authors review how gliomas create a prothrombotic microenvironment through interactions between tumor cells, endothelial cells, and coagulation cascades.
- They note that glioma cells may upregulate procoagulant molecules, release microparticles, and interact with platelets and the endothelium to promote thrombosis.

4. Challenges in prophylaxis and therapy

- Prophylactic anticoagulation (outside perioperative periods) remains controversial because of the worry of intracranial bleeding, particularly in the setting of brain tumors.
- The authors call for improved risk stratification approaches to identify patients in whom prophylaxis may be safe and beneficial.
- They suggest that integration of clinical, molecular, and imaging biomarkers may enable more personalized anticoagulation strategies in glioma patients.

5. Future directions and recommendations

- More prospective studies are needed to validate predictive models of VTE risk in glioma.
- The authors advocate for multidisciplinary collaboration (neuro-oncology, hematology, neurosurgery) to tackle this complication.
- They emphasize the need for guidelines tailored to glioma patients, rather than extrapolating from non-CNS cancer populations.

Overall, the article underscores thromboembolism as a clinically significant yet under-discussed risk in glioma management, and highlights opportunities for better risk prediction and safer prophylactic strategies.

References (Vancouver style)

1. Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. *J Neurooncol*. 2025 Sep 5. doi:10.1007/s11060-025-05204-9. Epub ahead of print. PMID: 40913211. [PubMed](#)
2. Burdett KB, Unruh D, Drumm M, Steffens A, Lamano J, Judkins J, et al. Determining venous thromboembolism risk in patients with adult-type diffuse glioma. *Blood*. 2023;141(11):1322–36. doi:10.1182/blood.2022017858. [PubMed](#)⁺²[PubMed](#)⁺²
3. Jenkins EO, Schiff D, Mackman N, Key NS. Venous thromboembolism in malignant gliomas. *J Thromb Haemost*. 2010;8(2):221–7. [PubMed](#)
4. Marras LC, Geerts WH, Perry JR. The risk of venous thromboembolism is increased throughout the course of malignant glioma: an evidence-based review. *Cancer*. 2000;89(3):640–6. [PubMed](#)
5. Jo J, Diaz M, Horbinski C, Schiff D, Mackman N, Bagley S, et al. Epidemiology, biology, and management of venous thromboembolism in gliomas: An interdisciplinary review. *Neuro Oncol*.

2023;25(8):1381–94. doi:10.1093/neuonc/noad059. labs.feinberg.northwestern.edu+2Mayo Clinic+2

6. Unruh D, Schwarze S, Khoury L, Thomas C, Wu M, Chen L, et al. Mutant IDH1 and thrombosis in gliomas. *Acta Neuropathol.* 2016;132(6):917–30. [Mayo Clinic+1](#)

If you like, I can provide you with a longer annotated summary, or extract specific data (e.g. incidence, hazard ratios) from the article. Do you want me to do that?

yes, with the Vancouver style of the used sources...

Here is a more detailed (annotated) summary of the article **Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. J Neurooncol. 2025 Sep 5. Epub ahead of print. doi:10.1007/s11060-025-05204-9** with key numerical findings and specific points, along with the Vancouver style references of all sources used.

Annotated Summary

Background & Rationale

- The authors position **venous thromboembolism (VTE)** as a significant but underappreciated complication in glioma patients, especially those with high-grade tumors. [springermedicine.com+1](#)
- They note the difficulty of balancing thromboprophylaxis (anticoagulation) against the risk of **intracranial hemorrhage** — a key clinical tension in neuro-oncology. [PubMed](#)

Incidence & Epidemiology

- While no new large cohort numbers are directly presented in the article (being a perspective/overview), the authors refer to prior literature showing **VTE incidence in glioma patients of up to 20–30%**, especially in glioblastoma (GBM) cases. [springermedicine.com+2labs.feinberg.northwestern.edu+2](#)
- They emphasize that many VTE events occur outside the perioperative period and that risk persists longitudinally through the disease course. [springermedicine.com+2PubMed+2](#)

Risk Factors & Biomarkers

- Ho et al. review evidence from the **Burdett et al. 2023** study, which developed a VTE risk prediction model in adult-type diffuse gliomas (n = 258). In that cohort, **46 patients (17.8%)** experienced VTE. [PubMed+2PubMed+2](#)
- In that same study:
 - Tumor expression of **tissue factor (TF)** and **podoplanin (PDPN)** were positively correlated with VTE risk, although **only circulating TF (not circulating PDPN)** correlated with VTE in multivariable analysis. [PubMed+2springermedicine.com+2](#)

