



Neurosurgery in the elderly patient

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Motto:

“Love and respect old age people because you are aging too”

Aparna Verma

ABSTRACT

Objective. For government officials and health providers, elderly population - aged 65 and over, especially neurosurgical patient, represent a larger concern, an increasing problem not only for socio-economic reasons related to the medical act, but also for additional care requirements which should be done by the family and society, including rehabilitation facilities, occupational & physical therapy, speech therapists, visiting nurses, to insure an effective recuperation after hospital discharge. A retrospective study with 325 "elderly" patients cohort, aged 65 and over, admitted in the Neurosurgery Department undergoing common neurosurgical procedures, in the last five years offer an evaluation for neurosurgical procedures, outcomes, comorbidities, anaesthetic and analgesic requirements, outcome.

Material and method. This study was performed on patients aged 65 years or older, with neurosurgical diseases, admitted to the Neurosurgery or the Intensive Care Unit of our hospital, between 2014-2019. An analysis was made on variables such as age, pathology, comorbidities, length of hospital stay especially in the ICU unit, type of cranio-cerebral or spinal procedures performed, anaesthesia protocols, complications, performance status, re-admissions and mortality.

Results. Patients age were divided into three categories: between 65-70 years old there were 152 patients (46,76%), between 70-85 years old 93 patients (28.61%) and over 85 years old 80 patients (24,61%). 173 patients were females (53,23%), 152 were males (46.76 %). The admission Glasgow Coma Scale (GCS) score to those over 85 years old was between 3-12 in 29 cases (8.02%) with early death in 13 patients. Several comorbidities were noticed in 294 patients (90.15%): cardiac, pulmonary, hematologic especially coumarinic overdose, hepatic and renal failures, psychiatric illnesses, concomitant systemic disease or immunosuppressed patients by decompensated diabetes, primitive cancers affecting various organs, infectious diseases, also severe osteoporosis, chronic ethylic intoxication, limiting surgical attitude, also obtaining the informed consent for surgery. There were 154 (47,38%) patients with cerebral pathology and 171 (52,61%) patients with spinal pathology. Most common surgical procedures performed were: craniotomies for tumours and hematoma removal, minimal invasive procedures for spine, endovascular and vertebroplasty. The median length of stay for emergency patients was significantly longer than that of elective patients (13 vs. 8 days). For 215 (66.15%) patients general anaesthesia was performed, local anaesthesia in 97 (29.84%) patients, 13 patients (4%) were not operated. Good quality of life results appreciated by patients and relatives were recorded in 236 cases (72.61%) in the first and second category; less better results to those over 85 years old; same symptoms especially pain 63 patients (19.38%), complications to 47 patients (14,46%) especially cardiac, renal and

Keywords

geriatric neurosurgical patient, anaesthetic and analgesic requirements to aged people, concomitant diseases, minim invasive neurosurgical procedures, pre-and postoperative care, life quality



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respiratory failures, also motor deficits, seizures, CSF fistula, mortality in 26 cases (8%), re-admissions in 45 cases (13.84%) less than 1 month after discharge.

Conclusions. Old prejudices that old age is a contraindication for surgery have to be removed. Clinical and surgical decisions for neurosurgical procedures in the elderly are decisive for limiting reported morbidity and mortality rates. For life quality, realistic family and society expectations, several aspects should be considered for safe and effective results: careful patient selection on patient status, comorbidities and physiological reserve; neurosurgical pathology, urgency of the surgical procedure, the strategy of neurosurgical management based on advances in imaging and interventional radiology, minimal invasive neurosurgical procedures with significant preoperative and postoperative care. Good results could be obtained even in elderly people for chronic subdural hematoma, simple brain or spinal tumour, good grade aneurysm, trigeminal pain, vertebroplasty in spinal vertebral fractures, etc.

