SKALSKA-DZIOBEK, Nina, NARUSZEWICZ, Maria, MIDRO, Aleksandra, CETNAROWSKI, Przemysław, ZAGÓRSKI, Karol, KOZIK, Mateusz, MAŁAGOCKA, Weronika and CHYBOWSKA, Karolina. Suicidal risk in patients diagnosed with central nervous system tumors – current state of knowledge: Comprehensive review. Quality in Sport. 2024;30:56768. eISSN 2450-3118.
https://doi.org/10.12775/QS.2024.30.56768
https://apcz.umk.pl/QS/article/view/56768

The journal has been 20 points in the Ministry of Higher Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Higher Education and Science of 05.01.2024. No. 32553.
Has a Journal's Unique Identifier: 201398. Scientific disciplines assigned: Economics and finance (Field of social sciences); Management and Quality Sciences (Field of social sciences).
Punkty Ministerialne z 2019 - aktualny rok 20 punktów. Załącznik do komunikatu Ministra Szkolnictwa Wyższego i Nauki z dnia 05.01.2024 r. Lp. 32553. Posiada Unikatowy Identyfikator Czasopisma: 201398.
Przypisane dyscypliny naukowe: Ekonomia i finanse (Dziedzina nauk społecznych); Nauki o zarządzaniu i jakości (Dziedzina nauk społecznych).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 07.12.2024. Revised: 28.12.2024. Accepted: 30.12.2024. Published: 30.12.2024.

Suicidal risk in patients diagnosed with central nervous system tumors – current state of knowledge: Comprehensive review

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Abstract

Introduction and objective: Central nervous system (CNS) tumors, particularly brain tumors, significantly impact mental health, leading to conditions like depression, anxiety, and suicidality. This study examines the prevalence and risk factors for these disorders in CNS tumor patients, focusing on brain tumors.

Material and methods: A comprehensive review was conducted to assess suicidality and prevalence of various mental diseases in patients with CNS tumors, focusing on brain tumors. Studies were identified through PubMed, Embase, and Google Scholar, including research on CNS tumors and associated mental health conditions. Key outcomes examined included depression, anxiety, and suicidality.

State of knowledge: Gliomas and glioblastomas are strongly linked to mental health challenges, with depression and anxiety being most common. Suicidality is notably higher in CNS tumor patients, influenced by tumor-related neurological and functional impairments. Despite this, mental health care integration into neuro-oncology remains inadequate.

Conclusions: CNS tumor patients are at high risk for mental health disorders and suicidality, highlighting the need for early intervention and multidisciplinary care. Better integration of mental health support can improve patient outcomes and quality of life.

Keywords: “Central nervous system tumors”; “Anxiety”; “Depression”; “Suicide”; “Glioma”; “Glioblastoma”; “Meningioma”

Introduction

Suicidality among patients with central nervous system (CNS) tumors is a complex and often underexplored issue. The diagnosis of a CNS tumor brings significant physical and psychological challenges, including neurological impairments, cognitive changes, and emotional distress. These factors, coupled with the often poor prognosis, create a unique vulnerability to suicidal ideation and behaviors. Recognizing patients at risk of suicidality is essential for delivering prompt psychiatric care in neuro-oncological settings, aiming to prevent potential harm[1].

In 2021, the WHO released an updated classification of CNS tumors. Despite the previous version being introduced only five years earlier, in 2016, significant progress in understanding the molecular biology of CNS tumors—particularly the identification of clinically relevant molecular subtypes - highlighted the need for a revised system[2].

The updates in the new classification of the most common primary adult tumors - gliomas (such as oligodendrogliomas, astrocytomas, and ependymomas) and meningiomas. It emphasizes the key genomic alterations defining each group, providing clinicians with a framework for understanding these changes when exploring treatment options, including clinical trials and targeted therapies, and discussing prognostic implications with patients[3].

Purpose

This article aims to explore the prevalence, risk factors, and potential strategies for prevention and support in this specific patient population.

Material and methods

A comprehensive literature review was conducted to analyze the prevalence and characteristics of suicidality among patients with central nervous system (CNS) tumors, with a particular focus on brain tumors. Articles were identified through systematic searches of PubMed, Embase, and Google Scholar databases. The search included both original research and review articles published in English.

