Prognosis of intracranial meningiomas with TERTp mutation: A systematic review with meta-analysis.

Giovana C Bitolo[1]; Christopher A Lima[1]; Pedro A Nogueira[2]; Bianca G Wanderley[2]; Marcus Vinicius C Maldaun, MD, PhD[3]; Mateus D Fabbro, Md, PhD[2]; Cleiton Formentin, MD, PhD[2]

[1]University Nine of July; [2]State University of Campinas; [3]Syrian-Lebanese Hospital

INTRODUCTION AND OBJECTIVES

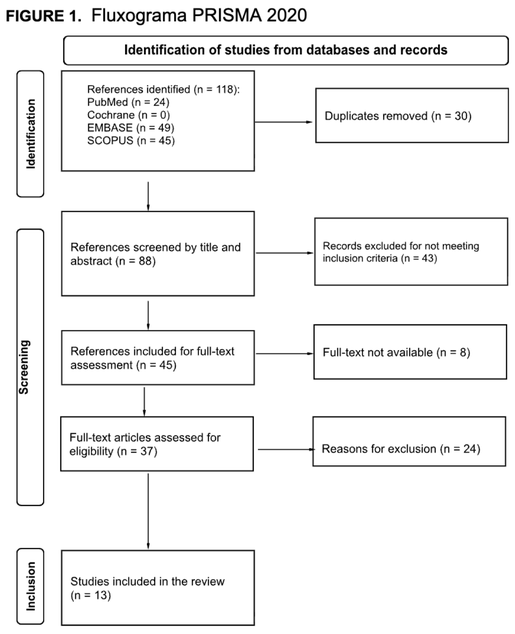
Intracranial meningiomas, the most common primary brain tumors in adults, originate from arachnoid cells of the leptomeninges (LYNES, J. et al., 2022). TERT promoter mutations (C228T/C250T) are notable molecular alterations linked to telomerase activation and more aggressive, recurrent tumor behavior compared to wild-type tumors (SPIEGL-KREINECKER, S. et al., 2018). Although these mutations have been recognized by the World Health Organization (WHO) as markers of tumor aggressiveness, their precise impact on patient survival and recurrence rates remains insufficiently defined in the literature.

This meta-analysis aimed to clarify the prognostic impact of TERTp mutations on overall survival (OS), progression-free survival (PFS), and recurrence in patients with intracranial meningioma, addressing the central question of how these mutations influence outcomes.

METHODOLOGY

This systematic review and meta-analysis, following PRISMA 2020 and PICOTT, searched PubMed, Embase, and Web of Science for terms related to "Meningioma," "TERT Promoter," and "Prognosis." It included adults with histologically confirmed intracranial meningiomas (WHO grades I–III, 2021) treated surgically, comparing TERT promoter-mutated tumors to wild-type. Outcomes were PFS, recurrence, and OS from studies with ≥2 years follow-up. Data were extracted from HRs, medians, or recurrence rates. Bias was assessed by funnel plots and Egger's test, and statistical analyses in RStudio included meta-analyses, sensitivity analysis, and Baujat plots.

