South Health and Policy. 2026; 5:239
doi: 10.56294/shp2026239

REVIEW

Neurological emergencies in cancer: pathophysiological and prognostic implications with a focus on the elderly

Emergencias neurológicas en el cáncer: implicaciones fisiopatológicas y pronosticas con enfoque en el adulto mayor

Ana Esperanza Jeréz Alvarez[1], Ariel Sosa Remón[1], Jhossmar Cristians Auza-Santivañez[2], Miguel Emilio García Rodríguez[1], Arian Jesús Cuba Naranjo[3], Yudiel Pérez Yero[4], Jorge Márquez-Molina[5], Freddy Ednildon Bautista-Vanegas[6]

[1]Universidad de Ciencias Médicas de La Habana. Instituto de Oncología y Radiobiología. La Habana, Cuba.
[2]Ministerio de Salud y Deportes. Instituto Académico Científico Quispe-Cornejo. La Paz, Bolivia.
[3]Universidad de Ciencias Médicas de Granma. Hospital Militar Carlos Arvelo. Unidad de Cuidados Intensivos. Venezuela.
[4]Universidad de Ciencias Médicas de Granma. Hospital Provincial Clínico-Quirúrgico Celia Sánchez Manduley. Cuba.
[5]Hospital del Norte Cochabamba. Servicio de emergencias. Cochabamba, Bolivia.
[6]Kliniken Beelitz GmbH - Brandenburg Deutschland. Germany.

Cite as: Jeréz Alvarez AE, Sosa Remón A, Auza-Santivañez JC, García Rodríguez ME, Cuba Naranjo AJ, Pérez Yero Y, et al. Neurological emergencies in cancer: pathophysiological and prognostic implications with a focus on the elderly. South Health and Policy. 2026; 5:239. https://doi.org/10.56294/shp2026239

Submitted: 30-12-2024 **Revised:** 06-04-2025 **Accepted:** 15-06-2025 **Published:** 01-01-2026

Editor: Dr. Telmo Raúl Aveiro-Róbalo

Corresponding Author: Jhossmar Cristians Auza-Santivañez

ABSTRACT

Introduction: neurological emergencies in cancer patients are associated with high mortality. This mortality rate is particularly prevalent in the older adult population, for whom limited scientific evidence exists.
Objective: to describe the pathophysiological mechanisms and prognosis of the main neurological emergencies that occur in older patients with cancer and lead to their admission to the Intensive Care Unit.
Method: to this end, a narrative review of the literature available in databases and search engines such as PubMed, Medline, Scopus, Scielo, and Google Scholar was conducted using the search terms: neuro-oncological emergencies, neurological complications, oncological intensive care, prognostic factors for cancer mortality, and their English translations. The review was conducted between November 2024 and March 2025. Forty-nine references from articles that met the inclusion criteria were used.
Results: among the main results, it is worth highlighting that the main neurological complications described are predominantly metabolic encephalopathy, stroke, status epilepticus, and intracranial hypertension. These factors share mechanistic relationships with neurocritical patients in general, although cancer appears to be a significant factor in their onset and mortality prognosis. This is accompanied by other variables of prognostic interest such as advanced age, cancer stage, individual functional status, hyperglycemia, sepsis, septic shock, and artificial ventilation.
Conclusions: it is concluded that pathophysiological and prognostic knowledge of critically ill older neuro-oncology patients is still limited and warrants multiple investigations in their own clinical context. This is because the greatest available evidence corresponds to young adult neurocritical patients without cancer.

Keywords: Older Adult; Cancer; Neuro-Oncological Emergency; Prognostic Factors; Mortality; Intensive Care; Neurocritical Patients; Advanced Age.

RESUMEN

Introducción: las emergencias neurológicas en pacientes con cáncer suponen una elevada mortalidad. La

cual se acrecienta en la población adulta mayor, de la cual se dispone escaza evidencia científica.
Objetivo: describir los mecanismos fisiopatológicos y el pronóstico de las principales emergencias neurológicas que aparecen en pacientes adultos mayores con padecimientos oncológicos y suscitan su ingreso en la Unidad de Cuidados Intensivos.
Método: para ello se realizó una revisión narrativa de la literatura disponible en bases de datos y motores de búsqueda como PubMed, Medline, Scopus, Scielo y Google académico bajo los términos: emergencias neurooncológicas, complicaciones neurológicas, cuidados intensivos oncológicos, factores pronósticos de mortalidad en cáncer y sus traducciones al idioma inglés. La revisión se realizó entre los meses de noviembre de 2024 y marzo de 2025. Se utilizaron 49 referencias de artículos que cumplieron con los criterios de inclusión.
Resultados: entre los principales resultados destacan que las principales complicaciones neurológicas descritas son la encefalopatía predominantemente metabólica, el ictus, el estado epiléptico y la hipertensión intracraneal. Dichos elementos comparten relaciones mecanicistas a los pacientes neurocríticos de forma general, aunque, el cáncer parece ser un factor de peso en su aparición y pronóstico de mortalidad. Junto a otras variables de interés pronóstico como la edad avanzada, el estadio del cáncer, el estado funcional del individuo, la hiperglucemia, sepsis, shock séptico o la ventilación artificial.
Conclusiones: se concluye que los conocimientos fisiopatológicos y pronósticos de los pacientes adultos mayores neurooncológicos críticos aún son escasos y suscitan múltiples investigaciones en su propio contexto clínico. Esto es debido a que la mayor evidencia disponible corresponde a los pacientes adultos jóvenes neurocríticos sin cáncer.

Palabras clave: Adulto Mayor; Cáncer; Emergencia Neurooncológica; Factores Pronósticos; Mortalidad; Cuidados Intensivos; Neurocríticos; Edad Avanzada.

INTRODUCTION

Clinical outcomes following a neurological emergency are worse for cancer patients and may result in critical illness requiring admission to the Intensive Care Unit (ICU). Conditions such as cerebrovascular accident (CVA), coma, intracranial hypertension (ICH), and the need for artificial mechanical ventilation (AMV) represent a subject of debate due to the bioethical burden of uncertain prognosis. Recently published studies report that the frequency of ICU admissions for neurological reasons in cancer patients varies between 3 % and 23 %.[1]

Currently, about 50 % of cancer patients have some neurological manifestation, and these are one of the leading causes of hospitalization in these individuals. At the National Cancer Institute of Mexico, the most frequent causes of neurological care in the last 15 000 consultations included neuropathy (26 %), central nervous system (CNS) tumor activity (15 %), seizures (12 %), headache (11 %), cerebral vascular disease (7 %), abnormal movements (6 %), dementia or cognitive impairment (6 %), primary CNS tumors (6 %). The importance of neurological emergencies lies in the high morbidity, the degree of disability, their mortality, and the short therapeutic window to become irreversible.[2] At the Institute of Oncology and Radiobiology of Cuba, in 2023, the main reason for admission was encephalopathies (34,7 %), followed by stroke (22,5 %) and postoperative tumor neurosurgery (25,8 %). Mortality was high overall, with an emphasis on an older adult population, especially in those who received AMV.[1]

In older adults with cancer, the pathophysiological burden on the prognosis of the complication is high, as it depends not only on the effect of the malignancy on the outcome but also on the effects on a vulnerable CNS due to cellular senescence of the brain tissue. This results in poor neurodynamic compliance structural changes associated with multiple neurotransmitter modifications, neuroreceptors, and neuronal transport alterations.[3]

However, older adults with cancer and neurological emergencies requiring admission to neurocritical care have been poorly studied, and there is a discontinuity of evidence on the subject. Therefore, this review aims to describe the pathophysiological mechanisms and prognosis of the main neurological emergencies that occur in older adult patients with oncological conditions, leading to their admission to the ICU.

