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Review Article

Meningioma recurrence: Time for an online prediction tool?

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ABSTRACT

Background: Meningioma, the most common brain tumor, traditionally considered benign, has a relatively high risk of recurrence over a patient's lifespan. In addition, with the emergence of several clinical, radiological, and molecular variables, it is becoming evident that existing grading criteria, including Simpson's and World Health Organization classification, may not be sufficient or accurate. As web-based tools for widespread accessibility and usage become commonplace, such as those for gene identification or other cancers, it is timely for meningioma care to take advantage of evolving new markers to help advance patient care.

Methods: A scoping review of the meningioma literature was undertaken using the MEDLINE and Embase databases. We reviewed original studies and review articles from September 2022 to December 2023 that provided the most updated information on the demographic, clinical, radiographic, histopathological, molecular genetics, and management of meningiomas in the adult population.

Results: Our scoping review reveals a large body of meningioma literature that has evaluated the determinants for recurrence and aggressive tumor biology, including older age, female sex, genetic abnormalities such as telomerase reverse transcriptase promoter mutation, *CDKN2A* deletion, subtotal resection, and higher grade. Despite a large body of evidence on meningiomas, however, we noted a lack of tools to aid the clinician in decision-making. We identified the need for an online, self-updating, and machine-learning-based dynamic model that can incorporate demographic, clinical, radiographic, histopathological, and genetic variables to predict the recurrence risk of meningiomas.

Conclusion: Although a challenging endeavor, a recurrence prediction tool for meningioma would provide critical information for the meningioma patient and the clinician making decisions on long-term surveillance and management of meningiomas.

Keywords: Machine learning, Meningioma, Recurrence risk tool, Recurrence, Risk prediction tool

INTRODUCTION

Not all meningiomas are benign. Harvey Cushing began his surgical career, apparently believing that they are highly benign neoplasms, and in his famed monograph from 1938, he described reoperation performed in 43 of 295 patients, among whom 72 patients with partly resected tumors later died.[20] Based on the 2021 World Health Organization (WHO) criteria, which rely on histology and some genetic information, approximately 80% of meningiomas are grade 1, 18% grade 2, and 2% grade 3.[71] Although the WHO grading scale is the current standard of care

informing meningioma treatment strategies, it is important to note that approximately 30% of grade 1 and 50% of grade 2 tumors recur, suggesting that some tumors are biologically different and more aggressive compared to other tumors.[21] The current WHO classification can misclassify tumors based on its histopathological grading and may not reliably predict tumor behavior, leading to inappropriately assigned adjuvant treatment and surveillance strategies for some patients. Indeed, meningioma is a heterogenous and chronic disease that exhibits diverse behaviors.[50] In a seminal publication in 1957, Simpson described a transformative grading system for predicting meningioma recurrence and defining the objectives of meningioma surgery.[88] Although the tenets of maximal safe resection for meningioma cannot be understated, the current neurosurgical era of advanced neuroimaging has called this grading scheme into question when informing the management of meningiomas.[5,10,16,66] While radiotherapy after subtotal resection (STR) of meningioma is effective, its therapeutic efficacy remains unclear in those with gross-total resection.[1,24,37,40,47,56] Although recent meta-analyses have demonstrated the potential benefit of adjuvant radiotherapy for grade 2 and 3 meningiomas, they are limited by study heterogeneity and reporting parameters.[49,93,99] Despite numerous publications on meningioma, the individual risk of recurrence after meningioma surgery is not well understood. Furthermore, the pooling of data from various centers is challenging due to heterogeneity in the data, definitions, and reporting; therefore, these data should be harmonized.[69] Predicting recurrence based on the WHO grading or Simpson scale alone in modern meningioma management is inadequate and should be revised based on the improved understanding of cytogenetics, mutations, and epigenetics. For instance, molecular profiling of glioma has provided the potential to develop novel therapies.[13,52,92]

Improving risk stratification and predicting meningioma recurrence is critical for tailoring subsequent management and surveillance strategies. Risk prediction models have been developed to improve patient care using evidence-based tools to guide clinical decision-making, which have been effective for numerous oncological conditions such as breast and colon cancers.[68,75,103] Other benefits of web-based risk assessment tools include avoiding overtreatment and its potential side effects, reducing financial costs to society, and enabling shared decision-making between patients and treating physicians.