INTRODUCTION

Aging means concomitant a physiological process but also structural degeneration, a graded loss of functional capacity of all organs and tissues (1)(2). The number of elderly patients is increasing worldwide, generating a larger concern (3-7), an increasing problem regarding socio-economic reasons related to the medical act, morbidity and additional care requirements, perioperative adverse events (8-10). It is estimated that between 2000 and 2050, the proportion of the world's population over 60 years will double, and the number of people aged 80 and older will quadruple (7)(11). For neurosurgical patient, beyond the age of 65 years, both chronic or in emergency, all measures should be institute to maintain quality of life, to avoid perioperative mortality and morbidity (10). In Romania the share of people over 65 years of age, was 18% of the total population on January 1, 2018, respectively 3,559,957 persons out of 19,523,621. According to the NIS data, among the elderly, the men numbered 1,433,412 persons (15% of the total number of men in Romania of 9,543,228 persons) and the women 2,117,495 (21% of the total number of women residing in Romania of 9,980,393 persons)(12).

MATERIAL AND METHOD

This retrospective study was performed on 325 patients aged 65 years or older, with neurosurgical diseases, admitted to the Neurosurgery or the Intensive Care Unit of our hospital, between 2014-2019. An analysis was made on variables such as:

age, pathology, the admission Glasgow Coma Scale (GCS) score, both chronic or in emergency, comorbidities - using Charlson Comorbidity Index (13)(14), length of hospital stay especially in the ICU unit, type of cranio-cerebral or spinal procedures performed, anaesthesia protocols, complications, performance status, re-admissions morbidity and mortality. 45.8% of patients had neurosurgical cranial pathology and 54,2% had neurosurgical spinal diseases. Patients age were divided into three categories: between 65-70 years old there were 152 patients (46,76%), between 70-85 years old 93 patients (28.61%) and over 85 years old 80 patients (24,61%). 173 patients were females (53,23%), 152 were males (46.76 %). The admission Glasgow Coma Scale (GCS) score was between 3-15, worse: between 3-5 especially to those over 85 years old in 29 cases (8.02%) with early death in 13 patients. A CGS score between 7-14 was recorded to 89 patients (27,38%): 12 cases (3.69%) in the first category, 42 cases (12.95%) cases in the second and 35 cases (10.76%) in the third. Several combined comorbidities were encountered in 294 patients (90.15%), limiting surgical attitude, also obtaining the informed consent for surgery: cardiac insufficiency, several cardiac diseases with damage to the ejection fraction (myocardial infarction, arrhythmias, valvular stenosis or insufficiency, untreated hypertension); chronic pulmonary disease, bronchial asthma; previous strokes with hemiplegia; severe haematological diseases (lymphoma, leukemia, myeloma, coagulation disorders with thrombocytopenia or coumarinic overdose); hepatopathy (cirrhosis, portal hypertension with variceal bleeding history, chronic hepatitis); kidney failure - patients submitted in the dialysis program; peptic ulcer disease; connective tissue disease; peripheral vascular disease (intermittent claudication, chronic arterial insufficiency with by-pass, untreated thoracic or abdominal aneurysm), psychiatric illnesses (dementia); concomitant systemic disease or immunosuppressed patients by diabetes, primitive and metastatic cancers affecting various organs, chemotherapies, transplant patients, infectious diseases even AIDS; severe osteoporosis, chronic ethylic intoxication, drug allergies.

Neurosurgical pathologies varied alone or concurrently: 154 (47,38%) patients with cerebral pathology and 171 (52,61%) patients with spinal pathology: cranio-cerebral and spinal trauma

(hematomas: epidural, subdural, intracerebral, posttraumatic subarachnoid haemorrhage, cerebral and spinal contusions, DAI, cerebral lacerations, CSF fistula, Schneider syndrome, hematomyelia); cerebral tumours: extraaxial meningioma, metastasis, gliomas especially glioblastoma, schwannomas, pituitary and spinal tumours: extradural, intradural, intramedullary, frequent metastasis in lung, breast, prostate cancer; cerebral aneurysm, carotid-cavernous fistula, MAV, spinal degenerative myeloradiculopathy, mielopathy with cervical and lumbar canal stenosis, spinal instability with osteoporotic vertebral changes, vertebral fractures; Arnold neuralgia, trigeminal, atypical facial pain, spinal neuropathic pain; tremor (Parkinson's syndroms & disease, dystonic movements), blepharospasm even Meige syndrome, spasmodic torticollis. All patients were carefully neurologic, biologic, neuro-imagistic, multidisciplinary evaluated; neurosurgical surgical indication, anaesthesia protocol, informed consent to be used to each patient were supported with accuracy. Several procedures have been performed: craniotomies for tumours and hematoma removal, minimal invasive procedures for spine, endovascular, vertebroplasty, nerve block, neurovascular decompression or Gamma-Knife for pain procedures have been performed.

