Journal of Current Hematology & Oncology Research

Original Article

DOI: 10.51271/JCHOR-0079

Retrospective analysis of glial tumors in light of the 2016 WHO classification of central nervous system tumours diagnosed at a single center between 2005 and 2016

Nilay Bakoğlu Malinowski*[1,2], Emel Çakır[1,3], İsmail Saygın[1]

[1]Department of Medical Pathology, Faculty of Medicine, Karadeniz Technical University, Trabzon, Turkiye
[2]Department of Medical Pathology, Faculty of Medicine, İstanbul Medipol University, İstanbul, Turkiye
[3]Department of Medical Pathology, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, İstanbul, Turkiye

Cite this article: Bakoğlu Malinowski N, Çakır E, Saygın İ. Retrospective analysis of glial tumors in light of the 2016 WHO classification of central nervous system tumours diagnosed at a single center between 2005 and 2016. *J Curr Hematol Oncol Res.* 2026;4(2):31-39. doi:10.51271/JCHOR-0079

***Corresponding Author:** Nilay Bakoğlu Malinowski, bakoglunilay@gmail.com

Received: 11/02/2026 ◆ **Accepted**: 12/04/2026 ◆ **Published**: 18/05/2026

ABSTRACT

Aims: The 2016 WHO Classification of Tumors of the Central Nervous System introduced a paradigm shift by integrating molecular features with traditional histomorphology. This study aims to retrospectively re-evaluate glial tumor cases from a major tertiary center in light of these evolving classification criteria and provide a baseline for future molecular research.

Methods: A retrospective analysis was conducted on 395 glial tumor cases diagnosed at the Karadeniz Technical University Faculty of Medicine, Department of Pathology, between 2005 and 2016. The cases were re-grouped according to the 2016 WHO criteria. Due to the lack of molecular data available during the archival period, cases were categorized under the "not otherwise specified" (NOS) group to establish a comprehensive database.

Results: Among the 395 cases analyzed, glioblastoma was identified as the most frequent histological subtype (n=235). A male predominance was observed (56.5%), with mean and median ages of 48.21 and 50 years, respectively. The most common anatomical location was the frontal lobe, and histological grade IV was the most prevalent grade. Statistical analyses revealed a highly significant association between advancing age and higher tumor grade ($\chi 2=68.45$, $p<.001$), while gender distribution remained homogeneous across major histological groups ($p= 0.042$). These demographic and distribution data were consistent with global literature.

Conclusion: The findings align with international demographic trends while highlighting the practical challenges of transitioning to molecular-based classifications. While the subsequent 2021 WHO Classification further emphasizes IDH status, "histologically defined" or "NOS" designations remain crucial for regions where molecular testing infrastructure is limited. This study provides a robust archival baseline that facilitates future molecular studies and serves as a reference for glial tumor characterization in resource-constrained settings.

Keywords: Central nervous system, 2016 WHO classification, glial tumors

INTRODUCTION

Glial tumors are the most common type of brain tumors. Twenty percent (20%) of glial tumors are low-grade glial tumors.[1] The most frequently seen tumour is glioblastoma.[2] For nearly a century, the classification of brain tumors was determined based on their histomorphological characteristics, which rely on assumed cellular origins and microscopic similarities. These similarities were characterized by the light microscopic appearance of Hematoxylin & Eosin (H&E)-stained sections, immunohistochemical expressions, and electron microscopic appearances. The 2007 WHO (World Health Organization) classification grouped glial tumors as oligodendroglial or astrocytic according to their phenotype, regardless of whether they were clinically similar or distinct.[3] Genetic studies conducted in the past two decades have contributed to a better understanding and classification of these tumors.[4] The importance of the genetic profile is increasing because some genetic alterations (e.g., isocitrate dehydrogenase (IDH) mutation in diffuse gliomas) have been found to have significant prognostic meaning.[5,6] The 2016 WHO classification categorized brain tumors not only by light microscopy findings but also by incorporating molecular studies. According to the WHO 2016 classification criteria for central nervous system (CNS) tumors, gliomas are grouped as diffuse astrocytic and oligodendroglial tumors, other astrocytic tumors, ependymal tumors, and other gliomas. Diffuse astrocytic and oligodendroglial tumors were subclassified as diffuse astrocytoma, anaplastic astrocytoma, glioblastoma, diffuse midline glioma, oligodendroglioma, anaplastic oligodendroglioma, oligoastrocytoma, and anaplastic oligoastrocytoma. Diffuse astrocytomas were divided into three categories: IDH-mutant, IDH-wildtype, and not otherwise specified (NOS), while 'gemistocytic

astrocytoma' was specified as a subtype of diffuse astrocytoma. Similarly, anaplastic astrocytoma and glioblastoma were also classified according to IDH mutation. Giant cell glioblastoma, gliosarcoma, and 'epithelioid glioblastoma,' which was absent in the 2007 WHO classification, were defined as subtypes of glioblastoma. Diffuse midline glioma was specified as H3K27M-mutant. Oligodendroglioma and anaplastic oligodendroglioma were divided into two categories: IDH-mutant and 1p/19q co-deleted, and NOS. Oligoastrocytoma and anaplastic oligoastrocytoma were defined as NOS. Other astrocytic tumors were divided into four subgroups: pilocytic astrocytoma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma, and anaplastic pleomorphic xanthoastrocytoma, which was absent in the 2007 WHO classification. Ependymal tumors were divided into five groups: subependymoma, myxopapillary ependymoma, ependymoma, ependymoma RELA fusion-positive, and anaplastic ependymoma. Ependymoma, in turn, was defined in three subgroups as papillary, clear cell, and tanycytic ependymoma, and the 'cellular type' from the WHO 2007 classification was removed.[7] However, the 2021 classification incorporates additional information derived from genomic studies[8,9] various changes have been made regarding the diagnostic principles and nomenclature of diffuse gliomas, which have led to important implications for clinical practice and the design and interpretation of clinical research.[10] According to the 2021 classification, the main group "diffuse astrocytic and oligodendroglial tumors" defined in 2016 has been divided into "adult-type and pediatric-type diffuse astrocytomas" for cases above and below 18 years of age. The "other astrocytic" and "other gliomas" groups have been moved into the "circumscribed astrocytic tumors" group. Within the diffuse astrocytic and oligodendroglial tumors group, diffuse midline glioma has been separated into low-grade and high-grade, and "pediatric diffuse gliomas" have been included in the high-grade classification, with the term H3K27M 'mutant' being replaced by 'altered.' Furthermore, six new molecular types have been defined and added to the pediatric diffuse glioma groups.[11]