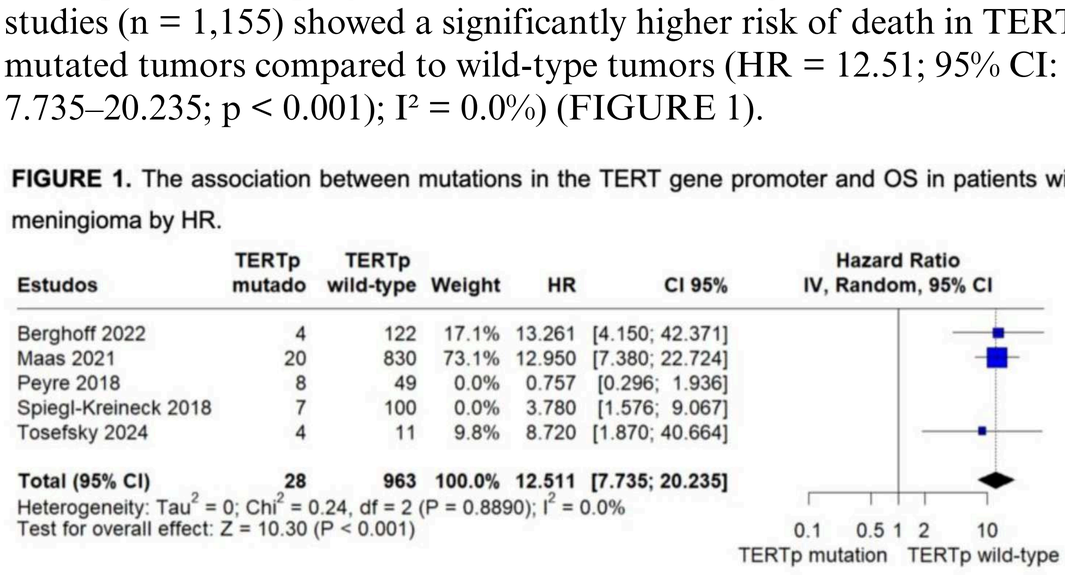
FIGURE 1. Fluxograma PRISMA 2020



RESULTS

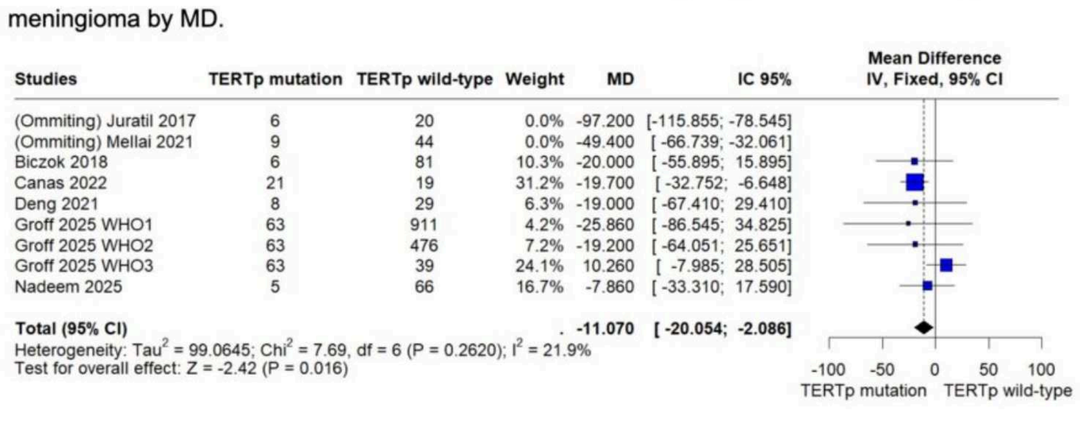
The meta-analysis revealed a strong association between mutations in the TERTp and worse prognosis in intracranial meningiomas. For OS, five studies (n = 1,155) showed a significantly higher risk of death in TERTp-mutated tumors compared to wild-type tumors (HR = 12.51; 95% CI: 7.735–20.235; $p < 0.001$); $I^2 = 0.0\%$) (FIGURE 1).

FIGURE 1. The association between mutations in the TERT gene promoter and OS in patients with meningioma by HR.



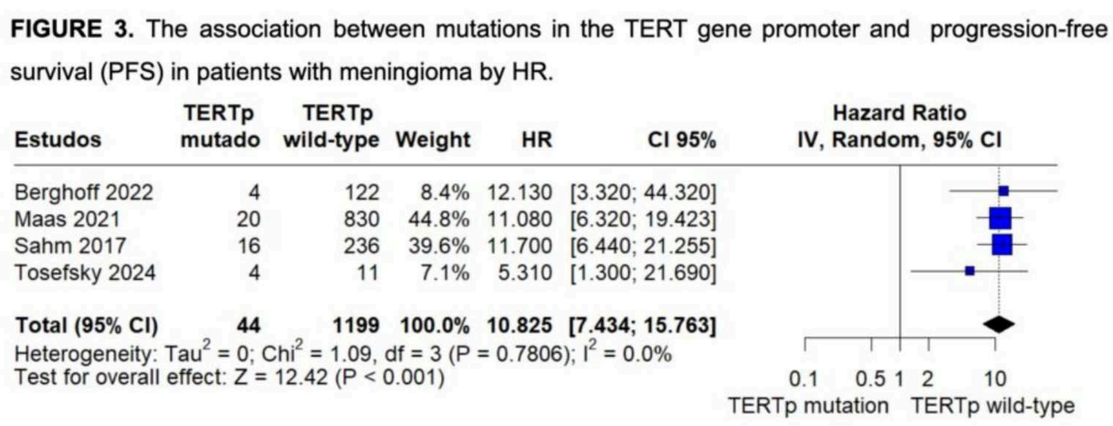
The mean difference (MD) assessed in seven studies (n = 1,724) confirming the finding was an 11-month reduction in survival for TERTp-mutated tumors (95% CI: -20.05 to -2.08; $p = 0.016$; $I^2 = 21.9\%$) (FIGURE 2).