METHOD

A narrative review of the literature was performed using an unrestricted search in English and Spanish. The search period included the last 10 years. A search was carried out in databases and search engines such as PubMed, Medline, Scopus, Scielo, and Google Scholar under the terms neuro-oncological emergencies, neurological complications, oncological intensive care, prognostic factors of mortality in cancer, and their translations into English. Inclusion criteria were open-access articles, original articles, narrative and systematic reviews, and consensus documents. Abstract articles and those describing the topic in the pediatric population were excluded from the present review. The review was conducted between November 2024 and March 2025.

Forty-nine references of articles that met the inclusion criteria were used. The pathophysiological, clinical, and prognostic implications of the main CNS emergencies in cancer patients and their implications in the older adult target population are described.

RESULTS AND DISCUSSION

Neurological emergencies in patients with malignancy require early attention in the ICU due to their high morbidity and mortality. Some oncoepidemiological, neurological, and intensive care-related factors have been described. However, the critical neuro-oncology population has been poorly studied, as is the case for neurocritical patients in general.[1]

Ischaemic stroke is the rapid development of clinical signs resulting from disturbances in brain or global function, with symptoms persisting for 24 hours or more or leading to death with no obvious cause other than vascular origin. Stroke represents one of the most frequent causes of mortality and morbidity worldwide. While strokes can occur at any age, approximately three-quarters of them occur in those over 65 years of age, and the risk doubles in each decade after the age of 55. In addition, older adults have a higher risk of mortality, more extended hospital stays, and a higher risk of institutionalization.

Their hospital stay may be prolonged by acute non-neurological complications such as swallowing disorders, pneumonia, urinary tract infection, deep vein thrombosis, and pulmonary embolism, among the most frequent. These disorders are associated with stroke severity and location.[4,5] Compared to the general population, cancer patients have a higher prevalence of ischaemic stroke, with an annual incidence of 7 %. This can be as high as a 50 % probability of occurrence of the event at the end of life of an individual with malignancy. It is estimated that up to 5 % of patients with ischaemic stroke of cryptogenic etiology will be diagnosed with a malignant neoplasm at some point in their lives.[6]

Mechanisms of cancer-related ischaemic stroke include hypercoagulability due to tumor production of mucin, leading to platelet-rich thrombus formation; release of procoagulant molecules such as tissue factor and cancer procoagulant; and output of procoagulant cytokines such as tumor necrosis factor-alpha, IL-1, and IL-6, which together enhance the coagulation cascade (more common in patients with adenocarcinoma); hyperviscosity leading to small vessel obstruction of small blood vessels (usually in multiple myeloma, polycythemia vera, Waldenstrom's macroglobulinemia or Bing-Neel syndrome, acute myelogenous leukemia, or chronic lymphocytic leukemia); and direct tumor effect either by tumor compression of blood vessels through invasion or edema, as seen in brain metastases, primary CNS tumors and with myeloid leukemia. This mechanistic pathway is very similar to CNS involvement by secondary entities, such as those described in nootropic viruses (especially the association of ischaemic stroke with SARS-CoV-2).[6,7]

Regarding prognosis, advanced cancer stage, which is directly related to overall tumor burden and extent of disease, is associated with a risk of stroke recurrence and carries a poor prognosis with a threefold increased risk of death, along with elevated D-dimer levels, systemic metastases, age, functional status, adenocarcinoma, and diabetes as independent predictors.[8]

Intracranial hypertension (ICH), cerebral herniation, and cerebral edema. Intracranial pressure (ICP) is defined as the pressure measured within the intracranial vault.

It is a dynamic pressure consisting of systolic, diastolic, and mean derivative pressure and can fluctuate physiologically. Standard ICP is typically 10 to 20 cmH2O or 7 to 14 mmHg. ICP is governed by the ratio of brain tissue volumes, cerebrospinal fluid (CSF), and intracranial blood in the arterial and venous compartments. Expansion of any of these leads to a compensatory decrease in one or more others, resulting in limited changes in ICP. In addition, the skull is considered non-expandable after the closure of the fontanelles, and therefore, once these compensatory mechanisms are exhausted, an increase in volume results in a pathological increase in ICP.[9] Elevated ICP, hydrocephalus, and herniation can directly result from neoplastic mass effect or meningeal involvement. In most patients with elevated ICP, the onset is heralded by subacute, progressive, or new headache, which may awaken the patient from sleep and is often aggravated by coughing, straining, or lying down. In the case of a gradually enlarging tumor, the headache may be accompanied by progressive focal neurological deficits and seizures due to the mass effect of the cancer itself and associated peritumoral vasogenic edema. In meningeal involvement, headache results from communicating hydrocephalus and may not be accompanied by focal deficits. In metastases, most travel to the brain by hematogenous spread.

Tumour microemboli appear to lodge in distal arteries, narrow capillaries ('watersheds'), and grey-white matter. The increase in ICP is due to the effect of the tumor mass and neoplastic-induced brain edema of the blood-brain barrier, partly caused by the local production of vascular endothelium.[10] ICH has three distinct phases, including a compensation phase in which the initial increase in any intracranial components results in a shift of blood and cerebrospinal fluid (CSF) along the spinal axis, keeping ICP within normal.