According to GLOBOCAN data CNS tumor cases in Turkiye increased from 2,087 in 2012 to 3,907 in 2020.[12-14] CBTRUS (Central Brain Tumor Registry of The United States) data indicate that 32.8% of CNS tumors are malignant with a higher prevalence in males (55%) while benign tumors are more frequent in females (64%).[2] Between 2016-2020 the average annual age-adjusted incidence rate (AAAIR) was 25.34 per 100,000, consistently appearing higher in females than males.[14] Anatomically, the meninges represent the most common tumor site, increasing from 36.4% in 2014 to 42% in 2022, followed by the frontal and temporal lobes. Histologically, meningioma remains the most frequent diagnosis (41.8% in 2022), followed by pituitary tumors and glioblastoma. Glioblastoma is the most prevalent malignant histology, accounting for 51.5% of cases in 2022, while gliomas overall comprise approximately 22.9% to 27% of all CNS tumors.[15,16] The development of CNS tumors is influenced by various environmental and occupational factors, with ionizing radiation and X-ray therapy identified as the most definitive risk factors for meningioma, sarcoma, and astrocytoma.[17-19] Histological grading, which determines the biological behavior of a neoplasm, plays a key role in specific chemotherapy protocols and adjuvant radiation treatments. Grade 1 and 2 tumors (low grade) exhibit lower potential for malignant progression into high grade (grade 3 and +) tumors.[20,21]

Although the fifth edition of the WHO Classification of Tumours of the CNS (2021) introduced significant changes—including the transition to Arabic numerals for grading and the integration of molecular markers such as IDH-mutation status and CDKN2A/B homozygous deletion for diagnosis—these updates are still being integrated into longitudinal statistical reporting. The molecular landscape of gliomas is defined by specific genetic alterations that serve as critical diagnostic, prognostic, and predictive markers[14,23,24] (**Figure 1**).[25,26] Notably, 1p/19q codeletion is established as a predictive marker for response to procarbazine, CCNU, and vincristine (PCV) chemotherapy in oligodendroglial tumors.[27-29] While increased EGFR activity is frequently observed in advanced-stage tumors and aids in characterization, other biomarkers such as MGMT promoter methylation status remain vital for predicting treatment response in IDH-wildtype glioblastoma.[30,31] Under the current diagnostic framework, IDH-wildtype diffuse gliomas (grades II-III) require investigation of TERT promoter mutations, EGFR amplification, and chromosome +7/–10 gain/loss to confirm molecular status. Furthermore, specific clinical contexts necessitate targeted testing: H3 K27 alterations for midline tumors, H3 G34 for pediatric and young adult IDH-wildtype cases, and MYB/MYBL1 or FGFR1 for pediatric low-grade patterns.[32] Modern classification now groups diffuse gliomas based on growth patterns integrated with driver mutations in IDH1 and IDH2.[5] In practice, while many markers like ATRX and TP53 can be assessed via immunohistochemistry, confirming 1p/19q codeletion status typically requires specialized molecular techniques such as fluorescence in situ hybridization (FISH).[33] According to the 2016 WHO classification, diagnosis was designated as NOS if molecular studies could not be performed or did not yield meaningful results. In the 2021 classification, the NOS designation has been removed, and all glial tumors are classified according to the molecular results; however, the histologically-based classification remains valid for countries lacking molecular laboratories or those with low income (**Figure 2**).[5] Under the 2021 update, the classification of adult-type diffuse gliomas is primarily dependent on IDH1/2 mutation and 1p/19q codeletion status, resulting in three distinct groups: IDH-mutant and 1p/19q-codeleted oligodendroglioma, IDH-mutant astrocytoma (1p/19q non-codeleted), and IDH-wildtype glioblastoma. This revision strictly separates IDH-mutant from IDH-wildtype disease—a necessity given the substantial survival discrepancy between the two, even among tumors sharing the same histopathological feature.[34] We aimed to retrospectively evaluate glial tumor cases diagnosed at Karadeniz Technical University Faculty of Medicine Hospital between 2005 and 2016 according to the 2016 WHO classification, intending to create a resource to contribute to future molecular studies.

METHODS

The study was conducted in accordance with the Declaration of Helsinki. This study was approved by the Karadeniz Technical University Faculty of Medicine Ethics Committee (Date: 28.11.2016, Decision No: 2016169). The authors

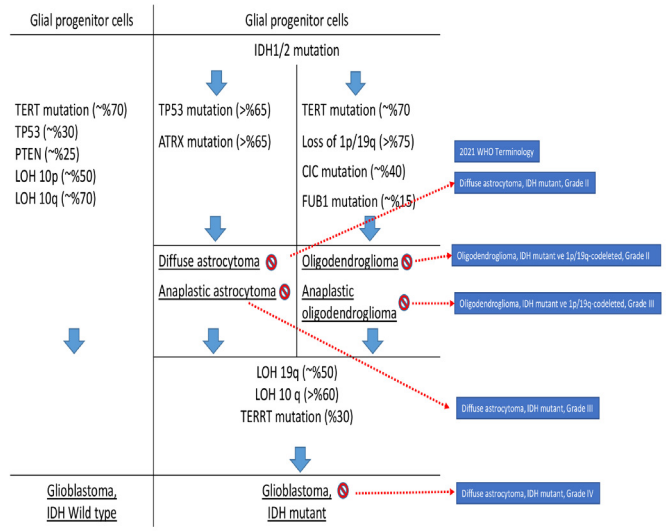

Figure 1. Genetic parameters of glial cells and the IDH1/2 molecular pathway, IDH status in glioblastomas, and terminological shifts between 2016 and 2021. The left panel shows the genetic pathway based on the primary vs. secondary glioblastoma distinction (WHO 2016); the right panel (highlighted in blue) illustrates how this terminology evolved in the WHO 2021 classification.
IDH: Isocitrate dehydrogenase

