Survival Analysis of CNS patients in Bangladesh – focusing the multidisciplinary approaches among 149 patients in a single center retrospective analysis from 2018- 2023.

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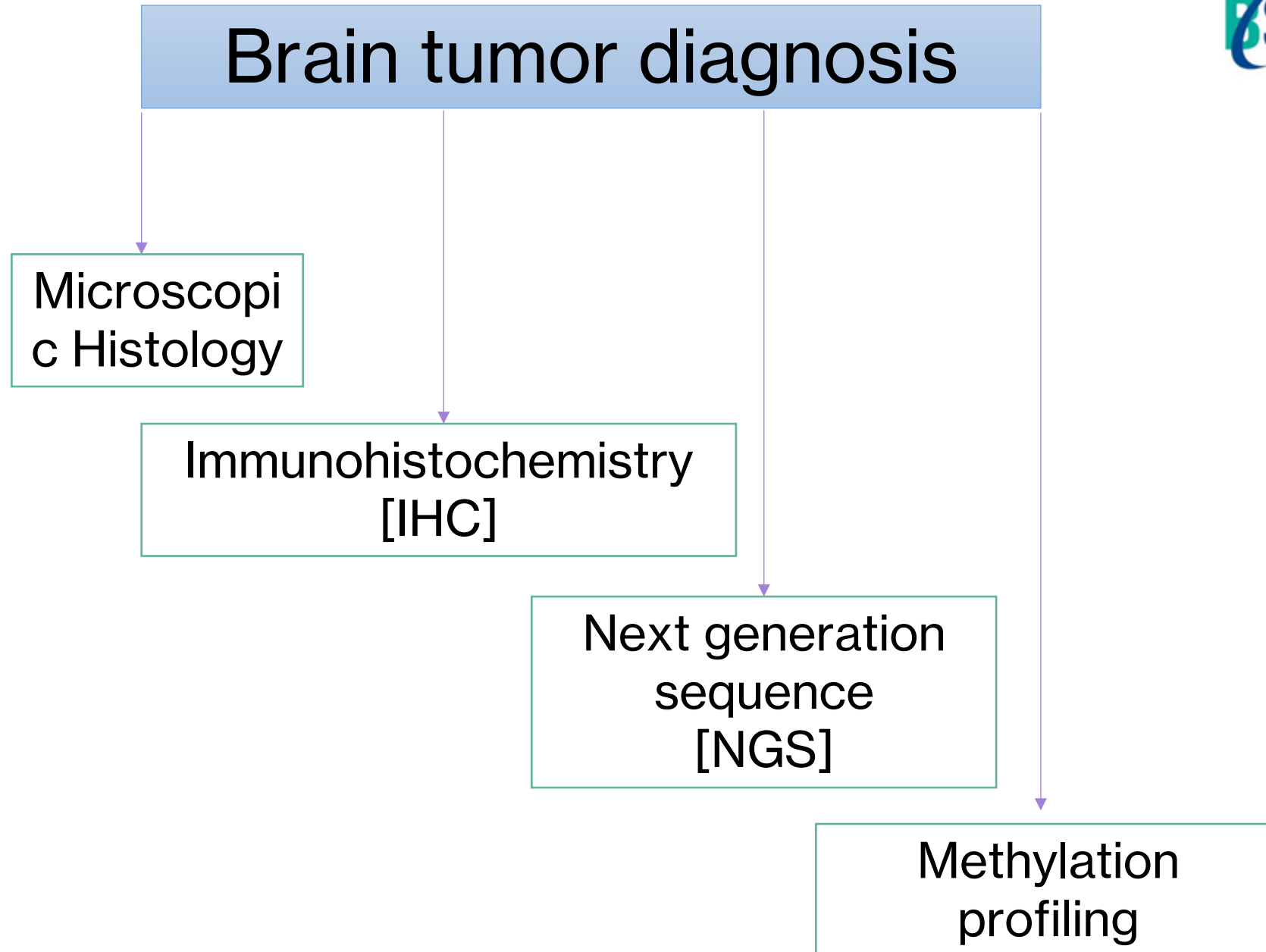# Contents

Introduction, Incidents & Etiology

- Brain and other CNS tumours are the 2nd most common cancer in adolescents and young adults, and represent the 8th most common cancer in older adults.

- Average annual age-adjusted incidence rates for all glial tumours is 5·95 per 100 000 people in the USA.

- Most primary brain tumours are sporadic and without a known cause. Cancer-causing mutations in glioma primarily originate as a consequence of endogenous, rather than exogenous, factors.

Iorgulescu JB, Sun C, Neff C, et al. *Neuro Oncol* 2022; **24:** 1989–2000.
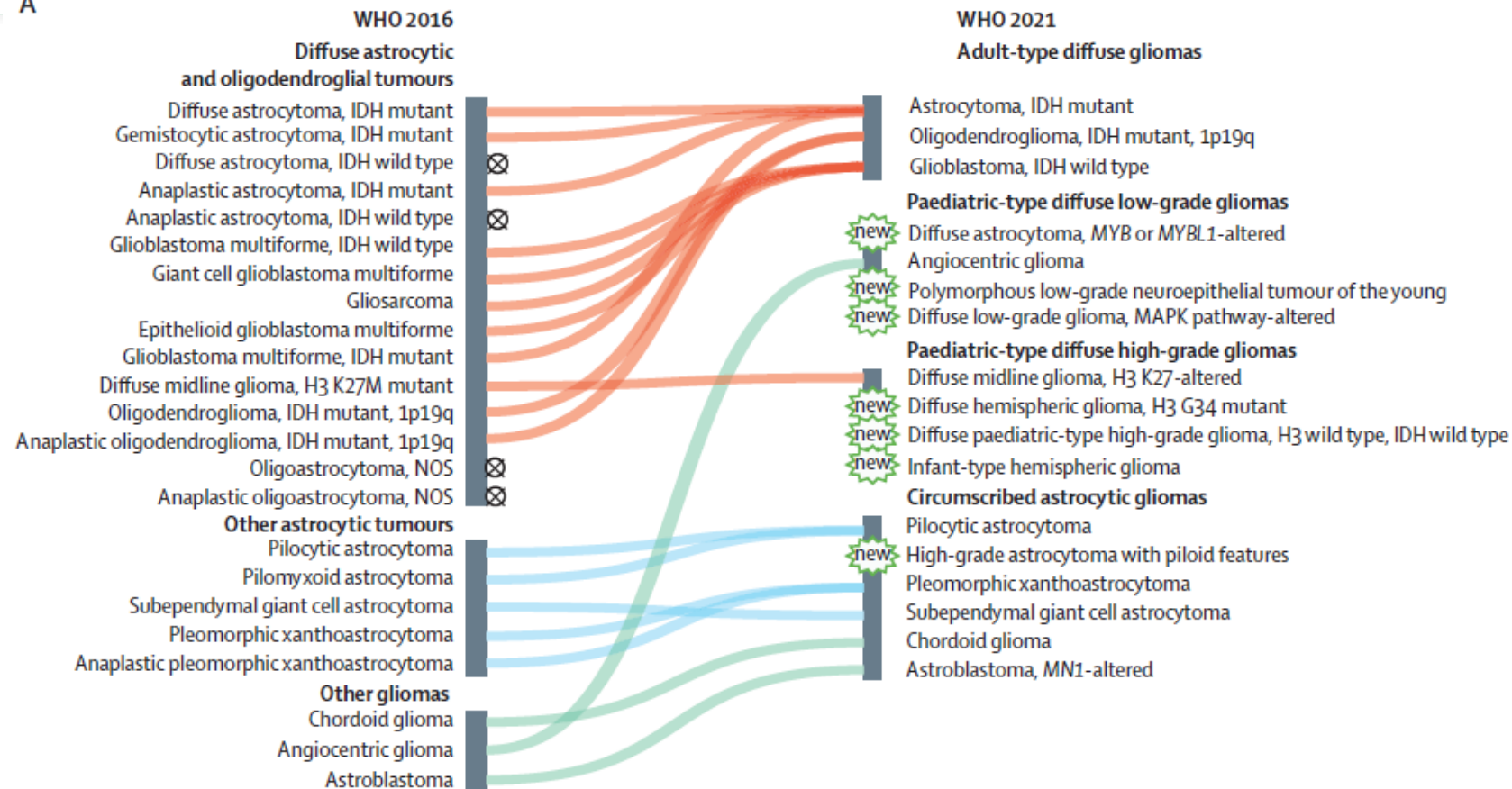
Pathological Classifications

- CNS tumor classification is based on the World Health Organization Classification of CNS tumors