Consider a 40-year-old working mother presenting with an anterior parafalx meningioma. She underwent gross total resection (GTR), and the tumor was classified as WHO grade 2. *What is the risk of recurrence? Should she receive radiotherapy? Is there a drug treatment? How often should she be imaged?* The answers to these questions remain controversial. Hence, developing a prognostic tool integrating clinical, surgical, radiological, and molecular data can transform treatment from the current one-size-fits-all approach to patient-specific management, allowing patient stratification for radiation and/or newer drug therapy, which currently cannot be performed. Here, we reviewed predictors and factors influencing meningioma recurrence and presented the idea of developing an individualized yet universal, web-based risk prediction tool for intracranial meningioma recurrence following surgical resection, which physicians and patients can access.

RACE, SEX, FUNCTIONAL STATUS, AND AGE

The influence of race on the outcome of meningioma surgery is complex and multifactorial. Several studies showed that African American race is a risk factor for meningioma recurrence;[6,25] however, this difference was lacking or insignificant in other studies.[65,66] In the latest report from the Central Brain Tumor Registry of the United States (CBTRUS), Caucasian and non-Hispanic ethnicity were predictors of poor survival in high-grade meningiomas.[71] Nonetheless, it is well-documented that the incidence of meningioma, including WHO 2 and 3, is significantly higher among African American patients.[22,48] Although the difference may be related to genetic predisposition, other factors, such as socioeconomic status or the likelihood of receiving maximum resection, should also be considered.[27] Data have also revealed a discrepancy in the incidence of this disease between sexes, with meningioma found to be more common in females.[27,48] Of concern, Kshettry *et al*. reported a higher incidence of the WHO 2 and 3 meningioma in females 35–64 years of age, whereas the incidence was higher in males aged 75 years and older.[48] The relationship between sex and the risk of meningioma recurrence remains controversial.[36,70] The previous studies have demonstrated an association between meningioma recurrence and male sex.[42,54] Similarly, CBTRUS data have shown that male patients with malignant meningioma have poorer survival rates.[71] Hence, given the sex distribution of meningioma, a role for hormonal factors or sex-related genetic alterations may explain the difference, and treatment strategies can also consider the role of hormonal therapy.[79,94,97,101,105] Another predictor of recurrence is the Karnofsky Performance Scale (KPS). Meningioma recurrence is higher among patients with lower KPS scores.[41,66] Finally, there is an exponential trend in the increasing incidence of meningioma with age; rates continue increasing even after 85 years of age.[48,71] In contrast, the WHO grade 2 and 3 meningioma rates exhibit a peak between ages 75 and 84 years, with a subsequent decrease in the incidence.[48] Similarly, multiple studies showed that a later age at diagnosis is a poor prognostic factor and/or predictor of meningioma recurrence.[30,71,104]

This difference may be related to tumor-intrinsic factors or merely because extensive resection is discouraged in older patients.[95] Older patients represent a unique population for which meningioma treatment strategies might differ based on comorbidities, functional quality of life, and surgical and anesthetic risks. Although younger patients demonstrate a better prognosis, meningioma is a chronic disease, and depending on several factors, approximately half of these patients will experience recurrence after 20 years.[39]

WHO GRADING, BRAIN INVASION, AND KI-67/MIB-1

Since the early 1970s and until at least the late 1990s, several grading systems have been published for meningioma, leading to considerable controversy. Older systems suffered from a lack of designation for high-grade meningioma, extreme vagueness, and subjectivity in criterion.[19,62] In 2000, the WHO classification system extensively revised the grading scheme for meningioma, introducing more defined criteria for high-grade tumors.[46] Furthermore, meningiomas exhibit a heterogeneous morphology; the WHO classification further divided the three grades into 15 subtypes.[52] Grades 2 and 3, each consisting of three variants, represent ~18% and ~2% of all meningioma, respectively; these grades are aggressive with a high rate of recurrence,[52,71] with approximately 50% and 80% of grade 2 and 3 meningiomas, respectively, recurring in 5 years.[21]

