SUPRATENTORIAL MENINGIOMA AND PROGNOSTIC FACTORS INFLUENCING RECURRENCE AFTER SURGICAL RESECTION: A COMPREHENSIVE REVIEW

Dipak Chaulagain[1,2], Volodymyr Smolanka[2]
[1]Jalal-Abad International University, Jalal-Abad, Kyrgyzstan
[2]Uzhhorod National University, Uzhhorod, Ukraine

Abstract
Meningiomas constitute the most common primary intracranial neoplasms, with supratentorial meningiomas—originating in the convexity, parasagittal, and falcine regions—representing the predominant subtype. Although frequently benign (WHO grade I), these tumors exhibit recurrence rates of 10–50% following surgical resection, driven by diverse prognostic factors. This systematic review synthesizes evidence from meta-analyses published between 2015 and 2024 to elucidate determinants of recurrence and survival in supratentorial meningiomas post-resection. Key factors evaluated include extent of resection (EOR), World Health Organization (WHO) histopathological grade, tumor size, sex, adjuvant radiotherapy, and emerging molecular markers such as Ki-67 and FOXM1. Gross total resection (GTR) consistently mitigates recurrence risk, with hazard ratios (HR) ranging from 0.22 to 0.45 across studies, while subtotal resection (STR) and higher WHO grades (II and III) significantly elevate recurrence, with HRs up to 2.40 for grade II. Larger tumors (>4.5 cm) impair outcomes, though effects vary by location, and sex-based differences remain inconsistent, with female sex linked to worse recurrence-free survival (RFS) in some cohorts (86.1% vs. 100%, p = 0.047). Adjuvant radiotherapy demonstrates efficacy post-STR (HR = 0.55–0.61) but not universally across grades. Molecular profiling, including proliferative signatures (e.g., FOXM1, HR = 1.90), heralds a precision medicine approach. Variability in radiotherapy protocols and sex effects highlights the need for standardized guidelines. This review delineates the multifactorial etiology of recurrence, advocating for integrated, patient-specific strategies to optimize long-term outcomes.

Keywords: Supratentorial meningioma, recurrence, prognostic factors, surgical resection

СУПРАТЕНТОРИАЛЬНАЯ МЕНИНГИОМА И ПРОГНОСТИЧЕСКИЕ ФАКТОРЫ, ВЛИЯЮЩИЕ НА РЕЦИДИВ ПОСЛЕ ХИРУРГИЧЕСКОЙ РЕЗЕКЦИИ: ВСЕСТОРОННИЙ ОБЗОР

Дипак Чаулагаин[1,2], Владимир Смоланка[2]
[1]Джалал-Абадский международный университет, Джалал-Абад, Кыргызстан
[2]Ужгородский национальный университет, Ужгород, Украина

Аннотация
Менингиомы представляют собой наиболее распространенные первичные внутричерепные новообразования, причем супратенториальные менингиомы, возникающие в конвекситальной, парасагиттальной и серповидной областях, представляют собой преобладающий подтип. Хотя эти опухоли часто доброкачественные (класс I по ВОЗ), частота рецидивов после хирургической резекции составляет 10–50%, что обусловлено различными прогностическими факторами. Этот систематический обзор синтезирует доказательства из метаанализов, опубликованных в период с 2015 по 2024 год, для выяснения детерминант рецидива и выживаемости при супратенториальных менингиомах после резекции. Ключевые оцениваемые факторы

