World Neurosurgery: X 18 (2023) 100167

Contents lists available at ScienceDirect

World Neurosurgery: X

journal homepage: www.journals.elsevier.com/world-neurosurgery-x

Meningioma grading based on positron emission tomography: A systematic review and meta-analysis

Panagiotis Filis [a,b], George A. Alexiou [a,*], Andreas Zigouris [a], Chrissa Sioka [c], Nikolaos Filis [a], Spyridon Voulgaris [a]

[a] Department of Neurosurgery, University of Ioannina, School of Medicine, Greece
[b] Department of Hygiene and Epidemiology, School of Medicine, University of Ioannina, Greece
[c] Department of Nuclear Medicine, University of Ioannina, Greece

ARTICLE INFO

Keywords:
PET
Mendingioma
Meta-analysis

ABSTRACT

Introduction: Meningiomas are the most common central nervous system tumor in adults. Knowledge of the tumor grade can guide optimal treatment timing and shape personalized follow-up strategies. Positron emission tomography (PET) has been utilized for the metabolic assessment of various intracranial space-occupying lesions. Herewith, we set out to evaluate the diagnostic accuracy of PET for the noninvasive assessment of meningioma's grade.

Materials and methods: The Medline, Scopus and Cochrane databases were systematically searched in March 2022 for studies that evaluated the sensitivity and specificity of PET compared to the gold standard of histological diagnosis in the grading of meningiomas. Summary statistics will be calculated and scatter plots, summary curve from the HSROC model and posterior predictions by empirical Bayes estimates will be presented.

Results: Five studies consisting of 242 patients with a total of 196 low-grade (Grade 1) and 46 high grade (Grade 2/3) meningiomas were included in our analysis. Three of the included studies used ^{18}F-FDG, one study used ^{18}F-FLT and one used(Whiting et al., 2011) 18 F-FET as PET tracers. The pooled sensitivity was 76% (95% CI: 52%–91%) and the pooled specificity was 89% (95% CI: 83%–93%). The diagnostic odds ratio was 27.17 (95% CI: 9.22–80.06), the positive likelihood ratio was 7.18 (95% CI: 4.54–11.34) and the negative likelihood ratio was 0.26 (95% CI: 0.11–0.61).

Conclusion: PET is a promising and viable option as a noninvasive imaging tool to differentiate the meningioma grades. However, currently it cannot overtake the gold standard of histological grade confirmation. More studies are required for further validation and refinement of this imaging technique and assessment of other radiotracers as well.

1. Introduction

Meningiomas are the most common central nervous system tumors[1] and are classified by WHO (World Health Organization) in grades 1, 2 and 3.[2] WHO grade 1 meningiomas are considered low-grade and are the most frequent (88–94%), while high-grade meningiomas, including WHO grade 2 (5–7%) and WHO grade 3 meningiomas (1–2%), are less frequent.[2–4] Surgical resection and radiotherapy are the main treatment options, while stereotactic radiosurgery is preferred in case of subtotal resection and small size and/or multiple lesions.

The term "benign tumor" encloses a percentage of moderate to severe disability despite total excision of a meningioma and in higher grade neoplasms there is a substantial risk of recurrence. Typically, patients with symptomatic meningiomas undergo surgical resection, except when co-morbidities and general status of patient are contraindications. In cases of an incidentally found meningioma with small size and no

Abbreviations: WHO, World Health Organization; MRI, magnetic resonance imaging; CT, computerized tomography; PET, positron emission tomography; SPECT, single-photon emission computerized tomography; 18F-FDG, fluorine-18 fluorodeoxyglucose; [18F]FLT, 3′-deoxy-3′-[18F]fluorothymidine; 18F-FET, O-(2-[18F]fluoroethyl)-L-tyrosine; 11C-MET, 11C-methionine; DOR, diagnostic odds ratio; LR+, positive likelihood ratios; LR−, negative likelihood ratios; 1/LR-, inverse of the negative likelihood ratio; CIs, 95% confidence intervals; HSROC, hierarchical summary receiver operating characteristic; SUVmax, maximum standardized uptake value; TGR, tumor-to-contralateral gray matter ratios; SUV, standardized uptake value; TBR, tumour-to-brain ratios.