- First published in 1979, last revised in 2021

- 2021 version incorporated a combination of molecular and histologic parameters

Louis, et al. Acta Neuropathologica, 2007
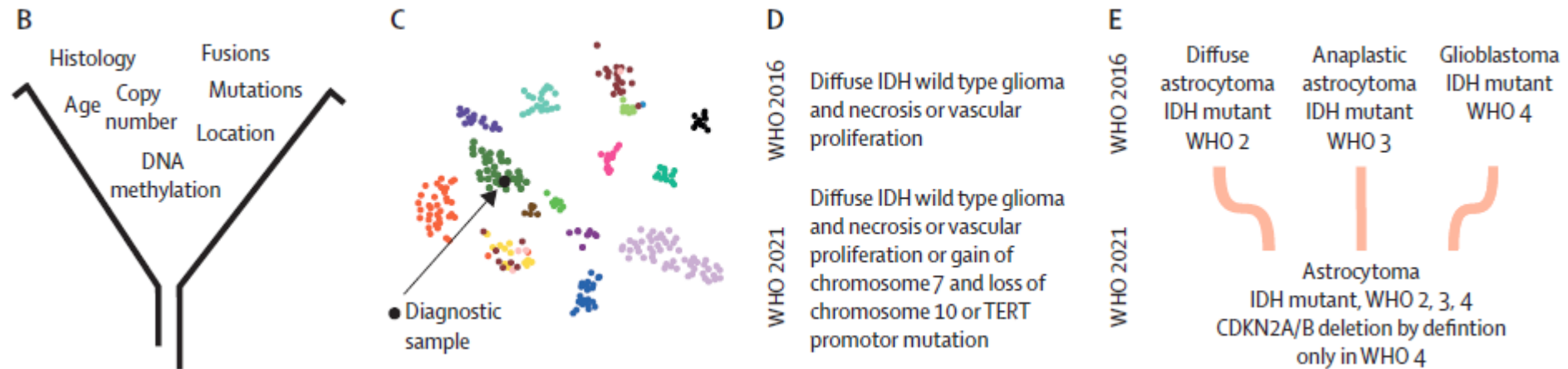
Classifications of CNS tumours - WHO 2021

A

WHO 2016
Diffuse astrocytic and oligodendroglial tumours
Diffuse astrocytoma, IDH mutant
Gemistocytic astrocytoma, IDH mutant
Diffuse astrocytoma, IDH wild type ⊗
Anaplastic astrocytoma, IDH mutant
Anaplastic astrocytoma, IDH wild type ⊗
Glioblastoma multiforme, IDH wild type
Giant cell glioblastoma multiforme
Gliosarcoma
Epithelioid glioblastoma multiforme
Glioblastoma multiforme, IDH mutant
Diffuse midline glioma, H3 K27M mutant
Oligodendroglioma, IDH mutant, 1p19q
Anaplastic oligodendroglioma, IDH mutant, 1p19q
Oligoastrocytoma, NOS ⊗
Anaplastic oligoastrocytoma, NOS ⊗
Other astrocytic tumours
Pilocytic astrocytoma
Pilomyxoid astrocytoma
Subependymal giant cell astrocytoma
Pleomorphic xanthoastrocytoma
Anaplastic pleomorphic xanthoastrocytoma
Other gliomas
Chordoid glioma
Angiocentric glioma
Astroblastoma

WHO 2021
Adult-type diffuse gliomas
Astrocytoma, IDH mutant
Oligodendroglioma, IDH mutant, 1p19q
Glioblastoma, IDH wild type
Paediatric-type diffuse low-grade gliomas
new Diffuse astrocytoma, *MYB* or *MYBL1*-altered
Angiocentric glioma
new Polymorphous low-grade neuroepithelial tumour of the young
new Diffuse low-grade glioma, MAPK pathway-altered
Paediatric-type diffuse high-grade gliomas
Diffuse midline glioma, H3 K27-altered
new Diffuse hemispheric glioma, H3 G34 mutant
new Diffuse paediatric-type high-grade glioma, H3 wild type, IDH wild type
new Infant-type hemispheric glioma
Circumscribed astrocytic gliomas
Pilocytic astrocytoma
new High-grade astrocytoma with piloid features
Pleomorphic xanthoastrocytoma
Subependymal giant cell astrocytoma
Chordoid glioma
Astroblastoma, MN1-altered

Central changes between the WHO 2016 and WHO 202169 classifications of CNS tumours :
(A) Overview of new sorting of diffuse and circumscribed gliomas from WHO 2016 to WHO 2021 and overview of newly introduced tumour classes. The symbol signifies an abandoned diagnostic term.

Primary brain tumours in adults van den Bent, Martin J et al. The Lancet, Volume 402, Issue 10412, 1564 - 1579

Central changes between the WHO 2016 and WHO 202169 classifications of CNS tumours

(B) Distillation of essential diagnostic criteria for every tumour class. (C) Introduction of DNA methylation-based tumour classification. (D) Introduction of molecular defining features for glioblastoma, IDH wildtype that allow diagnosis if histological features of glioblastoma (vascular proliferation or necrosis, or both) are lacking. (E) Consolidation of astrocytoma, IDH mutant into one type with three WHO grades. IDH=isocitrate dehydrogenase. NOS=not otherwise specified.

Primary brain tumours in adults van den Bent, Martin J et al. The Lancet, Volume 402, Issue 10412, 1564 - 1579

Survival Analysis of CNS patients in Bangladesh – focusing the multidisciplinary approaches among 149 patients in a single center retrospective analysis from 2018- 2023

- **Aims and Objective**
  - This study evaluates the overall survival (OS) of patients with central nervous system (CNS) malignancies in Bangladesh.
  - The study seeks to identify key prognostic factors affecting survival outcomes, providing insights to improve diagnostic, therapeutic, and resource allocation strategies in low-resource settings.

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Methods

- Central Nervous Tumor (CNS) tumor is variable survival status due to its location and age groups.

- We tried to find selected CNS tumors among adult and child with tri-modalities treatment and compared the survival and prognostic factors among 149 patients first time in Bangladesh.

Data Analysis
- A model with python created to analyze the survival in different groups.
- Kaplan-Meier survival analysis was used to estimate overall survival (OS), and the log-rank test was applied to compare survival curves between different patient subgroups.
- Cox proportional hazards regression was employed to assess the significance of potential prognostic factors on survival outcomes, A p-value of <0.05 was considered statistically significant for all tests.
- Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population, and results were presented as hazard ratios (HR) with 95% confidence intervals (CI).

Results

Among the 149 cases the median age 46.89 years with histology grouped in 4 major divisions of

- Ependymoma 11(7.4%),

- Oligodendroglioma 12(8.1%),

- Astrocytoma 48(32.2%),

- Glioblastoma (GBM) 78(52.3%).