Eligibility criteria included studies reporting on adult patients aged 18 to 70 years with CNS tumors and associated mental health conditions, such as depression, anxiety disorders, suicidal ideation, suicidal tendencies, or suicide attempts. Additionally, studies addressing suicide rates in this patient population were included. Particular emphasis was placed on those investigating the intersection of brain tumors and mental health outcomes.

Key search terms included combinations of "CNS tumors," "brain tumors," "suicidal ideation," "suicide attempts," "depression," "anxiety," and "mental health." Relevant data from the included articles were synthesized to highlight patterns, risk factors, and clinical implications regarding suicidality in this vulnerable population.

State of knowledge

The most prevalent types of CNS tumors

Table 1. presents the current classification from the 2021 World Health Organization (WHO) Classification of Tumors of the Central Nervous System. Below, the key facts regarding the most common CNS tumors are outlined.

Gliomas: astrocytomas, oligodendrogliomas, ependymomas

Gliomas are the most common primary tumors affecting the brain and spinal cord [4] . Their incidence generally increases with age, with glioblastoma showing the sharpest rise, ranging from 0.15 per 100,000 in children and 0.41 in young adults to 13.1 in those aged 65–75 years and 15.0 in individuals aged 75–84 [5,6] . These tumors originate from neuroglial stem or progenitor cells. Historically, they have been categorized based on histological features into astrocytic, oligodendroglial, or ependymal tumors and assigned WHO grades I–IV, reflecting varying levels of malignancy[5]. Glioblastoma WHO IV accounts for about 57% of gliomas and 48% of all primary malignant CNS tumors. Despite progress in multimodal treatment approaches, the prognosis remains poor[7].

Meningiomas

Meningiomas are predominantly benign tumors that arise from arachnoid cap cells [8] . Classified into three WHO grades, the majority (90%) are grade I[9]. Meningiomas account for 13–26% of all intracranial tumors. These tumors are more frequently observed in older adults and are more common in females[8]. Evidence of inherited susceptibility to meningioma comes from familial case reports and studies of candidate genes involved in DNA repair. Individuals with specific mutations in the neurofibromatosis type 2 (NF2) gene face a significantly elevated risk of developing meningiomas. Additionally, exposure to high doses of ionizing radiation is a well-established risk factor for these tumors[10]. Surgery is the primary treatment

approach, but complete resection is achievable in less than 50% of cases. Radiation therapy may be considered depending on the extent of resection, tumor location, and WHO grade[8,9].

Metastases to the CNS

Brain metastases occur in 15–30% of patients with cancer. Metastases to the central nervous system, frequently originating from lung cancer, breast cancer, and melanoma, are linked to poor survival rates [11] . Approximately 20% of cancer patients are expected to develop brain metastases. Moreover, the occurrence of brain metastases is a significant factor contributing to cancer-related mortality [12] . Various treatment methods may be applied. Young patients with minimal extracranial disease may benefit from surgical removal of a single brain metastasis, while radiosurgery or stereotactic radiotherapy may be effective for managing two to four brain metastases[13].

Lymphomas

Primary CNS lymphoma (PCNSL) is an uncommon subtype of extranodal non-Hodgkin lymphoma[14]. They are characterized by a relatively aggressive course and a low tendency for systemic spread. The prognosis for patients with PCNSL is often unfavorable. High-dose methotrexate-based chemotherapy regimens are the standard treatment for patients who are able to tolerate this approach[15].

Schwannomas

Schwannomas are peripheral nervous system tumors composed of various cell types. They originate from tumorigenic Schwann cells due to loss-of-function mutations in the NF2 tumor suppressor gene. Among cranial nerves, schwannomas most commonly affect the vestibular, trigeminal, and hypoglossal nerves[16].

Medulloblastomas

Medulloblastomas account for almost 10% of all brain tumors in children. These tumors are found in the posterior fossa and belong to biologically diverse group of embryonal tumors located in the cerebellum. The treatment of medulloblastomas, including surgical resection and radiotherapy, is often associated with significant morbidity, especially in young patients[17].

Table 1: World Health Organization Classification of Tumors of the Central Nervous System[18].