* Corresponding author.
E-mail address: galexiou@uoi.gr (G.A. Alexiou).

https://doi.org/10.1016/j.wnsx.2023.100167
Received 13 September 2022; Received in revised form 25 January 2023; Accepted 29 January 2023

peritumoral edema close observation with MRI could be an option. Once a meningioma recurs, it is more likely to recur again, resulting in a poor prognosis.[5–7] The factors that determine the rate of recurrence of the meningioma are extent of the resection, location of tumor, histopathological grade and biological aggressiveness.[6,8–13] An informative preoperative imaging study that could determine non-invasively meningioma grade could be extremely useful for surgical planning and follow-up.

In general, a combination of CT and MRI is the standard approach for diagnosis and planning of surgery. All treatment decisions should be personalized for a patient in order to have better outcomes. Additionally, PET is a promising molecular imaging technique that provides metabolic tumor information complementing the MR imaging examination and provides an *in vivo* profile of tumor proliferation. Many tracers can be used in PET (such as ^{18}F-FDG, ^{11}C-MET, F-FET or ^{18}F-FLT), with the most widely used being the 18 F-FDG. Glucose consumption of meningioma assessed by PET using ^{18}F-FDG has been used in several studies as an index of tumor aggressiveness and its histopathological grade.[14] Thus, it is possible that it can be used to predict the risk of meningioma recurrence. Herewith, we performed a systematic review and meta-analysis to provide a comprehensive summary and quantitative synthesis of information on the accuracy of PET to distinguish the meningioma grade using various tracers.

2. Materials and Methods

2.1. Search strategy and study selection

This systematic review and meta-analysis has adopted the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines[15] and was written according to the Meta-analysis of Observational Studies in Epidemiology proposal.[16]

The Medline, Scopus and Cochrane databases were systematically searched in March 2022 for studies of any duration and design that provided both sensitivity and specificity measures of PET compared to the gold standard of histological diagnosis in the grading of patients with meningioma. The search algorithm included: "positron emission tomography", "PET", "meningioma" and "grade". Two independent investigators screened the studies by titles and abstracts. The potentially eligible articles underwent full-text evaluation. If consensus on eligibility was not reached between the two reviewers, a third investigator provided assistance. The search was supplemented by citation analysis and reference list scanning of all the eligible articles. Studies were excluded if the publication language was not in English, the majority of patients had brain tumors other than meningiomas, if there was no histologic confirmation of the meningioma grading, as well as if the sensitivity and specificity were not provided or adequate data for their computation were accessible.

2.2. Data extraction

Two authors independently performed the data extraction of the eligible studies in a standardized form consisting of: name of the first author, year of publication, radiopharmaceutical agent used in PET, number of patients, number of grade 1 meningiomas, number of grade 2/3 meningiomas, sensitivity and specificity measures at optimal cut-off.

2.3. Quantitative synthesis, analysis and risk of bias

The true-positive, false-positive, true-negative, and false-negative rates occurring from the sensitivity and specificity were used to calculate the pooled sensitivity, specificity, diagnostic odds ratio (DOR), the positive (LR+) and negative (LR−) likelihood ratios, the inverse of the negative likelihood ratio (1/LR-), as well as their respective 95% confidence intervals (CIs). Moreover, scatter plot, summary curve from the HSROC model, as well as posterior predictions by empirical Bayes estimates were utilized. The estimation was based on meta-analysis of diagnostic accuracy using hierarchical logistic regression.[17] All statistical analyses were performed with Stata version 14. To assess the risk of bias in each study, the Quality Assessment of Diagnostic Accuracy Studies 2 tool was utilized.[18]

3. Results

3.1. Study selection and characteristics

The systematic review flow chart is described in Fig. 1. The search yielded 241 results from the Medline (n = 114), Scopus (n = 125) and Cochrane (n = 2) databases, which were screened by title and abstract. Twelve articles were retrieved for full-text review. After exclusion of the studies[19–25] that did not provide data for tumor grade and also did not allow the calculation of diagnostic accuracy, five cohort studies were considered eligible for our analysis.[3,4,26–28] These five studies included 242 patients with a total of 196 low-grade (Grade 1) and 46 high-grade (Grade 2/3) meningiomas. The characteristics of the studies are presented in Table 1.