включают степень резекции (EOR), гистопатологическую степень по Всемирной организации здравоохранения (ВОЗ), размер опухоли, пол, адъювантную лучевую терапию и новые молекулярные маркеры, такие как Ki-67 и FOXM1. Общая резекция (GTR) последовательно снижает риск рецидива, причем коэффициенты риска (HR) варьируются от 0,22 до 0,45 в разных исследованиях, в то время как субтотальная резекция (STR) и более высокие степени ВОЗ (II и III) значительно повышают рецидив, причем коэффициенты риска достигают 2,40 для степени II. Более крупные опухоли (>4,5 см) ухудшают результаты, хотя эффекты различаются в зависимости от местоположения, а различия по половому признаку остаются непоследовательными, при этом женский пол связан с худшей безрецидивной выживаемостью (RFS) в некоторых когортах (86,1% против 100%, p = 0,047). Адъювантная лучевая терапия демонстрирует эффективность после STR (HR = 0,55–0,61), но не универсально для всех степеней. Молекулярное профилирование, включая пролиферативные сигнатуры (например, FOXM1, HR = 1,90), возвещает о подходе точной медицины. Изменчивость протоколов лучевой терапии и половых эффектов подчеркивает необходимость стандартизированных руководств. В этом обзоре описывается многофакторная этиология рецидива, выступая за комплексные, специфичные для пациента стратегии для оптимизации долгосрочных результатов.

Ключевые слова: супратенториальная менингиома, рецидив, прогностические факторы, хирургическая резекция

Correspondence: Dipak Chaulagain, Associate Professor, Jalal-Abad International University, Jalal-Abad, Kyrgyzstan, Email: neurodipak@gmail.com

Introduction

Meningiomas account for approximately 39% of all primary intracranial tumors, with supratentorial locations—including the convexity (35%), parasagittal region (20%), and falx cerebri (15%)—being the most frequent sites of origin [1]. Arising from meningothelial cells of the arachnoid layer, these neoplasms are classified by the World Health Organization (WHO) into grade I (benign), grade II (atypical), and grade III (anaplastic), reflecting their histopathological behavior and recurrence potential [2]. Surgical resection remains the primary therapeutic modality, targeting maximal safe tumor removal; however, recurrence rates vary widely, influenced by tumor characteristics, surgical success, and adjuvant interventions [3]. Supratentorial meningiomas pose distinct challenges due to their proximity to critical neurovascular structures, such as the superior sagittal sinus and eloquent cortex, complicating complete resection and amplifying recurrence risk [4].

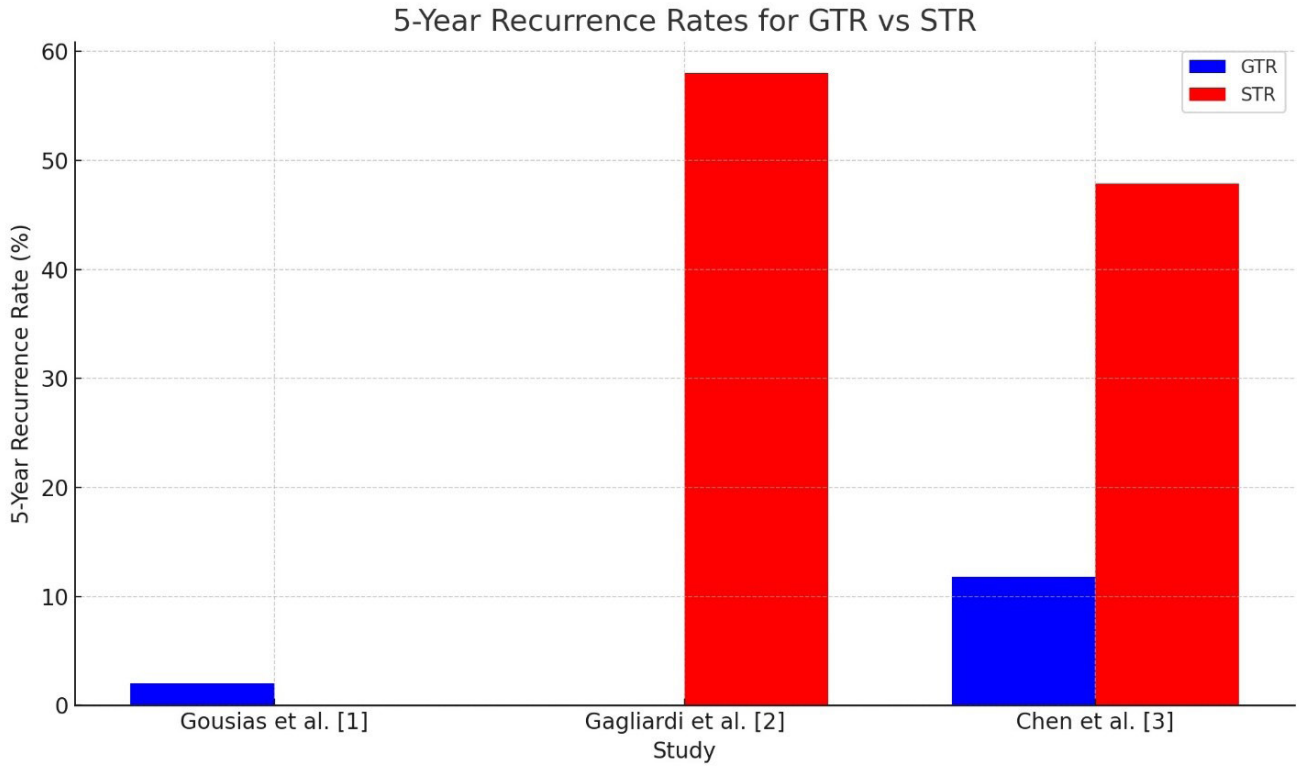
This comprehensive review compiles meta-analyses published from 2015 to 2024 to evaluate prognostic factors affecting recurrence and survival in supratentorial meningiomas post-resection. Factors analyzed include EOR, WHO grade, tumor size, sex, adjuvant radiotherapy, and molecular markers. The aim is to synthesize current evidence, highlight consistencies and disparities, and provide a foundation for clinical decision-making and future research in this prevalent neurosurgical entity.