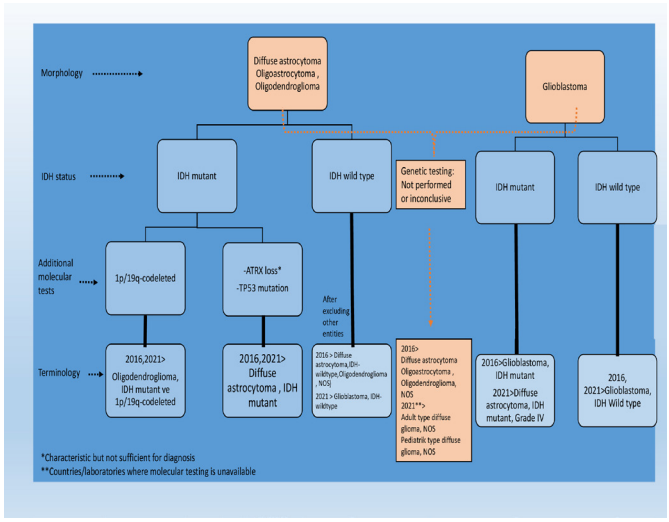

Figure 2. Comparison of genetic parameters used in clinical practice and terminology according to the 2016 and 2021 WHO classifications. While the 2016 WHO classification follows a histology-first followed by IDH mutation sequence, the 2021 WHO adopts IDH mutation as the primary step. A key change, besides the separation of adult and pediatric glial tumors, is that high-grade glial tumors with IDH mutations are now defined as "Astrocytoma, IDH-mutant, grade 4" instead of "glioblastoma, grade 4."
IDH: Isocitrate dehydrogenase

declared that this study has received no financial support. Our study consisted of glial tumors diagnosed at the Pathology Laboratory of Karadeniz Technical University Faculty of Medicine between 2005 and 2016. A total of 428 glial tumor cases were identified in our laboratory. Twenty-nine cases were excluded from the study because their histological grades were not assigned. The cases included in this study were diagnosed by experienced senior neuropathologists at a tertiary referral center, following the diagnostic gold standard of the respective period. To ensure the integrity of the archival data and to avoid potential inter-observer variability, the original pathological diagnoses and histological grades were strictly maintained. This approach preserves the real-world diagnostic performance of the center during the 11-year study period.

Statistical Analysis

The data analyses were performed on a total of 395 glial tumor cases. Parameters that could be compared, such as demographic findings (age, sex, and location), were determined based on the pathological diagnosis. Statistical analyses were performed by grouping the cases according to the 2016 WHO classification. The cases were evaluated across four main histological groups: 1) Diffuse astrocytic and oligodendroglial tumors, 2) Other astrocytic tumors, 3) Ependymal tumors, and 4) Other gliomas. The main groups were further divided into subgroups. In our study, all subgroups were compared with demographic characteristics. Statistical analyses were conducted with support from the Department of Public Health at Karadeniz Technical University Faculty of Medicine using SPSS 23.00. The 'sensitivity-specificity' test was applied for the use of qualitative data. Count data were expressed as percentages. While qualitative data were specified as numbers and percentages, measurement data were used by providing the median and mean values. Statistical analyses were performed using SPSS software (SPSS v23). Continuous variables such as age were expressed as mean, median, and range. Categorical variables (sex, location, subtype) were presented as frequencies and percentages. To evaluate the relationship between histological subtypes and clinical parameters (age groups, sex, and anatomical localization), Pearson Chi-square (x^2) tests or Fisher's exact tests were utilized where appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Demographic data for all glial tumors (histological subtypes, case numbers and percentages, case count per histological subtype, minimum, maximum age, mean, and median age values) are summarized in **Table 1**.

Distribution of Glial Tumors According to Their Histological Subtypes

The study cohort comprised a total of 395 glial tumor cases, which were categorized into four primary groups according to the 2016 WHO classification system. The most prevalent category was diffuse astrocytic and oligodendroglial tumors, accounting for 319 cases (80.8%), followed by ependymal tumors (49 cases; 12.4%) and other astrocytic tumors (27 cases; 6.8%); notably, no cases of "other gliomas" (group 4) were identified within the archive. Within the dominant first group, glioblastoma was the most frequent histological subtype (235 cases; 73.7%), followed by diffuse astrocytoma (13.8%), oligodendroglioma (4.7%), anaplastic astrocytoma (4.1%), and anaplastic oligodendroglioma (3.8%). Regarding group 2 ("other astrocytomas"), pilocytic astrocytoma constituted nearly the entire subset (26 of 27 cases), while group 3 (ependymal tumors) was primarily represented by ependymoma (67.3%), with smaller distributions of myxopapillary ependymoma (22.4%), anaplastic ependymoma (8.2%), and subependymoma (2%). Aggregated data across the entire 395-case series identifies glioblastoma as the overall most common diagnosis (59.5%), followed in descending order of frequency by diffuse astrocytoma (11.1%), all ependymoma (8.4%), and pilocytic astrocytoma (6.6%), with all remaining subtypes individually accounting for less than 4% of the total archive.

Table 1. Histological subtypes of all glial tumors: case numbers and percentages, case distribution across subtypes, minimum and maximum age ranges, and mean and median age values

Glial tumors	Percentage	Female	Male	Minimum age	Maximum age	Mean age	Medium age
Diffuse astrocytic and oligodendroglial tumors	80.80%	131	188	1	82	53.06	56
Diffuse astrocytoma	11.10%	20	24	1	81	42.57	41
Anaplastic astrocytoma	3.30%	3	10	7	76	46.31	37
Glioblastoma	59.50%	95	140	1	82	56.83	59
Oligodendroglioma	3.80%	7	8	13	71	38.27	37
Anaplastic oligodendroglioma	3%	6	6	30	57	43.58	45
Other astrocytic tumors	6.80%	15	12	2	41	14.74	14
Pilocytic astrocytoma	6.60%	15	11	2	41	14.69	13.6
Pleomorphic xanthoastrocytoma	0.30%	0	1	16	16	16	16
Ependymal tumors	12.40%	26	23	1	75	35.1	35
Myxopapillary ependymoma	2.80%	5	6	12	65	37.18	35
Ependymoma	8.40%	19	14	1	75	38.18	38
Anaplastic ependymoma	1%	1	3	2	17	9	8.5
Subependymoma	0.30%	1	0	15	15	15	15
Total	100%	172	223	1	82	48.21	50

Distribution of Glial Tumors by Sex

The study cohort comprised 395 glial tumor cases, exhibiting a male predominance of 56.5% (n=223) compared to 43.5% females (n=172). Across both gender cohorts, glioblastoma was identified as the most prevalent histological entity, representing 55.2% of female and 62.8% of male cases. In both groups, diffuse astrocytoma followed as the second most common subtype, occurring in 11.6% of females and 10.8% of males. Subsequent distributions for both cohorts included ependymoma, pilocytic astrocytoma, and various anaplastic variants, as detailed in **Table 1**. Analysis of sex-based distribution within the WHO 2016 classification groups revealed distinct patterns. Group 1 (diffuse astrocytic and oligodendroglial tumors; n=319) showed a significant male bias at 58.9%. Within this category, glioblastoma (n=235) and diffuse astrocytoma (n=44) both demonstrated a higher frequency in males (59.6% and 54.5%, respectively), while anaplastic oligodendrogliomas displayed an equal gender distribution (50% each). Conversely, a slight female predilection was observed in group 2 (other astrocytomas, 55.6%) and group 3 (ependymal tumors, 53.1%). Specifically, females constituted the majority of cases for pilocytic astrocytoma (57.7%) and ependymoma (57.6%). In contrast, rarer entities such as anaplastic ependymoma and pleomorphic xanthoastrocytoma were predominantly or exclusively identified in male patients (**Table 1**).