A decompensation phase occurs once the compensation limit has been reached and a progressive increase in the pressure exerted by the CSF within the cerebral ventricles begins, resulting in ICH. A herniation phase, which occurs when increased pressure in one of the cranial compartments bounded by rigid structures such as

the cerebral sickle, cerebellar tent, or foramen magnum, causes displacement of brain parenchyma through these structures, resulting in herniation of brain tissue.[11] ICH complements the devastating effects of cerebral herniation and intracranial compartment syndrome. Brain herniation, defined as the displacement of brain tissue from its normal location, represents the most frequent cause of death secondary to tumor progression. It occurs in 73 % of neuro-oncology patients admitted to end-of-life care. Increased intracranial pressure secondary to tumor growth causes parenchymal displacement, leading to brain herniation.[1,12]

Cerebral edema is a potentially devastating complication of brain metastases and brain tumors

The two main types of cerebral edema are vasogenic, an increase in fluid in the extracellular space, and cytotoxic, an increase in cellular fluid. Brain tumors cause vasogenic edema, and its mechanism is related to vascular endothelial growth factor (VEGF) and its key role in tumor angiogenesis and edema. Newly formed tumor blood vessels are structurally and functionally abnormal, with a compromised blood-brain barrier, leading to leakage of fluid into the surrounding brain parenchyma. VEGF can also alter occludin function, induce endothelial fenestration, and cause nitric oxide synthesis and release, leading to tight junctions and increased capillary permeability.[6,13]

Potentiating factors that worsen tumor-associated edema are seizures, the use of chemotherapeutic agents (e.g., interleukin-2), and radiotherapy. Radiation necrosis after stereotactic radiosurgery can mimic brain tumors with accompanying brain edema. It may be focal (from one lesion) or diffuse (post-anoxic-ischaemic liver edema) and is mainly eliminated via CSF. It can displace brain tissue, affect consciousness, and cause deformation and irreversible brainstem damage.[13] Alternatively, non-tumoural lesions with focal mass effects can cause intracellular (cytotoxic) edema that does not respond to steroids.

Causes include: 1) hypertensive hematomas, 2) traumatic or non-traumatic intracranial hemorrhage, 3) ischaemic infarcts in the distribution of a large vessel such as the carotid artery or the main trunk of the middle cerebral artery, and 4) vasculitis (if ischemia or hemorrhage predominates and the vasculitis is not due to an autoimmune process). A third group presents with elevated ICP with diffuse cerebral cytotoxic edema due to widespread cellular injury and includes the following: (1) hypoxia due to cardiorespiratory arrest; (2) refractory convulsive status epilepticus; (3) hepatic or renal failure and (4) hydrocephalus (in neoplastic meningitis).[14]

Table 1 shows the results of investigations in which stroke and ICH were prognostic in this population.

Table 1. Main prognostic factors for mortality in cancer patients with stroke or ICH

Authors	Objective and characteristics of interest of the study	Main results of interest
Cerebrovascular Accident		
Gon et al.[15]	Stroke mortality in a large cohort of patients	Population older than 60 years accounted for 68,9 % (475 003 patients) with the highest incidence in the 60-69 age group (29,3 % of the total). PPM: men (OR: 1,4; 95 % CI: 1,38-1,54; p<0,001). Age group: 60-69 years (OR: 11,89; 95 % CI: 7,13-19,85; p<0,001). 70-79 years (OR: 28,34; 95 % CI: 17,02-47,20; p<0,001). ≥80 years (OR: 85,78; 95 % CI: 51,54-142,76; p<0,001). Distant metastases (OR: 1,67; 95 % CI: 1,41-1,98; p<0,001).
Kang-Po et al.[16]	30-day and 1-year stroke-related mortality in patients with active cancer. Retrospective study.	MS: 68,3 ± 16,04 years; p= 0,098. PPM at 30 days: Initial NIHHs Score (OR: 1,160; 95 % CI: 1,011-1,332; p=0,03). INR alterations (OR: 108 317,295; 95 % CI: 3,737-3,140E9; p=0,02).
Navi et al.[17]	To examine whether haematological and embolic biomarkers after ischaemic stroke are associated with subsequent adverse clinical outcomes. Prospective study in 50 patients.	MS: 69 years (RIQ: 60-76). PPM or stroke recurrence: D-dimer (OR: 1,6, 95 % CI: 1,2-2,0). P-selectin (OR: 1,9; 95 % CI: 1,4-2,7), sICAM-1 (OR: 2,2; 95 % CI: 1,6-3,1). sVCAM-1 (OR: 1,6; 95 % CI: 1,2-2,1). Microembolism (OR 2,2, 95 % CI 1,1-4,5).
Pana et al.[18]	To analyse ischaemic stroke mortality in patients with metastatic cancer. Prospective study	MS: 70 years (RIQ: 62-78; p≤0,001). PPM: metastases (OR: 2,16; 95 % CI: 1,90-2,45; p≤0,001), mainly from respiratory, pancreatic and colorectal cancers..
Jin et al.[19]	To create and validate a prognostic nomogram for one-year ischaemic stroke mortality. Prospective study.	MS: 68,92 years (range: 57,33-78,86 years; p=0,51). PPM: age (OR: 1,04; 95 % CI: 1,036-1,058; p≤0,001). Active cancer (OR: 3,38; 95 % CI: 2,021-5,722; p≤0,001). Solid tumour with metastases (OR: 5,64; 95 % CI: 2,42-13,81; p≤0,001).
Intracranial Hypertension		

Sosa-Remón et al.[20]	To describe factors associated with mortality in patients with solid tumours and neurological complications in an ICU. Prospective study	MS of the deceased: 60 ±8,67 years. ICH present in 7 patients (6 deceased; p<0,05).
Decavèle et al.[21]	Describing prognostic factors in patients with primary central nervous system lymphoma	MS of deceased: 60 years (limits: 53-69; p=0,96). PMM (univariate analysis): ICH (20 patients, 34 %; p=0,05).
Tan et al.[22]	To identify potential prognostic factors in cancer patients admitted to an ICU. Retrospective study.	MS: 61 years (cut-off: 18-88). PPM (univariate analysis): ICH due to tumour mass effect (8 patients; 8 %; p≤0,001).
Neuman et al.[23]	To describe the prognosis of patients with gioblastoma and need for artificial mechanical ventilation. Retrospective study	MS: 65,2±8,7 years (limits: 50-75). PPM (univariate analysis): ICH (2 patients; 9,2 %; p=0,03).

Note: MS: median age. PPM: main predictors of mortality. NIHHs: National Institutes of Healt Stroke Scale. INR: international normalised ratio. IQR: interquartile range. ICH: intracranial hypertension.