Brain invasion was considered to have prognostic implications but was not included as a criterion for atypia until the 2007 version of the WHO grading system.[19] Consequently, certain pathologists regarded lesions with brain invasion as grade 2 despite showing histological features of grade 1 meningioma.[12,48,82] In the 2016 classification, brain invasion was formally added as a stand-alone criterion for diagnosing atypical grade 2 meningioma.[52] Notably, the use of different histopathological techniques and methods in defining brain invasion has led to conflicting conclusions and interpretations of the results; hence, the impact of brain invasion on patient prognosis has been questioned in several studies, with some authors suggesting its removal from the WHO classification system. Few authors have demonstrated a clear association between brain invasion and recurrence-free survival in grade 2 and 3 meningiomas.[15,90] A recent study compared 25 patients with invasive otherwise benign meningioma and 40 brain-invasive atypical meningioma. The authors found that brain invasion was an independent prognostic factor for progression-free survival.[4] In contrast, Pizem *et al*. observed no significant difference in recurrence-free survival among 19 patients with brain-invasive otherwise benign meningioma.[76] Spille *et al*. showed that the recurrence rate was similar between grade 1 meningioma and 20 patients with invasive grade 1 meningioma.[89] Similarly, in a cohort of 61 patients with brain invasive otherwise benign meningioma, only four tumors recurred, suggesting a low recurrence rate for this cluster of tumors.[15] In another cohort of 200 patients with atypical meningioma, brain invasion was not correlated with an increased risk of recurrence.[29] A recently published systematic review and meta-analysis indicated that overall, brain invasion was a significant predictor for recurrence; however, brain invasive otherwise grade 1 meningioma had a comparable prognosis to that of noninvasive grade 1 meningioma and better prognosis than grade 2 meningioma (WHO 2016 classification).[64] Although brain invasion was not included as a grading criterion for many years, its prognostic value has been described in the WHO grading system since 1993 and previously by Harvey Cushing in 1938, who considered its occurrence as a sign of malignancy.[45,20] However, it remains unclear whether brain invasive otherwise grade 1 and 2 meningioma should be treated similarly.

Cell proliferation is an important element of oncogenesis.[96] Ki-67/MIB-1, a widely used immunohistochemical biomarker for cell proliferation, along with MIB-1, a monoclonal antibody that detects an epitope on Ki-67 antigen, is expressed during active phases of the cell cycle.[19,51] In general, the Ki-67/MIB-1 proliferation index increases in proportion with the WHO grading of meningioma, which is used as an adjunct to the WHO criteria and is considered as a surrogate marker for recurrence.[19,100] In addition, high Ki-67 expression was detected in meningioma with brain invasion, suggesting a link between brain invasion and proliferative activity.[6] Haddad *et al*. revealed that MIB-1, posterior fossa location, presence of nuclear atypia, and STR were independently associated with an increased risk of meningioma recurrence. The authors demonstrated that achieving GTR with MIB-1 >4.5% carries a similar risk of recurrence as in patients who underwent STR of grade 1 meningioma, highlighting the need for close follow-up or even additional therapy among those with MIB-1 >4.5%.[36] In a recent systematic review of the prognostic value of Ki-67/MIB-1, a higher Ki-67 expression level was associated with worse overall survival and a higher rate of recurrence, particularly Ki-67 >4%.[50] In contrast, a recent study reported that Ki-67 was not an appropriate predictor for recurrence but was a valuable marker for time to recurrence.[61] Although several authors support the usefulness of the Ki-67/MIB-1 proliferation index in meningioma prognosis, some studies revealed insignificant results, likely due to diversity in the cutoff values, staining techniques, and definitions.[19,51] Overall, recurrence predictors are lacking, particularly for grade 1 meningioma. Therefore, utilization of Ki-67/MIB-1 in conjunction with other predictors may improve the framework for risk stratification of patients into high- or low-risk groups.

LOCATION AND RADIOLOGICAL FEATURES

Another important factor that correlates with the extent of resection, recurrence, and outcome is the anatomical tumor location. Although tentorial, falcine, and parafalcine locations were found to be predictors of recurrence, the latter two may be attributed to the frequent invasion of sagittal sinus, rendering complete resection problematic.[26,59] In addition, a higher incidence of recurrence was observed in posterior fossa meningioma, which may be related to the increased prevalence of neurofibromatosis type 2 (*NF2*) mutation in posterior fossa meningioma.[36,101] However, in a large cohort of 1218 patients with meningioma, the skull base location was a strong and independent risk factor for recurrence.[54] Of concern, skull-base meningioma may have different biology and pathology compared to non-skull base and within skull base locations; medial skull base meningioma was less likely to be grade 2, with lower rates of an elevated Ki-67 proliferation index and a lower likelihood of recurrence compared to meningioma in the lateral skull base and non-skull base locations.[58] Tumor size was also shown to be highly predictive of recurrence and associated with worse survival. Magill *et al*. reported that larger meningiomas were more likely to be atypical.[57] Interestingly, one study showed an increased risk of meningioma recurrence only for tumor sizes >6 cm.[32] In addition, peritumoral edema is a major obstacle during surgery and has been identified as a predictor of early recurrence.[11] Although grade 1 tumors can exhibit peritumoral edema, grade 2 tumors exhibit it significantly more frequently.[80]