Types	**Subtypes**	
Gliomas, glioneuronal tumors, and neuronal tumors	Adult-type diffuse gliomas	1. Astrocytoma, IDH-mutant 2. Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted 3. Glioblastoma, IDH-wildtype
	Pediatric-type diffuse low-grade gliomas	1. Diffuse astrocytoma, MYB- or MYBL1-altered 2. Angiocentric glioma 3. Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) 4. Diffuse low-grade glioma, MAPK pathway-altered
	Pediatric-type diffuse high-grade gliomas	1. Diffuse midline glioma, H3 K27-altered 2. Diffuse hemispheric glioma, H3 G34-mutant 3. Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype 4. Infant-type hemispheric glioma
	Circumscribed astrocytic gliomas	1. Pilocytic astrocytoma 2. High-grade astrocytoma with piloid features 3. Pleomorphic xanthoastrocytoma 4. Subependymal giant cell

		astrocytoma 5. Chordoid glioma 6. Astroblastoma, MN1-altered
	Glioneuronal and neuronal tumors	1. Gangliоglioma 2. Desmoplastic infantile ganglioglioma/desmoplastic infantile astrocytoma 3. Dysembryoplastic neuroepithelial tumor 4. Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters 5. Papillary glioneuronal tumor 6. Rosette-forming glioneuronal tumor 7. Myxoid glioneuronal tumor 8. Diffuse leptomeningeal glioneuronal tumor 9. Gangliocytoma 10. Multinodular and vacuolating neuronal tumor 11. Dysplastic cerebellar gangliocytoma 12. Central neurocytoma 13. Extraventricular neurocytoma 14. Cerebellar liponeurocytoma
		1. Supratentorial ependymoma

	Ependymal tumors	2. Posterior fossa ependymoma 3. Spinal ependymoma 4. Myxopapillary ependymoma 5. Subependymoma
Choroid plexus tumors	1. Choroid plexus papilloma 2. Atypical choroid plexus papilloma 3. Choroid plexus carcinoma	
Embryonal tumors	1. Medulloblastoma 2. Atypical teratoid/rhabdoid tumor 3. Cribiform neuroepithelial tumor 4. Embryonal tumor with multilayered rosettes 5. CNS neuroblastoma, FOXR2-activated 6. CNS tumor with BCOR internal tandem duplication	
Pineal tumors	1. Pineocytoma 2. Pineal parenchymal tumor of intermediate differentiation 3. Pineoblastoma 4. Papillary tumor of the pineal region 5. Desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant	
Cranial and paraspinal nerve tumors	1. Schwannoma 2. Neurofibroma 3. Perineurioma 4. Hybrid nerve sheath tumor 5. Malignant melanotic nerve sheath tumor 6. Malignant peripheral nerve sheath tumor 7. Paraganglioma	
	1. Meningothelial meningioma 2. Fibrous meningioma	

Meningioma	3. Transitional meningioma 4. Psammomatous meningioma 5. Angiomatus meningioma 6. Microcystic meningioma 7. Secretory meningioma 8. Lymphoplasmacyte-rich meningioma 9. Metaplastic meningioma 10. Chordoid meningioma 11. Clear cell meningioma 12. Atypical meningioma 13. Papillary meningioma 14. Rhabdoid meningioma 15. Anaplastic meningioma	
Mesenchymal, non-meningothelial tumors	Soft tissue tumors	1. Fibroblastic and myofibroblastic tumors 2. Vascular tumors 3. Skeletal muscle tumors 4. Uncertain differentiation
	Chondro-osseous tumors	1. Chondrogenic tumors 2. Notochordal tumors
Melanocytic tumors	1. Diffuse meningeal melanocytic neoplasms 2. Circumscribed meningeal melanocytic neoplasms	
Hematolymphoid tumors	1. Lymphomas 2. Histiocytic tumors	
Germ cell tumors	1. Mature teratoma 2. Immature teratoma 3. Teratoma with somatic-type malignancy 4. Germinoma	

	5. Embryonal carcinoma 6. Yolk sac tumor 7. Choriocarcinoma 8. Mixed germ cell tumor
Tumors of the sellar region	1. Adamantinomatous craniopharyngioma 2. Papillary craniopharyngioma 3. Pituicytoma, granular cell tumor of the sellar region, and spindle cell oncocytoma 4. Pituitary adenoma/PitNET 5. Pituitary blastoma
Metastases to the CNS	1. Metastases to the brain and spinal cord parenchyma 2. Metastases to the meninges

The association between CNS tumors and mental disorders

Risk factors

Key risk factors for suicidality included the presence of severe neurological deficits, uncontrolled pain, functional decline, and the psychological burden of a poor prognosis. Younger age (18–40 years), a history of pre-existing mental health disorders, and limited social support were also associated with higher rates of suicidality[19].