Bar Chart of hpr
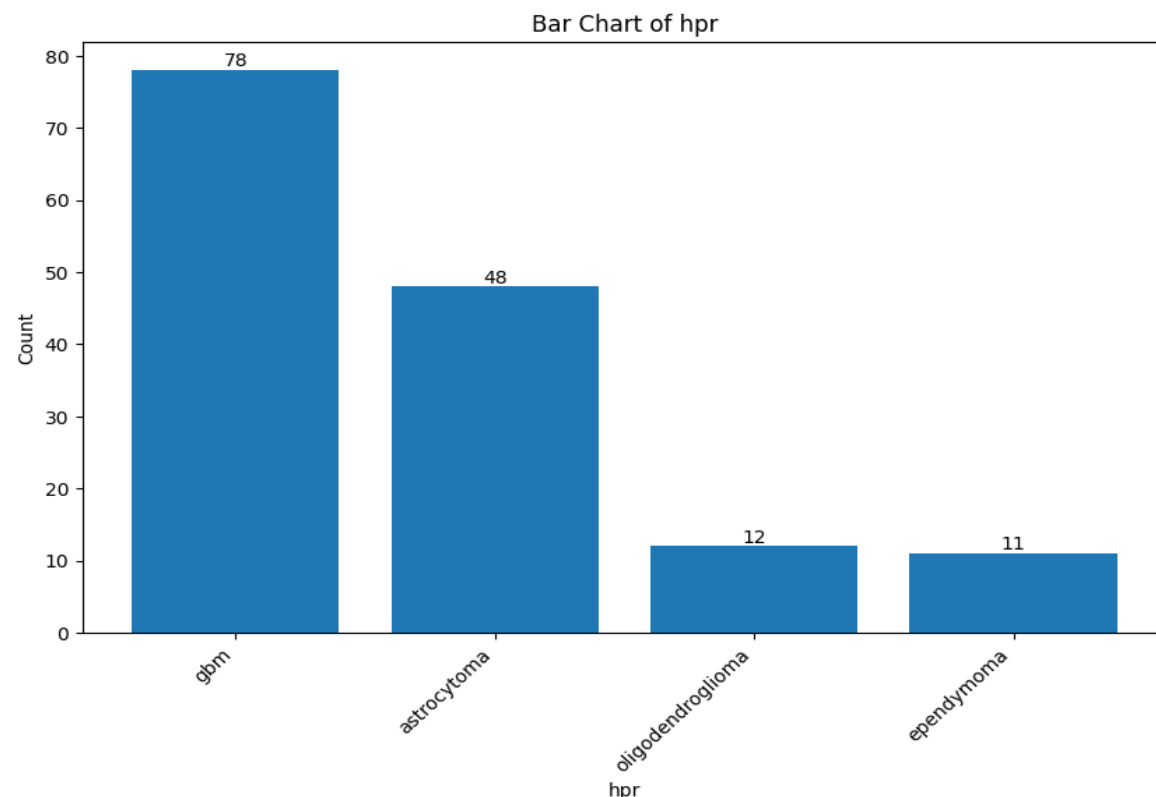
Age, Sex Distribution
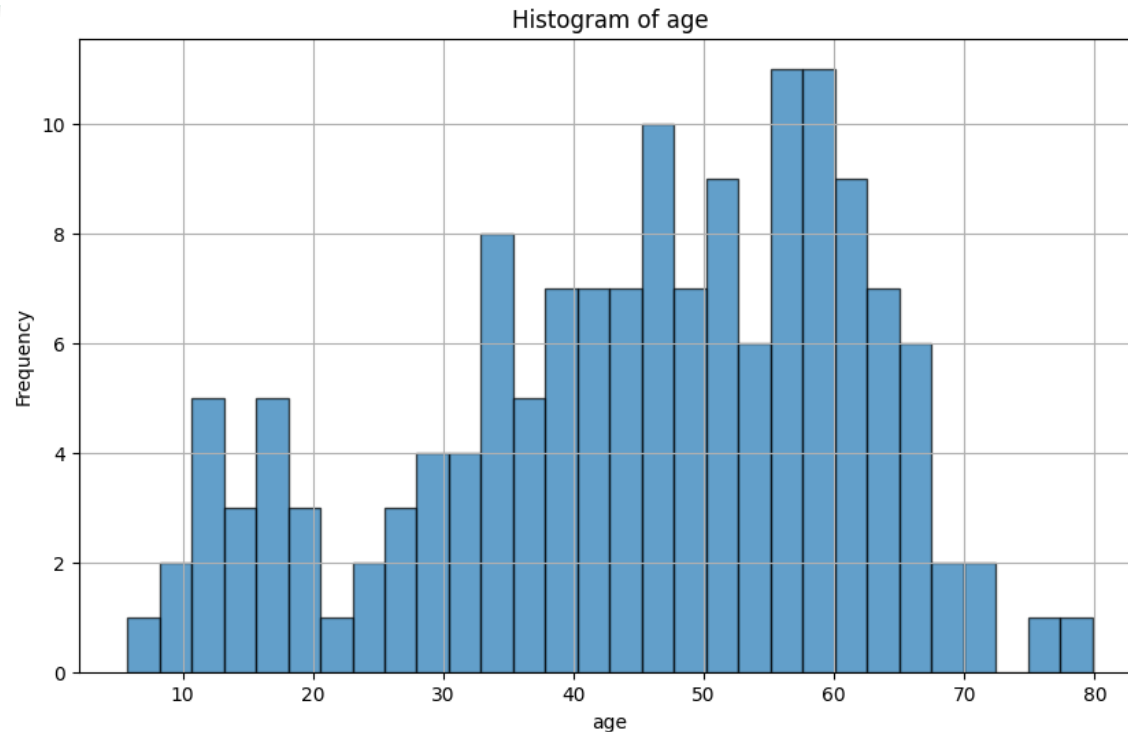
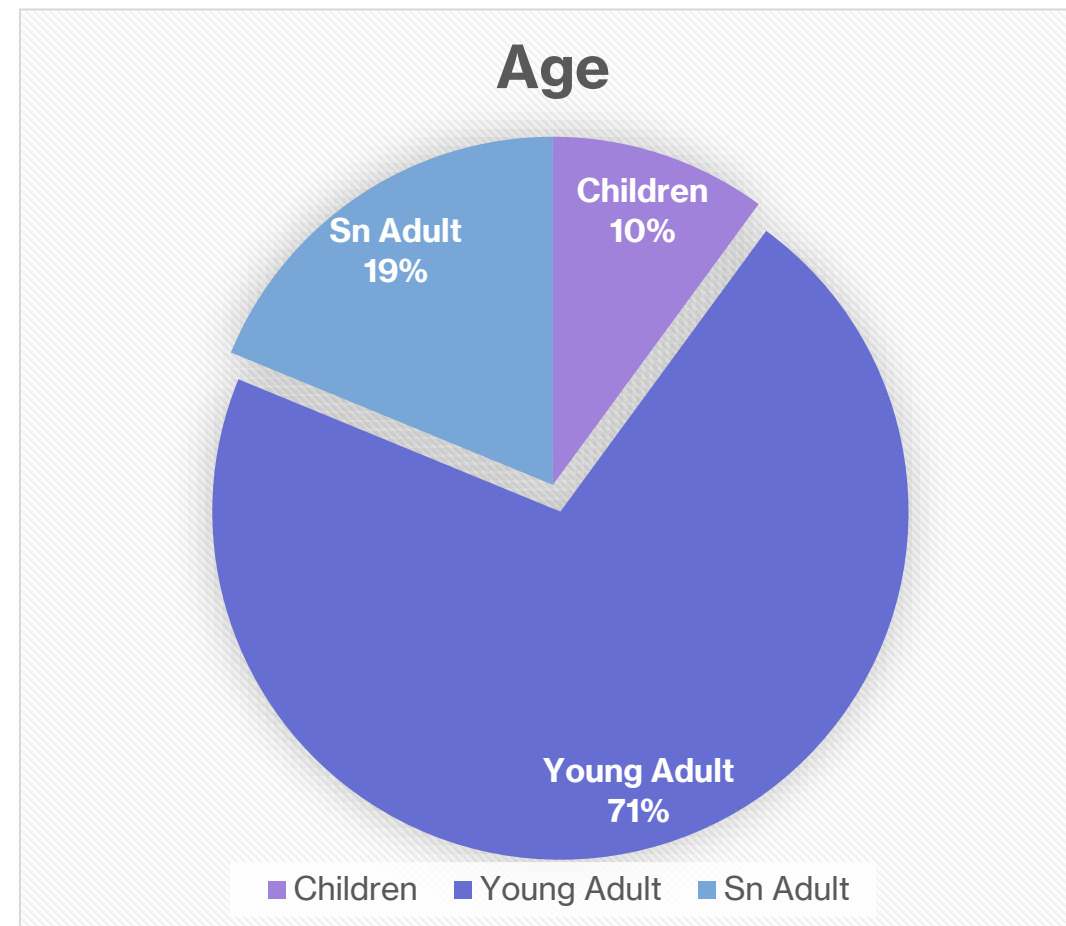Distribution of patients according to age median age 46.89 years, ranging from 5-79 years
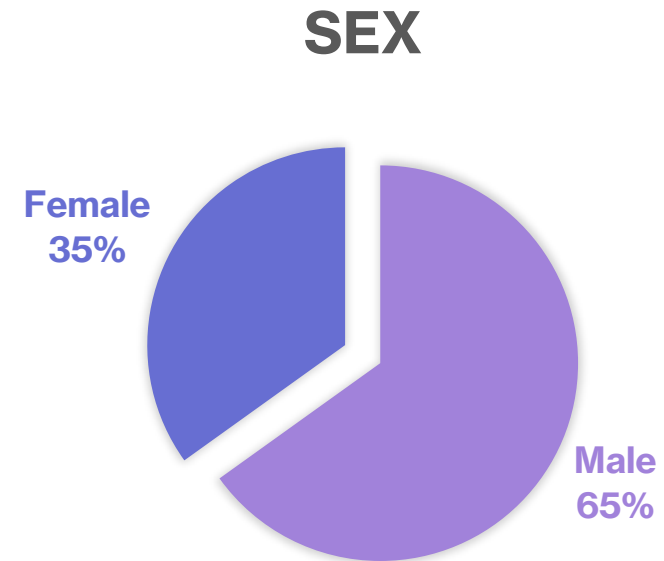
Distribution of patients according to sex

Results

Age group is proposed :

- 1-18 children (10%)

- 18-60 young adult (71%) &

- Above 60 Sn. Adult (19%).

The median overall survival was found 19.2m (95% CI, 14.3-26.7) and the male: female gender ratio is 17.9m:24.4m.

The individual histological median survival was lowest in GBM 11.7m & in Astrocytoma- 21.9m.