Distribution of Glial Tumors by Age

The study population (n=395) exhibited an age range of 1 to 82 years, with a mean age of 48.21 years and a median of 50 years. Analysis by WHO classification groups revealed distinct chronological profiles: the "diffuse astrocytic and oligodendroglial tumors" group showed the highest mean age (53.06 years), whereas "other astrocytomas" (primarily pilocytic) and "ependymal tumors" occurred in significantly younger populations, with mean ages of 14.74 and 35.10 years, respectively (**Table 1**). Age-specific histological trends were highly pronounced when stratified by the 50-year threshold. In the under-50 cohort (n=185), glioblastoma was the most frequent diagnosis (32.4%), followed by diffuse astrocytoma (15.7%) and ependymoma (14.6%). In sharp contrast, the over-50 cohort (n=210) was heavily dominated by glioblastoma, which accounted for 83.3% of all cases in this demographic. Further stratification into three age tiers—pediatric/adolescent (<20), young adult (20–39), and mature adult (>39)—underscored a clear pathological shift: Under 20 years (10.6%): Pilocytic astrocytoma was the predominant entity (47.6%), while glioblastoma was rare (16.7%).20–39 years (18.5%): The diagnostic landscape was more heterogeneous, led by diffuse astrocytoma (24.7%) and ependymoma (20.5%).Over 39 years (70.9%): Glioblastoma became the definitive majority (76.8%), followed by diffuse astrocytoma (8.2%). Notably, anaplastic ependymomas were confined to a pediatric/adolescent window (mean age: 9 years), whereas glioblastomas reached their peak incidence in the sixth decade of life (mean age: 56.83). These findings highlight a strong correlation between advancing age and the increased prevalence of high-grade glial malignancies (**Table 1**).

Distribution of Glial Tumors According to Their Locations

Among the 395 glial tumor cases analyzed, the frontal lobe was the most prevalent site of localization, accounting for 28.4% of cases (n=112), followed by the parietal (26.3%) and temporal (23.3%) lobes. Less frequent sites included the spinal cord (10.1%), the posterior fossa (7.6%), and the occipital lobe (2.3%), with minimal involvement observed in the ventricles, basal ganglia, and corpus callosum. Histological sub-analysis revealed distinct anatomical preferences: diffuse astrocytomas (n=44) and oligodendrogliomas (n=15) predominantly favored the frontal lobe at 38.6% and 86.7%, respectively, while anaplastic astrocytomas (n=13) were most common in the temporal lobe (38.5%). Glioblastomas (n=235) demonstrated a relatively even distribution across the temporal (32.3%), parietal (31.9%), and frontal (29.8%) lobes. Notably, pilocytic astrocytomas (n=26) showed a strong predilection for the posterior fossa (73.1%), whereas ependymal tumors were largely concentrated in the spinal cord, including 100% of myxopapillary ependymomas (n=11) and 69.7% of standard ependymomas (n=33). Conversely, anaplastic ependymomas were primarily localized to the

posterior fossa (75%). Rare instances, such as pleomorphic xanthoastrocytoma and subependymoma, were isolated to the parietal lobe and lateral ventricle, respectively.

Distribution of Glial Tumors According to Their Histological Grades

In 395 glial tumors, 235 cases (59.5%) were found to be grade 4. The number of grade 2 cases is 91 (23%), grade 1 cases is 39 (9.9%), and grade 3 cases is 30 (7.6%). The majority of the 44 diffuse astrocytoma cases are grade 2, with 42 cases (95%), while the remaining 2 cases (4.5%) are grade 3.

Comparative Analysis of Histological Subtypes, Age, Sex, and Localization

The clinico-anatomical distribution and histological grading of the 395 glial tumor cases are summarized in **Table 2**. Statistical analysis revealed a highly significant correlation between histological subtype and anatomical localization (Fisher's exact test, $p<0.001$). The frontal lobe was the most frequent site overall (28.4%); however, distinct predilections were observed for specific subtypes: 86.7% of oligodendrogliomas were localized to the frontal lobe, while 73.1% of pilocytic astrocytomas were situated in the posterior fossa. Notably, all myxopapillary ependymomas (100%) and a vast majority of standard ependymomas (69.7%) were identified within the spinal cord. Regarding demographics, a significant association was found between patient age and tumor type (x^2 test, $p<0.001$). While the cohort's median age was 50 years, glioblastoma (the most prevalent subtype at 59.5%) showed a marked concentration in the older population, representing 83.3% of all cases in patients aged ≥50. Conversely, pilocytic astrocytoma was the dominant diagnosis in the pediatric and adolescent group (under 20 years), accounting for 47.6% of cases in that bracket. Gender distribution also showed a statistically significant male predominance overall (56.5%, $p=0.042$), which was most pronounced in the anaplastic astrocytoma subgroup (76.9% male). Finally, histological grading reflected a high prevalence of aggressive malignancies, with grade IV (glioblastoma) constituting 59.5% of the total cohort, followed by grade II tumors (23%).

DISCUSSION

Histologic Subtypes

Glioblastoma remains the most prevalent primary malignant brain tumor globally.[35-37] In our cohort, glioblastoma accounted for 59.5% of cases, aligning with the 2022 CBTRUS report, which identifies diffuse astrocytic and oligodendroglial tumors as the most frequent CNS category (18.8%), with glioblastoma maintaining the highest incidence (14.2%).[38] Following glioblastoma, diffuse astrocytomas constituted our second largest group (11.1%), a distribution consistent with most Western literature but contrasting with data from the Brain Tumor Registry of Japan (BTJ), where anaplastic astrocytomas occurred more frequently.[39] While recent literature emphasizes the prognostic weight of molecular markers—noting that IDH-wildtype cases comprise the vast majority (78.5%) of glioblastomas[39] —our cases are classified as NOS due to a lack of molecular profiling. Despite this, the transition from the 2016 to the 2021 WHO Classification does not significantly alter our primary categorical findings. The 319 diffuse tumors in our study would largely redistribute into the 2021 "adult-type diffuse gliomas" category (306 cases), while our "other astrocytic tumors" would align with "circumscribed astrocytic gliomas." Critically, the demographic trends observed in our cohort—including age, sex, and localization—remain diagnostically valid and clinically relevant across both classification frameworks. A recent study at Prof. Dr. Cemil Taşcıoğlu City Hospital in Turkiye (2023) confirm that high-grade gliomas (HGG) dominate clinical cohorts in Turkish tertiary centers.[40] In a Turkish study published in the Turkish Neurosurgery (2021), glioblastoma was consistently the primary diagnosis, mirroring our 59.5% rate.[41]