3.2. Quantitative analysis and risk of bias

The pooled sensitivity was 76% (95% CI: 52%–91%) and the pooled specificity was 89% (95% CI: 83%–93%). The diagnostic odds ratio was 27.17 (95% CI: 9.22–80.06), the positive likelihood ratio was 7.18 (95% CI: 4.54–11.34), the negative likelihood ratio iwas 0.26 (95% CI: 0.11–0.61) and the inverse of the negative likelihood ratio was 3.79 (95% CI: 1.64–8.74) (Table 2). Fig. 2 presents the SROC plot of the PET data for detection of meningioma grade. Studies are indicated by circles sized according to the total number of individuals in each study. Fig. 3 consists of a summary curve for the HSROC model, a summary operating point, a 95% confidence region for the summary operating point and a 95% prediction region (confidence region for a forecast of the true sensitivity and specificity in a future study. The greater "shrinkage" in sensitivity compared to the specificity observed in Fig. 4, which presents the empirical Bayes estimates of the sensitivity and specificity in each study, is indicative of small variance of sensitivity on the logit scale and the fact that most studies have fewer patients with high-grade meningioma than patients with low-grade meningioma, leading to more precise estimates of specificity than of sensitivity. The risk of bias assessment in each study using the Quality Assessment of Diagnostic Accuracy Studies 2 tool (QUADAS 2) is depicted in Figs. 5 and 6. All the patients had histopathological confirmation of the intracranial meningioma. The PET scanning procedure was sufficiently described in all of the studies. However, the exclusion and inclusion criteria for the patient selection were not sufficiently described in every study and thus the risk of bias was deemed unclear for these domains. Finally, none of the studies showed high risk of bias.

4. Discussion

Due to the high incidence of meningiomas, a reliable noninvasive imaging technique to assess tumor malignancy could transform the clinical practice and guide optimal treatment timing as well as shape personalized follow-up strategies. Conventional MRI approaches cannot provide reliable information for meningioma grading, although perfusion imaging has yielded better results.[2,29] However, it should be noted that recent advances in the field of radiomics, combining MRI and machine learning, have shown promising applications for the imaging and grading of meningiomas.[30–32] This systematic review and meta-analysis aimed to comprehensively present the diagnostic accuracy of PET in distinguishing the meningioma grade driven from the current published evidence.

The present results indicated that PET can detect meningioma grade with a sensitivity of 76% and specificity of 89%. These results can be subsequently translated as a satisfactory detection rate of high-grade

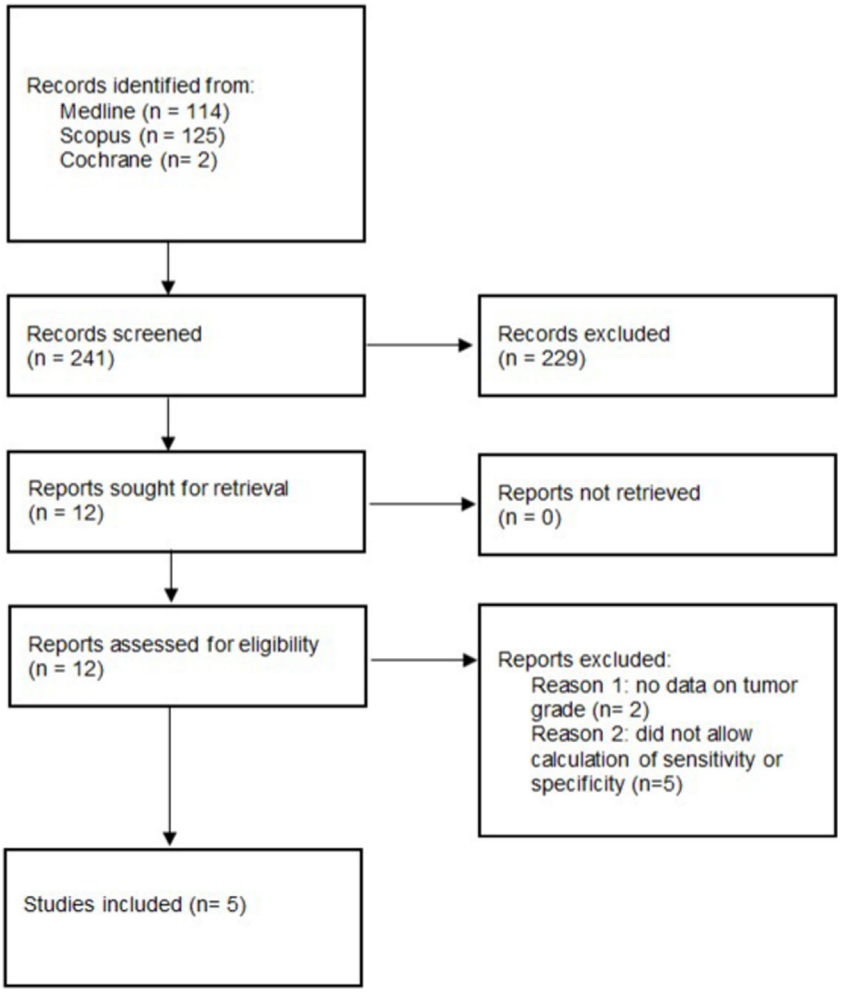

Fig. 1. Review flow chart.