Median Survival Time and Confidence Intervals

Description	Value
Median Survival Time	19.23
95% CI Lower Bound	14.30
95% CI Upper Bound	26.77

Median Over Survival of CNS Patient in Bangladesh

Survival Analysis in CNS Patient
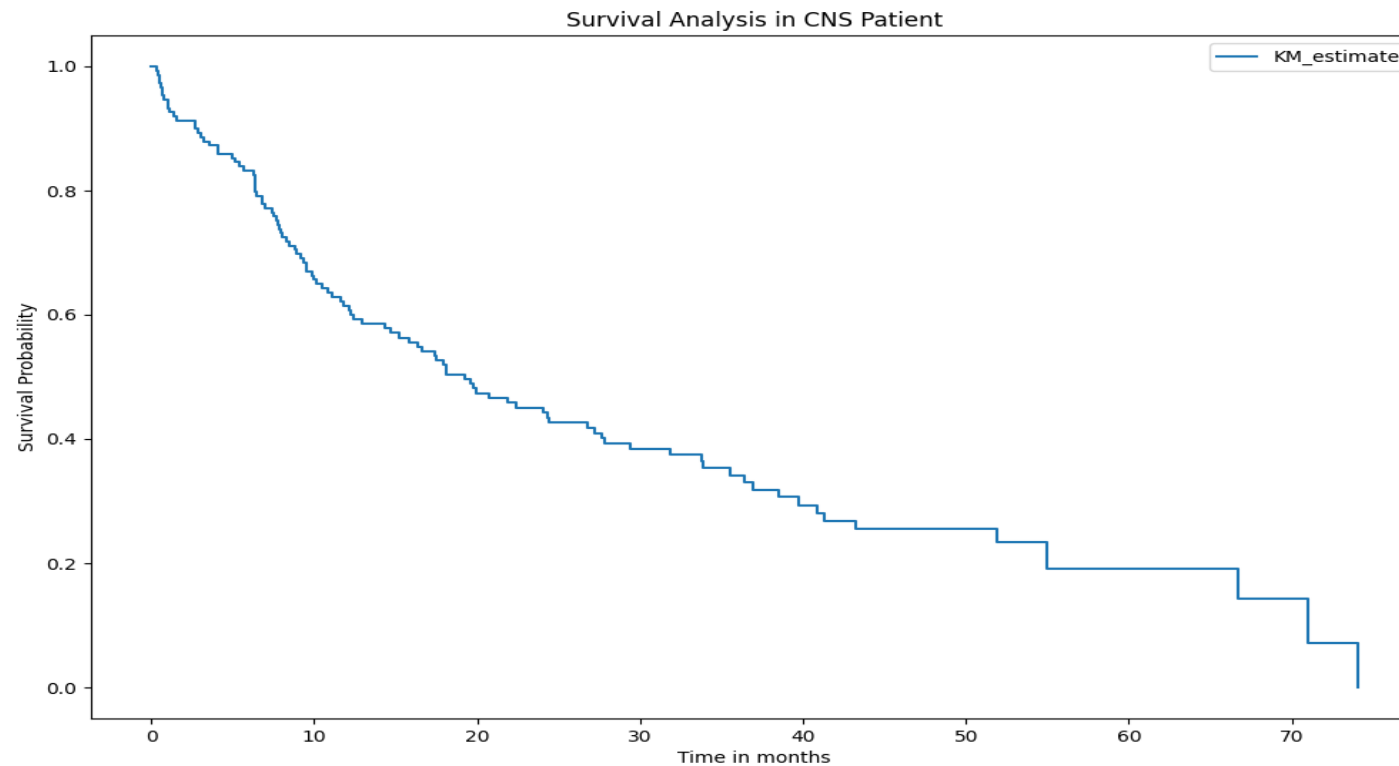
Median Survival of CNS Patient in Bangladesh based on Gender

Sex	Median Survival Time	95% CI Lower	95% CI Upper
Female	24.4	9.5	41.33
Male	17.93	11.77	24.07

Log rank p test results on Survival of different Gender Group

Group1	Group2	p-value	Significant
Male	Female	0.2349	False

Median Over Survival of CNS Patient in Bangladesh based on Gender

Bar Chart of tumour_location
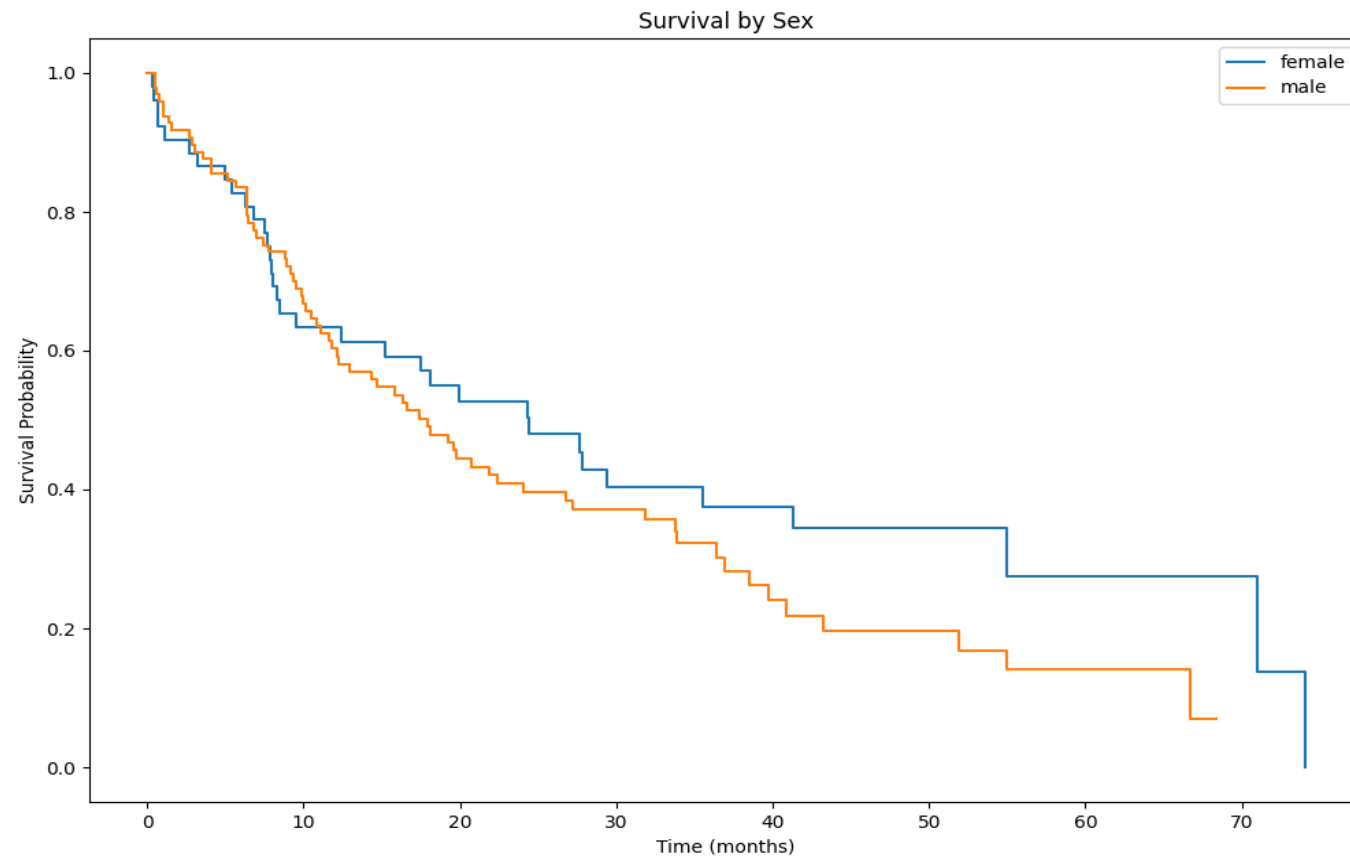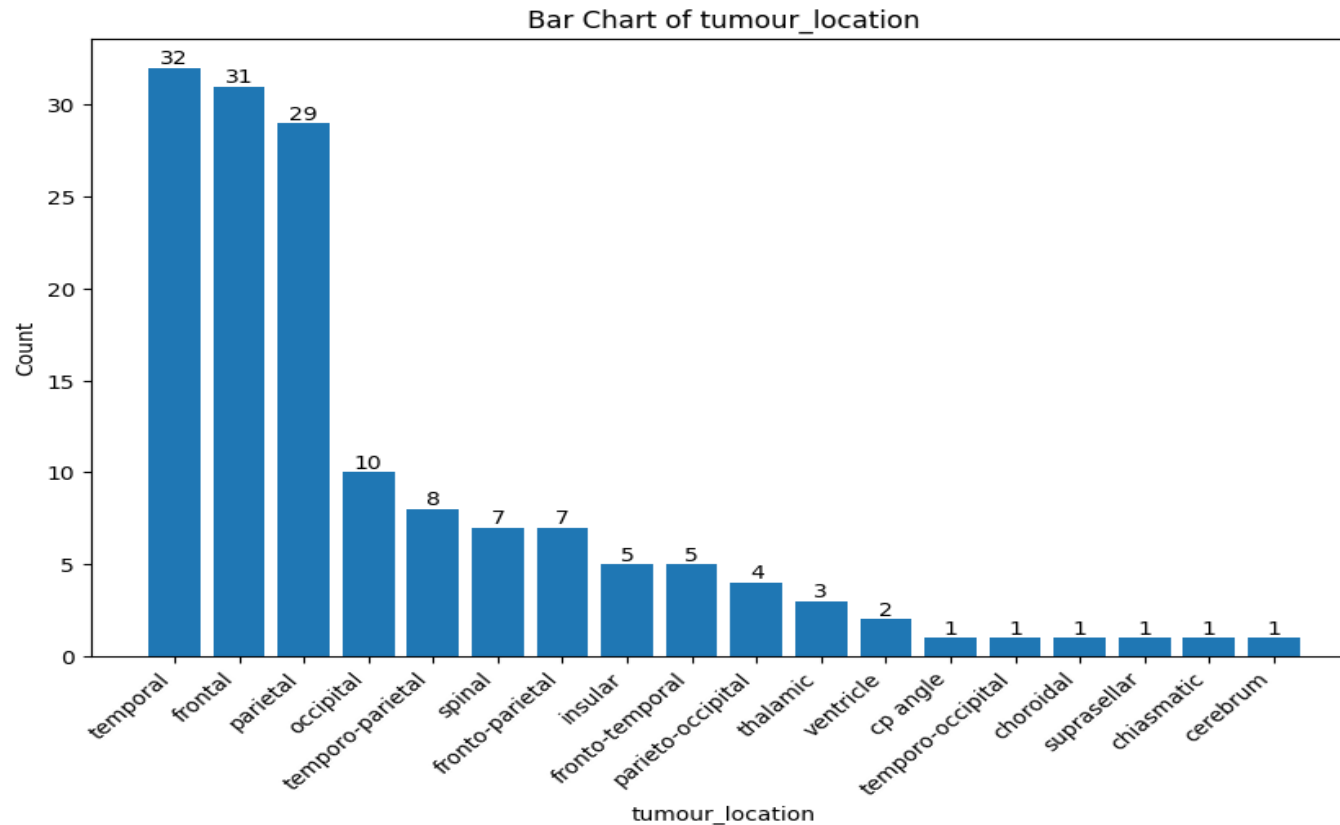
- Position of tumor predominantly in right side of brain 53.7%.