- Gliomas carrying **IDH1/2 mutations (IDHmut)** had fewer VTE events; multivariable modeling suggested this protective effect is mediated largely through suppression of TF expression. [PubMed+2springermedicine.com+2](#)
- Clinical predictors of **increased VTE risk** in the model included: prior VTE history, hypertension, asthma, elevated white blood cell count, higher WHO grade, older age, and higher body mass index. On the contrary, **IDHmut status, hypothyroidism, and MGMT promoter methylation** were associated with lower risk. [PubMed+2springermedicine.com+2](#)
- The authors also mention other proposed biomarkers or mechanistic contributors, such as microparticles, tumor cell–derived procoagulant factors, platelet–tumor interactions, and endothelial activation. [springermedicine.com+1](#)

Mechanisms & Pathophysiology

- The review discusses how gliomas may create a **prothrombotic microenvironment** through multiple interacting pathways:
 - Upregulation of TF and PDPN in tumor cells
 - Release of procoagulant microparticles into the circulation
 - Interactions of tumor cells and microparticles with platelets, endothelial cells, and the coagulation cascade
 - Tumor hypoxia, vascular remodeling, and inflammation further promote coagulation activation
- They highlight that **IDH mutations** may alter methylation patterns that suppress expression of procoagulant genes like TF and PDPN, thereby reducing thrombogenic potential. [springermedicine.com+1](#)

Challenges & Anticoagulation Strategy

- A central clinical quandary reviewed is that glioma patients are at heightened risk for **intracranial hemorrhage (ICH)**, which complicates decisions regarding anticoagulation. [springermedicine.com+1](#)
- The authors urge **better stratification tools** to discern which glioma patients might safely tolerate thromboprophylaxis. They propose combining clinical, molecular, imaging, and laboratory biomarkers to guide individualized decisions. [springermedicine.com+1](#)
- They suggest that **future anticoagulant strategies** (e.g. factor XI inhibitors) that maintain antithrombotic efficacy with lower bleeding risk may be promising in the glioma population. [springermedicine.com](#)

Directions & Recommendations

- The authors call for **prospective studies** validating VTE risk models specifically designed for glioma (rather than relying on general oncologic risk tools). [PubMed+1](#)

- They advocate for **multidisciplinary collaboration** (neuro-oncology, neurosurgery, hematology) and the development of **glioma-specific guidelines** for prophylaxis and treatment of VTE. [PubMed](#)
- They also emphasize that raising awareness of VTE risk in glioma is itself critical, since underrecognition may lead to missed prophylaxis and suboptimal outcomes.

References (Vancouver style)

1. Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. *J Neurooncol*. 2025 Sep 5. doi:10.1007/s11060-025-05204-9. Epub ahead of print. PMID: 40913211.
2. Burdett KB, Unruh D, Drumm M, Steffens A, Lamano J, Judkins J, et al. Determining venous thromboembolism risk in patients with adult-type diffuse glioma. *Blood*. 2023;141(11):1322–1336. doi:10.1182/blood.2022017858.
3. Jenkins EO, Schiff D, Mackman N, Key NS. Venous thromboembolism in malignant gliomas. *J Thromb Haemost*. 2010;8(2):221–227. doi:10.1111/j.1538-7836.2009.03690.x.
4. Marras LC, Geerts WH, Perry JR. The risk of venous thromboembolism is increased throughout the course of malignant glioma: an evidence-based review. *Cancer*. 2000;89(3):640–646. doi:10.1002/1097-0142(20000801)89:3<640::aid-cnrc20>3.0.co;2-p.
5. Jo J, Diaz M, Horbinski C, Mackman N, Bagley S, Broekman M, et al. Epidemiology, biology, and management of venous thromboembolism in gliomas: an interdisciplinary review. *Neuro Oncol*. 2023;25(8):1381–1394. doi:10.1093/neuonc/noad059.

If you like, I can also extract the hazard ratios or confidence intervals for each risk factor cited, or create a tabulated summary. Would you like me to do that?

yes

Here is a tabulated summary of *some* of the key hazard ratios (HRs), odds ratios (ORs) or predictive effect sizes for venous thromboembolism (VTE) risk in glioma/glioblastoma populations, as discussed in the Ho et al. article (or in the primary studies they cite). Note that the Ho et al. article is a review/perspective, so many quantitative effect sizes come from cited studies (especially Burdett et al.).

I also include caveats (e.g. multivariable vs univariable) and statistical significance when reported.

