

RESEARCH ARTICLE

Time to surgery after radiological diagnosis of brain tumours in Pakistan: A nationwide cross-sectional study

Mohammad Hamza Bajwa,¹ Mashal Murad Shah,² Muhammad Usman Khalid,³ Muhammad Shahzad Shamim,⁴ Erum Baig,⁵ Naveed Zaman Akhunzada,⁶ Altaf Ali Laghari,⁷ Muhammad Faraz Raghbi,⁸ Saad bin Anis,⁹ Pakistan Brain Tumour Consortium, Sameen Siddiqi,¹⁰ Syed Ather Enam¹¹

Abstract

Objective: To investigate waiting times for brain tumour surgery in Pakistan from a nationwide sample and highlight specific affected patient populations.

Methods: A nationwide study was conducted as part of the Pakistan Brain Tumour Epidemiology Study; data from 32 high-volume neurosurgical centres were collected. The national sample included 2,750 patients. Time to surgery was calculated by the difference in dates recorded for radiological diagnosis and the date of the first surgery. This was further stratified according to demographic factors, histopathological diagnosis, type of surgical procedure performed and survival outcomes.

Results: The data of 1,474 patients for time to surgery was available. Patients travelling to public hospitals had significantly longer mean wait times (94.07 (CI: 85.29, 102.84) vs 75.14 (CI: 54.72, 95.56) days, $p < 0.001$). Significant differences were seen between patients of various age groups, as adolescents (116.63 (CI: 65.27, 167.98) days) and young adults (103.34 (CI: 85.96, 120.72) days) had higher waiting times compared to middle-aged (72.44 (CI: 61.26, 83.61) days) and older (48.58 (CI: 31.17, 65.98) days) adults. No difference was seen between the genders. A significantly longer time to surgery was observed for middle- and lower-socioeconomic class patients. Those undergoing gross total resection of the tumour had significantly ($p < 0.001$) longer waiting times for surgery when compared to STR (sub-total resection), biopsy, and CSF-diversion procedures, for all tumour types. Patients diagnosed with meningioma had the most prolonged waiting periods (106 (CI: 76, 95) days). Gliomas had a mean waiting period of 88 (CI: 73, 103) days across the country. Low-grade gliomas had significantly ($p = 0.031$) longer mean waiting times (99.73 (CI: 61.91, 127.36) days) in comparison to high-grade gliomas (70.13 (CI: 43.39, 89.69) days). A significant difference was seen between waiting times for patients who survived surgical procedures for a brain tumour on the most recent follow-up and those who had expired (91.87 (CI: 79, 107.74) vs 77.41 (CI: 59.90, 94.91) days, $p < 0.001$).

Conclusion: Prolonged delays to surgery are a significant barrier within low-and-middle-income countries, leading to adverse outcomes for patients. Patients undergoing brain tumour surgery at public hospitals from lower or middle SES and electing for gross resections were more likely to have longer delays.

Keywords: Treatment delay, Neuro-oncology, Time to surgery, Neurosurgery.

(JPMA 72: S-93 [Suppl. 4]; 2022) DOI: <https://doi.org/10.47391/JPMA.11-S4-AKUB15>

Introduction

Delay in brain tumour management has been linked to poor outcomes; while great strides have been made in earlier diagnosis and initiating chemotherapy and radiation therapy, surgical resection remains the mainstay of treatment for most brain tumours.¹ While the holistic nature of neuro-oncological treatment leads to better

survival outcomes, long waiting lists for surgical care and adjuvant treatment often add to the patients' stress. Patients who must wait extended periods to receive the multidisciplinary care associated with cancer treatment often have a negatively impacted quality of life. Therefore surgical wait times must be reduced to ensure patient wellbeing.² Additionally, delays can lead to tumour progression and worsening of symptoms and increase the probability of postoperative complications.³ The current approach to brain tumours requires multiple investigations, consultations, tumour board meetings, and goals-of-care discussions before setting a date for surgery.⁴

Delays in surgery can be detrimental for some brain tumours as the disease may progress and may even

Affiliation at the time of study

^{1-4,7,8,10,11}The Aga Khan University Hospital, Karachi, ⁶Rehman Medical Institute, Hayatabad, Peshawar, ⁹Shaukat Khanum Cancer Memorial Hospital, Lahore, Pakistan. PBTC Group Names: End of the supplement

Current affiliation

⁵University of Pennsylvania, USA.

