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TREATMENT OF SUPRATENTORIAL BRAIN TUMOURS IN OLDER AND VERY OLD PATIENTS: FROM THE CONCEPT OF BIOLOGICAL AGE TO PERSONALISED MANAGEMENT

УЛГАЙГАН ЖАНА КАРЫЛЫК КУРАКТАГЫ АДАМДАРДА БАШ МЭЭНИН СУПРАТЕНТОРИАЛДЫК ШИШИКТЕРИН ДАРЫЛОО: БИОЛОГИЯЛЫК КУРАК КОНЦЕПЦИЯСЫНАН ЖЕКЕЛЕШТИРИЛГЕН ТАКТИКАГА

ЛЕЧЕНИЕ СУПРАТЕНТОРИАЛЬНЫХ ОПУХОЛЕЙ ГОЛОВНОГО МОЗГА У ЛИЦ ПОЖИЛОГО И СТАРЧЕСКОГО ВОЗРАСТА: ОТ КОНЦЕПЦИИ БИОЛОГИЧЕСКОГО ВОЗРАСТА К ПЕРСОНАЛИЗИРОВАННОЙ ТАКТИКЕ

Akylbek Akmatalievich Akmataliev
Акматалиев Акылбек Акматалиевич
Акматалиев Акылбек Акматалиевич

Candidate of Medical Sciences, neurosurgeon, National Hospital under the Ministry of Health of the Kyrgyz Republic, corresponding author
м.и.к., врач-нейрохирург, КРнын Саламаттык сактоо министирлигинин Улуттук госпиталы, жооптуу автор
к.м.н., врач-нейрохирург, Национальный госпиталь при Министерстве здравоохранения Кыргызской Республики, автор, ответственный за переписку
akmataliev.akylbek@gmail.com
ORCID: 0000-0002-7337-2601

Buranbek Djamgyrchievich Dyusheev
Дюшеев Буранбек Джамгырчиевич
Дюшеев Буранбек Джамгырчиевич

Doctor of Medical Sciences, neurosurgeon, National Hospital under the Ministry of Health of the Kyrgyz Republic
м.и.д., врач-нейрохирург, КРнын Саламаттык сактоо министирлигинин Улуттук госпиталы
д.м.н., профессор, врач-нейрохирург,Национальный госпиталь при Министерстве здравоохранения Кыргызской Республики
ORCID: 0009-0007-6138-4203

Nurlan Tolobekovich Kachiev
Качиев Нурлан Толобекович
Качиев Нурлан Толобекович

Candidate of Medical Sciences, neurosurgeon, National Hospital under the Ministry of Health of the Kyrgyz Republic
м.и.к., врач-нейрохирург, КРнын Саламаттык сактоо министирлигинин Улуттук госпиталы
к.м.н., врач-нейрохирург, Национальный госпиталь при Министерстве здравоохранения Кыргызской Республики
ORCID: 0000-0003-4117-478X

Ulan Abdillaevich Karimov
Каримов Улан Абдиллаевич
Каримов Улан Абдиллаевич

neurosurgeon, Osh Inter-regional Unified Clinical Hospital
врач-нейрохирург, Ош областтар аралык бириккен клиникалык ооруканасы
врач-нейрохирург, Ошская межобластная объединенная клиническая больница
ORCID: 0009-0008-6171-4281

TREATMENT OF SUPRATENTORIAL BRAIN TUMOURS IN OLDER AND VERY OLD PATIENTS: FROM THE CONCEPT OF BIOLOGICAL AGE TO PERSONALISED MANAGEMENT

Abstract.

Population ageing is reshaping the neurosurgical caseload: the share of older and very old patients in specialised departments continues to grow. The aim of this work is to summarise current evidence on the epidemiology, molecular biology and clinical management of supratentorial gliomas and meningiomas in geriatric patients. A narrative review of publications from the past decade was performed, covering international clinical guidelines, randomised trials, systematic reviews and population registry data. In this age group, meningiomas predominate among non-malignant tumours and glioblastomas without isocitrate dehydrogenase mutation among malignant ones, while wider access to imaging increases the detection of asymptomatic meningiomas. The contribution of multimodal neuroimaging to delineating tumour infiltration is discussed. Reducing postoperative mortality depends not only on surgical technique but also on standardised prolonged postoperative care that accounts for comorbidity and the risk of hospital-acquired infection. Developing guidelines for personalised management of such patients remains a priority.