Table 1
Characteristics of the included studies.

Author	Year of publication	Number of patients	PET tracer	Grade 1 meningiomas	Grade 2/3 meningiomas	Sensitivity %	Specificity %
Bashir	2020	17	^{18}F-FLT	13	4	100	95
Okuchi	2015	67	^{18}F-FDG	56	11	72.7	87.5
Cornelius	2015	24	^{18}F-FET	18	6	83	83
Lee	2009	59	^{18}F-FDG	43	16	43	95
Cremerius	1997	75	^{18}F-FDG	66	9	89	88

Table 2
Summary statistics.

	Summary Estimate	95% Confidence Interval
Sensitivity	0.76	0.52 to 0.91
Specificity	0.89	0.83 to 0.93
Diagnostic Odds Ratio (DOR)	27.17	9.22 to 80.06
Positive Likelihood Ratio (LR+)	7.18	4.54 to 11.34
Negative Likelihood Ratio (LR-)	0.26	0.11 to 0.61
Inverse of the negative likelihood ratio (1/LR-)	3.79	1.64 to 8.74

meningiomas (grade 2 and 3) and high distinction rate of low-grade meningiomas (grade 1). The positive likelihood ratio of 7.18 shows that a PET scan positive for high grade meningioma raises the probability for its later histological diagnosis by 35–40%, while the negative likelihood ratio of 0.26 shows, by the same effect, that a negative PET scan for high grade meningioma reduces the probability of its histological diagnosis by 30%.[33] The value of 3.79 for the inverse of the negative likelihood ratio is also satisfactory. Larger values of the inverse of the negative likelihood ratio indicate a more accurate test, and comparing this with the positive likelihood ratio can indicate whether a positive or negative test result has greater impact on the odds of disease.[17]

Three of the included studies used fluorine-18 fluorodeoxyglucose (^{18}F-FDG).[4,27,28] Okuchi et al[27] presented sensitivity of 72.7% and specificity of 87.5% for maximum standardized uptake value (SUVmax) optimal cutoff 7.2. The authors did not only evaluate PET for grading meningioma but also thallium-201 SPECT and showed promising results for both. Cremerius et al[28] using tumor-to-contralateral gray matter ratios (TGR) and a different threshold of 1.05 in primary meningioma and 0.85 in tumor recurrence achieved sensitivity of 89% and specificity of 88%. In this study, fasting before the imaging was shown to improve the diagnostic accuracy of FDG-PET. Conversely, Lee et al[4] was the study that reported the lowest sensitivity of 43% for TGR optimal cutoff 1.0, which

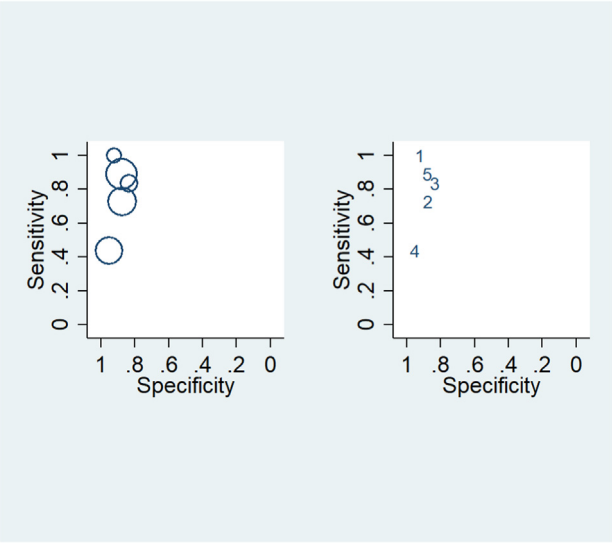

Fig. 2. SROC plot of the PET data for detection of meningioma grade. Left panel: Studies indicated by circles sized according to the total number of individuals in each study. Right panel:
Studies indicated by study ID numbers. 1: Bashir 2020, 2: Okuchi 2015, 3: Cornelius 2015, 4: Lee 2009, 5: Cremerius 1997.