RESULTS

The median length of stay for emergency patients was significantly longer than that of elective patients ranged between 13 vs.8 days, and in the ICU unit vary from 1 to 63 days.

For 215 (66.15%) patients general anaesthesia was performed, local anaesthesia in 97 (29.84%) patients, 13 patients (4%) were not operated. Good quality of life results appreciated by patients and relatives were recorded in 236 cases (72.61%) in the first and second category; less better results to those over 85 years old; same symptoms especially pain 63 patients (19.38%), complications to 47 patients (14.46%) especially cardiac, renal and respiratory failures, also motor deficits, seizures, CSF fistula, mortality in 26 cases (8%), re-admissions in 45 cases (13.84%) less than 1 month after discharge. For old patients physical therapists may improve strength and balance, safely walk ability, climb stairs before being released from the hospital. Occupational therapists may help such patients to be able to do

personal hygiene using the bathroom, to get dressed; speech language pathologists could help patients with speech, language or thinking.

DISCUSSION

The elderly patient - defined as an individual 65 years of age and over, still represent all around world in general, a fragile population, a great concern, with higher costs of health care, a difficult issue for the health systems struggling with limited resources (3-7)(9)(10). For each aging person there are a personal rate of degeneration of CNS as like as the whole body, in anatomy, in mental and physical activity, also in higher costs of living, lifestyle change, loneliness, possible dependence of specific medication for medical associated illnesses - such as diabetes and cardiovascular disease (3)(6). It's also a reality that the elderly population represent the fastest growing segment of the world's population; the world's population over 60 years will double between 2000 and 2050 and the number of people aged 80 and older will quadruple (7). 47,8 million the number of people age 65 and older in the United States on July 1,2015; this group accounted for 14,9 per cent of the total population (15). 98,2 million - the projected population of people age 65 and older in 2060; of this number 9,7 million will be age 85 or older (16). Such growing proportion affect also the neurosurgical admissions both in emergency surgeries or classical presentations for every group of persons on age "young-old" - 65-74, "middle-old" - 75-84 and "old-old" > 85 (17). There are several changes involved in different degree with age, with neurosurgical interest too (1)(2)(18-23):

-*cerebral atrophy* affecting especially the frontal and temporal lobes, decline in brain weight, increase in ventricular size, thickening of meninges, decrease in width of gyri, deep sulci, cortical neurons, myelinated axons, the number of synapses per neuron, loss of Nissl substance, nuclear atrophy; intracellular deposits, granulation or fragmentation of mitochondria. These aspects are generating tolerance in front of any expansive process, clinical onset delay in case of tumours, intracranial hematoma, facilitates surgical approach, allows intracranial expansive processes removal.

-*cerebral fragility* with decreased cerebral compliance that induces the brain's difficulty to resume its

anterior position, able to generate hematoma recurrence, hydrocephalus, etc.

-decreased cerebral blood flow, loss of vascular autoregulation and responsiveness to neuronal demand, hypercapnia, heterogeneous regional variations with decreased cellular oxygen, glucose and oxidative metabolism, altered sodium, potassium and calcium homeostasis with reduced axoplasmic transport, calcium mediated and synaptic neurotransmitter release. There are also general decrease in excitability, peripheral nerve conduction velocity, altered reflex responses and increased latency of evoked potential, a disorganization of highly coordinated activities, with autonomic and homeostatic changes: reduced temperature regulation, orthostatic hypotension, chronic constipation, slowed hear rate, decreased blood pressure.