Keywords: neuro-oncology; older and very old patients; meningioma; glioblastoma; frailty; neuroimaging; postoperative care

Улгайган жана карылык курактагы адамдарда баш мээнин супратенториалдык шишиктерин дарылоо: биологиялык курак концепциясынан жекелештирилген тактикага

Аннотация

Калктын картаюусу нейрохирургиялык агымдын түзүмүн өзгөртүүдө: адистештирилген стационарларда улгайган жана карылык курактагы бейтаптардын үлүшү туруктуу өсүүдө. Иштин максаты — гериатриялык бейтаптарда супратенториалдык глиомалардын жана менингиомалардын эпидемиологиясы, молекулярдык биологиясы жана клиникалык жүргүзүлүшү боюнча заманбап маалыматтарды жалпылоо. Акыркы он жылдыктагы басылмаларга нарративдик сереп жүргүзүлдү: эл аралык клиникалык колдонмолор, рандомизацияланган изилдөөлөр, системалуу серептер жана популяциялык каттоолордун маалыматтары. Бул курактык топто залалсыз шишиктердин арасында менингиомалар, залалдуу шишиктердин арасында изоцитратдегидрогеназанын мутациясы жок глиобластомалар басымдуулук кылары көрсөтүлдү, ал эми томографиянын жеткиликтүүлүгүнүн өсүшү белгисиз өткөн менингиомалардын аныкталышын көбөйтүүдө. Шишиктин инвазия чегин тактоодо мультимодалдык нейровизуализациянын ролу негизделди. Операциядан кийинки өлүмдүн азайышы хирургиялык техника менен гана эмес, полиморбиддүүлүктү жана госпиталдык инфекциялардын коркунучун эске алуу менен узартылган операциядан кийинки мезгилди жүргүзүүнү стандартташтыруу менен да аныкталат. Мындай бейтаптарды жекелештирилген жүргүзүү боюнча методикалык сунуштарды иштеп чыгуу

Лечение супратенториальных опухолей головного мозга у лиц пожилого и старческого возраста: от концепции биологического возраста к персонализированной тактике

Аннотация

Старение населения меняет структуру нейрохирургического потока: доля пациентов пожилого и старческого возраста в профильных стационарах устойчиво растёт. Цель работы — обобщить современные данные об эпидемиологии, молекулярной биологии и клиническом ведении супратенториальных глиом и менингиом у гериатрических пациентов. Выполнен нарративный обзор публикаций последнего десятилетия: международных клинических руководств, рандомизированных исследований, систематических обзоров и данных популяционных регистров. Показано, что в этой возрастной группе преобладают менингиомы среди доброкачественных новообразований и глиобластомы без мутации изоцитратдегидрогеназы среди злокачественных, а растущая доступность томографии увеличивает выявление бессимптомных менингиом. Обоснована роль мультимодальной нейровизуализации в уточнении границ опухолевой инвазии. Снижение послеоперационной летальности определяется не только хирургической техникой, но и стандартизацией ведения пролонгированного послеоперационного периода с учётом полиморбидности и риска госпитальных инфекций. Приоритетной задачей остаётся разработка методических рекомендаций по персонализированному ведению таких пациентов.

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Ачкыч сөздөр: нейроонкология; улгайган жана карылык курак; менингиома; глиобластома; карылык астения; нейровизуализация; операциядан кийинки багуу

Ключевые слова: нейроонкология; пожилой и старческий возраст; менингиома; глиобластома; старческая астения; нейровизуализация; послеоперационное ведение

Introduction

Modern Demographic Changes and Anatomical and Physiological Features of the Aging Organism

Health systems in the twenty-first century have met population aging at a pace without precedent. The World Health Organization designated 2021–2030 the "Decade of Healthy Ageing," a label that signals how far the age structure of the world population has shifted (WHO, 2021). Projections for 2050 put the share of people over 60 at roughly 22% of the population, double the present proportion and more than 2 billion in absolute terms; those aged 80 and above are expected to triple in number and reach 426 million (UN DESA, 2020). Central Asia follows the same curve, the Kyrgyz Republic included. Specialized hospitals therefore admit steadily more geriatric patients and need management protocols written for them.