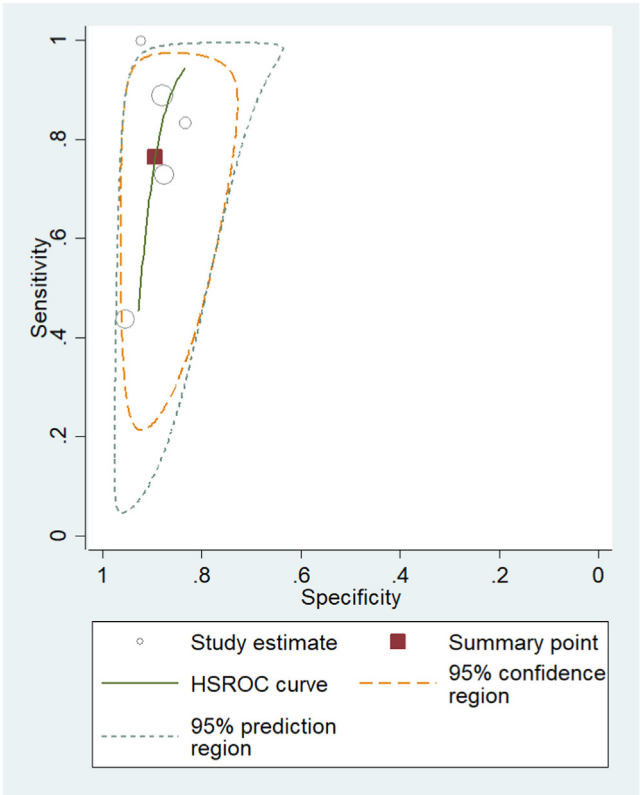

Fig. 3. Plot of the HSROC model.

was in line with other articles that did not support FDG-PET.[34,35] At this point it is important to highlight the heterogeneity in the reporting of the study results. Generally, due to the fact that glucose consumption of normal gray matter is a rather stable parameter, the use of the TGR may be preferred to correct for variations of input function, which is not considered in the calculation of the standardized uptake value (SUV).[28]

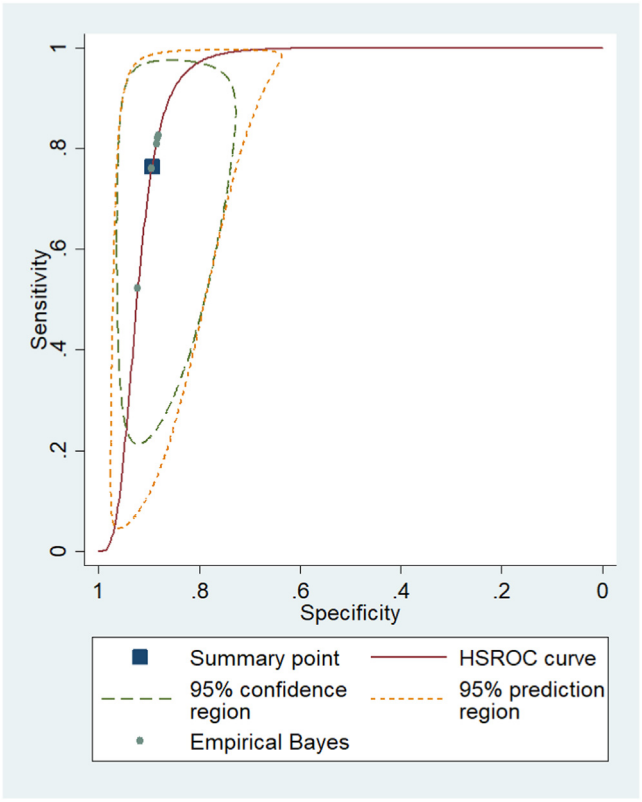

Fig. 4. Empirical Bayes estimates of the sensitivity and specificity in each study.

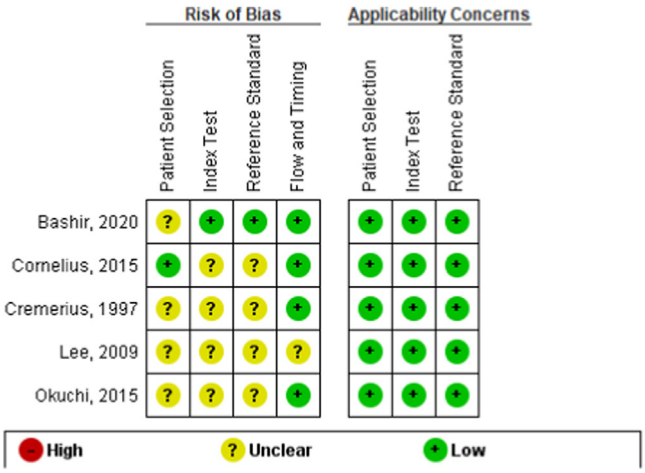

Fig. 5. Risk of Bias assessment with QUADAS 2.