- 70.5% of them achieved GTR due to the use of neuronavigation and 4% patients have only biopsy due to inoperability.

- Highest location of tumor was found to have in temporal, frontal & parietal region about 62% together.

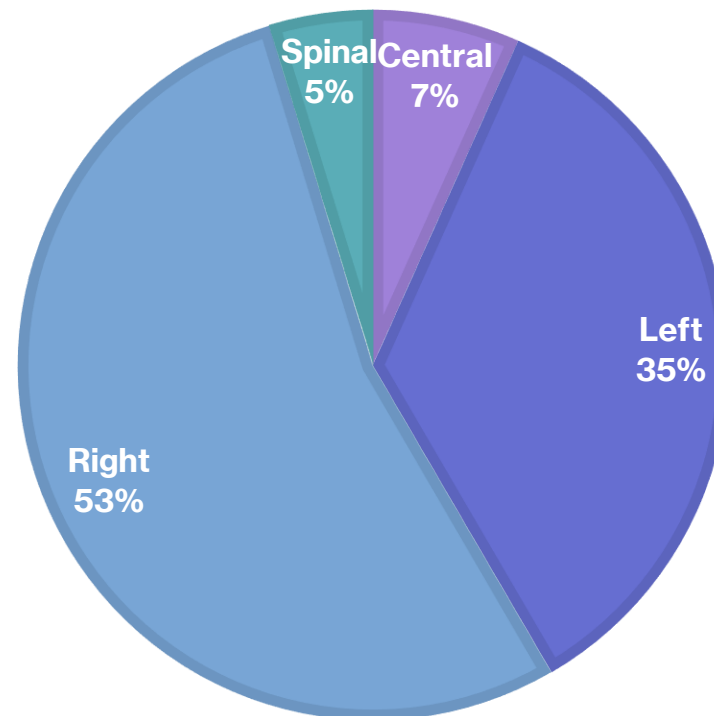# Median Overall Survival of CNS patient in Bangladesh based on Tumour Location

Survival by Tumour Location
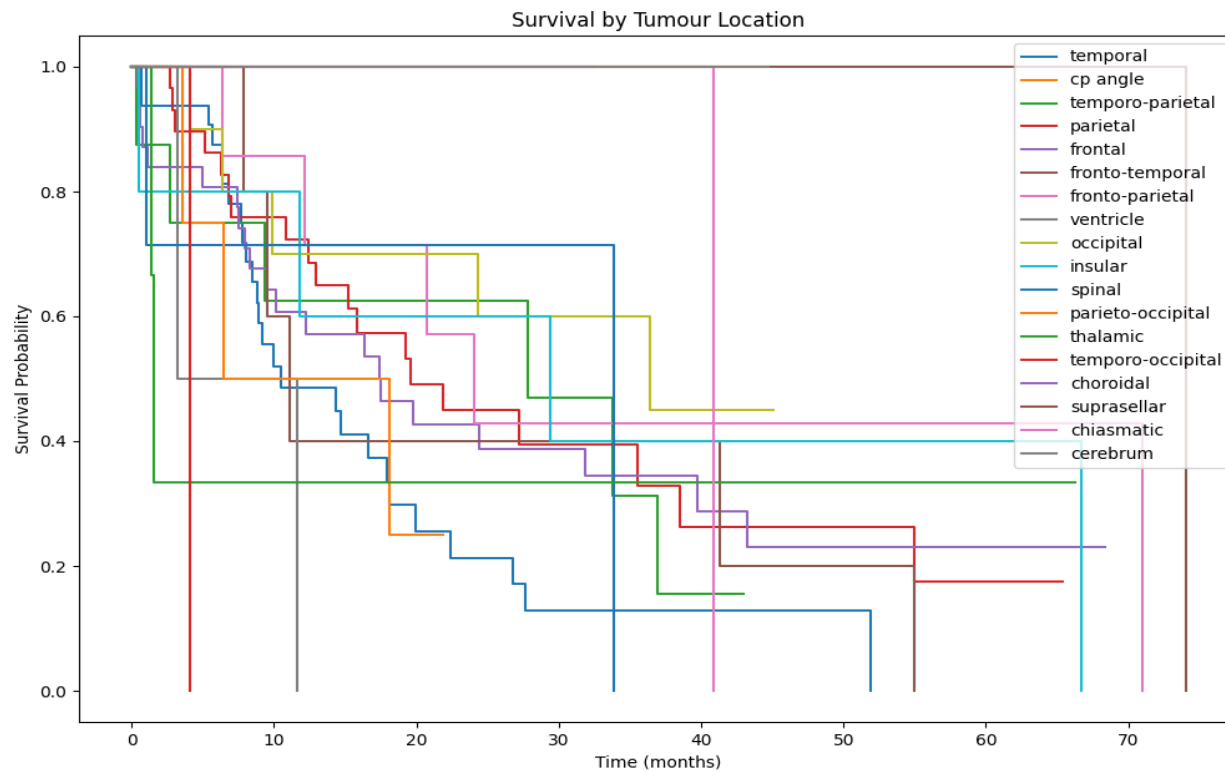
Tumour Location	Median Survival Time	95% CI Lower	95% CI Upper
temporal	10.47	8.03	18.1

Laterality

LATERILITY

■ Central ■ Left ■ Right ■ Spinal

Spinal 5%
Central 7%
Left 35%
Right 53%

Median Survival of CNS Patient in Bangladesh based on Different Age Group

Age Group	Median Survival Time	95% CI Lower	95% CI Upper
Children	74.03	6.77	74.03
Young	22.4	17.47	31.87
Senior Adult	7.73	5.7	9.83

Log rank p test results on Survival of Different Age Group

Group1	Group2	p-value	Significant
Children	Young	0.1239	False
Children	Senior Adult	0.005	True
Young	Senior Adult	0.0004	True

Survival Analysis of CNS patient in Bangladesh based on Age Group
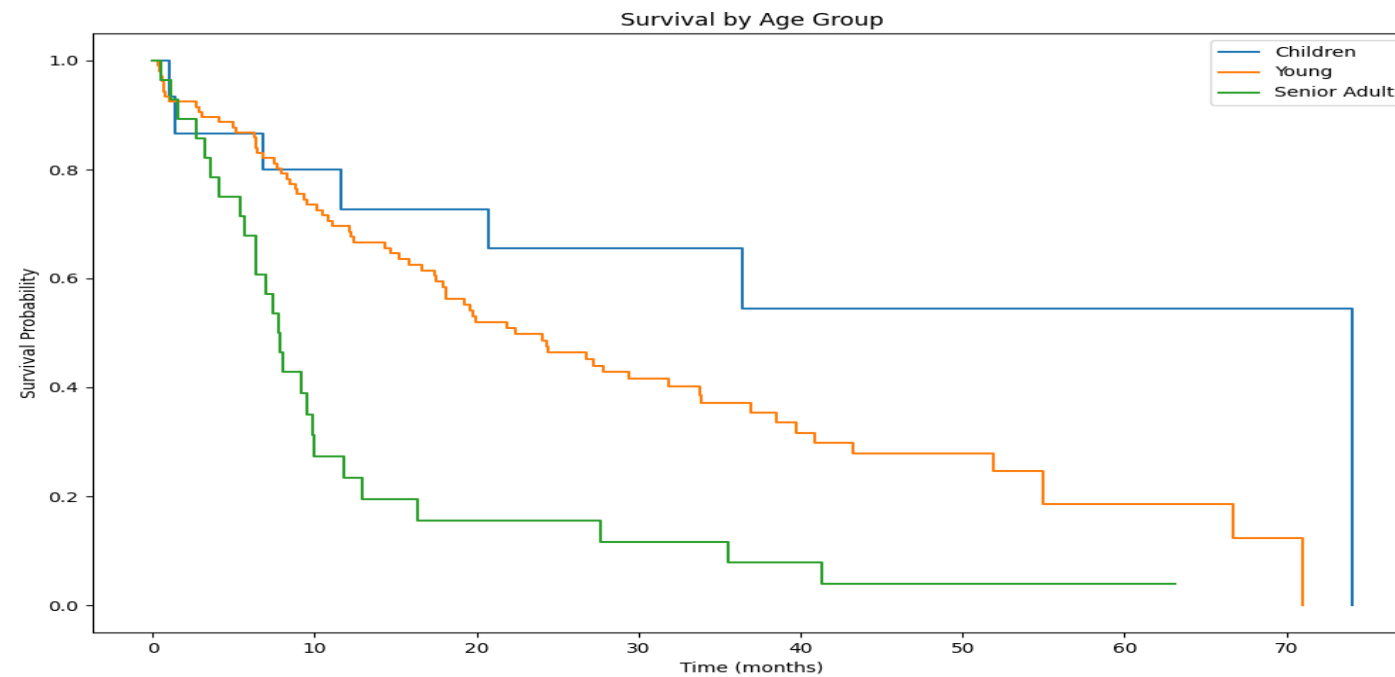
If we compare with the histology with grading the results of median survival also similar like in G-IV 11.7m (95% CI-8.93-17.47) whereas in case of G-III 24.4m (95% CI 18.1-66.67) & in G-II 54.97m (95% CI- 21.9-74.03).