After severe brain damage, impaired consciousness and impairment of brainstem reflexes induce hypoventilation and precipitate bronchial aspiration and subsequent death. Thus, airway patency is a primary goal to preserve life. Clinical assessment of brain stem reflexes is part of routine neuromonitoring of stroke patients admitted to the ICU. These help localize the lesion and guide therapeutic support in the critically ill patient. Stem reflexes are more helpful in localizing the lesion according to the cranial nerve involved than the abnormal motor response. Loss of these (total or partial) is part of the clinical features of ICH and brain herniation. As prognostic factors, the disappearance of the photomotor reflex is associated with worse outcomes, with 90 % of patients with absent corneal reflex dying within 24 hours. Finally, an absent vestibular-ocular reflex is associated with a poor short-term prognosis.[23,24,25]

Encephalopathy and cancer

Changes in mental status may occur in a patient with normal mental function or may occur in the context of a chronic cognitive disorder, such as dementia or mental retardation. In the medical literature, the terms altered mental status, mental status changes, confusion, encephalopathy, and delirium are often used interchangeably. Encephalopathy and delirium are more relevant as diagnostic keywords. More recently, an expert panel established that the preferred term to use in this context is acute encephalopathy, which also includes delirium as a subsyndromal substrate. Other definitions, such as acute brain failure or dysfunction, acute confusional state, or altered mental status, are left out of this spectrum.[14,26]

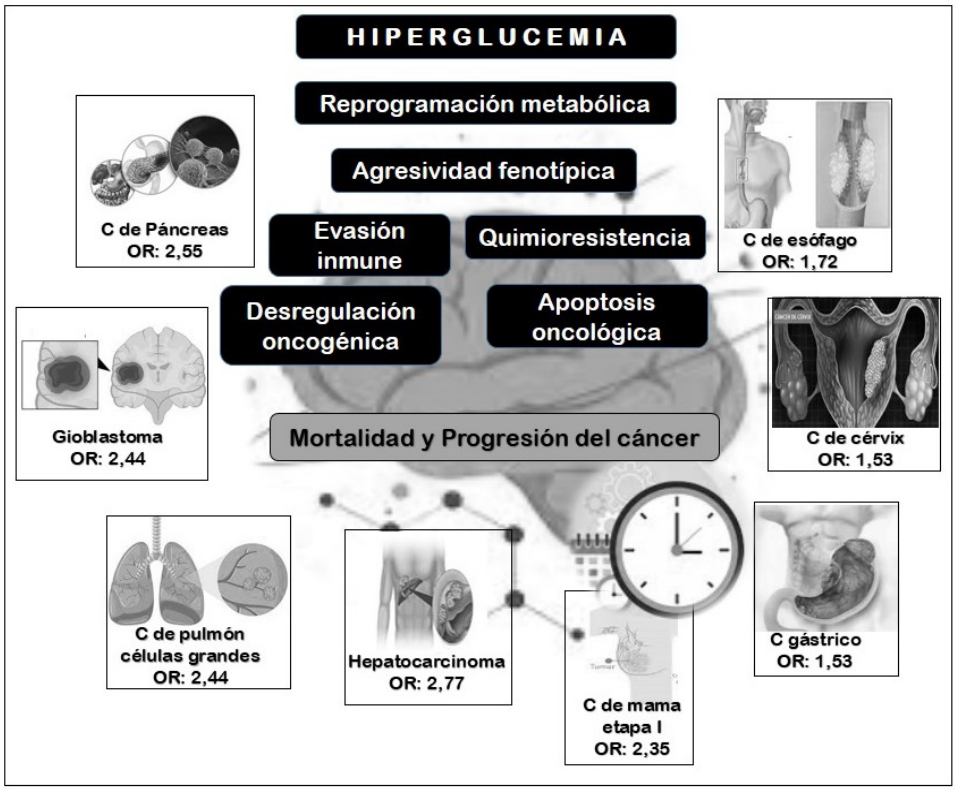
Encephalopathies are primarily consequences of systemic disorders and produce global neurological dysfunction. The ascending reticular activating system (ARAS) is usually affected, especially its thalamocortical component. Neoplasms form part of the risk factors for suffering from it and are sources of admission to the ICU. The usual mode of presentation is diffuse encephalopathy in the form of a confusional picture, although on occasion, it may be associated with a coma or neurological facility.[1,27] Generally speaking, the mechanisms involved in the involvement of the RAAS in the course of encephalopathy are: 1) Cerebral edema, hepatic encephalopathy, and hypoosmolar encephalopathy. 2) Drug-induced delirium: disruption of normal neurotransmitter function (dopamine, acetylcholine, glutamate, GABA). 3) Electrolyte disturbance with impairment of membrane excitability. 4) Nutritional disorders that alter cellular energetics and cause neuronal death. 5) Toxins (carbon monoxide or cyanide) impeding oxygen supply with mitochondrial dysfunction and haematoencephalic membrane disruption with accumulation of systemic toxins and plasma constituents in the cerebrospinal fluid (protein elevation).[27] In cancer, delirium is a life-threatening complication. Delirium is often overlooked by emergency healthcare professionals, with a misdiagnosis rate of 41 %. Its frequency ranges from 57-85 % in cancer patients to 15-30 % in hospitalized patients. In older adults, the diagnosis and delayed management of encephalopathy is challenging due to the paucity of presenting signs and symptoms.[14,28] John et al.[28] studied 251 elderly Indians with encephalopathy. Of these, 186 (74,1 %) were in the age group 60-75 years, with a mean age of 70,78. There were 48 (19,1 %) deaths, of which 38 (79,1 %) had one or more comorbidities. Early presentation to hospital (within 6 hours of symptom onset), higher level of consciousness, and Glasgow score at presentation were markers of good prognosis in these elderly patients. However, patients with septic encephalopathy had the worst prognosis. Outside neurological causes, in adults with malignancy, encephalopathy as a complication and prognosis has been identified in those undergoing anticancer immunotherapy (cytokine release syndrome, cellular immunity effector-associated neurotoxicity syndrome, chemotherapy-associated reversible posterior encephalopathy syndrome, etc).[29,30,31,32]

Seizures and status epilepticus

Status epilepticus is characterized by repeated seizures for at least 20-30 minutes or two or more seizures in a row without recovery of consciousness in between. It can occur at tumor presentation (29 %), during tumor progression (23 %), and even when tumors are stable (23 %). Clinical manifestations of non-convulsive status epilepticus are non-specific and may include personality changes, fluctuating mental status, focal myoclonic jerks, or abnormal eye movements. Status epilepticus occurs in approximately 20 % of patients with tumor epilepsy. Approximately 3-12 % of adult patients with status epilepticus have CNS tumors.[12,33] Molecular factors are postulated to play a role in the epileptogenesis of brain tumors. Isocitrate dehydrogenase 1 (IDH1) and 2 (IDH2), causative mutations in low-grade gliomas, are associated with an increased risk of increased seizure risk. The IDH1 mutation is expressed in 70-80 % of low-grade gliomas, compared to only 5-10 % of high-grade gliomas. Mutated IDH1 catalyzes isocitrate to 2-hydroxyglutarate (2-HG), structurally similar to glutamate, instead of a-ketoglutarate in the Krebs cycle. Accumulation of 2-HG can activate N-methyl-D-aspartate (NMDA) receptors and promote tumor-associated epilepsy. Glutamate, a known 'tumor growth factor' in gliomas, is also implicated in epileptogenesis. Increased glutamate concentration and altered expression of the glutamate transporter are associated with tumor-associated seizures. Mortality is higher in older people and in those with an identifiable tumor. More specifically, mortality is similar or slightly higher when the precipitant of status epilepticus is a brain tumor.[10] Infections and metabolic disturbances are other important causes of seizures in cancer patients. Treatment-related immunosuppression induces an increased risk of infection with less common pathogens. Hyponatraemia is a well-established cause of seizures in cancer patients, especially in tumors originating in or affecting the lungs (small cell lung cancer), pleura, or spinal cord. Dysnatraemia, hypocalcemia (often associated with tumor lysis syndrome), hyperglycemia (usually secondary to corticosteroid therapy or pancreatic insufficiency), and hypoglycemia (secondary to tumor production of insulin or insulin-like growth factors) can be associated with seizures and should be detected and corrected if identified.[34]