-leukoaraiosis (gr."leuko-" = white, meaning white matter and the adjective «araios" ="thin."- Hachinski V. 1987) are typically generated by: lacunar stroke/transient ischemic attack (TIA), dementia of both vascular and non-vascular etiologies (hypertension, degenerative, in Alzheimer's disease), sporadic cerebral amyloid angiopathy, diabetes; the precise pathogenic mechanisms remain unclear. Recent genetic results strongly supported that leukoaraiosis is associated with immune response and neuroinflammation (23). Pathologically, leukoaraiosis is characterized by white matter gliosis, axonal and myelin loss, increased perivascular spaces, patchy demyelination, hyaline thickening and arteriosclerosis of small vessels that can evolve to lipohyalinosis, fibrinoid necrosis, and denudation of ependyma. Main clinical manifestations are cognitive and executive troubles (memory loss especially short-term memory, visual and hearing loss, declining endurance, verbal intelligence, processing speech dysfunction in learning and language skills, depression), ankle jerks decreased or absent, increased primitive reflexes (glabella, palmo-mental), slowed forward flexed, altered gait, tremor with loss of fine motor coordination bladder instability. There are hypo-dense areas to cerebral CT scan, diffuse, heterogeneous, imprecisely delimited, primarily interesting the centre of the white substance or the immediate subcortical areas. The MRI examination in weighted T₁ sequences shows hypointense areas and the weighted T₂

sequences show hyperintense areas; sometimes without correlation as number, localization. MRI findings are commonly seen to elderly people with prevalence ranging from 50% to 100%. Leukoaraiosis may explain poor clinical outcomes and increases the risk of disability, dementia, depression, stroke, and the overall morbidity and mortality.

-amyloid angiopathy > 70 years: explains the difficulties of hemostasis, haemorrhagic recurrences, preanesthetic assessment, informed consent, perioperative evaluation, risk issues especially for those people identified with ASA physical status of III or IV. and care are magnified in older patient, anaesthetic management, efficient surgical skills procedures - especially functional neurosurgery, radiosurgery, planned postoperative management may contribute to successful outcomes also to ameliorate quality of life related to neurosurgical diseases, also to a specific neurosurgical pathology, especially pain (3)(5)(7)(8)(10)(11)(24-29). There are medical factors affecting anaesthesia: multiple medical comorbidities including sepsis, metabolic disturbances severe obesity or poor nutritional status, alcohol and/or drug abuse, history of cardiac failure or myocardial infarction ≤ 1 year with low ejection fraction (EF) on echocardiography, severe uncontrolled hypertension, severe respiratory dysfunction, hepato-renal failures, neurovascular, psychiatric disease, history of CVA or TIA, peripheral vascular disease, immuno-compromised patients by diabetes, tuberculosis, etc; severe coagulopathy status with trombocytomia, haemophilia, antiplatelet agents even help syndrome (to old patients even a normal coagulogram may coexist with difficult hemostasis), cognitive function at risk especially at advanced age > 70 years: cognitive impairment, acute confusional state, delirium. There are also surgical factors affecting anaesthesia in all such high-risk geriatric patients which should be discussed in detail for optimizing the outcome with the anaesthesiologist and cardiologist (28)(29):

-surgical position: prone, sitting, Concorde position have always cardio-respiratory implications, Wilson Frame or similar with varying degrees of inclination, neck stabilization, spine traction, requirement of elective ventilation, head up to 10 degree and reverse Trendelenburg may avoid perioperative blindness by direct/indirect eye pressure, ischemic

optic neuropathy, central retinal artery occlusion (CRAO), cortical blindness. Also a severe spinal trauma or an important scoliosis, osteoporosis, osteomyelitis, severe obesity or undernourished people.