The advent of advanced neuroimaging has brought a recent interest in radiomics in meningioma, a technique that uses detailed quantitative analysis on the differences in pixels of a radiographic image (i.e., computed tomography, magnetic resonance imaging [MRI], and positron emission tomography) to provide more in-depth analysis of a tumor, including volumetric information, intensity distributions, spatial relations, and textural heterogeneity. In meningioma, a growing body of evidence has identified multiple radiomics features with the potential to predict meningioma grade and recurrence. Patel *et al.* describe a myriad of studies in their systematic review that has focused on radiomics applications in meningioma, including meningioma classification, segmentation, tumor grade prediction, and tumor recurrence prediction.[73] Many studies have also developed machine learning algorithms that use radiomics features combined with other clinical and surgical predictors of meningioma recurrence.[31,63] The future for meningioma imaging research lies in the integration of MRI-based radiomics features into validated models to inform treatment strategies including intraoperative strategies and adjuvant therapy considerations.

EXTENT OF RESECTION

For many decades, maximal safe resection of the tumor and dural attachment has been defined as the gold standard approach for meningioma surgery and a strong predictor of recurrence.[2,3,39] In this context, the Simpson grading system, a 5-point scale with a stepwise decline in the risk of meningioma recurrence following aggressive resection remains relevant, but its value and accuracy in guiding modern meningioma surgery remains controversial.[78,85,88] Perhaps, the strongest limitation of the Simpson grading system is its reliance on the subjective intraoperative surgeon's impression, which often does not correlate with postoperative imaging. Furthermore, unless the score is documented in the operative note itself, scores retrieved retrospectively can be notoriously inaccurate. Indeed, earlier reports indicated a wide range of tumor recurrence after what was considered as Simpson grade 1 resection (9–55%).[85] Later, studies suggested that the high recurrence rate is likely due to regional multifocality; consequently, a modification to the original score was proposed, introducing Simpson grade 0 (i.e., additional removal of 2 cm of the dura).[8,44] Although the new strategy has led to a lack of recurrence after 5 years, the strategy cannot be applied except for in cases of small convexity lesions.[44] In addition, applying the score in certain locations is challenging; certainly, the universality of Simpson grading remains an area of debate.[85] Przybylowski *et al*. demonstrated that Simpson I showed a lower recurrence rate; nonetheless, Simpson grade 2 and 3 exhibited a similar recurrence-free survival as Simpson grade 1V with adjuvant radiosurgery.[78] Other authors reported no difference in the rates of progression among Simpson grades 1–3.[72,91] Hence, some have recommended classifying the extent of resection as either GTR or STR.[60] To overcome the variability in STR, Materi *et al*. used volumetric tumor measurements and found that the residual volume was associated with a high growth rate.[59] Tumor volumetric assessment provides a more accurate estimate of the extent of resection than traditional methods of relying on the detection of any residual tumor by the naked eye. Recently, common data elements for meningioma were developed. The consortium suggested using a less subjective measure, such as the radiographic extent of resection: GTR (Simpson I–III) or STR (Simpson IV and V).[69] A less subjective and more clinically relevant estimate of the extent of resection is desired when developing an online prediction tool for meningioma recurrence.

GENETICS AND MOLECULAR CHARACTERISTICS

The current understanding of molecular genomics of meningiomas has rapidly evolved to elucidate major genetic and epigenetic alterations that drive clinical behavior. Multiple studies have shown that these are thought to be