Correspondence: Syed Ather Enam. Email: ather.enam@aku.edu

worsen in terms of symptoms and staging. This becomes more complex with regard to the type of cancer. Large cohort studies in breast surgery have shown a poor survival outcome in patients with longer preoperative waiting times.⁵ This effect has not been replicated in studies on gastric cancer, with a recent cohort showing no effect on survival for preoperative waiting times up to 90 days. Brain tumour studies have shown that patients treated promptly before developing more debilitating symptoms tend to have better survival.⁶ This seems intuitive given that brain tumours often impinge on critical structures — good functional outcomes with improved survival depend on timely neurosurgical intervention. More importantly, tumour growth in malignant brain tumours can progressively infiltrate functional tissue, further deteriorating functional and survival outcomes. However, this impact has not been studied previously, particularly in LMICs.

This study aimed to determine the current waiting times for brain tumour surgeries in a developing country such as Pakistan. We investigated the impact this has on patients, and which specific demographics are most likely to face longer delays before surgery. Through quantifying this issue, we intend to highlight the importance of timely and prompt neuro-oncological surgery in our part of the world.

Methodology

As described in a previous paper,⁷ data were collected

Table-1: Time to brain tumour surgery according to hospital sector, age group, gender, and socioeconomic status of the patient.

		N (%)		Time to Surgery			p-value
				Mean	Confidence Interval		
Hospital Sector	Public	995	67.50%	94.07	85.29	102.84	<0.001
	Private	479	32.50%	75.14	54.72	95.56	
Age Group	Children (<15 years)	176	12.20%	88.11	70.63	105.6	0.004
	Adolescent (15-19 years)	94	6.50%	116.63	65.27	167.98	
	Young Adult (20-39 years)	594	41.30%	103.34	85.96	120.72	
	Middle-aged adults (40-59 years)	472	32.80%	72.44	61.26	83.61	
	Older adults (60-99 years)	104	7.20%	48.58	31.17	65.98	
Gender	Male	854	57.90%	83.75	73.89	93.62	0.268
	Female	618	41.90%	93.8	77.53	110.07	
	Not specified	2	0.10%		-513.07	605.07	
Socio-Economic Status	Lower Class (e.g. blue-collar workers, labourers, daily wagers)	704	47.80%	80.55	69.63	91.47	<0.001
	Middle Class (e.g. graduates, mid-level office workers, homeowners)	536	36.40%	111.95	94.29	129.61	
	Upper Middle Class (e.g. professionals such as doctors, lawyers, engineers, etc.)	76	5.20%	62.87	42.1	83.64	
	Upper Class (e.g. land owners, big businesses, etc.)	10	0.70%	69	18.25	119.75	
	Not specified	148	10.00%		20.54	79.56	
Glioma Grade	High Grade	215	49.10%	70.13	43.39	89.69	0.031
	Low Grade	223	50.90%	99.73	61.91	127.36	
Current Status	Alive	746	50.60%	91.87	79	104.74	<0.001
	Deceased	158	10.70%	77.41	59.9	94.91	
	Information currently not available	570	38.70%		70.72	100.58	

as part of the Pakistan Brain Tumour Epidemiology Study, a nationwide, hospital record-based study of 32 high-volume neurosurgical centres. Data collected included patient demographics, hospital sector, histopathological diagnosis, and current status on most recent follow-up as assessed on clinic visits or telephonic confirmation. Overall, the national sample included 2750 patients.

The current study investigated patients with recorded dates of first radiological diagnosis and first surgery from this sample. The time to surgery was calculated by the difference in dates by days. Cases with either of these specific dates missing were excluded. This was further stratified according to patient demographic factors, histopathological diagnosis, type of surgical procedure performed, and survival outcomes. For statistical analysis, SPSS Version 23.0 and STATA Version 16.0 were used; data normality was checked with the Kolmogorov-Smirnov test. For parametric data, means were compared with student t-test and ANOVA, while non-parametric data were analysed using Mann-Whitney U and Kruskal-Wallis H tests of significance. All statistical tests were two-sided, and a p-value of <0.05 was taken to be significant.