FIGURE 2. The association between mutations in the TERT gene promoter and OS in patients with meningioma by MD.



For PFS, four studies (n = 1,243) indicated a significantly higher risk of progression in TERTp-mutated patients (HR = 10.82; 95% CI: 7.43–15.76; $p < 0.001$), with high consistency ($I^2 = 0\%$) (FIGURE 3).

FIGURE 3. The association between mutations in the TERT gene promoter and progression-free survival (PFS) in patients with meningioma by HR.



The MD in PFS was evaluated in 6 studies (n = 2,360), showing a mean progression 28.65 months earlier in this group (95% CI: -36.55 to -20.76; $p < 0.001$), with low heterogeneity ($I^2 = 15.7\%$) (FIGURE 4)

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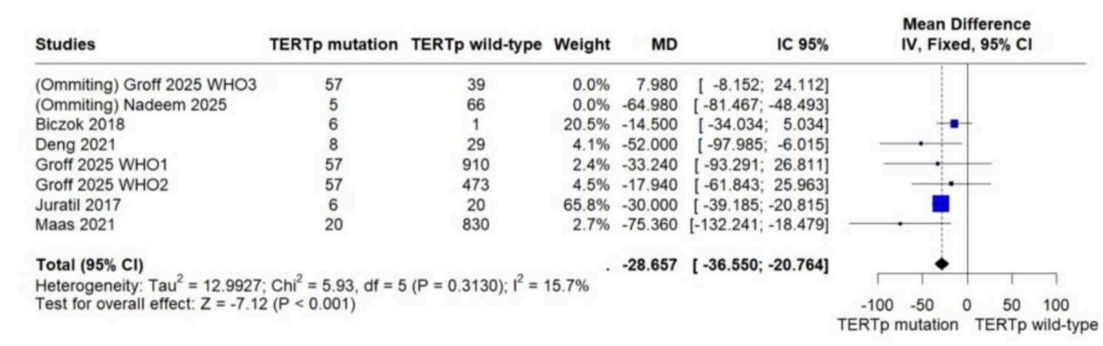

Studies excluded from the analysis showed statistically negligible weight and potential artificial impact on heterogeneity, increasing the model's robustness.

CONCLUSION

Meningiomas with TERTp mutation have poor prognosis, with reduced OS and shorter PFS. Their presence increases the risk of death by over twelve times and recurrence by eleven times compared to wild-type TERTp. This proves that this mutation serves as a molecular marker for risk stratification, personalized therapy, support refined prognostic stratification and suggest early adjuvant therapy and closer oncological follow-up.