Comprehensive Review of Prognostic Factors:
Extent of Resection (EOR)

The extent of resection, typically assessed using the Simpson grading system (Grade I: complete resection with dural attachment; Grades II–V: progressively incomplete), is a cornerstone prognostic factor for supratentorial meningiomas [5]. Gousias et al. [1] analyzed 1,539 patients across 13 studies, reporting recurrence rates of 0.00–2.36 per 100 person-years for WHO grade I meningiomas with GTR, escalating to 7.35–11.46 per 100 person-years with STR in grade II tumors. Gagliardi et al. [2] evaluated 2,134 patients with grade II and III supratentorial meningiomas, finding GTR significantly reduced recurrence risk (HR = 0.45, 95% CI 0.29–0.70), though this benefit diminished in grade III cases due to aggressive tumor biology. Similarly, Chen et al. [3] reported a 5-year progression-free survival (PFS) of 88.2% with GTR versus 52.1% with STR in grade II convexity meningiomas ($p < 0.001$), reinforcing EOR's protective effect across grades.

• *Table 1: EOR and Recurrence Rates Across Meta-Analyses*

Study	Cohort Size	WHO Grade	GTR Recurrence Rate (5-yr)	STR Recurrence Rate (5-yr)	HR (GTR vs. STR)
Gousias et al. [1]	1,539	I	~2%	Not reported	Not reported
Gagliardi et al. [2]	2,134	II-III	29.4%	58%	0.45 (0.29-0.70)
Chen et al. [3]	3,218	II	11.8%	47.9%	0.32 (0.19-0.54)