Sex

The 2016 CBTRUS report indicates a female predominance (57.9%) in the overall incidence of brain tumors. In contrast, malignant tumors are more common among males, who represent 55.2% of such cases. Furthermore, all glial tumor types—excluding pilocytic astrocytomas—demonstrate a higher frequency in the male population.[2] According to

Table 2. Clinicopathological characteristics and anatomical distribution of glial tumors in relation to histological grading and patient demographics (n=395)

Histological subtype	n (%)	Mean age	Gender (F/M)	Primary localization (%)	WHO grade
Glioblastoma	235 (59.5%)	56.8	95 / 140	Temporal (32.3%)	IV
Diffuse astrocytoma	44 (11.1%)	42.6	20 / 24	Frontal (38.6%)	II
Ependymoma	33 (8.4%)	38.2	19 / 14	Spinal cord (69.7%)	II
Pilocytic astrocytoma	26 (6.6%)	14.7	15 / 11	Post. fossa (73.1%)	I
Oligodendroglioma	15 (3.8%)	38.3	7 / 8	Frontal (86.7%)	II
Anaplastic astrocytoma	13 (3.3%)	46.3	3 / 10	Temporal (38.5%)	III
Anaplastic oligo	12 (3.0%)	43.6	6 / 6	Frontal/parietal (50%)	III
Myxopapillary epend	11 (2.8%)	37.2	5 / 6	Spinal cord (100%)	I
Anaplastic ependymoma	4 (1.0%)	9.0	1 / 3	Post. fossa (75%)	III
Others (PXA, subepend.)	2 (0.6%)	-	1 / 1	Various	I/II
Total/overall	395 (100%)	48.2	172 / 223	Frontal (28.4%)	-
Statistical analysis		p<0.001*	p=0.042	p<0.001*	

F: Female, M: Male

2022 worldwide cancer statistics, primary malignant brain tumors exhibited a male disparity; of the 321,731 diagnosed cases, 173,699 were male and 148,032 were female.[42] Males predominated in several categories, including diffuse astrocytic and oligodendroglial tumors (48% to 35%), other astrocytic tumors (3% to 2.9%), ependymal tumors (3.9% to 2.9%), and other gliomas (4.4% to 4.3%). Conversely, oligodendroglioma and oligoastrocytoma showed a female-to-male disparity favoring females. Similarly, a retrospective Japanese study of glial tumors reported a cohort of 149 females and 238 males, with a median age of 60 (range 3–88 years).[43] In alignment with existing literature, our findings showed a male predominance (56.5%) in glial tumors. Contrary to the 2015–2019 data, however, female predominance was observed in both pilocytic astrocytomas and ependymal tumors. Furthermore, Ohgaki et al.[24] reported glioblastoma incidence rates of 3.32 and 2.24 per 100,000 for males and females, respectively. In the United States, higher incidence rates have been reported, specifically 2.88 and 4.63 per 100,000 for females and males, respectively. CBTRUS reports from 2009–2013 identified a 1.57-fold higher incidence of glioblastoma in males compared to females, a figure that declined to 1.4 in the 2015–2019 period. Similarly, a study based in the UK documented a higher male-to-female ratio of 1.66.[44] The corresponding ratio in our study was 1.47, falling within the range reported in the literature. A Turkish study (Bilgin et al.,[40] 2021) reported a mean age of 56.4 for primary glioblastoma with a 56.9% male ratio. This almost perfectly matches our mean age (56.8) and male percentage (56.5%). Data from Erciyes University (2017) regarding childhood glial tumors in Turkiye shows a median age of median age at diagnosis was 17 months, with pilocytic astrocytoma being the most common.[45] Our pediatric concentration in the 0–9 age group (45%) aligns with these national statistics.

Age

Age-stratified distribution and pediatric vs. adult disparities CNS neoplasms represent the most prevalent malignancy in the 0–14 age group, with incidence rates increasing significantly into adulthood.[46] Our cohort's demographic profile strongly correlates with these global trends, with 375 of 395 cases occurring in patients older than 10 years. While CBTRUS 2009–2013 data identifies a peak incidence in the ≥85 age group (84.52 per 100,000), our findings confirm that glial tumors remain predominantly a disease of the elderly, evidenced by the marked statistical divergence between pediatric and adult populations.[2,12] The pediatric landscape: pilocytic astrocytoma in the pediatric population, pilocytic astrocytoma emerged as the predominant subtype. In our study, this was particularly evident in the 0–9 age range, where it accounted for 45% of glial tumors—a finding that mirrors the 2015–2019 CBTRUS data (incidence: 1.13).[47] Notably, this subtype was entirely absent in our cohort over 50 years of age. While the BTJ identifies diffuse astrocytoma as the most frequent subtype in patients under 20, our data showed pilocytic astrocytoma (47.6%) as the primary diagnosis, followed by glioblastoma (16.7%). This higher-than-expected frequency of glioblastoma in our younger patients represents a slight deviation from the BTJ findings but aligns with 2023 CBTRUS updates, which rank malignant ependymal tumors and glioblastomas as secondary frequent types in the 0–19 bracket.[13,36] Adult and elderly populations: glioblastoma dominance for patients over 50, glioblastom was the overwhelmingly dominant subtype, representing 83.3% of cases. This aligns with the mean age of 62 years reported by Ohgaki et al.,[24] and the median age of 65 documented for IDH-wildtype astrocytomas. The age-dependent increase in glioblastoma incidence—rising from 5% in our 0–9 age group to 61.3% in those older than 10—confirms the progressive risk associated with advancing age identified in the BTJ and CBTRUS datasets.[40,49] Our median age results showed a minimal discrepancy of only 1–2 years compared to international literature, reinforcing that our cohort serves as a representative model for the typical pediatric-to-adult distribution of glial neoplasms.