Results

Patients with recorded dates of first radiological diagnosis and first surgery made up 1474 (53.6%) of the patients in this study. Demographically, a majority of the cohort were

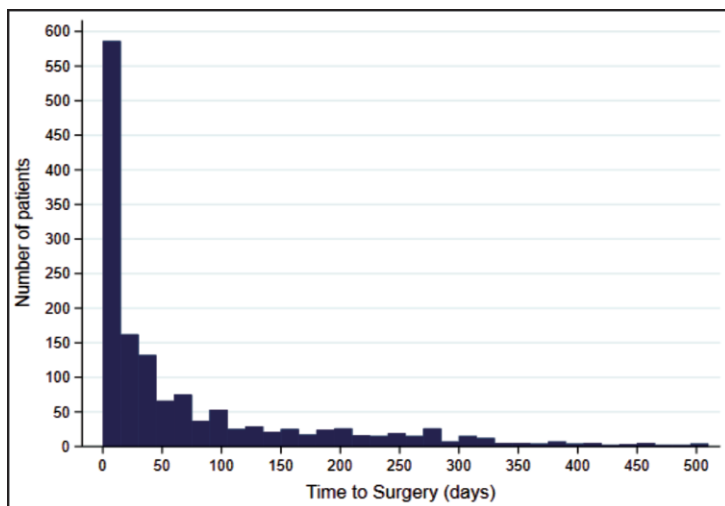


Figure-1: Distribution of time to surgery for patients undergoing brain tumour surgery in Pakistan (2019).

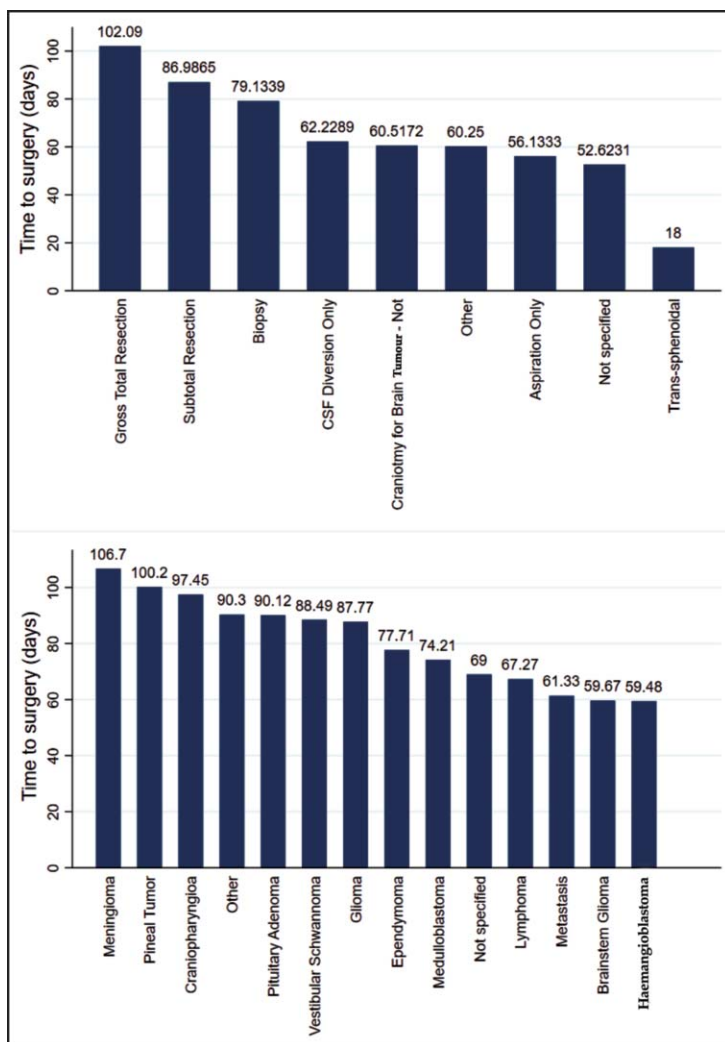


Figure-2: Time to surgery according to surgical procedure and histopathological diagnosis.

young adults ($n=594$, 41.3%) or middle-aged adults ($n=472$, 32.8%), male ($n=854$, 57.9%), and from a lower socioeconomic status ($n=704$, 47.8%). More patients received brain tumour surgery at government hospitals ($n=995$, 67.5%). Figure-1 shows the pattern of distribution of patients according to waiting time for surgery across Pakistan.