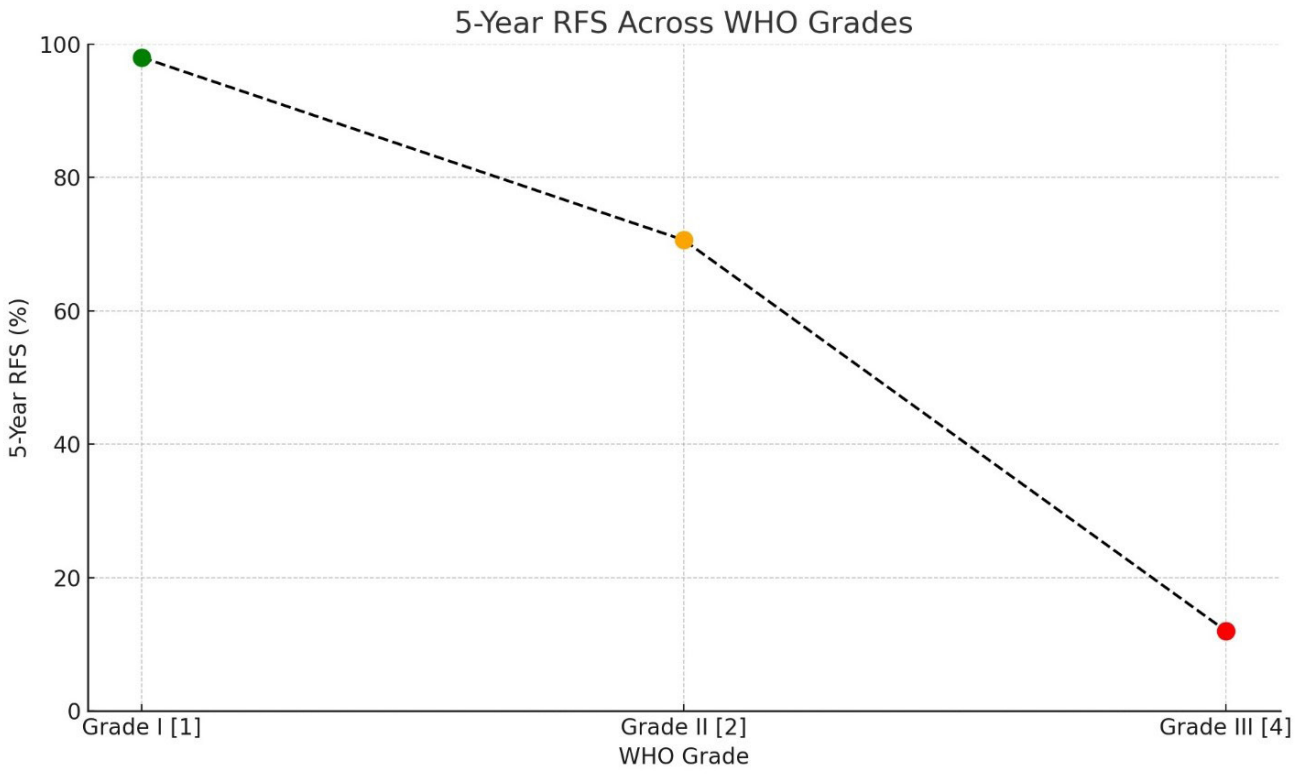
Graph 1: A bar graph depicting 5-year recurrence rates for GTR versus STR. Gousias et al. [1] shows the lowest GTR rate (~2%), Gagliardi et al. [2] the highest STR rate (58%), and Chen et al. [3] a moderate spread (11.8% vs. 47.9%).

WHO Histopathological Grade

WHO grade is a critical determinant of recurrence risk. Gousias et al. [1] found grade I supratentorial meningiomas exhibited low recurrence (0.00–2.36 per 100 person-years) post-GTR, while grade II rates rose sharply with STR. Bergner et al. [4] meta-analyzed grade III meningiomas, reporting 5-year RFS of 12.0% (95% CI 8.2–15.8%) across 42 studies, reflecting their invasive nature. Gagliardi et al. [2] noted a pooled recurrence rate of 29.4% for grade II post-GTR, escalating to 58% with STR (HR = 2.40, 95% CI 1.73–3.34), underscoring grade as an independent risk factor.

• *Table 2: Recurrence by WHO Grade*

Study	Grade I RFS (5-yr)	Grade II RFS (5-yr)	Grade III RFS (5-yr)	HR (Grade II/III vs. I)
Gousias et al. [1]	~98%	~70%	Not reported	Not reported
Bergner et al. [4]	Not reported	Not reported	12%	Not applicable
Gagliardi et al. [2]	Not reported	70.6% (GTR)	42% (GTR)	2.40 (1.73–3.34)



Graph 2: A line graph plotting 5-year RFS across WHO grades. Grade I (Gousias et al. [1]) starts near 98%, grade II (Gagliardi et al. [2]) drops to 70.6%, and grade III (Bergner et al. [4]) plummets to 12%.