Location

Anatomical distribution analysis revealed that 80% of glial tumors in this cohort were localized within the cerebral lobes, with the frontal lobe (28.4%) being the most prevalent site, followed by an equal distribution between the parietal and temporal lobes (26.3% each). While these findings generally align with CBTRUS 2016–2020 data—which identifies the frontal and parietal regions as primary sites (16.6% and 7.4%, respectively)—our results demonstrate a distinct temporal lobe parity.[13,50] Subtype-specific topography corroborated the strong frontal lobe affinity reported by the BTJ for oligodendrogliomas (86.7%), yet diverged regarding diffuse astrocytomas, which showed an equal prevalence in the temporal and parietal lobes (22.7%) after the frontal region.[36] Furthermore, our data showed a temporal lobe predominance for high-grade cases, contrasting with UK-based and Istanbul University studies that identified the frontal lobe as the primary site for glioblastoma (24.9% and predominant, respectively).[34] Regarding infratentorial distribution, our findings reflected the lower prevalence noted in the literature, with ependymal neoplasms being the predominant diagnosis in these regions, whereas pilocytic astrocytomas (3.8%) and standard ependymomas (3%) showed minimal frontal involvement.[36] These discrepancies, including the equal prevalence of oligodendroglioma in both the parietal and frontal lobes, suggest notable regional variations in glial tumor topography compared to established populations like those described by Yoshikazu et al.[48] While many global studies cite the frontal lobe as the most common site, a recent study in Turkiye for low grade gliomas and our findings show a temporal lobe lead.

Grade

In our study, more than half of the cases were classified as grade 4, while grade 3 was the least frequent. Although no changes were made in the WHO 2016 grading system itself, considering the updates introduced in the WHO 2021 classification, many IDH-wildtype grade 2 and 3 astrocytomas can now be reclassified as grade 4 glioblastoma. A study focusing on the 2016 revision of high-grade oligodendroglial tumors observed a shift from grade 3 to grade 4, accompanied by an increased incidence of glioblastoma. This shift was more pronounced in cases previously diagnosed as grade 3 oligoastrocytoma, as approximately 50% were reclassified as glioblastoma (either IDH-mutant or IDH-wildtype). Furthermore, while the 2016 WHO classification demonstrated high prognostic value, it was concluded that the distinction between grade 3 and grade 4 was not prognostic for either IDH-mutant/1p/19q-intact gliomas or IDH-wildtype gliomas; this has sparked a

debate regarding the grading of these tumors. Notably, no significant prognostic difference was found between IDH-mutant/1p/19q-intact gliomas and IDH-wildtype grade 3 and 4 gliomas.[53,54]

Contextualizing Histopathological Findings within the WHO 2021 Classification Framework

While our findings are categorized based on the 2016 WHO Classification, it is critical to evaluate the observed clinico-pathological patterns through the lens of the 2021 WHO Classification (5th Edition), which has fundamentally decoupled morphology from molecular identity. For instance, the striking frontal lobe predilection (86.7%) observed in our oligodendroglioma cases serves as a robust clinical surrogate that aligns with the current requirement for IDH mutation and 1p/19q co-deletion—the molecular hallmarks now defining this entity. Similarly, our data highlights a high prevalence of glioblastoma (59.5%), particularly in the over-50 demographic; however, under the 2021 criteria, these would be strictly stratified as IDH-wildtype, whereas high-grade cases in our younger cohorts (20–39 years) might now be reclassified as Astrocytoma, IDH-mutant, grade 4. Furthermore, the anatomical clustering of our ependymal tumors—notably the spinal concentration of myxopapillary and standard variants—mirrors the 2021 framework's move toward site-specific molecular subgroups. By mapping these histological distributions, our study provides a necessary phenotypic baseline. This morphologic-anatomical map not only validates traditional diagnostic patterns but also serves as the essential scaffolding upon which future molecular re-stratification can be built, ensuring that the transition from NOS-based reporting to integrated molecular diagnostics is grounded in established clinical trends.

Limitations

Despite the comprehensive nature of this demographic analysis, our study has several limitations that warrant consideration. The primary constraint is the absence of molecular diagnostic data—such as IDH1/2 mutation status, 1p/19q codeletion, and ATRX expression—due to technical and financial limitations during the study period. Consequently, a significant portion of our cohort was classified under the 'NOS' designation, as mandated by the WHO 2016 and 2021 criteria when molecular parameters are unavailable. Furthermore, the retrospective and single-center design of the study may limit the generalizability of our findings to the broader population. However, we believe that providing this baseline morphological and demographic data remains crucial, as it establishes a necessary framework for future research that will integrate molecular subtyping as laboratory infrastructure continues to expand.

CONCLUSION

When analyzed under the four primary categories of the 2016 WHO classification, 319 (80.8%) of the 395 glial tumor cases in our study were identified within the 'diffuse astrocytic and oligodendroglial tumors' group. Additionally, 49 cases (12.4%) were categorized as 'ependymal tumors,' while 27 cases (6.8%) were classified as 'other astrocytic tumors.' The fourth category, 'other gliomas,' was not represented in our series as no such diagnoses were rendered in our department during the study period. Because the 2016 WHO classification is fundamentally based on molecular parameters and our cases were diagnosed without access to molecular testing, all such cases were classified under the NOS category. Due to financial constraints and time limitations, cases falling under the diffuse astrocytoma and oligodendroglial tumor headings were consolidated under the NOS designation. By establishing this comprehensive database, we aim to facilitate the integration of molecular analyses into future doctoral and residency theses within our department. Furthermore, by providing essential demographic data, our study will serve as a foundational guide for subsequent subtyping research, thereby reducing the future institutional workload. As classification and prognostic stratification become increasingly reliant on molecular features, the clinical significance of laboratory biomarker testing continues to rise. In current pathological practice, while surrogate immunohistochemical markers such as IDH1/2 and ATRX provide a practical and accessible diagnostic framework, it is essential to recognize that more advanced molecular techniques, specifically FISH, remain indispensable for the definitive assessment of 1p/19q codeletion status. The WHO 2021 classification has expanded the trend initiated in 2016 by utilizing core molecular biomarkers to define neoplasia and substantially reducing the reliance on morphological features for tumor classification. The terminology regarding tumor grading has also been simplified; while molecular features now dictate the classification, the integration of histopathological and molecular analyses determines the grade. In line with the 2021 update, our diagnostic approach for adult-type diffuse gliomas prioritized IDH1/2 mutation and 1p/19q codeletion status, categorizing cases into three distinct groups: IDH-mutant and 1p/19q-codeleted oligodendroglioma, IDH-mutant astrocytoma, and IDH-wildtype glioblastoma. In summary, we highlight that the molecular divergence between IDH-mutant and IDH-wildtype disease remains the most reliable prognostic indicator. Given the substantial discrepancy in survival between these two groups, this classification should be maintained as a priority over traditional histopathology alone. The expansion of molecular laboratory infrastructure in our country over the past decade has paved the way for deeper insights through molecular diagnostics. Nevertheless, incorporating these biomarkers into national cancer registries remains a complex undertaking requiring ongoing professional development. In the interim, considering the current limitations in some laboratory settings, the demographic profiles established in this study maintain their clinical significance as they will facilitate the categorization of future molecular cohorts.