Median Survival of CNS Patient in Bangladesh based on Different Tumor Grade

Grade	Median Survival Time	95% CI Lower	95% CI Upper
Grade iv	11.77	8.93	17.47
Grade iii	24.4	18.1	66.67
Grade ii	54.97	21.9	74.03

Log rank p test results on Survival of Different Tumor Grade

Group1	Group2	p-value	Significant
Grade iv	Grade iii	0.035	True
Grade iv	Grade ii	0.0006	True
Grade iii	Grade ii	0.3655	False

Grade Median Overall Survival of CNS patient in Bangladesh based on Tumor Grade


Survival by Grade
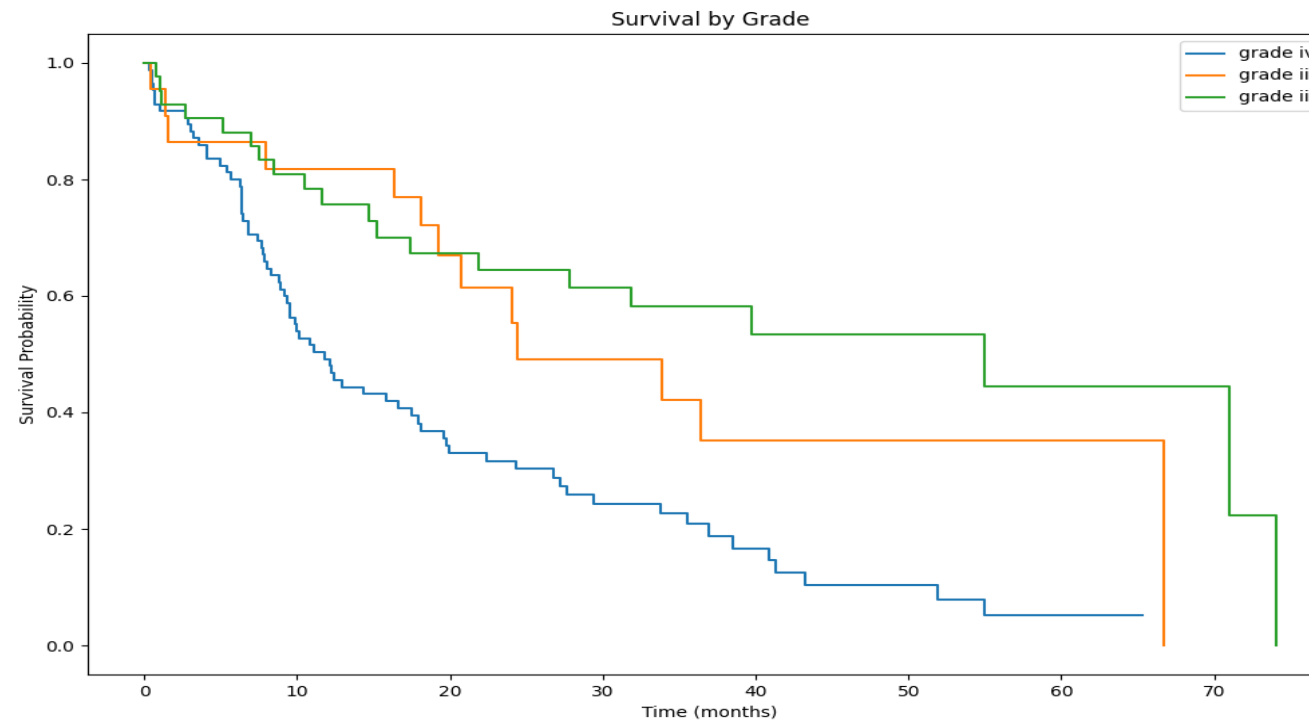
HPR & Grade Distribution
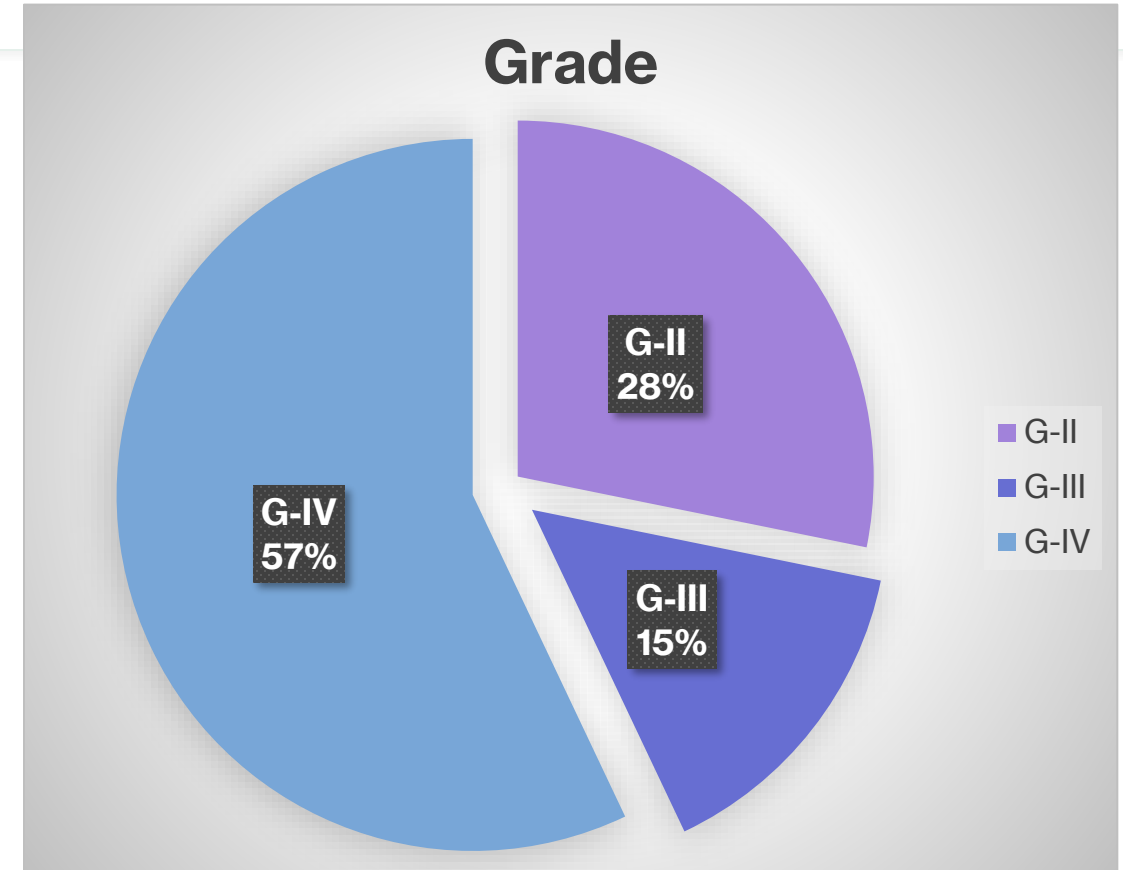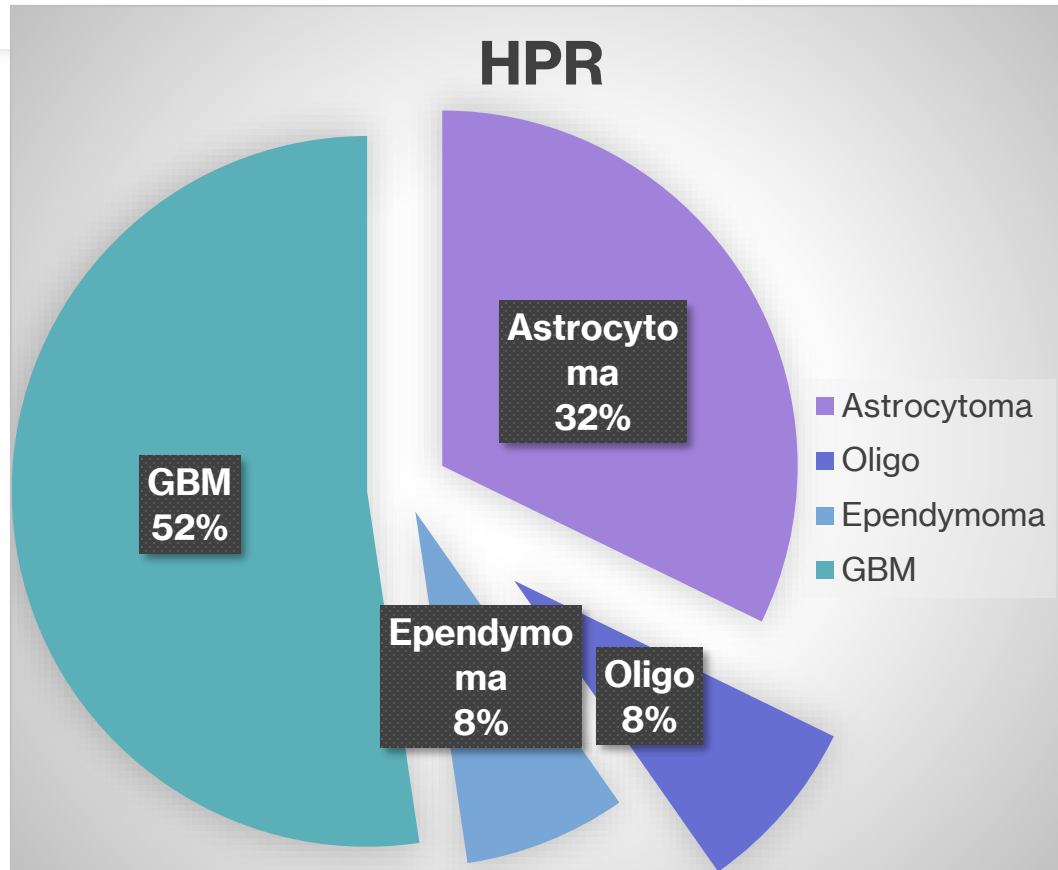
Surgery type also plays an important role in our study, STR & GTR 18.07m vs 19.73m, however the NTR group showed the lowest survival 5.4m as expected in biopsy only group too. 23.5% of IDH mutation positive patients has better survival than 18.1% negative patients (21.9m vs 16.63m)