Other emergencies with implications for neurocritical cancer patients include hyperglycemia

The hyperglycaemic stress response is part of the adaptive metabolic response to critical illness, especially hypoxia, hemorrhage, and sepsis. It involves neuroendocrine and immune pathways leading to insulin resistance and hepatic glucose production by gluconeogenesis and glycogenolysis. In recent years, the concept of stress-related hyperglycemia has been developed and replaced by the idea of dysglycaemia and its three domains: hyperglycemia, hypoglycemia, and glycaemic variability. Each of the three domains is associated with an increased risk of mortality in patients admitted to the ICU.



Source: adapted from Ramteke et al.[39]

Figure 1. Pathophysiological implications of hyperglycaemia in cancer and prognosis

The strongest association with mortality is demonstrated for hypoglycemia, with additive adverse effects for hyperglycemia and glycaemic variability. Advances in continuous glucose monitoring systems and insulin therapy algorithms may reduce glycaemic variability and hypoglycemia, but the benefits in clinical practice have not yet been established in clinical trials.[35] The neurocritically ill patient develops a hypermetabolic and hypercatabolic response to injury. In such circumstances, blood glucose levels increase due to insulin resistance due to metabolic stress. Hyperglycaemia in these patients is associated with increased morbidity and mortality. Brain activity requires high energy consumption, mainly 30 % of plasma glucose. Glucose supply must be continuous, as the brain has no reserves.

The brain has no reserves. The gradient between plasma and brain glucose values is 110-126 mg/dl, suggesting wider cut-off points for glycaemic control in these patients. The American Dietetic Association recommends for critically ill patients that insulin therapy should be initiated to treat persistent hyperglycemia≥ 180 mg/dL and that the glucose level should be maintained between 140 and 180 mg/dL, a point on which American and European guidelines agree. Similarly, the Neurocritical Care Society recommends keeping glucose below 200 mg/dL for patients in the neurocritical unit and avoiding hypoglycemia (serum glucose concentrations < 80 mg/dL). Aggressive corrections of hyperglycemia are not recommended due to the high risk of hypoglycemia and associated neurological dysfunction. A drastic reduction in blood glucose values by strict controls (<110 mg/dL) has been shown to promote an increase in the lactate-pyruvate-glutamate ratio in the brain, increasing brain damage.[36,37,38]

There is little comprehensive literature on the hyperglycemia-cancer-mortality correlation, and a lack of clarity in understanding these comorbid conditions contributes to higher mortality rates. Hence, a critical analysis of the elements responsible for increased mortality due to concomitant hyperglycemia-cancer is warranted. Given the changing lifestyles of the human population, the increase in metabolic disorders, and the glucose addiction of cancer cells, the complications related to hyperglycemia in cancer underline the need for further in-depth research (figure 1).[39]

Sepsis and septic shock

Sepsis is the leading cause of admission to the ICU. Patients aged 80 years and older have a higher mortality from this cause compared to those aged 60-79 years. Age, sarcopenia, and functional status are independent predictors of mortality, which can be as high as 60 % (1,3 - 1,5 to that of young adults). Other predictors, such as prolonged hospital stay, progression to septic shock, and multi-organ dysfunction, are described. Early care (less than 6 hours after onset of the event) is associated with improved survival. Studies in Cuban ICUs detail other prognostic factors such as an APACHE II score ≥15 (OR: 10,7; 95 % CI: 2,84-40,42; p=0,000) and SOFA ≥5 points (OR: 43,9; 95 % CI: 2,33-826,6; p=0,001).[40,41] The five most influential factors in the occurrence of sepsis and septic shock are 1) immunosenescence, 2) altered immunoinflammatory response, 3) procoagulant state and apoptosis, 4) comorbidities, and 5) immunosuppressive drugs.[40] An interesting observation is that cancer patients have implicit risk factors that characterize the pathophysiology of the complication in malignancy.

There are pathophysiological similarities between cancer and sepsis that favor the interaction between these two processes. Indeed, some conditions related to malignancies and adverse drug reactions can mimic sepsis and may make it difficult to differentiate between these entities. In particular, certain aggressive hematological diseases, such as acute leukemia and high-grade B-cell lymphoma, can present multiple organ dysfunctions through various pathways, such as tissue infiltration by tumor cells, anatomical compression, the intracellular release of metabolites, altered coagulation and haemophagocytic lymphohistiocytosis. Available antineoplastic therapies, including T-cell-based therapies or differentiating agents, can also produce acute systemic inflammatory syndromes that mimic sepsis.

Differentiating these entities is vitally important because the treatment of these proinflammatory conditions varies significantly.[42] Nazer et al.[43], in a recent meta-analysis, reported that the weighted ICU mortality for sepsis and/or septic shock in cancer patients was 48 % (95 % CI 43 %-53 %; I2 = 80,6 %). The variables most commonly associated with mortality are those related to the underlying disease (mainly hematological malignancies) and its status (uncontrolled cancer and poor functional status), the presence of one or more organ dysfunctions, and the need for organ support. Other variables identified as risk factors for mortality are advanced age, comorbidities, location of infection (mainly pneumonia), and polymicrobial infection.

The year of ICU admission has also been shown to significantly influence outcomes in cancer patients, with mortality rates decreasing over time.[42] Although septic shock is less common in the neurological ICU than in the medical ICU, it may be related to the patient's primary neurological injury or as a complication of a patient's admission to the ICU (e.g., ventilator pneumonia or central line-related infections). Patients with neurocritical illness are an under-recognized population at high risk of sepsis. It affects more than one-third of neurocritically ill patients and occurs mostly in the first week of admission. History of diabetes, serum transferrin, and sequential organ failure assessment score on admission are early predictors. Sepsis results in significantly worse outcomes and higher medical costs.[44,45] In neuro-oncology patients, the presence of sepsis

and/or septic shock behaves similarly to other patients with malignancies and shares the same mechanistic pathways. In addition, it is now known that various neurological entities may predispose to infections such as pneumonia, sepsis, and septic shock because of the multiple connections between the various affected organs and the brain. A recently studied phenomenon called ¨organ-brain crosstalk¨.