better indicators of meningioma tumor biology than the current WHO grade.[18,55,68,83,84,102] Sporadic meningiomas with major genomic subgroups have been classified as follows: *NF2* mutations (with or without *SMARC1B*), *TRAF7*-associated (*KLF4* or *PI3K* pathway with *AKT1, PIK3CA, and PIK3R1*), hedgehog signaling molecules (*SMO, SUFU, and PRKAR1A*), *POLR2A*-associated, or *SMARCE1* mutations.[38,68,102] Each of these is driven by specific somatic driver mutations, as outlined in Table 1.[81] The most common genetic alteration associated with meningioma is in the tumor-suppressor gene *NF2*, which is on chromosome 22q12.2 and observed in 40–60% of all meningiomas.[17,34] *NF2* mutant meningioma harbor more genetic alterations and greater genomic instability, higher WHO grade, and a greater risk of tumor recurrence.[17,33,77] In addition, they are commonly located on the convexity and posterior skull base and are present in young patients and those with multiple meningiomas.[77] Similarly, loss of 1p is commonly detected in high-grade meningioma and is associated with aggressive clinical behavior.[35,86] Additional karyotype abnormalities were also observed. In multivariate analysis of 302 meningiomas, alterations of the 1p, 1q, 7, 9, 10, 14, 18, and 22 chromosomes were associated with a high incidence of relapse.[23]

More recently, two other mutations have been proposed to be highly involved with the formation of *de novo* aggressive meningiomas or transformation to more aggressive meningiomas. Mutations in the promoter of the telomerase reverse transcriptase (TERT) gene have been reported in 6% of meningioma, with 80% co-occurring with mutations or deletions at the *NF2* locus.[83] Meningioma harboring TERT promoter mutations exhibit a high rate of recurrence and malignant behavior. Among cases with TERT promoter mutations, the time to progression was 10.1 months compared to 179 months in the wild-type group.[83] Furthermore, loss of the CDKN2A/CDKN2B locus on chromosome 9q was observed in malignant meningioma and was associated with poor survival.[9,74] The latest WHO 2021 classification has been updated to incorporate molecular data and now includes TERT promoter mutations and/or CDKN2A/B deletion as a diagnostic criterion for the WHO grade 3 meningioma, irrespective of the histological features of anaplasia. Other molecular biomarkers with prognostic value include H3K27me3 loss of nuclear expression and methylome profiling.[53] H3K27me3-negative meningiomas are associated with rapid progression.[43] DNA methylation analyses have provided an advancement in the understanding of meningioma behavior and have been shown to correlate with tumor recurrence and prognosis more than that of the WHO grade alone. Based on DNA methylation profiling, Sahm et al. classified meningioma into six methylation classes (MC): benign MCs (ben-1, ben-2, ben-3), intermediate MCs (int-A and int-B), and malignant MC (mal).[84] Compared to MCs ben, MC int-A and B were associated with higher rates of recurrence; MC mal was distinguished as a malignant tumor.[84,87] Furthermore, the methylation cluster showed better prognostic value at estimating progression free-survival and overall survival than each of the individual mutations.[7]

Nassiri *et al.* generated a meningioma recurrence score using a methylome model combined with prognostic clinical factors and found it to be a reliable, individualized estimate of recurrence risk.[68] More recently, Nassiri *et al.* introduced four consensus molecular groups of meningioma

Table 1: Genetic alterations in meningiomas.

Gene	Full Name	Locus	Association	Incidence
NF2	Neurofibromin 2	22q12.2	Convexity; posterior to coronal suture/ lateral sphenoid wing with bone invasion; aggressive clinical course, shorter progression free survival	50%
SMARCB1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily b, member 1	22q11.23	Falcine; anterior to coronal suture	
TRAF7	TNF receptor-associated factor 7	16p13.3	Sphenoid wing; higher grade characteristics	25%
KLF4	Kruppel-like factor 4	9p31	Lateral skull base	10%
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha	3q26.32	Sphenoid wing	10%
AKT1	v-Akt murine thymoma viral oncogene homolog 1	14q32.33		20%
SMO	Smoothened, frizzled class receptor	7p32.1	Olfactory groove/planum sphenoidale	45%
POLR2A	RNA polymerase II subunit A	17p13.1	Sellar/clival/posterior fossa	
SMARCE1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	17q21.2	Higher grade tumors	
CDKN2A	Cyclin-dependent kinase inhibitor 2A	9p21.3	Transformation to higher grade	
TERTp	Telomerase reverse transcriptase promoter		Transformation to higher grade	6%

based on combined analysis of DNA somatic copy-number aberrations, DNA somatic point mutations, DNA methylation, and messenger RNA abundance. The identified groups more accurately predicted recurrence-free survival, and the molecular classification was superior to that of the WHO grading system.[67]

Although incorporating genomic and molecular features with clinical and histopathological data is critical for improving the understanding of disease prognosis and providing patient-specific management, most molecular data/testing have not been adopted for clinical practice yet, limiting their integration into a prediction tool.