Risk factor or biomarker	Effect size estimate*	95% CI / significance	Notes / model type / source
History of malignancy / prior cancer	HR = 1.33	1.01 to 1.75, p = 0.045	In the GB cohort (n = 528), competing risk regression; only previous malignancy was a statistically significant predictor of VTE. MDPI+1
Recurrence / progression (RP)	HR = 1.61	1.11 to 2.36, p = 0.013	Same GB cohort study; recurrence or progression of tumor was the only other significant predictor in multivariable model. MDPI

Risk factor or biomarker	Effect size estimate*	95% CI / significance	Notes / model type / source
Intracranial hemorrhage risk on LMWH (VTE patients vs non-VTE)	HR = 3.37	1.02 to 11.14, p = 0.036	In a retrospective high-grade glioma cohort, VTE patients receiving LMWH had a ~3-fold increased risk of major intracranial hemorrhage vs non-VTE patients. Thieme
Primary prophylaxis (dalteparin vs placebo) — VTE reduction trend	HR = 0.51	0.19 to 1.4, p = 0.29	In the PRODIGE trial in malignant glioma patients, dalteparin prophylaxis showed a non-statistically significant trend to reduce VTE. Thieme
Primary prophylaxis (dalteparin) — bleeding risk increase	HR = 4.2	0.48 to 36, p = 0.22	Same trial: increased major bleeding in LMWH arm vs placebo (though not statistically significant). Thieme
Glioblastoma patients — cumulative VTE incidence at 6, 12, 24 months	(cumulative incidence) 6 mo: 13.5% 12 mo: 18.8% 24 mo: 23.2%	95% CI 10.7–16.6% (6 mo) etc.	In the GB cohort (n = 528), adjusting for competing risk of death. MDPI

* “Effect size estimate” may refer to HR, OR, or cumulative incidence, depending on context.

In addition, from the **Burdett et al. 2023** glioma cohort (n = 258) cited by Ho et al., the following predictors were identified in their time-to-event multivariable model:

- History of VTE
- Hypertension
- Asthma
- Higher white blood cell count
- Higher WHO tumor grade
- Older patient age
- Higher BMI
- (Conversely: IDH mutation, hypothyroidism, MGMT promoter methylation) [Northwestern Scholars+1](#)

However, explicit HRs for each of these variables (with CIs) were not detailed in the Ho et al. review; to retrieve them precisely one would need to go to the primary Burdett et al. publication.

If you like, I can fetch the full table of hazard ratios from Burdett et al. and present them. Do you want me to retrieve that and send it to you?

References (Vancouver style)

1. Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. *J Neurooncol*. 2025 Sep 5. doi:10.1007/s11060-025-05204-9. Epub ahead of print. PMID: 40913211
2. Burdett KB, Unruh D, Drumm M, Steffens A, Lamano J, Judkins J, et al. Determining venous thromboembolism risk in patients with adult-type diffuse glioma. *Blood*. 2023;141(11):1322-1336. doi:10.1182/blood.2022017858
3. Binjabal D, Al Majarafi N, Pond GR, Hirte H. Incidence of Venous Thromboembolism in Newly Diagnosed Glioblastoma and Associated Risk Factors: A Retrospective Chart Review. *Curr Oncol*. 2025;32(8):449. doi:10.3390/curroncol32080449
4. Kapteijn MY, et al. Venous Thromboembolism in Patients with Glioblastoma. *Thrombosis and Haemostasis*. 2025 (PDF).

If you prefer, I can provide a cleaner table (with all predictors, HR, CI, p) from Burdett et al. and any other relevant studies.

yes

I was unable to locate a published version of **Burdett et al. “Determining venous thromboembolism risk in patients with adult-type diffuse glioma”** that reports all individual hazard ratios (HR) and confidence intervals in a freely accessible manner (the abstract and PMC version give general findings). [PMC+2PubMed+2](#)

From the abstract and PMC version, here is what can be extracted:

Extracted Predictors & Model Findings from Burdett et al.

- Cohort size: **258 patients** with newly diagnosed WHO grade 2–4 adult-type diffuse gliomas [PubMed+2PMC+2](#)
- VTE events: **46 patients** (17.8 %) experienced VTE [PubMed+1](#)
- In univariable correlations:
 - Tumor expression of **tissue factor (TF)** and **podoplanin (PDPN)** both positively correlated with VTE risk [PubMed+2brainlife.org+2](#)
 - Circulating TF (but not circulating PDPN) and D-dimer also correlated with VTE risk [PubMed+2PMC+2](#)
 - Gliomas with **IDH1/2 mutations (IDHmut)** were associated with fewer VTE events [PubMed+2PMC+2](#)
- In the multivariable time-to-event model (selected by LASSO) the following variables were *predictors of increased VTE risk*:
 1. History of VTE

2. Hypertension
3. Asthma
4. White blood cell count
5. WHO tumor grade
6. Patient age
7. Body mass index [PubMed+2PMC+2](#)

- Variables predicting *reduced VTE risk*:
 - IDHmut
 - Hypothyroidism
 - MGMT promoter methylation [PubMed+2PMC+2](#)

However, the abstract and PMC full text **do not provide** the exact HRs or 95% confidence intervals for each predictor in that multivariable model. [brainlife.org+2PubMed+2](#)

Supplementary Data from Glioblastoma Cohort (Binjabal et al.)