How vulnerable these patients are at baseline follows from involutional processes in the central nervous system (CNS). Morphometry and neuroimaging place the loss of brain parenchymal volume at about 5% per decade after the age of 40; past 70 the atrophy accelerates, and the subarachnoid spaces and ventricular system widen along with it (Fjell and Walhovd, 2010; Resnick et al., 2003). Perfusion studies show global cerebral blood flow falling by 10–20% over the same span. Microcirculation changes as well: capillary basement membranes thicken, cerebral amyloid angiopathy develops, vasoreactivity declines (Fjell and Walhovd, 2010). An aging brain carrying this burden tolerates retraction, swings in perfusion pressure, and operative stress poorly.

Frailty in combination with multimorbidity is the organizing concept of contemporary geriatric neurosurgery (Zhu et al., 2023). What predicts outcome is biological status, not chronological age. Advanced atherosclerosis, ischemic heart disease, arterial hypertension, and diabetes mellitus aggravate one another, while the age-related decline in immunological reactivity narrows compensatory reserve further. Coexisting cerebrovascular disease blurs the classical neurological picture on top of that. Tumors are consequently found late, at large or giant size, when the surgical risk is already high.

A systematic review with meta-analysis in neuro-oncology tied frailty consistently to perioperative complications, mortality, and length of hospital stay (Zhu et al., 2023). A wider review of the neurosurgical literature reached the same conclusion (Pazniokas et al., 2021). Pharmacokinetics shift with age and demand equal precision from the anesthesia team: in a prospectively collected cohort of patients aged 65 years and older operated on for intracranial tumors, 46% had at least one neurosurgical complication, and 29.4% left the hospital in worse functional condition than they entered it (Ferroli et al., 2021). Targeted antimicrobial protocols and dedicated management of the prolonged postoperative period belong to the treatment itself, not to its optional extras.

Epidemiology of Supratentorial Meningiomas and Gliomas in Elderly and Very Old Patients

The epidemiology of primary intracranial tumors moves with the age structure of the population. The Central Brain Tumor Registry of the United States reports an overall incidence of primary CNS tumors of 24.8 cases per 100,000 population; rates are highest above 65 years and peak beyond 107 cases per 100,000 in the group aged 85 years and older (Ostrom et al., 2024). Supratentorial tumors make up as much as 85–90% of the neuro-oncological disease burden in elderly and very old patients, with meningiomas and malignant gliomas at the top (Ostrom et al., 2024).

Meningiomas are still the most common primary intracranial tumor and supply roughly 57% of all non-malignant CNS neoplasms (Ostrom et al., 2024). Incidence rises directly with age: about 9.5 per 100,000 in the general population against more than 30 cases per 100,000 in patients older

than 75 years (Ostrom et al., 2024; Vernooij et al., 2007). Hemispheric meningiomas of the convexity, parasagittal region, and falx show marked sex dimorphism and affect women more than twice as often as men (Ostrom et al., 2024). Incidentalomas warrant separate attention. Screening and autopsy series using high-resolution MRI now detect asymptomatic meningiomas in 2.5–3% of people older than 60 years and in almost 10% of those older than 80 years (Vernooij et al., 2007). The neurosurgeon then faces a dilemma between active intervention and surveillance, to be settled against the patient's somatic status and expected life expectancy.

Glioblastoma dominates the malignant neuroepithelial tumors of this age group and supplies more than 51% of all malignant primary CNS neoplasms (Ostrom et al., 2024). Incidence peaks between 70 and 84 years, predominantly among men (Ostrom et al., 2024). Molecularly and epidemiologically, the geriatric population is defined by primary glioblastomas that arise de novo and carry an isocitrate dehydrogenase wild-type genotype (IDH-wildtype) (Eckel-Passow et al., 2015; Louis et al., 2021).

Delayed diagnosis is a clinical problem in its own right. Neurological deficits get attributed to vascular dementia, Alzheimer's disease, or chronic cerebral ischemia (Pazniokas et al., 2021; Zhu et al., 2023), so supratentorial neoplasms surface only once clinical decompensation is pronounced.

Molecular Genetic and Biological Features of Meningeal and Glial Tumors in Elderly and Very Old Patients

Personalized medicine has made the molecular genetic profile of intracranial neoplasms decisive, as the WHO Classification of Tumors of the Central Nervous System (2021) established (Louis et al., 2021). A tumor's genetics matter as much as its histological structure. In elderly and very old patients the molecular landscape of supratentorial neoplasms departs substantially from what younger patients show, which accounts both for resistance to standard therapy and for the separate therapeutic algorithms geriatric neuro-oncology requires (Eckel-Passow et al., 2015).