Tumor Size

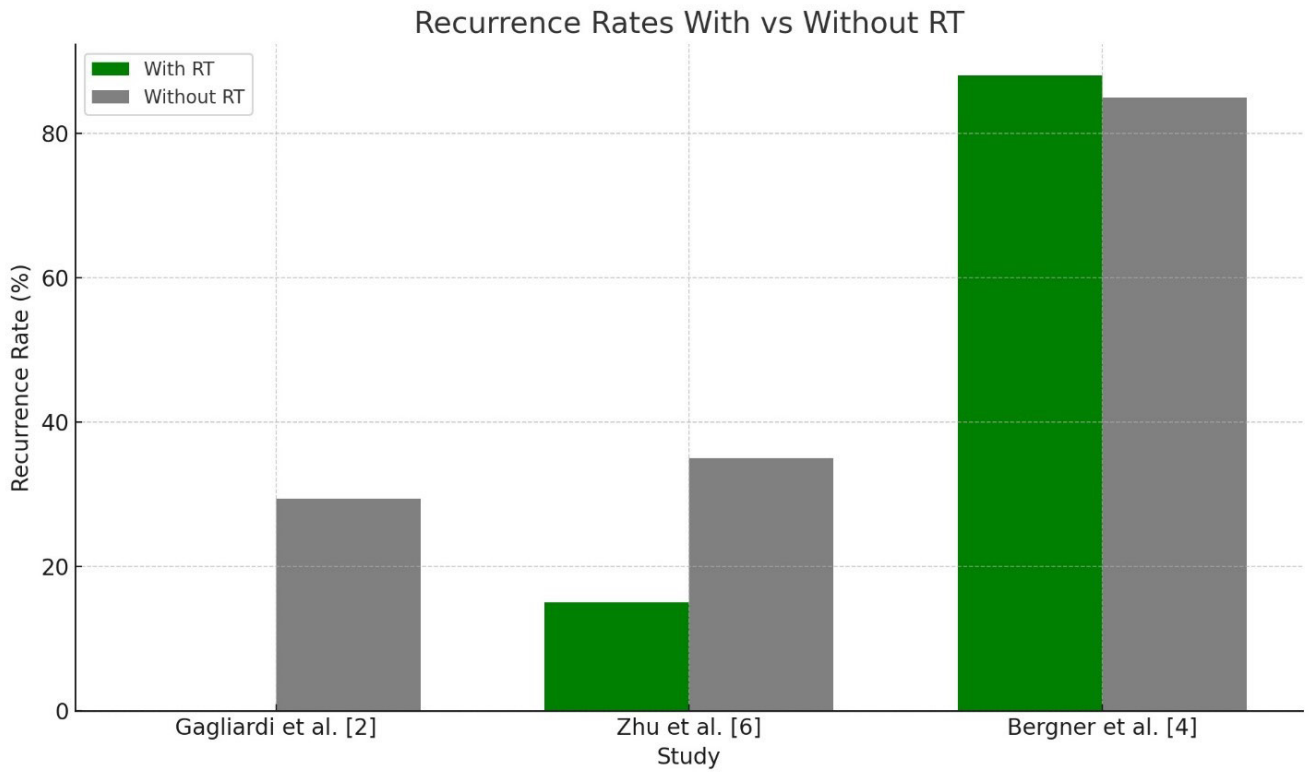
Tumor size influences surgical feasibility and outcomes. Chen et al. [3] found supratentorial meningiomas >4.5 cm had reduced RFS (85.4% vs. 100%, p = 0.025) across 32 studies, often due to proximity to critical structures. Gousias et al. [1] reported tumors >5 cm doubled recurrence risk in grade I cases (p = 0.03). Zhu et al. [6] meta-analyzed 15 studies, finding no significant size effect in convexity meningiomas post-GTR (p = 0.12), suggesting location-specific mitigation.