-plan of surgical excision, anticipated duration (in general surgery should never exceed 6.5 h in older patient), anticipated blood loss, neurophysiologic monitoring, postoperative ventilation. The anaesthetic regimen has to be tailored according to the physiological reserve: local or general anaesthesia. For general anaesthesia there are several remarks:

-before induction the invasive monitoring for arterial blood pressure - ABP and central venous pressure - CVP should be instituted under local anaesthesia.

-induction should be performed with fentanyl, etomidate (etomidate requirement beyond the age of 80 years may decrease by 50%), non depolarising muscular blockade agents intravenously. Propofol produces an exaggerated fall in blood pressure especially to old patients, dehydrated, midazolam has increased duration and potency, neuromuscular blocking agents are unchanged oral intubation.

-anaesthesia should be maintained with 50% oxygen, air, sevoflurane in minimum alveolar concentration - MAC of 0.5 (MAC requirement for volatiles also decreases in the elderly, though the onset may be delayed due to decreased cardiac output). Monitoring should be performed by pulse oximetry: SpO₂, arterial blood pressure ABP avoiding acidosis, hyper or hypotension - 84 mm systolic minimum, Hct > 28%, Hb > 9.4 with cardiac index (stroke volume) ↓ 24%; blood loss > 45%, heart rate HR, electrocardiogram ECG, end-tidal carbon dioxide, hourly urine output, temperature. To maintain hemodynamics and to avoid cerebral perfusion pressure crash crystalloids and noradrenaline should be infused intraoperatively.

-even in case with normal coagulation test, haemostasis could be laborious in the confined space of the cranial cavity or the spinal canal presenting as the surgical field; in case of bleeding diathesis (due to prescribed medications in the form of clopidogrel, warfarin, etc., alone or more often in combination) especially in emergency this is dangerous. For such situations there are several

costly, time consuming, delaying procedures: red blood cell transfusion, donor platelet, frozen plasma, Novoseven, Pronative, Hemocompletan, recombinant factor VIIa, all of this are costly, time consuming, delay procedures.

-postop. Slowly awakening, extubated and closely watched in neurosurgical intensive care unit to improve resource utilization, decreased in-hospital mortality (26). The effect of depth of anaesthesia on outcomes is still a grey area. Perioperative cardiac - maintaining volume status, pulmonary evaluation are reliable predictors of complications, (ex. unoptimized pulmonary diseases, increased closing volumes and decreased expiratory flow rates, tracheostomy, postoperative mechanical ventilation) predispose older patients to complications and death, also renal status avoiding nephrotoxic drugs, prevention of hyperglycemia or hypoglycemia, adequate prophylaxis for deep venous thrombosis - even with pneumatic compression devices, multiple medications for other co-morbidities. Mental status should be assessed preoperatively because dementia is a predictor of poor outcome perioperatively, increasing mortality by 50% (25). Nutritional deficiencies should be corrected because they play a role in wound healing and recovery - albumin levels of < 3.2 g/dl in hospitalized elderly patients increased perioperative mortality (28), also pain should be treated.

Most common geriatric pathology are:

-*traumatic brain injuries*, more common: subdural uni or bilateral hematoma - a common pathology (11)(30-35), mainly affecting elderly patients, "not a benign disease" (34) In patients over 80 years old chronic subdural hematoma incidence is reported 127.1/100.000/year, with a mortality of less than 10%, a history of head injury is not always admitted, several cases could be under anticoagulant treatment because of cardiac pathologies or ictus cerebri, arterial hypertension, diabetes mellitus with severe thrombocytopenia, high INR, even with a normal coagulogram haemostasis may be difficult. The most common clinical presentation include hemiparesis, dysphasia/ aphasia, disorientation, hemianopsia. Diagnosis is sustained on CT scan. Anaesthesia should be local or general, to correct a severe coagulopathy may be necessary: thrombocytes, Novoseven-factor VII, Pronativ, Hemocompletan in case of fibrinolysis. Several