Meningiomas in older patients have a molecular biology of their own. Grade 1 covers most of them, yet age-related changes in the tumor microenvironment, namely cellular senescence, remodeling of the extracellular matrix, and local immunosuppression, may sustain growth. Molecular grading carries practical weight: a homozygous CDKN2A/B deletion or a TERT promoter mutation in a histologically "typical" meningioma moves it into the Grade 3 category and forces postoperative management to be reconsidered (Maas et al., 2021).

Above 65 years, supratentorial glial tumors are represented almost exclusively by IDH-wildtype glioblastomas (Eckel-Passow et al., 2015; Louis et al., 2021). Primary tumors account for more than 90–95% of glioblastomas at this age (Louis et al., 2021). Absent IDH1 and IDH2 mutations point to de novo development and to aggressive biological behavior. Alongside IDH status, glioblastomas in the aging brain carry mutations of the telomerase reverse transcriptase (TERT) gene promoter, epidermal growth factor receptor (EGFR) amplification, and loss of heterozygosity of chromosome 10 with PTEN inactivation (Eckel-Passow et al., 2015). Clinically the profile reads as rapid infiltrative growth, resistance to chemoradiotherapy, and an unfavorable prognosis: without adequate treatment, patients older than 65 years survive a median of no more than 3–4 months.

Methylation status of the O6-methylguanine-DNA methyltransferase (MGMT) gene promoter keeps its particular prognostic and predictive significance and is taken up below.

Specific Clinical Course and Differential Diagnostic Considerations

Supratentorial tumors present atypically in elderly and very old patients. Cerebral atrophy and enlarged cerebrospinal fluid spaces leave a reserve of intracranial volume, so a neoplasm can grow for a long period without symptoms while signs of intracranial hypertension stay masked. What appears instead of focal neurological symptoms is cognitive and memory impairment, apathy, personality change, and psychomotor slowing. That pattern imitates vascular dementia, dyscirculatory encephalopathy, or Alzheimer's disease and can send the diagnostic work-up down an erroneous path.

When the clinical presentation is this attenuated, multimodal neuroimaging carries more of the diagnosis. Standard contrast-enhanced MRI is frequently insufficient to separate glioblastoma, solitary metastasis, primary CNS lymphoma (which also becomes more frequent with age), and subacute ischemic stroke with a disrupted blood–brain barrier (Hu et al., 2015). The following methods can be added to the diagnostic protocol to close that gap.

- Perfusion MRI (DSC- and DCE-MRI) characterizes the tumor microcirculatory bed. High relative cerebral blood volume (rCBV) is typical of high-grade gliomas and separates tumor infiltration from areas of chronic ischemia and peritumoral edema (Hu et al., 2015).
- MR spectroscopy (MRS) shows a raised choline (Cho) peak with reduced N-acetylaspartate (NAA), which supports a neoplastic lesion and argues against pseudotumoral forms of demyelinating and infectious processes (Hu et al., 2015).
- PET with radiolabeled amino acids (11C-methionine, 18F-FET) is the method of choice for neuro-oncological imaging in the joint EANM/EANO/RANO recommendations (Law et al., 2019). Amino-acid tracers, unlike 18F-FDG, are taken up poorly by the normal cortex of the aging brain. That contrast makes it possible to define the true boundaries of infiltrative growth beyond the area of contrast enhancement and to separate tumor progression from radiation necrosis (Law et al., 2019).

Mapping tumor boundaries accurately and functionally before surgery has direct surgical consequences, since it governs the choice of approach and the extent of resection that can be permitted.

Surgical Treatment, Anesthetic Management, and Prolonged Postoperative Care

Surgery for supratentorial tumors in elderly and very old patients has to hold oncological radicality and quality of life in balance. Small tumors found incidentally, without perifocal edema or neurological deficit, are better watched, and the slow growth of most Grade 1 meningiomas justifies the "wait-and-see" position (Kaul et al., 2015).

Resection "at any cost" has given way to the concept of maximum safe resection. Total removal of a meningioma (Simpson I–II) remains the standard for younger patients, whereas subtotal resection (Simpson III–IV) is now chosen deliberately and with growing frequency in the elderly and very old. Where major venous sinuses, large arteries, or functionally significant cortical areas are involved, decompression of the brain outranks radicality (Corell et al., 2022; Kaul et al., 2015).