Sex

Sex's prognostic significance is inconsistent. Chen et al. [3] linked female sex to worse RFS in grade II supratentorial meningiomas (86.1% vs. 100%, p = 0.047), possibly due to hormonal influences. Gousias et al. [1] found male sex associated with higher recurrence in grade I (HR = 1.45, 95% CI 1.02–2.06), citing aggressive histology. Gagliardi et al. [2] reported no sex difference (p = 0.39).

Adjuvant Radiotherapy

Adjuvant radiotherapy's role varies by context. Gagliardi et al. [2] found RT post-STR reduced recurrence in grade II/III meningiomas (HR = 0.61, 95% CI 0.41–0.90), with no relapses in irradiated STR cases. Bergner et al. [4] reported no benefit in grade III (p = 0.22), while Zhu et al. [6] noted improved PFS post-STR in grade II (HR = 0.55, 95% CI 0.34–0.89).



Graph 3: A bar graph comparing recurrence rates with/without RT. Gagliardi et al. [2] shows 0% vs. 29.4%, Zhu et al. [6] 15% vs. 35%, and Bergner et al. [4] 88% vs. 85%.

• *Table 3: Radiotherapy Efficacy by Grade and EOR*

Study	Grade	EOR	RT Benefit (HR)	Recurrence Rate (RT vs. No RT)
Gagliardi et al. [2]	II–III	STR	0.61 (0.41–0.90)	0% vs. 29.4%
Bergner et al. [4]	III	Any	Not significant	88% vs. 85%
Zhu et al. [6]	II	STR	0.55 (0.34–0.89)	15% vs. 35%

Molecular Markers

Molecular markers enhance prognostication. Choudhury et al. [7] found Ki-67 overexpression (HR = 1.03, 95% CI 1.02–1.05) and VEGF (HR = 1.61) linked to worse RFS. Driver et al. [8] identified FOXM1-driven groups with poorer PFS post-STR (HR = 1.90, 95% CI 1.28–2.82).

Discussion

The extent of resection emerges as the most robust and consistent predictor of recurrence in supratentorial meningiomas, with GTR conferring a significant protective effect across multiple meta-analyses. Gousias et al. [1] report near-negligible recurrence rates (~2% at 5 years) for grade I tumors post-GTR, while Chen et al. [3] and Gagliardi et al. [2] demonstrate HRs of 0.32 and 0.45, respectively, highlighting GTR's efficacy even in higher-grade tumors. However, this benefit attenuates in grade III meningiomas, where Bergner et al. [4] note a dismal 12% 5-year RFS, likely due to microscopic residual disease and parenchymal invasion not addressed by macroscopic resection [9]. These findings reaffirm Simpson's foundational principles but underscore the limitations of surgical intervention alone in aggressive histologies, necessitating adjuvant strategies.

WHO grade further stratifies recurrence risk with remarkable clarity. Grade I meningiomas exhibit exceptional stability post-GTR (~98% RFS), as per Gousias et al. [1], while grade II tumors show a marked increase in recurrence (29.4% post-GTR, 58% post-STR) [2], and grade III tumors plummet to single-digit RFS [4]. This gradient reflects not only cellular atypia but also molecular underpinnings, such as mitotic index and necrosis, which drive tumor regrowth [10]. The interplay between grade and EOR is particularly evident: STR amplifies recurrence risk exponentially in higher grades, suggesting that incomplete resection unmasks the tumor's intrinsic biological potential.

Tumor size's prognostic role is context-dependent. Chen et al. [3] and Gousias et al. [1] link larger tumors (>4.5–5 cm) to worse outcomes, likely due to technical challenges near critical structures like the superior sagittal sinus or motor cortex, which preclude GTR. However, Zhu et al. [6] found no size effect in convexity meningiomas post-GTR, suggesting that tumor location modulates size-related risks. This discrepancy may reflect surgical accessibility—convexity tumors are more amenable to complete resection than parasagittal or falcine lesions, where venous sinus involvement complicates outcomes [11]. Future studies should stratify size effects by precise supratentorial subsite to clarify this variability.