Median Overall Survival of CNS patient in Bangladesh based on IDH Mutation Status
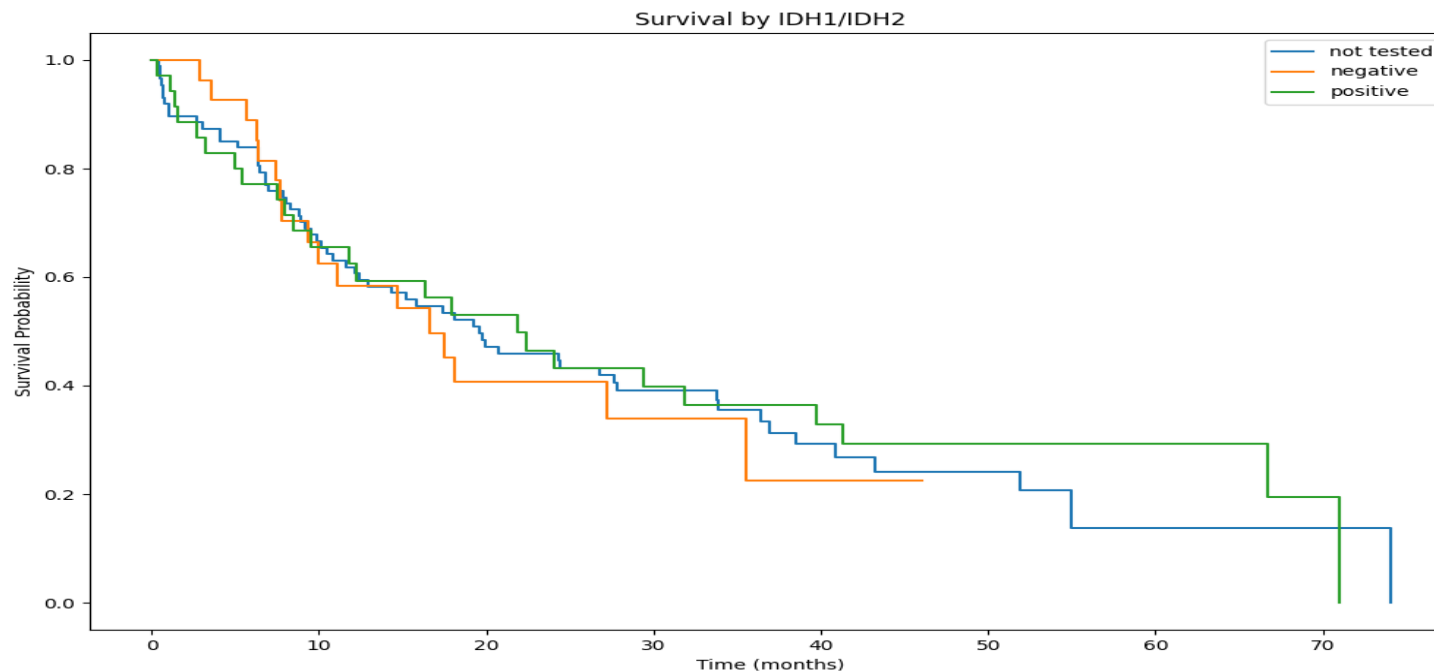
Survival Analysis of CNS Patient in Bangladesh based on IDH Mutation Status

IDH1/IDH2	Median Survival Time	95% CI Lower	95% CI Upper
Not tested	19.57	12.13	27.8
Negative	16.63	7.73	35.53
Positive	21.9	9.5	39.73

Log rank p test results on Survival based on IDH Mutation Status

Group1	Group2	p-value	Significant
Not tested	Negative	0.1189	False
Not tested	Positive	0.2813	False
Negative	Positive	0.0686	False

COX proportional hazard ratio in Forest Plot also in favor of in case of IDH & Surgery type & Histology as well.

## Survival Analysis of CNS Patient in Bangladesh based on Surgery Type

Surgery Type	Median Survival Time	95% CI Lower	95% CI Upper
STR	18.07	9.37	36.9
GTR	19.73	15.23	27.2
NTR	5.4	0.7	39.73

Log rank p test results on Survival based on IDH Mutation Status

Group1	Group2	p-value	Significant
STR	GTR	0.1337	False
STR	NTR	0.065	False
STR	Biopsy	0.9918	False
GTR	NTR	0.0585	False
GTR	Biopsy	0.8201	False
NTR	Biopsy	0.088	False