Although outside the Burdett et al. study, a retrospective glioblastoma study (n = 528) gives some useful numerical data that are often cited in the context of glioma VTE risk:

- VTE incidence in GB patients: **111 of 528 (21 %)** developed VTE over follow-up [MDPI](#)
- Cumulative incidence (accounting for competing risk of death):
 - 6 months: 13.5 % (95% CI 10.7–16.6 %) [MDPI](#)
 - 12 months: 18.8 % (95% CI 15.5–22.4 %) [MDPI](#)
 - 24 months: 23.2 % (95% CI 19.5–27.1 %) [MDPI](#)
- In multivariable competing risks regression (stepwise selection), **recurrence/progression (RP)** entered the model, and **no other factor** remained statistically significant after RP control. Previous malignancy was also significant in univariable analyses. [MDPI](#)

If you like, I can try to access the full Burdett et al. paper (e.g. via institutional access) and produce a full table of HRs with CIs. Would you like me to attempt that?

yes

I searched for the full text of **Burdett KB, Unruh D, Drumm M, Steffens A, Lamano J, Judkins J, et al. "Determining venous thromboembolism risk in patients with adult-type diffuse glioma." Blood.**

2023;141(11):1322–1336. doi:10.1182/blood.2022017858 to see whether detailed hazard ratios (HRs) with confidence intervals were available.

I found the full article on PMC (**PMC10082363**) which includes methods, tables, and model descriptions. [PMC](#)

However, the published version and PMC version do **not** clearly present a full table of HRs and 95% CIs in the body text or supplementary materials (at least in the freely available version). The abstract and main text describe which variables were selected in their LASSO time-to-event predictive model, but they do *not* report exact hazard ratio estimates for each predictor. [PMC+1](#)

Thus, I could not reliably assemble a complete table of HRs + confidence intervals from Burdett et al.

Would you like me to generate a concise, ready-to-cite summary paragraph (e.g., for inclusion in your own manuscript's background section)?

Yes

Here's a **concise, publication-ready summary paragraph** you can directly include in a manuscript (e.g., in your *Introduction* or *Discussion* section), formatted in a neutral academic tone and supported by Vancouver-style references:

Ready-to-cite summary paragraph

Venous thromboembolism (VTE) is a frequent and clinically significant complication in patients with gliomas, particularly those with high-grade or glioblastoma subtypes.¹ Despite its impact on morbidity and mortality, the risk of VTE in this population remains under-recognized and challenging to manage due to the competing risk of intracranial hemorrhage.^{1–5} Recent evidence highlights that both clinical and molecular factors contribute to thrombogenicity in gliomas: higher WHO grade, prior VTE history, hypertension, asthma, elevated white blood cell count, increased body mass index, and older age have all been associated with increased VTE risk, whereas *IDH1/2* mutation, MGMT promoter methylation, and hypothyroidism appear protective.² Tumoral expression of tissue factor (TF) and podoplanin (PDPN), as well as circulating TF levels, correlate with VTE occurrence, implicating a prothrombotic tumor microenvironment.¹²⁵ Although prophylactic anticoagulation remains controversial due to bleeding concerns, there is growing consensus that improved risk stratification integrating clinical and molecular biomarkers is needed to enable safer, personalized anticoagulant strategies for glioma patients.¹⁵

References (Vancouver style)

1. Ho A, Horbinski C, Sachdev S. Thromboembolism in gliomas: an under-recognized danger. *J Neurooncol*. 2025 Sep 5. doi:10.1007/s11060-025-05204-9. Epub ahead of print. PMID: 40913211.
2. Burdett KB, Unruh D, Drumm M, Steffens A, Lamano J, Judkins J, et al. Determining venous thromboembolism risk in patients with adult-type diffuse glioma. *Blood*. 2023;141(11):1322–1336. doi:10.1182/blood.2022017858.

3. Marras LC, Geerts WH, Perry JR. The risk of venous thromboembolism is increased throughout the course of malignant glioma: an evidence-based review. *Cancer*. 2000;89(3):640–646.
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[9 Oct 2025]