Bashir et al[26] is the first study investigating 3′-deoxy-3′-[^{18}F]fluorothymidine ([^{18}F]FLT) uptake in meningiomas and reported its viability to differentiate between WHO grades with very high sensitivity and specificity rates, but in a small study population. Cornelius et al[3] also studied a tracer other than ^{18}F-FDG. The authors showed that O-(2-[^{18}F] Fluoroethyl)-L-tyrosine (^{18}F-FET) at tumour-to-brain ratios (TBR) optimal cutoff 2.3 can reliable distinguish the meningioma grades with both sensitivity and specificity 83%. Other tracers may also show potential in diagnosing higher grade meningiomas.[21,25] Further research regarding more radiotracers, as well as research of the possible role of SPECT[36,37] in the grading of meningiomas is highly encouraged and awaited.

Despite the strengths of the current report, some limitations need also to be acknowledged. The published studies that reported estimates of diagnostic accuracy for grading of meningiomas with PET proved to be

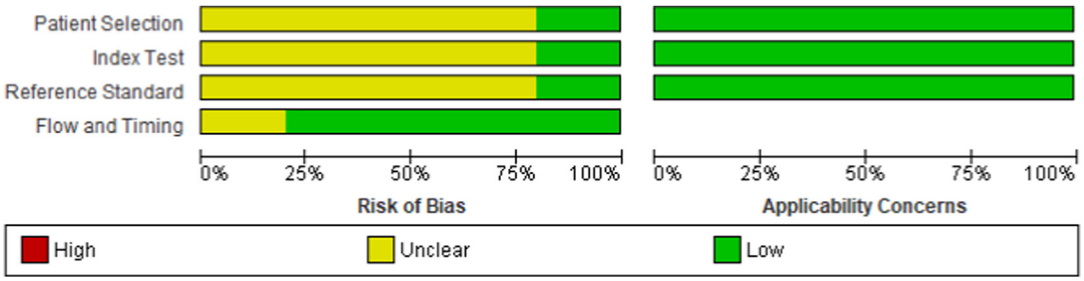

Fig. 6. Risk of Bias graph.

limited. Moreover, each one of the studies contained a very small patient population with high grade meningioma compared to the low grade group. Finally, heterogeneity on the use of PET tracers was noticed. Ideally, if enough information were available, analyses should be separate for each tracer, in order to additionally present comparisons between them.

5. Conclusion

In conclusion, our results suggest that PET holds promise as a companion noninvasive diagnostic tool for distinction of meningioma grade and could be especially useful for patient monitoring. This fact was evident from the meta-analysis, which showed satisfactory diagnostic accuracy with sufficient sensitivity and specificity. However, the histopathologic confirmation of the meningiomas will remain the golden standard. Larger, multicenter studies, with high patient accrual and testing of various radiopharmaceutical tracers are essential for further validation and refinement of this diagnostic procedure.

Authors contributions

PF, GA, AZ, CS and NF equally participated in the database search and data collection and extraction. All authors co-wrote the manuscript. S.V. and G.A.A. conceived and supervised the study and gave the final approval.

Data availability

All data generated or analyzed during this study are included in this published article (and its supplementary information files).