Neuronavigation, intraoperative ultrasonography, and neurophysiological monitoring support this approach technically. Combined with modern neuroanesthesia protocols, they keep traction injury to atrophic parenchyma to a minimum and lower the risk of ischemic complications in adjacent areas (Kingsly et al., 2023; Wu et al., 2024).

History shows how much has changed. In the early 2000s, craniotomy in patients older than 65–70 years counted as an intervention of extremely high risk. Retrospective analyses of large clinical databases from that period, among them the Medicare registry and European series, put 30-day postoperative mortality after resection of malignant gliomas at 12–15%, and at 20% in patients

older than 75 years; after resection of cerebral hemispheric meningiomas the figure ran 8–12%, driven mainly by fatal intraoperative hemorrhage and ischemic stroke (Barker, 2004; Caroli et al., 2005). Those views have since been revised. A population-based study drawn from the Swedish Brain Tumor Registry, covering 1,676 patients aged 65 years and older who underwent meningioma surgery between 1999 and 2017, recorded perioperative mortality of 3.1% and perioperative morbidity of 37.6%; age stayed associated with mortality, while tumor size and the presence of preoperative symptoms drove the risk of complications (Corell et al., 2022).

Formalized assessment tools carry the risk stratification. The Karnofsky Performance Status (KPS) and the Charlson Comorbidity Index (CCI) are the fundamental instruments for geriatric neuro-oncology patients (Pazniokas et al., 2021; Zhu et al., 2023). The CCI turns somatic disease burden, including ischemic heart disease, hypertension, diabetes mellitus, and chronic kidney disease, into a quantitative score. A high score, generally ≥3, correlates with more frequent severe systemic complications such as pulmonary embolism, pneumonia, and myocardial infarction, independently of tumor size and histology. For a very old patient with a CCI ≥3, the multidisciplinary team should weigh alternatives to open surgery, whether fractionated radiotherapy or observation, even when a convexity meningioma is technically operable (Kaul et al., 2015; Zhu et al., 2023).

Patients with KPS ≥70 and CCI ≤2, conversely, gain the most from active surgical management. The governing principle is to judge biological age and physiological reserves rather than decide on chronological age alone.

Recent publications add the modified Frailty Index (mFI) to KPS and CCI (Zhu et al., 2023). This tool catches a category of patients that conventional scales miss. A frail patient may hold an acceptable KPS, walk, manage self-care, and have no severe cardiac disease, and still answer the stress of intubation, blood loss, and anesthesia with a cascade of deterioration: delirium, acute kidney injury, multiorgan failure. Frailty follows neither chronological age nor the number of comorbid conditions directly, yet it cuts overall survival substantially (Zhu et al., 2023). Structural and pathological correlates give the phenomenon a neurobiological basis, since frail patients more often show a greater volume of white-matter hyperintensities and reduced gray-matter volume, reflecting a brain less able to resist damaging insults (Sciancalepore et al., 2026). In patients with glioblastoma older than 65 years, frailty assessed by mFI and comorbidity burden measured by CCI each retained independent prognostic value for overall survival (Schneider et al., 2020).

Radicality cannot be abandoned automatically either. Extent of resection (EOR) is significantly associated with survival in geriatric cohorts as well. Sanai et al. (2011) located the threshold below which the survival benefit disappeared at 78% of tumor volume; the volumetric analysis of Chaichana et al. (2014) put the threshold values at an EOR of 70% and a residual tumor volume of 5 cm^3, each parameter independently associated with survival and time to recurrence. Among a geriatric cohort of 342 patients, median overall survival after gross-total resection exceeded that after partial resection or biopsy by a significant margin (Heiland et al., 2018).

Adjuvant management warrants specific consideration too. MGMT promoter methylation is the key predictive biomarker in older patients and is detected in approximately 35–45% of the geriatric cohort (Eckel-Passow et al., 2015; Perry et al., 2017). The standard six-week Stupp chemoradiotherapy protocol often produces unacceptable hematological toxicity at this age (Perry et al., 2017; Wick et al., 2012). Three key randomized trials, the NOA-08 trial (Wick et al., 2012), the Nordic trial (Roa et al., 2004, 2015), and the Canadian–European CE.6 trial (Perry et al., 2017), supplied the basis for an alternative treatment strategy.