Median Overall Survival of CNS patient in Bangladesh based on Surgery Type

Survival by Surgery Type

Bar Chart of surgery type

Forest Plot of COX proportional hazard ratio
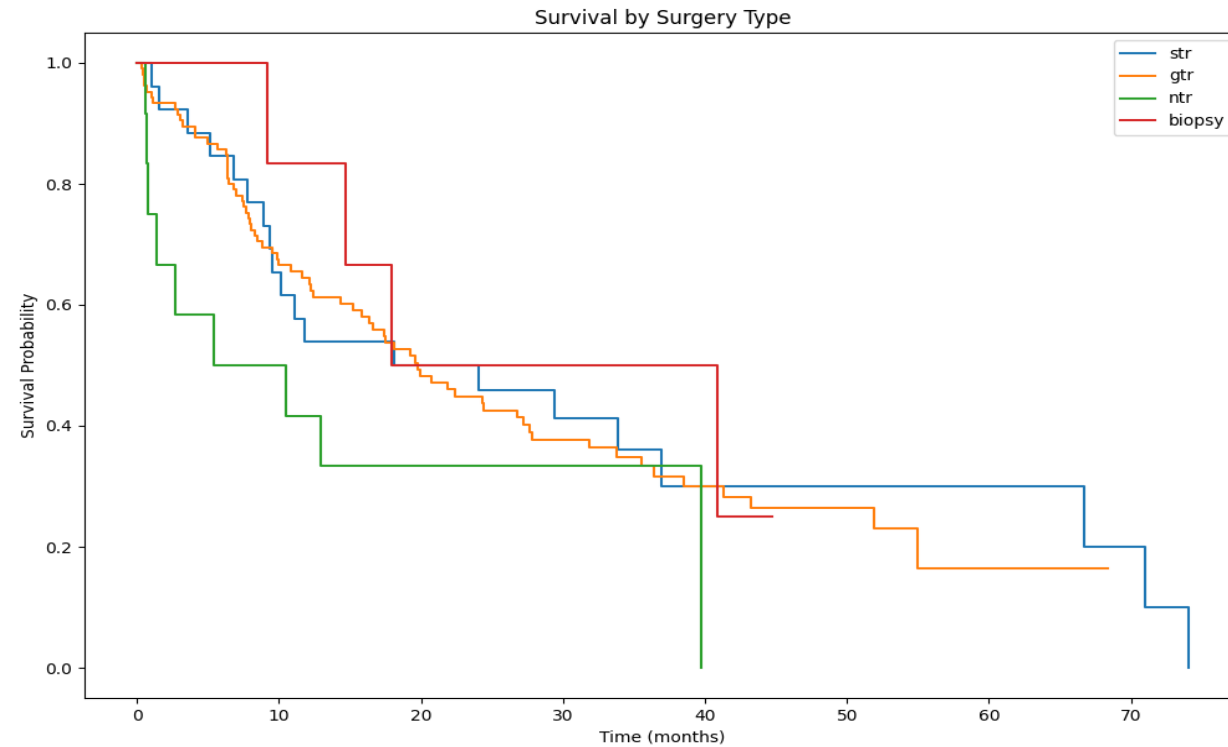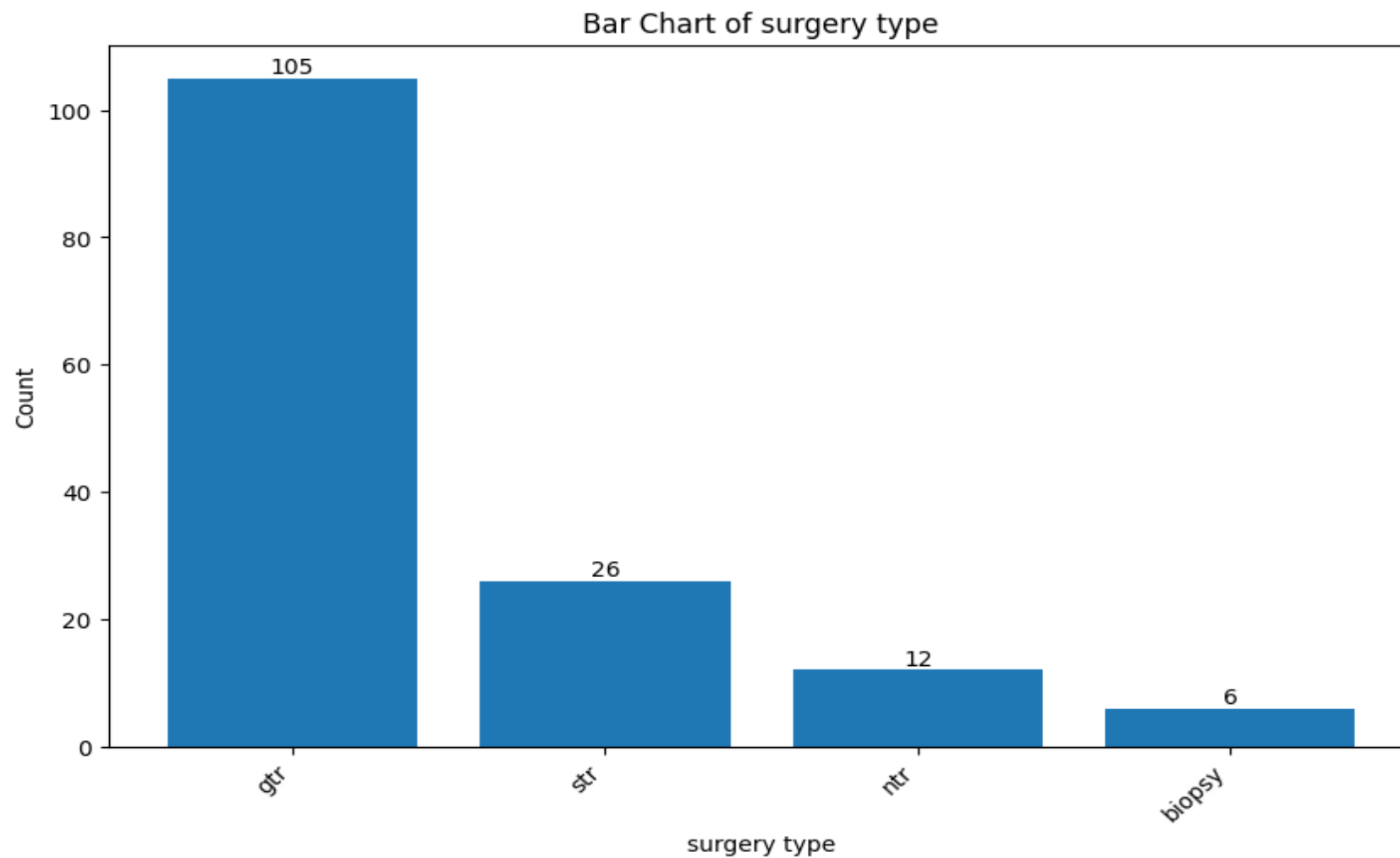
Forest Plot of Cox Proportional Hazards Model
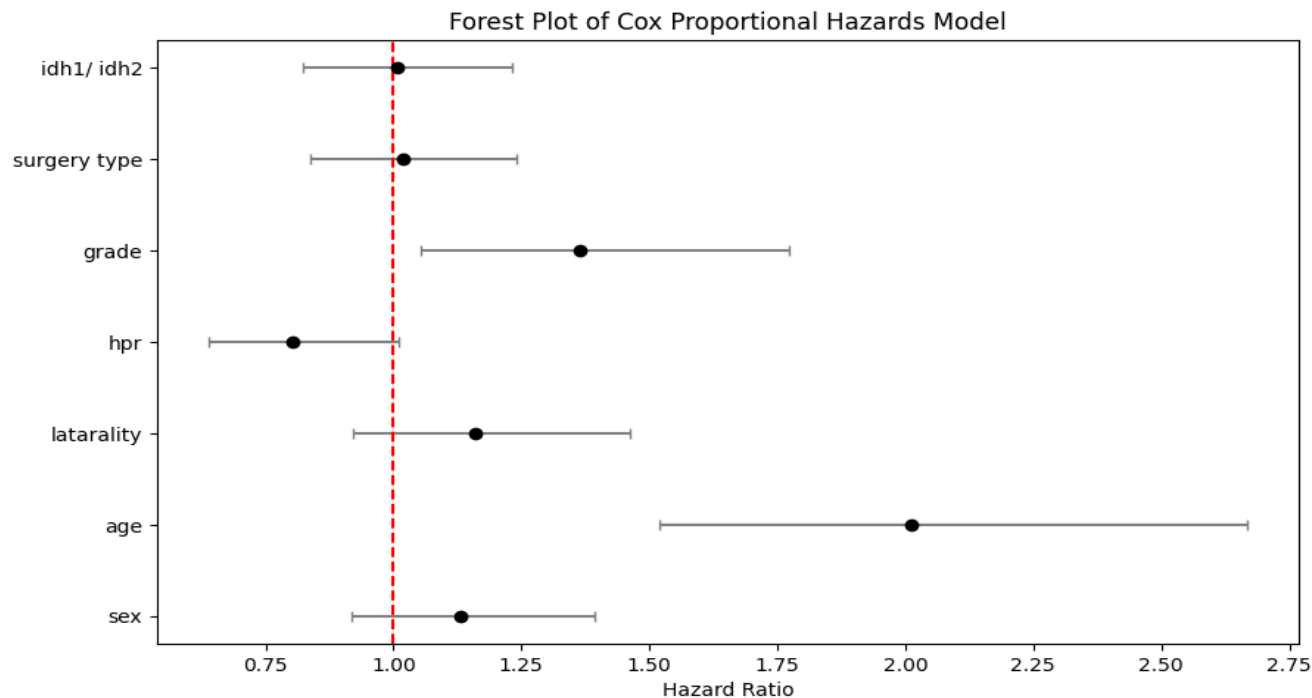
Age has the strongest association, with a hazard ratio (HR) of 2.0 (p < 0.001), indicating that as age increases, the risk of mortality also rises significantly. **Histopathology (HPR)** also impacts survival, with an HR of 0.78 (p = 0.0293), suggesting that certain tumor types are associated with reduced risk.
Tumor grade shows an HR of 1.35, nearing significance (p = 0.0982), indicating that higher grades may slightly elevate risk.
Variables such as **sex**, **surgery type**, and **IDH mutation** status had no significant impact on survival outcomes in this analysis.

Radiotherapy +-concurrent (CRT) and/or adjuvant chemotherapy (AdChT) with TMZ

- RT doses varies in 50Gy to 60Gy according to histology or group grade with 3DCRT/ IMRT/ VMAT facilities.

- Completion of majorities of group 106/149 patients completed 50-60Gy prescribed doses among them
    - 59.4-60Gy in 33-30# 74/106 patients,
    - 54Gy in 30-27#   22/106 patients and
    - rest of them 10 patients 45-50.4 Gy received.

- Incompletion of 5/149 patients due to poor general condition and completed 10-40Gy with prescribed doses of 45-60Gy.

- RT was not received among 23/149 patients.

- CRT/ AdChT was most of the time with Temozolamide (TMZ) and PCV also given only few patients.
    - CRT was given 96 patients whereas
    - 53 patients did not receive any form of CRT.
    - AdChT was received 84 patients.

Radiotherapy +-concurrent (CRT) and/or adjuvant chemotherapy (AdChT) with TMZ

- **Patients who received radiotherapy had a median survival of 27.5 months, significantly higher than those who did not receive radiotherapy (12.4 months, p = 0.008)**

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Conclusion

The analysis is little complicated in case of heterogeneous histology and location of CNS tumors. But with the model that created by python showed significant relationship and survival outcome. If the sample size also increases in number and the single histology selected to find out the comparison with other parameters, then the best survival outcome can be estimated.