ETHICAL DECLARATIONS

Ethics Committee Approval

This study was approved by the Karadeniz Technical University Faculty of Medicine Ethics Committee (Date: 28.11.2016, Decision No: 2016169).

Informed Consent

This retrospective study used pre-existing anonymized patient data. No additional intervention was performed, and there was no direct patient contact. The study was approved by the Ethics Committee, and the requirement for written informed consent was waived by the ethics committee.

Peer Review Process
This manuscript was subject to external peer review.

Conflict of Interest
The authors declare no conflicts of interest related to this study.

Financial Disclosure
The authors received no financial support for the conduct or publication of this research.

Author Contributions
Concept: NBM, EÇ; Design: NBM; Control: NBM, EÇ; Resources: NBM; Data Collection and/or Processing: NBM, İS; Analysis and/or Interpretation: NBM, İS; Literature Review: NBM; Writing the Article: NBM, EÇ, İS; Critical Review: NBM, EÇ, İS.

REFERENCES

1. Brunetti A, Alfano B, Soricelli A, et al. Functional characterization of brain tumors: an overview of the potential clinical value. *Nucl Med Biol.* 1996;23(6):699-715. doi:10.1016/0969-8051(96)00069-8
2. Ostrom QT, Gittleman H, Xu J, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2009–2013. *Neuro Oncol.* 2016;18:v1–v75. doi:10.1093/neuonc/now207
3. Leece R, Xu J, Ostrom QT, Chen Y, Kruchko C, Barnholtz-Sloan JS. Global incidence of malignant brain and other central nervous system tumors by histology, 2003–2007. *Neuro Oncol.* 2017;19(11):1553-1564. doi:10.1093/neuonc/nox091
4. Louis DN. The next step in brain tumor classification: "let us now praise famous men"… or molecules? *Acta Neuropathol.* 2012;124(6):761-762. doi:10.1007/s00401-012-1067-4
5. Leeper HE, Caron AA, Decker PA, Jenkins RB, Lachance DH, Giannini C. IDH mutation, 1p19q codeletion and ATRX loss in WHO grade II gliomas. *Oncotarget.* 2015;6(30):30295.
6. Weller M, Weber RG, Willscher E, et al. Molecular classification of diffuse cerebral WHO grade II/III gliomas using genome- and transcriptome-wide profiling improves stratification of prognostically distinct patient groups. *Acta Neuropathol.* 2015;129(5):679-693. doi:10.1007/s00401-015-1409-0
7. Louis DN, Perry A, Reifenberger G, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol.* 2016;131(6):803-820. doi:10.1007/s00401-016-1545-1
8. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. *Neuro Oncol.* 2021;23(8):1231-1251. doi:10.1093/neuonc/noab106
9. Tesileanu CMS, Dirven L, Wijnenga MMJ, et al. Survival of diffuse astrocytic glioma, IDH1/2 wildtype, with molecular features of glioblastoma, WHO grade IV: a confirmation of the cIMPACT-NOW criteria. *Neuro Oncol.* 2020;22(4):515-523. doi:10.1093/neuonc/noz200
10. Gritsch S, Batchelor TT, Gonzalez Castro LN. Diagnostic, therapeutic, and prognostic implications of the 2021 World Health Organization classification of tumors of the central nervous system. *Cancer.* 2022;128(1):47-58. doi:10.1002/cncr.33918
11. Van den Bent MJ, Geurts M, French PJ, et al. Primary brain tumours in adults. *Lancet.* 2023;402(10412):1564-1579. doi:10.1016/S0140-6736(23)01054-1
12. Ferlay JE, Lam F. Global cancer observatory: cancer today (Version 1.0). International Agency for Research on Cancer [Internet]. 2024. https://gco.iarc.who.int/today
13. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN estimates of ıncidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2021;71(3):209-249. doi:10.3322/caac.21660
14. Ferlay J, Colombet M, Soerjomataram I, et al. Cancer statistics for the year 2020: an overview. Int J Cancer. 2021. doi:10.1002/ijc.33588
15. Ostrom QT, Gittleman H, Fulop J, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. *Neuro Oncol.* 2015;17(Suppl 4):iv1-iv62. doi:10.1093/neuonc/nov189
16. Ostrom QT, Price M, Neff C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2016-2020. *Neuro Oncol.* 2023;25(12 Suppl 2):iv1-iv99. doi:10.1093/neuonc/noad149
17. Braganza MZ, Kitahara CM, Berrington de González A, Inskip PD, Johnson KJ, Rajaraman P. Ionizing radiation and the risk of brain and central nervous system tumors: a systematic review. *Neuro Oncol.* 2012;14(11):1316-1324. doi:10.1093/neuonc/nos208
18. Mack EE, Wilson CB. Meningiomas induced by high-dose cranial irradiation. *J Neurosurg.* 1993;79(1):28-31. doi:10.3171/jns.1993.79.1.0028
19. Ostrom QT, Bauchet L, Davis FG, et al. The epidemiology of glioma in adults: a "state of the science" review. *Neuro Oncol.* 2014;16(7):896-913. doi:10.1093/neuonc/nou087
20. Louis DN, Ohgaki H, Wiestler OD, Cavenee WK, World Health Organization (WHO) classification ot tumours of the central nervous system, 3rd edition, International Agency for Research on Cancer. Lyon. 2007.
21. Network TC. Corrigendum: Comprehensive genomic characterization defines human glioblastoma genes and core pathways. *Nature.* 2013;494(7438):506. doi:10.1038/nature11903
22. Torp SH, Solheim O, Skjulsvik AJ. The WHO 2021 Classification of Central Nervous System tumours: a practical update on what neurosurgeons need to know—a minireview. Acta Neurochir. 2022;164(9):2453-2464. doi:10.1007/s00701-022-05301-y
23. Riemenschneider MJ, Jeuken JW, Wesseling P, Reifenberger G. Molecular diagnostics of gliomas: state of the art. *Acta Neuropathol.* 2010;120(5): 567-584. doi:10.1007/s00401-010-0736-4
24. Ohgaki H, Kleihues P. Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendroglial gliomas. *J Neuropathol Exp Neurol.* 2005;64(6):479-489. doi:10.1093/jnen/64.6.479
25. Korshunov A, Meyer J, Capper D, et al. Combined molecular analysis of BRAF and IDH1 distinguishes pilocytic astrocytoma from diffuse astrocytoma. *Acta Neuropathol.* 2009;118(3):401-405. doi:10.1007/s00401-009-0550-z
26. Ohgaki H, Kleihues P. Epidemiology and etiology of gliomas. *Acta Neuropathol.* 2005;109(1):93-108. doi:10.1007/s00401-005-0991-y
27. Aldape K, Burger PC, Perry A. Clinicopathologic aspects of 1p/19q loss and the diagnosis of oligodendroglioma. *Arch Pathol Lab Med.* 2007;131(2):242-251. doi:10.5858/2007-131-242-CAOQLA
28. Van den Bent MJ, Brandes AA, Taphoorn MJ, et al. Adjuvant procarbazine, lomustine, and vincristine chemotherapy in newly diagnosed anaplastic oligodendroglioma: long-term follow-up of EORTC brain tumor group study 26951. *J Clin Oncol.* 2013;31(3):344-350. doi:10.1200/JCO.2012.43.2229
29. Cairncross G, Wang M, Shaw E, et al. Phase III trial of chemoradiotherapy for anaplastic oligodendroglioma: long-term results of RTOG 9402. *J Clin Oncol.* 2013;31(3):337-343. doi:10.1200/JCO.2012.43.2674
30. Ueki K, Nishikawa R, Nakazato Y, et al. Correlation of histology and molecular genetic analysis of 1p, 19q, 10q, TP53, EGFR, CDK4, and CDKN2A in 91 astrocytic and oligodendroglial tumors. *Clin Cancer Res.* 2002;8(1):196-201.
31. Li L, Dutra A, Pak E, et al. EGFRvIII expression and PTEN loss synergistically induce chromosomal instability and glial tumors. *Neuro Oncol.* 2009;11(1):9-21. doi:10.1215/15228517-2008-081
32. Park YW, Vollmuth P, Foltyn-Dumitru M, et al. The 2021 WHO classification for gliomas and implications on imaging diagnosis: part 1—Key points of the fifth edition and summary of imaging findings on adult-type diffuse gliomas. *J Magn Reson Imaging.* 2023;58(3):677-689. doi:10.1002/jmri.28743
33. Whitfield BT, Huse JT. Classification of adult-type diffuse gliomas: impact of the World Health Organization 2021 update. *Brain Pathol.* 2022;32(4):e13062. doi:10.1111/bpa.13062
34. Hartmann C, Hentschel B, Simon M, et al. Long-term survival in primary glioblastoma with versus without isocitrate dehydrogenase mutations. *Clin Cancer Res.* 2013;19(18):5146-5157. doi:10.1158/1078-0432.CCR-13-0017
35. Prayson RA. Neuropathology. In: Foundations in diagnostic pathology. Philadelphia, PA: Elsevier Churchill Livingstone; 2007:160-309.
36. Ohgaki H, Dessen P, Jourde B, et al. Genetic pathways to glioblastoma: a population-based study. *Cancer Res.* 2004;64(19):6892-6899. doi:10.1158/0008-5472.CAN-04-1337
37. Ohgaki H, Kleihues P. The definition of primary and secondary glioblastoma. *Clin Cancer Res.* 2013;19(4):764-772. doi:10.1158/1078-0432.CCR-12-3002