Perry et al. (2017, p. 1030) added temozolomide to hypofractionated radiotherapy (40 Gy in 15 fractions) and raised median overall survival across the whole cohort from 7.6 to 9.3 months; the subgroup with a methylated MGMT promoter gained most, from 7.7 to 13.5 months. The practical

algorithm follows from this: hypofractionated radiotherapy alone for an unmethylated promoter; combination therapy with temozolomide for a methylated promoter, or temozolomide monotherapy where somatic comorbidity is substantial (Perry et al., 2017; Wick et al., 2012).

Functionally oriented surgery is widening its scope in this cohort as well. Awake craniotomy for tumors involving functionally significant areas can be performed in older patients, provided baseline cognitive function is preserved and hearing is not severely impaired (Grossman et al., 2013). In the comparative study of Grossman et al. (2013) the procedure was tolerated well and proved safe in patients older than 65 years, while gross-total resection of high-grade glioma in that group brought longer survival, and prognostic factors relevant to younger patients held their significance. Later series, including cohorts of patients older than 75 years, confirm that the technique is feasible with careful patient selection (Himic et al., 2026). Much of that success rests with the anesthesiology team and its total intravenous anesthesia (TIVA) protocols, built on ultra-short-acting agents that avoid marked hemodynamic instability and prolonged post-anesthetic respiratory depression.

Even an optimally executed operation guarantees nothing, however. For elderly and very old patients the major risks sit in the prolonged postoperative period. Complications arose in almost half of the operated patients in the cohort cited above, and their presence, together with the surgical complexity of the intervention, determined functional outcomes at discharge and at three months (Ferroli et al., 2021). Infectious-inflammatory and thromboembolic complications lead the list of threats; nosocomial infections, among them ventilator-associated pneumonia, postoperative meningitis, and urinary tract infections, occur more often because of age-related immunosuppression and multimorbidity (Ferroli et al., 2021; Pazniokas et al., 2021).

Altered metabolism imposes further limits. Reduced glomerular filtration rate and hepatic clearance turn empirical antimicrobial therapy in elderly and very old patients into a potential source of nephrotoxicity and hepatotoxicity. Antimicrobial Stewardship Programs (ASP) in neurocritical care units answer that problem (Yu et al., 2023). Local microbiological surveillance should guide therapy, along with therapeutic drug monitoring in blood and cerebrospinal fluid, assessment of penetration across the blood–brain barrier, early mobilization, and nutritional support (Yu et al., 2023). Minimizing intraoperative tissue trauma therefore has systemic as well as surgical significance: it reduces the need for complex pharmacological correction and shortens the stay in the intensive care unit (Heiland et al., 2018; Pazniokas et al., 2021).

Conclusion

Population aging asks neurosurgery to adapt its treatment standards for supratentorial tumors. In elderly and very old patients these neoplasms, represented predominantly by meningiomas and IDH-wildtype glioblastomas, follow distinct biological, molecular genetic, and clinical patterns. An attenuated initial presentation leads predictably to delayed diagnosis and to hospitalization during neurological decompensation. Multimodal neuroimaging (amino-acid PET, perfusion MRI) and the concept of maximum safe resection, supplemented by intraoperative mapping techniques, keep surgical trauma to the aging brain at a minimum (Chaichana et al., 2014; Grossman et al., 2013; Law et al., 2019). Prognosis increasingly depends on personalization of adjuvant strategies: on MGMT methylation status in high-grade gliomas (Perry et al., 2017; Roa et al., 2004; Roa et al., 2015; Wick et al., 2012) and on markers of aggressive behavior such as TERT and CDKN2A/B in meningiomas (Maas et al., 2021).

Successful outcomes depend critically on the quality of prolonged postoperative care. A high risk of systemic decompensation and infectious complications makes standardized postoperative care protocols and multidisciplinary rehabilitation a priority. Global and regional practice both lack methodological recommendations that set out step-by-step algorithms for

managing elderly and very old patients after neuro-oncological interventions (Heiland et al., 2018; Weller et al., 2021). Guidelines of that kind, covering the whole patient pathway from the operating room to the later stages of rehabilitation, should count as a priority for reducing postoperative mortality and improving functional outcomes.

Author Contributions

A. Akmataliev — conception and design of the review; D. Dyusheev — critical revision and editing of the manuscript; N. Kachiev — literature search and analysis.

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