As shown in Table-1, patients travelling to public sector hospitals had a significantly longer time for surgery (94.07 (CI: 85.29, 102.84) vs 75.14 (CI: 54.72, 95.56) days, $p<0.001$) compared to private hospitals. Significant differences ($p=0.004$) were also seen between patients of various age groups, as adolescents (116.63 (CI: 65.27, 167.98) days) and young adults (103.34 (CI: 85.96, 120.72) days) had higher waiting times compared to middle-aged (72.44 (CI: 61.26, 83.61) days) and older adults (48.58 (CI: 31.17, 65.98) days). Significant differences were not seen between genders when means were compared statistically ($p=0.268$). A significantly longer time to surgery was observed for middle (111.95 (CI: 94.29, 129.61) days) and lower (80.55 (CI: 69.63, 91.47) days) socioeconomic class patients.

Patients undergoing gross total resection of tumour had significantly ($p<0.001$) longer waiting times for surgery when compared to STR (sub-total resection), biopsy, and CSF-diversion procedures, for all tumour types (Figure-2). Patients diagnosed with meningioma had the most extended waiting periods (106 (CI: 76, 95) days). Gliomas had an average waiting period of 88 (CI: 73, 103) days across the country. Low-grade gliomas had significantly ($p=0.031$) longer waiting times (99.73 (CI: 61.91, 127.36) days) in comparison to high-grade gliomas (70.13 (CI: 43.39, 89.69) days). The shortest times to surgery were observed for haemangioblastomas (59.48 (CI: 26.98, 91.98) days), metastatic lesions (61.33 (CI: 33.05, 89.61) days), and brainstem gliomas (59.67 (CI: 15.08, 134.31) days). A significant difference was seen between waiting times for patients who survived surgical procedures for a brain tumour on the most recent follow-up and those who had expired (91.87 (CI: 79, 107.74) vs 77.41 (CI: 59.90, 94.91) days, $p<0.001$).

Discussion

Waiting times for brain tumour surgery within the country were prolonged according to the sample assessed. Our findings show significantly longer waiting times for public sector patients, regardless of tumour type. This is understandable considering

resource constraints within the public sector and a shortage of trained neurosurgeons to cater to the population. It is particularly concerning that patients aged 15-39 years had the most extended overall waiting times for surgery. This can be explained by (a) sample size bias as few older adult patients (60-99 years) had records available, and (b) as a developing country, the bulk of the population is made up of working age and young adults.

This data highlights the current crisis in providing timely surgery for young adult patients with brain tumours. Patients from lower and middle-socioeconomic classes were also seen to be at a significantly higher risk of delays in brain tumour surgery. On average, patients who underwent a gross resection of the tumour had to wait 102 days for surgery. In comparison, shorter and more technically feasible procedures such as biopsies and CSF diversion only had 77 day shorter waiting time periods. It is concerning that even for biopsy procedures, patients have, on average, had to wait 80 days for tissue diagnosis and then initiation of further adjuvant therapy. Delays in surgery will inevitably have a downstream effect on the progression of the disease, difficulty in providing a survival benefit through treatment, and significantly impacting a patient's quality of life when intervention is warranted.

While many studies have looked at the impact of waiting times from surgery to postoperative radiation therapy, few have considered the impact of healthcare systems on delays to surgical care in brain tumour surgery.^{8,9} An audit conducted in the UK in 2015 recorded an average of 50.82 days till surgical treatment after diagnosis.¹⁰ Similarly, a retrospective review in the USA from 2015 recorded a mean wait time for surgery of 11 days after the first scan, specifically in glioblastoma.¹¹ More recently, an extensive report was published from the Netherlands in 2022 — the mean time to surgery for glioblastoma was 18 days from the first MR scan. Interestingly, there was no significant difference in waiting times for resections and biopsy procedures within this cohort. This study also concluded longer wait times were associated with better survival, as patients with worse preoperative KPS scores were the ones more likely to undergo urgent surgery. However, delays in surgical resection negatively impacted KPS improvement.