38. Ostrom QT, Price M, Neff C, et al. CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2015–2019. *Neuro Oncol.* 2022;24(Suppl 5):v1-v95. doi:10.1093/neuonc/noac202
39. Narita Y, Shibui S; Committee of Brain Tumor Registry of Japan Supported by the Japan Neurosurgical Society. Trends and outcomes in the treatment of gliomas based on data during 2001–2004 from the brain tumor registry of Japan. *Neurol Med Chir (Tokyo).* 2015;55(Suppl 1):286-295.
40. Bilgin E, Duman BB, Altintas S, Cil T, Gezercan Y, Okten AI. Predictors of survival in Turkish patients with primary glioblastoma. *Turk Neurosurg.* 2021;31(4):641-653. doi:10.5137/1019-5149.JTN.33332-20.3
41. Sucuoğlu İşleyen Z, Seçmeler Ş, Sakin A, et al. Evaluation of the efficacy and tolerability of bevacizumab-based treatments in recurrent primary brain tumors: a multicenter real-world Turkish Oncology Group (TOG) study. *BMC Cancer.* 2026;26(1):347. doi:10.1186/s12885-026-15725-9
42. Bray F, Laversanne M, Sung H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin.* 2024;74(3):229-263. doi:10.3322/caac.21834
43. Iuchi T, Sugiyama T, Ohira M, et al. Clinical significance of the 2016 WHO classification in Japanese patients with gliomas. *Brain Tumor Pathol.* 2018;35(2):71-80. doi:10.1007/s10014-018-0309-0
44. Brodbelt A, Greenberg D, Winters T, et al. Glioblastoma in England: 2007-2011. *Eur J Cancer.* 2015;51(4):533-542. doi:10.1016/j.ejca.2014.12.014
45. Tumturk A, Ozdemir MA, Per H, et al. Pediatric central nervous system tumors in the first 3 years of life: pre-operative mean platelet volume, neutrophil/lymphocyte count ratio, and white blood cell count correlate with the presence of a central nervous system tumor. *Childs Nerv Syst.* 2017;33(2):233-238. doi:10.1007/s00381-016-3301-1
46. Siegel RL, Miller KD, Fuchs HE, Jemal A. Cancer statistics, 2022. *CA Cancer J Clin.* 2022;72(1):7-33. doi:10.3322/caac.21708
47. Jones DT, Gronych J, Lichter P, Witt O, Pfister SM. MAPK pathway activation in pilocytic astrocytoma. *Cell Mol Life Sci.* 2012;69(11):1799-1811. doi:10.1007/s00018-011-0898-9
48. Okamoto Y, Di Patre PL, Burkhard C, et al. Population-based study on incidence, survival rates, and genetic alterations of low-grade diffuse astrocytomas and oligodendrogliomas. *Acta Neuropathol.* 2004;108(1):49-56. doi:10.1007/s00401-004-0861-z
49. Kemerdere R, Yuksel O, Kacira T, et al. Low-grade temporal gliomas: surgical strategy and long-term seizure outcome. *Clin Neurol Neurosurg.* 2014;126:196-200. doi:10.1016/j.clineuro.2014.09.007
50. Tabouret E, Nguyen AT, Dehais C, et al. Prognostic impact of the 2016 WHO classification of diffuse gliomas in the French POLA cohort. *Acta Neuropathol.* 2016;132(4):625-634. doi:10.1007/s00401-016-1611-8
51. Whitfield BT, Huse JT. Classification of adult-type diffuse gliomas: Impact of the World Health Organization 2021 update. *Brain Pathol.* 2022;32(4):e13062. doi:10.1111/bpa.13062