PREDICTION TOOL FOR MENINGIOMA RECURRENCE

With this study, we propose the need for an online recurrence risk prediction tool because accurate prediction of meningioma recurrence following surgery is a critical part of the decision-making process to determine the need for adjuvant therapy and the appropriate surveillance strategies. Risk prediction models have been developed to improve patient care using evidence-based tools to guide clinical decision-making, which have been effective for a few oncological conditions such as breast and colon cancers.[28,75,103] Other advantages of risk prediction models include avoiding undertreatment or overtreatment and its potential side effects and patients' loss of quality of life, reducing financial costs to society, informing patients about the future course of their disease, and enabling shared decision-making between patients and physicians.[75,103] Breast cancer prognostic models date back to 1982, with 58 models that were developed between 1982 and 2016. Nottingham prognostic index (NPI) is an early and simple model that includes basic information such as nodal status, tumor size, and grade.[75] Over time, several attempts have been proposed to improve and modify the model by adding novel predictors such as hormonal receptor status and human epidermal growth factor receptor 2 (HER2) status. For example, PREDICT breast cancer prognostication is a widely used model which was developed in 2010 and has been updated multiple times since then.[14,98] The model reflects prognosis with sufficient accuracy by including clinical and histopathological data and only three molecular variables (Ki-67, HER2, and estrogen receptor status).[14] The challenge in meningioma research is that a plethora of recurrence and survival predictors exist, namely, molecular and genetic data, most of which are not yet widely adopted in clinical practice and, therefore, difficult to integrate into a prognostic model. Like breast cancer, any new model remains to be tested and validated and should undergo several modifications overtime to include novel predictors and ultimately improve accuracy and enhance the usage.

As a future direction, we hope that a risk prediction tool for meningioma recurrence can be built – one that can incorporate a deep learning framework with neural networks interfaced with a custom-built dashboard providing an interactive visualization (e.g., a Flask-based platform) and deployed to a cloud service for online access and operation (e.g., Microsoft Azure where data security is safeguarded by its compatibility to Health Insurance Portability and Accountability Act). Such a user interface can enable clinicians to upload data and generate the risk of recurrence for each patient from a predictive algorithm (for instance, a neural network-based model trained to predict patient-specific categories of risk, e.g., probable or unlikely with the ranges of risk values, for recurrence and/or transformation). This can be an important tool for entering and collecting data for future external validation and fine-tuning. For example, various variables, including patient clinical characteristics, tumor location, the extent of resection, WHO grading, presence of brain invasion, Ki-67/MIB-1 proliferation index, and *NF2* gene status, can be used to build this prediction model [Figure 1 and Table 2]. The selected variables are based on our review of the predictors and factors influencing meningioma recurrence and some of the variables used in meningioma-specific common data elements.[69] The current meningioma literature defines the importance of certain variables and identifies the predictors that influence meningioma development and proliferation more than others.[92] The model would be built to assign a certain weightage to these characteristics and then identify the risk probability. For example, a young female of Asian origin with a brain-invaded Grade 2 *NF2* mutated meningioma with a STR would have a higher recurrence risk compared to a similar patient without *NF2* mutation or brain-invasion; the greater importance of *NF2* mutation and brain invasion compared to the extent of resection would be factored into the risk prediction model. In addition, future iterations of the model would also factor in imaging markers for worse meningioma grade and prognosis. Imaging markers can also help with preoperative considerations. With the increasing utility of such a tool and being trained on the diverse input variables predicting the labeled outcomes, the accuracy of a built-in machine learning model is anticipated to be improved in perpetuity.

Table 2: Variables used in the current model.