A few factors limit the current study. Due to the retrospective nature of the nationwide study, waiting times were only available for a select subset of the national sample, limiting the generalisability of our findings. Moreover, waiting times for chemotherapy and

radiation therapy are unknown, which would significantly impact survival. Waiting times for surgery may be affected by socio-cultural practices and surgeon-dependant guidance regarding urgency or need for surgery. These limitations may explain variations in waiting times in our region. However, our study is the first report of waiting times for brain tumour surgery, particularly from a low-and-middle-income country; LMIC healthcare systems are distinct due to their emphasis on vertical programmes for infection, trauma, and diseases of known epidemiology and burden of disease. The findings of this study may help establish a benchmark for brain tumour surgical care and timely delivery.

Conclusion

Our publication highlights an essential metric in brain tumour care delivery — prolonged delays to surgery are a significant barrier within LMICs, leading to worse patient outcomes. As shown, patients undergoing brain tumour surgery at public sector hospitals from lower or middle socioeconomic statuses and elected for GTR were more likely to have longer delays to the surgical procedure. Specific tumour subtypes were also more likely to undergo delayed procedures, potentially impacting those patients' overall survival and postoperative functional outcomes.

Disclaimer: None to declare.

Conflict of Interest: None to declare.

Funding Disclosure: None to declare.

References

1. Brandes AA. State-of-the-art treatment of high-grade brain tumors. *Semin Oncol* 2003;30(Suppl 19):4-9. doi: 10.1053/j.seminoncol.2003.11.028.
2. Felder JM, Ducic I. Chronic Nerve Injuries and Delays in Surgical Treatment Negatively Impact Patient-reported Quality of Life. *Plast Reconstr Surg Glob Open* 2021;9:e3570. doi: 10.1097/GOX.0000000000003570.
3. Guan J, Karsy M, Brock AA, Couldwell WT, Kestle JRW, Jensen RL, et al. Impact of a more restrictive overlapping surgery policy: an analysis of pre- and postimplementation complication rates, resident involvement, and surgical wait times at a high-volume neurosurgical department. *J Neurosurg* 2018;129:515-23. doi: 10.3171/2017.5.JNS17183.
4. Nimmervoll BV, Boulos N, Bianski B, Dapper J, DeCuyper M, Shelat A, et al. Establishing a Preclinical Multidisciplinary Board for Brain Tumors. *Clin Cancer Res* 2018;24:1654-66. doi: 10.1158/1078-0432.CCR-17-2168.
5. Liederbach E, Sisco M, Wang C, Pesce C, Sharpe S, Winchester DJ, et al. Wait times for breast surgical operations, 2003-2011: a report from the National Cancer Data Base. *Ann Surg Oncol* 2015;22:899-907. doi: 10.1245/s10434-014-4086-7.
6. Yuile P, Dent O, Cook R, Biggs M, Little N. Survival of glioblastoma patients related to presenting symptoms, brain site and treatment variables. *J Clin Neurosci* 2006;13:747-51. doi:

- 10.1016/j.jocn.2005.10.011.
7. Baig E, Shah MM, Bajwa MH, Khalid MU, Khan SA, Hani U, et al. Conducting the Pakistan brain tumour epidemiology study — a report on the methodology. *J Pak Med Assoc* 2022;72(Suppl 4):s4-7.. doi: 10.47391/JPMA.11-S4-AKUB01
 8. Rasmussen BK, Hansen S, Laursen RJ, Kosteljanetz M, Schultz H, Nørgård BM, et al. Epidemiology of glioma: clinical characteristics, symptoms, and predictors of glioma patients grade I-IV in the the Danish Neuro-Oncology Registry. *J Neurooncol* 2017;135:571-9. doi: 10.1007/s11060-017-2607-5.
 9. Lutterbach J, Bartelt S, Momm F, Becker G, Frommhold H, Ostertag C. Is older age associated with a worse prognosis due to different patterns of care? A long-term study of 1346 patients with glioblastomas or brain metastases. *Cancer* 2005;103:1234-44. doi: 10.1002/cncr.20895.
 10. Umotong DE. PP79. Diagnosis To Treatment Time For Brain Tumours: Audit. *Neuro Oncol* 2017;19(Suppl 1):i21. doi: 10.1093/neuonc/now293.079.
 11. Young J, Muster R, Chandra A, Morshed R, Aghi M. Surg-14. Does waiting matter? How time from diagnostic mri to surgical resection affects outcomes in newly diagnosed glioblastoma. *Neuro Oncol* 2019;21(Suppl 6):vi242-3. doi: 10.1093/neuonc/noz175.1015.
-