Complex biological communication between distal organs is mediated by cellular, soluble, and neurohormonal actions based on a bidirectional pathway. Communication between the CNS and peripheral organs involves nerves, endocrine and immune systems, and the brain's emotional and cognitive centers. In particular, acute brain injury is complicated by neuroinflammation and neurodegeneration, causing multi-organ inflammation, microbial dysbiosis, gastrointestinal dysfunction and dysmotility, liver dysfunction, acute kidney injury, and cardiac dysfunction. This phenomenon has become increasingly popular, although information is still limited. [1,46,47] Marzorati et al.[48] studied a cohort of patients with neurological complications and hematological cancer. The mean age of the deceased was 64 years. Septic shock behaved as a predictor of death on multivariate analysis (OR: 1,95 (95 % CI: 1,04-3,72; p = 0,04).Finally, other prognostic factors studied in this subpopulation are worse functional status (ECOG III and IV; OR: 2,94; 95 % CI: 1,01-8,55, p=0,04), abnormality in the cerebrospinal fluid study (OR: 5,49; 95 % CI: 1,09-27,66; p=0,03) and need for vasopressors (OR: 6,47; 95 % CI: 1,32-31,66; p=0,03) and need for vasopressors (OR: 6,47; 95 % CI: 1,32-31,66; p=0,02), acute respiratory failure (OR: 2,18; 95 %: 1,14-4,25; p=0,02).[48,49]

CONCLUSIONS

Neurological emergencies in cancer patients are serious and life-threatening. The presence of stroke, ICH, encephalopathy, or status epilepticus increases the length of hospital stay and clouds the prognosis. From the literature review, there is little research involving cancer patients, neurological complications, and prognosis. Even less in older adult populations, who are severely affected by being excluded from most clinical trials on oncological and neurocritical intensive care. In older adults with cancer and neurological emergencies, the main prognostic factors for death are age (increased likelihood with increasing age), ICH, impaired functional status, and the presence of sepsis and septic shock, among others.

BIBLIOGRAPHIC REFERENCES

1. Sosa-Remón A, Cuba-Naranjo AJ, Jeréz-Alvarez, AE, García-Arias DM, Llana-Ramírez MR. Complicaciones neurológicas como motivo de ingreso en una Unidad de Cuidados Intensivos Oncológicos. Rev Chil Anest [internet] 2023 [consultado 26/02/2025];52(8):801-808. Disponible en: DOI: 10.25237/revchilanestv52n8-17

2. Cacho-Díaz B, Reyes-Soto, G. Urgencias neurológicas en el paciente con cáncer. En: Herrera-Gómez A, Ñamendys-Silva SA, Meneses-García, A autores. Manual de Oncología. Procedimientos médico-quirurgicos 6ta edición. Mcgraw-HILL Interamericana Editores, S.A. C.V [consultado 26/02/2025]; 2017 p: 28-29. Disponible en: www.mhhe.com/medicina/incan_onco_6e

3. Velázquez-Álvarez L, Méndez-Suárez G. Cambios anatómicos del sistema nervioso central asociados al envejecimiento. En: Carrillo-Esper R, Cabello-Aguilera R editores. Medicina crítica en el adulto mayor. Editorial Alfil, S.A de C.V. San Rafael, México [consultado 26/02/2025]; 2020 p: 19-24.

4. Auza-Santivañez JC, Lopez-Quispe AG, Carías A, Apaza Huanca B, Sosa-Remón A, Condo-Gutierrez AR et al. Improvements in functionality and quality of life after aquatic therapy in stroke survivors. AG Salud [internet]. 2023 [consultado 26/02/2025];1:15. Disponible en: https://doi.org/10.62486/agsalud202315

5. Méndez-Rojas EK, Tapia-Cárdenas MG. Complicaciones agudas hospitalarias en adultos mayores con Enfermedad Cerebrovascular asociadas a características neuro-geriátricas. CAMbios [internet]. 2022 [consultado 26/02/2025];21(1):e827. Disponible en: DOI: https://doi.org/10.36015/cambios.v21.n1.2022.827

6. Jo JT, Schiff D. Management of neuro-oncologic emergencies. En: Wijdicks EFM, Kramer AH editores. Handbook of Clinical Neurology, Vol. 141 (3th ed). Critical Care Neurology, Part II. Elsevier B.V. [consultado 26/02/2025]; 2017 p: 715-741. Disponible en: http://dx.doi.org/10.1016/B978-0-444-63599-0.00039-9

7. Sosa-Remón A, Cuba-Naranjo AJ, Jeréz-Alvarez, AE. Recomendaciones para el manejo ventilatorio invasivo con ictus isquémico y COVID-19. Rev Cuban Anestesiol Reanimac [internet]. 2022 [consultado 26/02/2025];21(1):e765. Disponible en: http://revanestesia.sld.cu/index.php/anestRean/article/view/765

8. Bowry R, Grotta JC. Stroke in Critically Ill Cancer Patients. En: Nates JL, Price KJ editores. Oncologic Critical Care. Springer Nature Switzerland AG [consultado 26/02/2025]; 2020 p: 1-12. Disponible en: https://

doi.org/10.1007/978-3-319-74698-2_35-1

9. Tadevosyan A, Kornbluth J. Brain Herniation and Intracranial Hypertension. Neurol Clin [internet]. 2021 [consultado 26/02/2025];39:293–318. Disponible en: https://doi.org/10.1016/j.ncl.2021.02.005

10. Therelked ZD, Scott BJ. Neuro-Oncologic Emergencies. Neurol Clinic [internet]. 2021 [consultado 26/02/2025];39(2):545-563. Disponible en: doi:10.1016/j.nlc.2021.01.012

11. Carvajal-Carpio L, Vargas-Mena R, Hidalgo-Azofeifa S. Fisiopatología del síndrome de hipertensión intracraneal. Sinergia [internet]. 2021 [consultado 26/02/2025];e719. Disponible en: https://doi.org/10.31434/rms.v6i10.719

12. Suarez-Meade P, Marenco-Hillembrand L, Sherman WJ. Neuro-oncologic Emergencies. Curr Oncol Rep internet]. 2022 [consultado 26/02/2025];24(8):975-984. Disponible en: doi: 10.1007/s11912-022-01259-3.