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

1. Marosi C, Hassler M, Roessler K, et al. *Meningioma. Critical reviews in oncology/hematology*. 2008;67(2):153–171. https://doi.org/10.1016/j.critrevonc.2008.01.010.
2. Louis DN, Ohgaki H, Wiestler OD, et al. The 2007 WHO classification of tumours of the central nervous system. *Acta Neuropathol*. 2007;114(2):97–109. https://doi.org/10.1007/s00401-007-0243-4.
3. Cornelius JF, Stoffels G, Filß C, et al. Uptake and tracer kinetics of O-(2-(18)F-fluoroethyl)-L-tyrosine in meningiomas: preliminary results. *Eur J Nucl Med Mol Imag*. 2015;42(3):459–467. https://doi.org/10.1007/s00259-014-2934-0.
4. Lee JW, Kang KW, Park SH, et al. 18F-FDG PET in the assessment of tumor grade and prediction of tumor recurrence in intracranial meningioma. *Eur J Nucl Med Mol Imag*. 2009;36(10):1574–1582. https://doi.org/10.1007/s00259-009-1133-x.
5. Dziuk TW, Woo S, Butler EB, et al. Malignant meningioma: an indication for initial aggressive surgery and adjuvant radiotherapy. *Journal of neuro-oncology*. 1998;37(2):177–188. https://doi.org/10.1023/a:1005853720926.
6. Goyal LK, Suh JH, Mohan DS, Prayson RA, Lee J, Barnett GH. Local control and overall survival in atypical meningioma: a retrospective study. *Int J Radiat Oncol Biol Phys*. 2000;46(1):57–61. https://doi.org/10.1016/s0360-3016(99)00349-1.
7. Hug EB, Devries A, Thornton AF, et al. Management of atypical and malignant meningiomas: role of high-dose, 3D-conformal radiation therapy. *Journal of neuro-oncology*. 2000;48(2):151–160. https://doi.org/10.1023/a:1006434124794.
8. Maier H, Ofner D, Hittmair A, Kitz K, Budka H. Classic, atypical, and anaplastic meningioma: three histopathological subtypes of clinical relevance. *J Neurosurg*. 1992;77(4):616–623. https://doi.org/10.3171/jns.1992.77.4.0616.
9. Takahashi JA, Ueba T, Hashimoto N, Nakashima Y, Katsuki N. The combination of mitotic and Ki-67 indices as a useful method for predicting short-term recurrence of meningiomas. *Surg Neurol*. 2004;61(2):149–155. https://doi.org/10.1016/s0090-3019(03)00575-5. ; discussion 55-6.
10. Modha A, Gutin PH. Diagnosis and treatment of atypical and anaplastic meningiomas: a review. *Neurosurgery*. 2005;57(3):538–550. https://doi.org/10.1227/01.neu.0000170980.47582.a5. discussion -50.
11. Simpson D. The recurrence of intracranial meningiomas after surgical treatment. *J Neurol Neurosurg Psychiatr*. 1957;20(1):22–39. https://doi.org/10.1136/jnnp.20.1.22.
12. Yang SY, Park CK, Park SH, Kim DG, Chung YS, Jung HW. Atypical and anaplastic meningiomas: prognostic implications of clinicopathological features. *J Neurol Neurosurg Psychiatr*. 2008;79(5):574–580. https://doi.org/10.1136/jnnp.2007.121582.
13. Jääskeläinen J. Seemingly complete removal of histologically benign intracranial meningioma: late recurrence rate and factors predicting recurrence in 657 patients. A multivariate analysis. *Surg Neurol*. 1986;26(5):461–469. https://doi.org/10.1016/0090-3019(86)90259-4.
14. Di Chiro G, Hatazawa J, Katz DA, Rizzoli HV, De Michele DJ. Glucose utilization by intracranial meningiomas as an index of tumor aggressivity and probability of recurrence: a PET study. *Radiology*. 1987;164(2):521–526. https://doi.org/10.1148/radiology.164.2.3496626.
15. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *J Clin Epidemiol*. 2009;62(10):1006–1012. https://doi.org/10.1016/j.jclinepi.2009.06.005.
16. Stroup DF, Berlin JA, Morton SC, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. *JAMA*. 2000;283(15):2008–2012. https://doi.org/10.1001/jama.283.15.2008.
17. Harbord RM, Whiting P. metandi: meta-analysis of diagnostic accuracy using hierarchical logistic regression. *STATA J*. 2009;9(2):211–229.
18. Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med*. 2011;155(8):529–536. https://doi.org/10.7326/0003-4819-155-8-201110180-00009.
19. Giovacchini G, Fallanca F, Landoni C, et al. C-11 choline versus F-18 fluorodeoxyglucose for imaging meningiomas: an initial experience. *Clin Nucl Med*. 2009;34(1):7–10. https://doi.org/10.1097/RLU.0b013e31818f4369.
20. Liu RS, Chang CP, Guo WY, et al. 1-11C-acetate versus 18F-FDG PET in detection of meningioma and monitoring the effect of gamma-knife radiosurgery. *J Nucl Med : official publication, Society of Nuclear Medicine*. 2010;51(6):883–891. https://doi.org/10.2967/jnumed.109.070565.
21. Mitamura K, Yamamoto Y, Norikane T, Hatakeyama T, Okada M, Nishiyama Y. Correlation of (18)F-FDG and (11)C-methionine uptake on PET/CT with Ki-67 immunohistochemistry in newly diagnosed intracranial meningiomas. *Ann Nucl Med*. 2018;32(9):627–633. https://doi.org/10.1007/s12149-018-1284-6.
22. Bashir A, Larsen VA, Ziebell M, Fugleholm K, Law I. Improved detection of postoperative residual meningioma with [(68)Ga]Ga-DOTA-TOC PET imaging using a high-resolution research tomograph PET scanner. *Clin Cancer Res : an official journal of the American Association for Cancer Research*. 2021;27(8):2216–2225. https://doi.org/10.1158/1078-0432.Ccr-20-3362.
23. Sommerauer M, Burkhardt JK, Frontzek K, et al. 68Gallium-DOTATATE PET in meningioma: a reliable predictor of tumor growth rate? *Neuro Oncol*. 2016;18(7):1021–1027. https://doi.org/10.1093/neuonc/now001.
24. Ikeda H, Tsuyuguchi N, Kunihiro N, Ishibashi K, Goto T, Ohata K. Analysis of progression and recurrence of meningioma using (11)C-methionine PET. *Ann Nucl Med*. 2013;27(8):772–780. https://doi.org/10.1007/s12149-013-0747-z.
25. Xiangsong Z, Xingchong S, Chang Y, Xiaoyan W, Zhifeng C. 13N-NH3 versus F-18 FDG in detection of intracranial meningioma: initial report. *Clin Nucl Med*. 2011;36(11):1003–1006. https://doi.org/10.1097/RLU.0b013e3182291c2a.
26. Bashir A, Vestergaard MB, Marner L, et al. PET imaging of meningioma with 18F-FLT: a predictor of tumour progression. *Brain : J Neurol*. 2020;143(11):3308–3317. https://doi.org/10.1093/brain/awaa267.