Variables
Age
Gender
Ethnicity
Tumor location
Extent of resection
WHO grading
Presence of brain invasion
Ki-67/MIB-1 proliferation index
NF2 gene status

WHO: World Health Organization

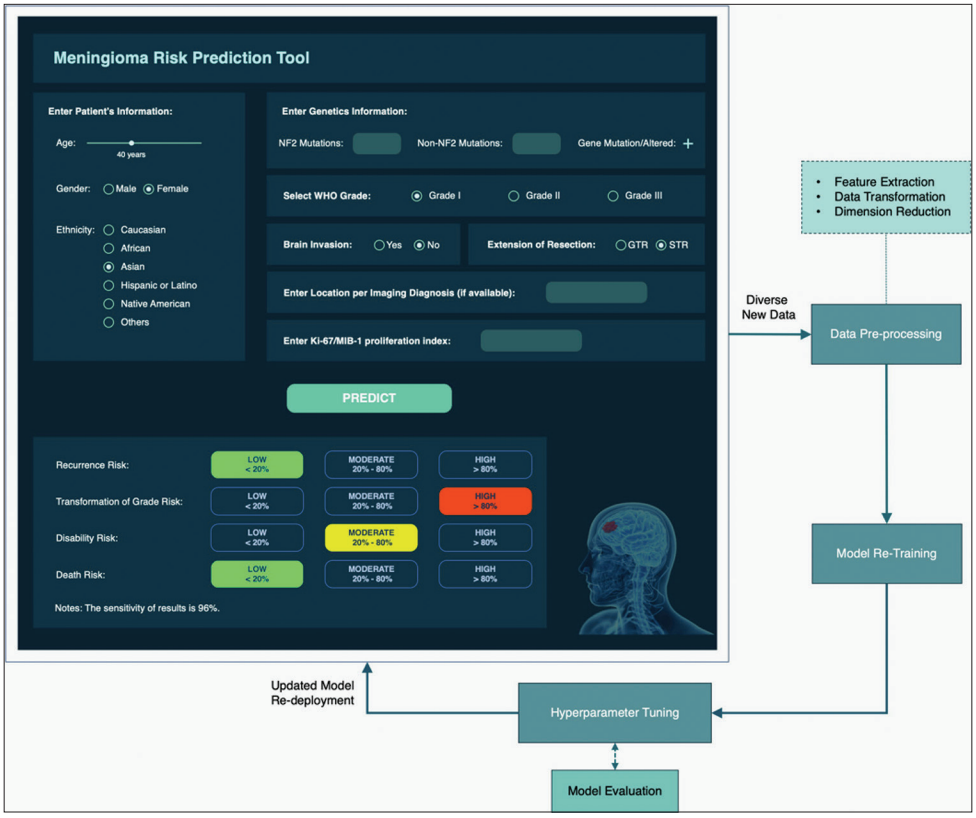

Figure 1: A graphical render of the proposed recurrence risk prediction tool for meningioma with behind the-scenes machine learning and in perpetuity refinement framework. NF: neurofibromatosis, GTR: gross-total resection, STR: sub-total resection

LIMITATIONS

To the best of our knowledge, there has been no report of a clinically validated prognostic model for predicting recurrence risk in meningioma that incorporates all the current evidence regarding clinical, radiographic, histopathologic, molecular, and outcome data of meningiomas. Despite the novelty and potential importance of the risk prediction model, the idea faces some limitations. Here, we present a theoretical framework for an online meningioma risk prediction model. We have not yet created such a model nor validated it with internal or external data; this remains a major limitation of this manuscript. This model that incorporates contemporary knowledge to select input variables remains to be tested and validated. With ongoing advances in the field of meningioma, these variables are expected to evolve continually which in turn influences the model, that is, a dynamic machine learning model. Indeed, toward widespread adoption, continued surveillance evaluation, testing, validation, and modification of the model would be necessary. Another limitation of the model is that several novel genomic and molecular data were not included as most are not clinically in use except for select lead academic centers. However, with a greater understanding of the field, more genomic and molecular data will be integrated into clinical practice and eventually into the prediction tool. Furthermore, the model is only suitable for surgically treated meningioma; hence, it cannot be used in patients with multiple or incidentally discovered meningioma.

CONCLUSION

In this scoping review, we identified the most relevant topics surrounding meningioma management and a need for an online recurrence risk prediction tool to improve patient-centered care. We highlighted the importance of predictors, including demographic, radiographic, surgical, histopathologic, and molecular factors. We introduce the idea of a risk prediction model for meningioma recurrence that can incorporate the most recent evidence in meningioma research and use a machine learning-based algorithm to provide the best methodological framework. With an increasingly aging population and increasing screening and detection of meningiomas, treatment and recurrence are gaining importance both for patient care and resource allocation for long-term surveillance. With the rise of patient-specific therapy, such a tool is timely and important for strategizing patient management as well as resource allocation accordingly.

Ethical approval

The Institutional Review Board approval is not required.

Declaration of patient consent

Patient's consent was not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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