13. Brock P, Toale KM, Tummala S. Neurologic Emergencies. En: Manzullo EF, Gonzalez CE, Escalante CP, Yeung SJ editores. Oncologic Emergencies. Springer New York Heidelberg Dordrecht London [consultado 26/02/2025]; 2016 p: 1-14. Disponible en: DOI 10.1007/978-1-4939-3188-0

14. Rai P, Shivaprasad A, Tremont-Lukats IW, Tummala S. Central Nervous System. En: Todd KH, Thomas CR, Alagappan K editores. Oncologic Emergency Medicine 2da edición. Springer Nature Switzerland AG [consultado 26/02/2025];2021 p: 207-223. Disponible en: https://doi.org/10.1007/978-3-030-67123-5_16

15. Gon Y, Zha L, Sasaki T, Morishima T, Ohno Y, Mochizuki H et al. Stroke mortality in cancer survivors: A population-based study in Japan. Thrombosis Research [internet]. 2023 [consultado 26/02/2025];222(1):140-148. Disponible en: https://doi.org/10.1016/j.thromres.2023.01.005

16. Lee KP, Huang HC, Tsai JY, Hsu LC. Effects of cancer on stroke recurrence and mortality: A single-center retrospective cohort study. eNeurologicalSci [internet]. 2023 [consultado 26/02/2025];32:100474. Disponible en: doi: 10.1016/j.ensci.2023.100474

17. Navi BB, Zhang C, Sherman CP, Genova R, LeMoss NM, Kamel H et al. Ischemic stroke with cancer: Hematologic and embolic biomarkers and clinical outcomes. J Thromb Haemost [internet]. 2022 [consultado 26/02/2025];20(9):2046-2057. Disponible en: doi: 10.1111/jth.15779

18. Pana TA, Mohamed MO, Mamas MA, Myint PK. Prognosis of Acute Ischaemic Stroke Patients with Cancer: A National Inpatient Sample Study. Cancers (Basel) [internet]. 2021 [consultado 26/02/2025];13(9):2193. Disponible en: doi: 10.3390/cancers13092193

19. Jin G, Hu W, Zeng L, Ma B, Zhou M. Prediction of long-term mortality in patients with ischemic stroke based on clinical characteristics on the first day of ICU admission: An easy-to-use nomogram. Front Neurol [internet]. 2023 [consultado 26/02/2025];14:1148185. Disponible en: doi: 10.3389/fneur.2023.1148185

20. Decavèle M, Dreyfus A, Gatulle N, Weiss N, Houillier C, Demeret S et al. Clinical features and outcome of patients with primary central nervous system lymphoma admitted to the intensive care unit: a French national expert center experience. J Neurol [internet]. 2021 [consultado 26/02/2025];268(6):2141-2150. Disponible en: doi: 10.1007/s00415-021-10396-x

21. Tan AC, Jacques SK, Oatley M, Guminski AD. Characteristics and outcomes of oncology unit patients requiring admission to an Australian intensive care unit. Intern Med J [internet]. 2019 [consultado 26/02/2025];49(6):734-739. Disponible en: doi: 10.1111/imj.14160

22. Neumann B, Onken J, König N, Stetefeld H, Luger S, Luger AL et al. Outcome of glioblastoma patients after intensive care unit admission with invasive mechanical ventilation: a multicenter analysis. J Neurooncol [internet]. 2023 [consultado 26/02/2025];164(1):249-256. Disponible en: doi: 10.1007/s11060-023-04403-6.

23. Asehnoune K, Roquilly A, Cinotti R. Respiratory management in patients with severe brain injury. Crit Care [internet]. 2018 [consultado 26/02/2025];22:76. Disponible en: https://doi.org/10.1186/s13054-018-1994-0

24. Sosa-Remón A, Jeréz-Alvarez AE, García-Arias DA, Cuba-Naranjo AJ, Galiano-Guerra G. Factores neurológicos asociados a la mortalidad en pacientes con accidente cerebrovascular y ventilación mecánica artificial. Rev Cuban Anestesiol Reanimac [internet]. 2021 [consultado 26/02/2025];20(2):e688. Disponible en: http://revanestesia.sld.cu/index.php/anestRean/article/view/688

25. Lay-Son L, Varas P. Coma anóxico-isquémico en 46 pacientes. Evolución a treinta días y su relación con los reflejos de tronco. RevMéd Chile [internet]. 2006 [consultado 26/02/2025];134:441-46. Disponible en: http://dx.doi.org/10.4067/S0034-98872006000400006

26. Slooter AJC, Otte WM, Devlin JW, Arora RC, Bleck TP, Claassen J et al. Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies. Intensive Care Med [internet]. 2020 [consultado 26/02/2025];46(5):1020-1022. Disponible en: doi: 10.1007/s00134-019-05907-4

27. Lovesio C. Medicina intensiva. 7ma ed. Buenos Aires: Editorial Corpus Libros Médicos y Científicos; 2017.

28. John B, Loomba V, John M. Etiology, Clinical Profile and Outcome of Encephalopathy in Elderly. J Assoc Physicians India [internet]. 2020 [consultado 26/02/2025];68(3):63-66. Disponible en: doi: https://journal-api.s3.ap-south-1.amazonaws.com/issues/May2020.pdf

29. Cerrella-Cano C, Junquera-Alonso E, Terroba-Alonso M, Cano-Calderero FX, Seoane-Blanco L, Armesto-González EM. Capecitabine-induced hyperammonemic encephalopathy. Rev Esp Enferm Dig [internet]. 2022 [consultado 26/02/2025];114(1):56. Disponible en: doi: 10.17235/reed.2021.8129/2021.

30. Lin AL, Avila EK. Neurologic Emergencies in the Patients With Cancer. J Intensive Care Med [internet]. 2017 [consultado 26/02/2025];32(2):99-115. Disponible en: doi: 10.1177/0885066615619582

31. Pistone A, Durieux V, Grigoriu B, Meert AP. Management of Acute Complications of Targeted Therapy in Patients With Cancer: A Review of Cases Managed in ICU. J Intensive Care Med [internet]. 2019 [consultado 26/02/2025];34(6):435-448. Disponible en: doi: 10.1177/0885066618787788

32. Roth P, Winklhofer S, Müller AMS, Dummer R, Mair MJ, Gramatzki D et al. Neurological complications of cancer immunotherapy. Cancer Treat Rev [internet]. 2021 [consultado 26/02/2025];97:102189. Disponible en: doi: 10.1016/j.ctrv.2021.102189

33. Espada-Zurera M, Martínez-Villena B, Carrero-Fernández AM. Manejo de las urgencias y emergencias neurooncológicas. Medicine [internet]. 2019 [consultado 26/02/2025];12(90):5293-302. Disponible en: https://doi.org/10.1016/j.med.2019.11.013

34. Gonzalez-Castro LN, Milligan TA. Seizures in patients with cancer. Cancer [internet]. 2020 [consultado 26/02/2025];126(7):1379-1389. Disponible en: doi: 10.1002/cncr.32708