27. Okuchi S, Okada T, Yamamoto A, et al. Grading meningioma: a comparative study of thallium-SPECT and FDG-PET. *Medicine*. 2015;94(6):e549. https://doi.org/10.1097/md.0000000000000549.
28. Cremerius U, Bares R, Weis J, et al. Fasting improves discrimination of grade 1 and atypical or malignant meningioma in FDG-PET. *J Nucl Med : official publication, Society of Nuclear Medicine*. 1997;38(1):26–30.
29. Saloner D, Uzelac A, Hetts S, Martin A, Dillon W. Modern meningioma imaging techniques. *Journal of neuro-oncology*. 2010;99(3):333–340. https://doi.org/10.1007/s11060-010-0367-6.
30. Hu J, Zhao Y, Li M, et al. Machine learning-based radiomics analysis in predicting the meningioma grade using multiparametric MRI. *Eur J Radiol*. 2020;131, 109251. https://doi.org/10.1016/j.ejrad.2020.109251.
31. Duan C, Zhou X, Wang J, et al. A radiomics nomogram for predicting the meningioma grade based on enhanced T(1)WI images. *Br J Radiol*. 2022;95(1137), 20220141. https://doi.org/10.1259/bjr.20220141.
32. Ugga L, Perillo T, Cuocolo R, et al. Meningioma MRI radiomics and machine learning: systematic review, quality score assessment, and meta-analysis. *Neuroradiology*. 2021;63(8):1293–1304. https://doi.org/10.1007/s00234-021-02668-0.
33. McGee S. Simplifying likelihood ratios. *J Gen Intern Med*. 2002;17(8):646–649. https://doi.org/10.1046/j.1525-1497.2002.10750.x.
34. Park YS, Jeon BC, Oh HS, Lee SM, Chun BK, Chang HKJJoKNS. *FDG PET/CT Assessment of the Biological Behavior of Meningiomas*. 2006;40(6):428–433.
35. Iuchi T, Iwadate Y, Namba H, et al. Glucose and methionine uptake and proliferative activity in meningiomas. *Neurol Res*. 1999;21(7):640–644. https://doi.org/10.1080/01616412.1999.11740989.
36. Alexiou GA, Vartholomatos G, Tsiouris S, et al. Evaluation of meningioma aggressiveness by (99m)Tc-Tetrofosmin SPECT. *Clin Neurol Neurosurg*. 2008;110(7):645–648. https://doi.org/10.1016/j.clineuro.2008.03.016.
37. Fotopoulos AD, Alexiou GA, Goussia A, et al. Tc-Tetrofosmin brain SPECT in the assessment of meningiomas-correlation with histological grade and proliferation index. *Journal of neuro-oncology*. 2008;89(2):225–230. https://doi.org/10.1007/s11060-008-9611-8, 99m.