REFERENCES

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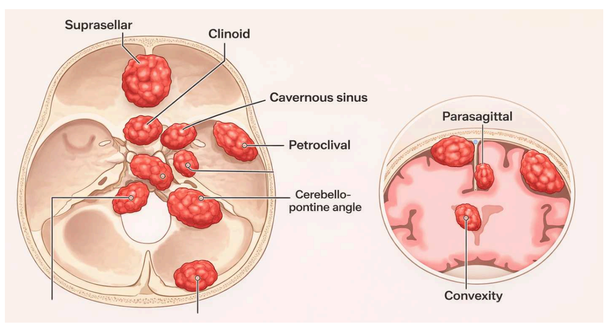
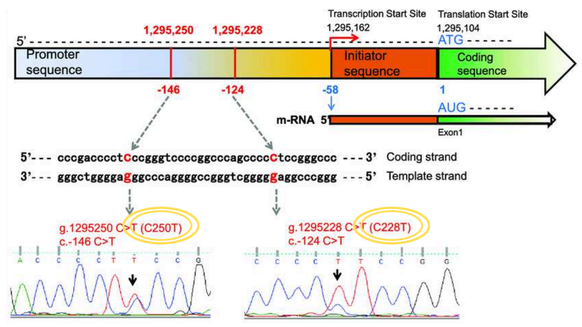
- Although these mutations have been recognized by the World Health Organization (WHO) as markers of tumor aggressiveness, their precise impact on patient survival and recurrence rates remains insufficiently defined in the literature.

FIGURE 1. Possible locations of meningiomas at the base of the skull (left) and cerebral convexity (right).



Source: Adapted from Neurotology and Acoustic Neuroma Center, 2024.

FIGURE 2. Structure of the wild-type TERT gene and representative of DNA of the TERT promoter.



Source: Adapted from Bae, 2016. ResearchGate.

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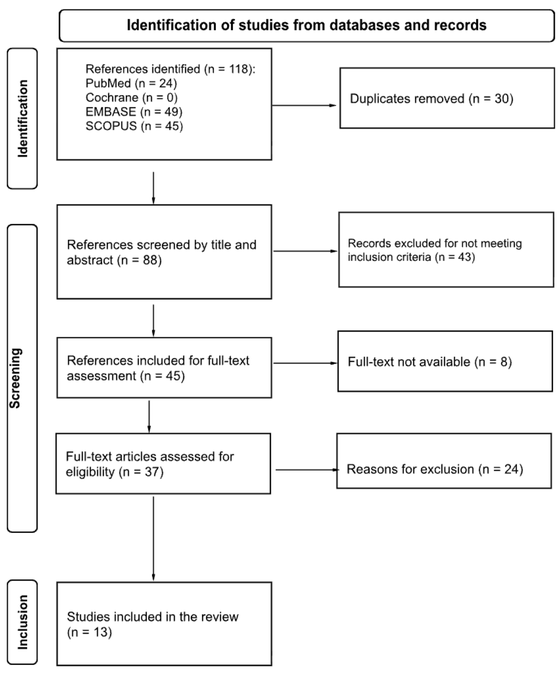

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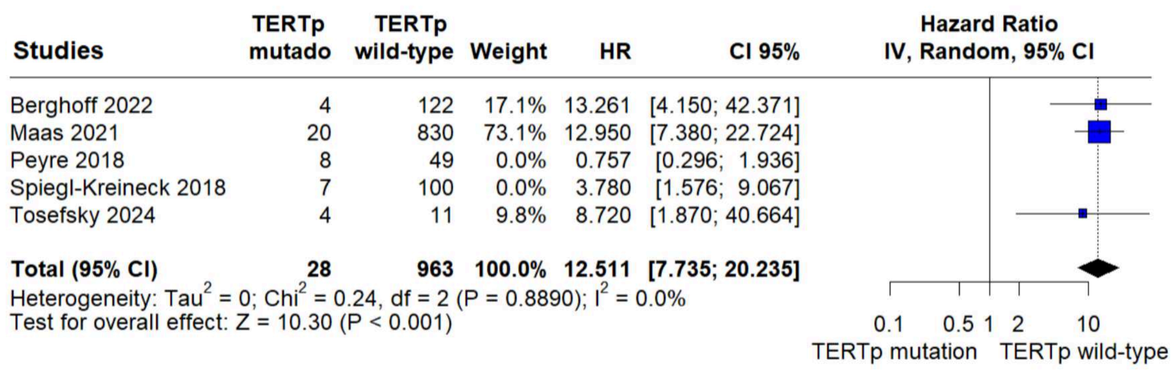