35. Balloni A, Lari F, Giostra F. Evaluation and treatment of hyperglycemia in critically ill patients. Acta Biomed [internet]. 2016 [consultado 26/02/2025];87(3):329-333. Disponible en: https://pmc.ncbi.nlm.nih.gov/articles/PMC10521884/

36. Jereb S, Asus N, Blumtritt M, Kreff Y, Magnífico L, Rebagliati V et al. Hiperglucemia en el paciente Neurocrítico. Diaeta (B.Aires) [internet]. 2015 [consultado 26/02/2025];33(150):7-11. Disponible en: https://www.scielo.org.ar/pdf/diaeta/v33n150/v33n150a01.pdf

37. Kramer AH, Roberts DJ, Zygun DA. Optimal glycemic control in neurocritical care patients: a systematic review and meta-analysis. Crit Care [internet]. 2012 [consultado 26/02/2025];16(5):R203. Disponible en: doi: 10.1186/cc11812

38. Gruenbaum SE, Bertasi RAO, Bertasi TGO, Gruenbaum BF, Bilotta F. Glycemic control. En: Prabhakar H editor. Essentials of Evidence-Based Practice of Neuroanesthesia and Neurocritical Care. Elsevier Inc [consultado 26/02/2025]; 2022 p: 389-394. Disponible en: https://doi.org/10.1016/B978-0-12-821776-4.00028-7

39. Ramteke P, Deb A, Shepal V, Bhat MK. Hyperglycemia Associated Metabolic and Molecular Alterations

in Cancer Risk, Progression, Treatment, and Mortality. Cancers (Basel) [internet]. 2019 [consultado 26/02/2025];11(9):1402. Disponible en: doi: 10.3390/cancers11091402

40. Ramirez-Rosillo FJ, Carrillo-Esper R, Cabello-Aguilera R, Laredo-Sánches EC. Sepsis en el adulto mayor. En: Carrillo-Esper R, Cabello-Aguilera R editores. Medicina crítica en el adulto mayor. Editorial Alfil, S.A de C.V. San Rafael, México [consultado 26/02/2025]; 2020 p: 315-321

41. Hernández-Oliva M, Hernández-Jiménez A, Padrón-Mora M, Pérez-Fleites GJ, Leyva-Hernández A. Factores pronósticos de mortalidad en pacientes ancianos con sepsis en cuidados intensivos. Rev haban cienc méd [Internet]. 2020 [consultado 26/02/2025];19(1):63-75. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1729-519X2020000100063&lng=es.

42. Gudiol C, Albasanz-Puig A, Cuervo G, Carratalà J. Understanding and Managing Sepsis in Patients With Cancer in the Era of Antimicrobial Resistance. Front Med (Lausanne) [Internet]. 2021 [consultado 26/02/2025];8:636547. Disponible en: doi: 10.3389/fmed.2021.636547

43. Nazer L, López-Olivo MA, Cuenca JA, Awad W, Brown AR, Abusara A, et al. All-cause mortality in cancer patients treated for sepsis in intensive care units: a systematic review and meta-analysis. Support Care Cancer [Internet]. 2022 [consultado 26/02/2025];30(12):10099–109. Disponible en: https://doi.org/10.1007/s00520-022-07392-wPMID:36214879

44. Ahjin-Kim J, Izzy S. Cardiac Complications in Neurocritical Care Patients. En: Nelson SE, Nyquist PA editores. Neurointensive Care Unit, Current Clinical Neurology. Springer Nature Switzerland AG 2020. p: 49-56 Disponible en: https://doi.org/10.1007/978-3-030-36548-6_4

45. Ma Z, Jiang Z, Li H, Lu A, Wu S, Lu H et al. Prevalence, early predictors, and outcomes of sepsis in neurocritical illnesses: A prospective cohort study. Am J Infect Control [Internet]. 2024 [consultado 26/02/2025];52(7):827-833. Disponible en: doi: 10.1016/j.ajic.2024.01.017

46. Robba C, Battaglini D, Samary CS, Silva PL, Ball L, Rocco PR, et al. Ischaemic stroke-induced distal organ damage: pathophysiology and new therapeutic strategies. Intensive Care Med Exp [Internet]. 2020 [consultado 26/02/2025];8(1):23. Disponible en: https://doi.org/10.1186/s40635-020-00305- 3 PMID:33336314

47. Battaglini D, De-Rosa S, Godoy DA. Crosstalk Between the Nervous System and Systemic Organs in Acute Brain Injury. Neurocrit Care [Internet]. 2024 [consultado 26/02/2025];40(1):337-348. Disponible en: doi: 10.1007/s12028-023-01725-1

48. Marzorati C, Mokart D, Pène F, Lemiale V, Kouatchet A, Mayaux J, et al. Groupe de Recherche en Réanimation Respiratoire en Onco-Hématologie (GRRR-OH). Neurological failure in ICU patients with hematological malignancies: A prospective cohort study. PLoS One [Internet]. 2017 [consultado 26/02/2025];12(6):e0178824. Disponible en: https://doi.org/10.1371/journal.pone.0178824 PMID:28598990

49. Legriel S, Marijon H, Darmon M, Lemiale V, Bedos JP, Schlemmer B et al. Central neurological complications in critically ill patients with malignancies. Intensive Care Med [Internet]. 2010 [consultado 26/02/2025];36(2):232–40. Disponible en: https://doi.org/10.1007/s00134-009-1709-8

FINANCING

The authors did not receive funding for the implementation of this study.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest..

AUTHORSHIP CONTRIBUTION

Conceptualization: Ana Esperanza Jeréz Alvarez, Ariel Sosa Remón.
Formal Analysis: Ana Esperanza Jeréz Alvarez.
Research: Jhossmar Cristians Auza-Santivañez, Ariel Sosa Remón.
Methodology: Ariel Sosa Remón,Jhossmar Cristians Auza-Santivañez.
Project management: Ariel Sosa Remón.
Supervision: Arian Jesús Cuba Naranjo.

Visualisation: Jorge Márquez-Molina.

Writing - original draft: Ana Esperanza Jeréz Alvarez, Ariel Sosa Remón, Jhossmar Cristians Auza-Santivañez, Miguel Emilio García Rodríguez, Arian Jesús Cuba Naranjo,Yudiel Pérez Yero, Jorge Márquez-Molina, Freddy Ednildon Bautista-Vanegas.

Writing - proofreading and editing: Ana Esperanza Jeréz Alvarez, Ariel Sosa Remón, Jhossmar Cristians Auza-Santivañez, Miguel Emilio García Rodríguez, Arian Jesús Cuba Naranjo,Yudiel Pérez Yero, Jorge Márquez-Molina, Freddy Ednildon Bautista-Vanegas.