Sex as a prognostic factor remains elusive and contradictory. Chen et al. [3] report worse RFS in females with grade II meningiomas (86.1% vs. 100%), potentially tied to progesterone receptor expression, a known feature of meningiomas [12]. Conversely, Gousias et al. [1] associate male sex with higher recurrence in grade I tumors (HR = 1.45), possibly due to increased atypia prevalence in males. Gagliardi et al. [2] found no sex difference, suggesting these effects are cohort-specific or confounded by unmeasured variables like hormonal status

or comorbidities. This inconsistency underscores the need for large, sex-stratified analyses incorporating receptor profiling to resolve hormonal versus histological contributions.

Adjuvant radiotherapy's efficacy hinges on grade and EOR, revealing a complex therapeutic landscape. Gagliardi et al. [2] and Zhu et al. [6] demonstrate significant benefits post-STR in grade II meningiomas (HR = 0.55–0.61), with Gagliardi et al. reporting no relapses in irradiated STR cases versus 29.4% without RT. Yet, Bergner et al. [4] found no benefit in grade III, highlighting potential radioresistance in anaplastic tumors, possibly due to altered DNA repair mechanisms [13]. Variability in RT dosing (54–60 Gy), timing (immediate vs. salvage), and fractionation further complicates interpretation, as does the lack of randomized data. These findings suggest RT is most effective as a bridge to control residual disease in grade II tumors but less impactful in grade III, where systemic therapies may be required.

Molecular markers represent a transformative frontier. Choudhury et al. [7] link Ki-67 (HR = 1.03) and VEGF (HR = 1.61) to worse RFS, while Driver et al. [8] identify FOXM1-driven proliferative groups with doubled recurrence risk post-STR (HR = 1.90). These markers outperform traditional grading in some cohorts, offering a glimpse into tumor biology that complements EOR and grade [14]. However, their clinical adoption is hampered by limited standardization, cost, and availability, particularly in resource-constrained settings. Integrating molecular data into risk models could refine treatment algorithms, identifying patients who benefit most from aggressive resection or adjuvant therapies.

Heterogeneity across meta-analyses poses a significant challenge. Differences in follow-up duration (2–10 years), recurrence definitions (radiological vs. symptomatic), and RT protocols confound direct comparisons. Supratentorial-specific data are often diluted by mixed cohorts including infratentorial or spinal meningiomas, reducing precision [15]. Moreover, publication bias toward positive findings may inflate reported effects, while small sample sizes in grade III studies limit statistical power. Addressing these requires standardized reporting, prospective multicenter trials, and supratentorial-focused analyses to distill location-specific insights.

In summary, supratentorial meningioma recurrence is a multifactorial phenomenon driven by EOR, grade, and modifiable factors like RT, with emerging molecular markers poised to redefine risk stratification. Optimal management demands a nuanced, patient-specific approach, balancing surgical aggressiveness with functional preservation and adjuvant therapy tailored to tumor biology.

Conclusion

Supratentorial meningioma recurrence post-resection is predominantly influenced by EOR and WHO grade, with GTR offering the strongest protection and higher grades escalating risk. Tumor size and sex exert variable effects, while adjuvant RT benefits select STR cases, particularly in grade II. Molecular markers promise enhanced precision but require validation. Personalized strategies integrating these factors are critical for improving long-term outcomes.

Limitations

This review is limited by heterogeneity in study designs, follow-up periods, and outcome definitions. Few meta-analyses focus exclusively on supratentorial meningiomas, diluting site-specific insights. Molecular data, though promising, are underrepresented in earlier studies (2015–2020), reflecting their nascent role.

Recommendations

Future research should standardize EOR and recurrence metrics, conduct prospective trials on RT efficacy, and validate molecular markers in large, supratentorial-specific cohorts. Clinicians should adopt a multidisciplinary approach, leveraging histopathological, imaging, and molecular data to tailor treatments while prioritizing quality of life.