Mental health conditions in CNS tumor patients

Patients with gliomas face the challenges of both a progressive neurological condition and cancer, which often lead to symptoms like depression and anxiety. These mental health issues are prevalent in glioma patients, with depression affecting 16-41% and anxiety 24-48%, as indicated by self-report questionnaires. Such symptoms can severely affect health-related quality of life and may also influence survival outcomes[20,21]. Brain tumors can manifest with a range of psychiatric symptoms, including depression, anxiety, psychosis, apathy/abulia, cognitive or personality changes, mania, panic attacks, and occasionally anorexia nervosa. These tumors may be identified during a patient's initial presentation to mental health services or in individuals with pre-existing psychiatric diagnoses [21,22] . Depression is reported in as many as 90% of cancer patients, however, there is currently no standardized screening tool specifically adapted for individuals diagnosed with brain tumors. Finze et al. demonstrated

that 87.5% of glioblastoma patients scored above 16 points on the Center for Epidemiologic Studies Depression Scale (CES-D) following surgery[23].

Suicidal risk in patients with CNS tumors

Suicidality includes a range of conditions, from suicidal ideation to suicidal behaviors, which cover suicide attempts and completed suicide. Suicidality and brain tumors are both critical, dangerous medical conditions, but their association is rarely discussed in the literature. Despite their profound effects on mental and physical well-being, there is limited research on how brain tumors may influence the risk of suicidality, indicating a need for further exploration[19].

Patients with brain tumors, particularly those with glioblastomas, exhibited a notably higher suicide rate compared to individuals with other CNS tumors or the general population. The studies highlighted a suicide incidence ranging from 1.2% to 3.4%, depending on tumor type and stage of progression[24].

Discussion and conclusions

The findings of this review highlight the profound psychological burden experienced by patients with CNS tumors, particularly those with brain tumors. Suicidality in this population is a complex issue driven by biological, psychological, and social factors.

The pathophysiology of CNS tumors, including their location and associated neurological impairments, often results in cognitive dysfunction, emotional instability, and diminished quality of life [25,26] . These factors significantly contribute to the development of depression, anxiety, and suicidal ideation. Brain tumors, such as glioblastomas, are particularly associated with heightened psychological distress due to their aggressive nature and poor prognosis[25–27].

Younger patients and those with limited social support appear to be at higher risk for suicidality. Younger individuals face unique challenges, such as the psychological impact of confronting a life-threatening diagnosis during critical life stages. Additionally, insufficient access to psychiatric care exacerbates the vulnerability of this population, emphasizing the need for targeted interventions[28,29].

This review underscores the importance of integrating mental health assessments into routine care for patients with CNS tumors. Early identification and management of depression and suicidal ideation are crucial to reducing the risk of suicide. A multidisciplinary approach, involving neuro-oncologists, psychiatrists, psychologists, and social workers, is essential to address the diverse needs of these patients. Targeted therapies addressing both the physical

and psychological aspects of CNS tumors could play a crucial role in improving patient outcomes and reducing suicidality in this population.

Limitations

The variability in study designs and methodologies among the included articles may limit the findings. Furthermore, evidence on specific interventions to reduce suicidality in CNS tumor patients remains scarce. Future research should focus on developing and evaluating integrated mental health care strategies tailored to various populations.

The association between mental health and CNS tumor pathology is vital for improving both psychological well-being and clinical outcomes in this vulnerable group.

Disclosures

Author contribution: Conceptulization: Karol Zagórski and Mateusz Kozik; ***methodology:*** Nina Skalska-Dziobek; ***software:*** Weronika Małagocka; ***check:*** Karolina Chybowska; ***formal analysis:*** Maria Naruszewicz; ***investigation:*** Aleksandra Midro; ***resources:*** Przemysław Cetnarowski; ***data curation:*** Nina Skalska-Dziobek; ***writing – rough preparation:*** Karol Zagórski; ***writing – review and editing:*** Mateusz Kozik, Weronika Małagocka, Karolina Chybowska; ***visualization:*** Przemysław Cetrnarowski; ***supervision:*** Maria Naruszewicz; ***project administration:*** Aleksandra Midro.

All authors have read and agreed with the final, published version of the manuscript.

Funding statement: No external funding was received to perform this review.

Institutional Review Board Statement: Not applicable – this review included analysis of the available literature.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflict of interest: The authors declare no conflict of interest.

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