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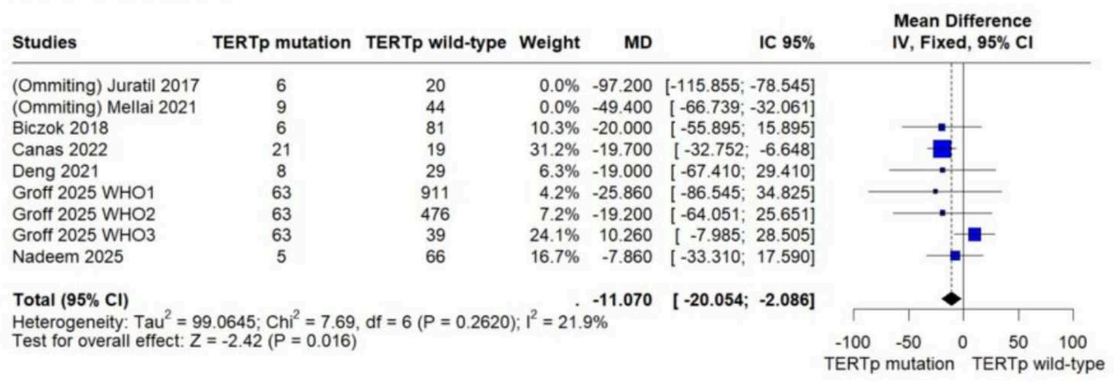

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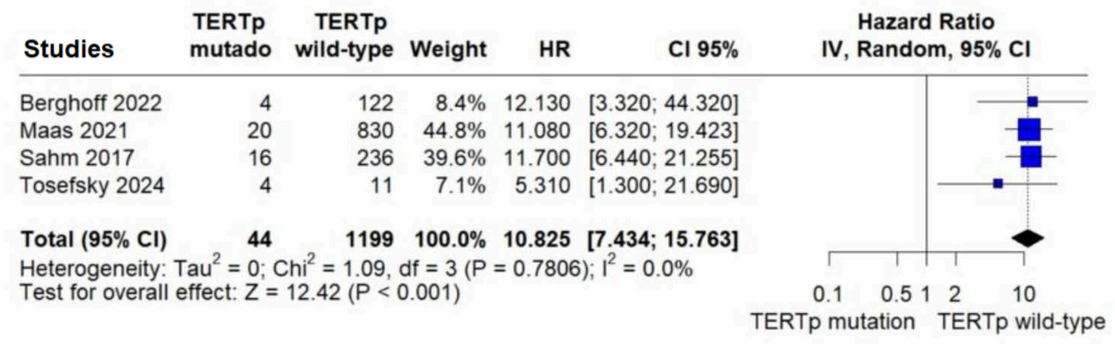

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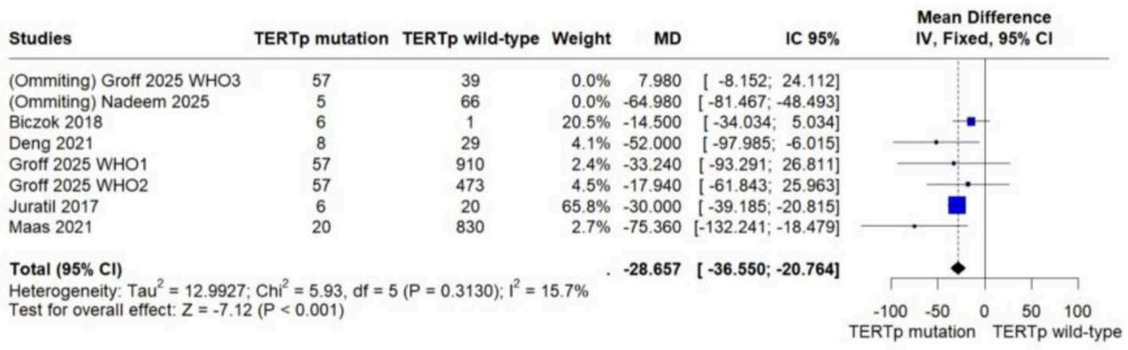

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References and contact information for the author and presenter

KEYWORDS: Meningioma; Progression-free survival; Gene expression regulation

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