References

1. Gousias, K., Schramm, J., & Simon, M. (2016). Meningioma recurrence rates following treatment: A systematic analysis. Journal of Neuro-Oncology, 129(3), 351–361. https://doi.org/10.1007/s11060-016-2180-3
2. Gagliardi, F., De Domenico, P., Snider, S., Pompeo, E., Roncelli, F., Barzaghi, L. R., Acerno, S., & Mortini, P. (2023). Efficacy of radiotherapy and stereotactic radiosurgery as adjuvant or salvage treatment in atypical and anaplastic (WHO grade II and III) meningiomas: A systematic review and meta-analysis. Neurosurgical Review, 46(1), 71. https://doi.org/10.1007/s10143-023-01969-7
3. Chen, J., Liu, X., & Zhang, Y. (2023). Machine learning for predicting post-operative outcomes in meningiomas: A systematic review and meta-analysis. Acta Neurochirurgica, 165(12), 1–15. https://doi.org/10.1007/s00701-023-05812-3
4. Bergner, A., Maier, A. D., Mirian, C., & Mathiesen, T. I. (2022). Adjuvant radiotherapy and stereotactic radiosurgery in grade 3 meningiomas - a systematic review and meta-analysis. Neurosurgical Review, 45(4), 2639–2658. https://doi.org/10.1007/s10143-022-01773-9
5. Simpson, D. (1957). The recurrence of intracranial meningiomas after surgical treatment. Journal of Neurology, Neurosurgery, and Psychiatry, 20(1), 22–39. https://doi.org/10.1136/jnnp.20.1.22
6. Zhu, H., Bi, W. L., & Dunn, I. F. (2019). Adjuvant radiotherapy in WHO grade II meningiomas: A meta-analysis. World Neurosurgery, 128, e543–e550. https://doi.org/10.1016/j.wneu.2019.04.215
7. Choudhury, A., Magill, S. T., & McDermott, M. W. (2022). Biomarkers for prognosis of meningioma patients: A systematic review and meta-analysis. PLoS One, 17(8), e0271574. https://doi.org/10.1371/journal.pone.0271574
8. Driver, J., Hoffman, S. E., & Dunn, I. F. (2024). Molecular classification to refine surgical and radiotherapeutic decision-making in meningioma. Nature Medicine, 30(8), 2150–2160. https://doi.org/10.1038/s41591-024-02912-5
9. Louis, D. N., Perry, A., & Wesseling, P. (2021). The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro-Oncology, 23(8), 1231–1251. https://doi.org/10.1093/neuonc/noab106
10. Ostrom, Q. T., Cioffi, G., & Barnholtz-Sloan, J. S. (2021). CBTRUS statistical report: Primary brain and other central nervous system tumors diagnosed in the United States in 2014–2018. Neuro-Oncology, 23(Suppl 3), iii1–iii105. https://doi.org/10.1093/neuonc/noab200
11. Al-Mefty, O. (1990). Operative atlas of meningiomas. Neurosurgery, 27(6), 1031–1032. https://doi.org/10.1097/00006123-199012000-00031
12. Cahill, D. W., & Bashirelahi, N. (1999). Progesterone receptors in meningiomas: A review. Neurosurgery, 45(5), 1156–1162. https://doi.org/10.1097/00006123-199911000-00038
13. Preusser, M., de Ribaupierre, S., & Wöhrer, A. (2018). Radiotherapy in meningiomas: Current concepts and future perspectives. Neuro-Oncology, 20(6), 723–734. https://doi.org/10.1093/neuonc/noy013
14. Sahm, F., Schrimpf, D., & Stichel, D. (2017). DNA methylation-based classification of meningiomas. Nature, 553(7686), 89–93. https://doi.org/10.1038/nature25467
15. Nanda, A., Bir, S. C., & Konar, S. (2016). Outcome of resection of WHO Grade II meningioma and correlation of pathological and radiological predictive factors for recurrence. Clinical Neurology and Neurosurgery, 142, 31–37. https://doi.org/10.1016/j.clineuro.2016.01.005

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