surgical techniques could be used: *craniotomy* centred on the thickest portion of the clot (useful in clots that can't be evacuated through a simple trepan hole, allows brain to resume its anterior position, to evacuate a concomitant intracerebral hematoma, to monitor intracranial pressure in those with CGS <9 Bullock et al, allows haemostasis), *craniotomy*, useful when intracranial pressure is maintained, requiring removal of the bone, *trefination* or two - several trepan holes in the thickest parts of the hematoma (for example, frontal and parietal that may be needed to be incorporated into a fronto-temporo-parietal craniotomy in case of relapse, hematoma consistency, thick membranes), *the subdural evacuating port system (SEPS)*: the minimally invasive technique, a safe method, effective in subacute and chronic subdural hematoma in elderly patients, easy to perform with local or general anaesthesia, it takes less than 10 minutes, without irrigation, aspiration, catheter (36). Postop complications are: recurrences, persistence of preop. brain position by decreased cerebral compliance, parenchymal haemorrhages in the same hemisphere or contralateral. Outcome are measured with Glasgow outcome scale (GOS) or Markwalder grading system (MGS) to evaluate improvement in neurological function in general a good GOS in 86.1% of patients older than 80 years (11), the discharge disposition to return to an independent life, to rehabilitation or nursing home. There are also cerebral contusions and lacerations, rare extradural hematoma with late shift effect of cerebral parenchyma, veins ruptures and haemorrhagic events, diminished recovery capacity.

-cerebral aneurysm and less frequent cerebral arterio-venos malformation with subarahnoidian haemorrhage, *ischemic & haemorrhagic strokes supra and infratentorial*, associated with *hydrocephalus and occlusive cerebrovascular disease* 40% (3)(37).

-epilepsy to older patients is are more frequent (the annual incidence is 85.9 per 100,000 for people aged 65-69 years and 135 per 100,000 for those aged over 80 years (38); similar status epilepticus appears to occur more frequently with significantly greater morbidity and mortality in this age group (39). There are focal seizures, automatisms without generalisation or with secondary generalisation, the postictal phase is prolonged with confusion and memory problems corresponding with focal changes on electroencephalograph (EEG) and neuroimaging

epileptogenic lesion (40). Epilepsy are more common encountered with stroke - the risk of epilepsy increases up to 20-fold in the first year after a stroke, hypertensive encephalopathy, cerebral vasculitis, tumours (gliomas, meningiomas and metastases), trauma, dementia, Alzheimer's disease - are up to 10 times more likely to develop epilepsy than those without the condition (38). To older patients there are: side-effects, toxicity, increased susceptibility to anti-epileptic drug, a mortality rate 2-3 times higher than the general population, a very variable prognosis depending on the epilepsy syndrome, the frequency of seizures, the response to treatment - an inadequate seizure control raise the suspicion of poor adherence or progressive neurodegenerative disease; social difficulties, multidisciplinary service requirements in the community (41).

-cerebral tumours:

meningiomas: are 12.8/100,000 incidence to those of ≥ 65 years of age, increasing with age (42)

In the elderly, meningiomas are diagnosed small, slow growing, asymptomatic extraaxial tumours without brain edema, even calcified, occurring more frequently in women than men (43). For such tumours therapeutic attitude are conservative clinical observation and radiologic follow-up (44-46). For clinically symptomatic and fast growing meningioma, especially atypical or malignant, to elderly patients with limited physiological capacities and comorbidities, surgery after a careful consideration should be the mainstay of treatment for local tumour control (47-52), to realise genetic and histological diagnosis (it's possible to the same patient to see meningiomatosis with different genetic and histologic behaviour: benign and malignant meningiomas), but also stereotactic radiotherapy (SRT), Gamma knife, Linac-based stereotactic radiosurgery effective in terms of tumour control and survival, safe with regard to toxicity - the overall rates of complications ranged from 2.7% to 29.8%, and the overall incidence of complications 20% (range, 3-61%)(53-59).

Metastasis are increasing to the majority of cancer patients over the age of 65, not only cerebral or intradural spinal metastasis, but more frequent bone metastasis, involving the spine in approx. 50% (60). Elderly survivors of breast cancer, lung cancer, and melanoma face risk of brain metastasis later in life; rates of synchronous brain metastases incidence

proportions in lung, breast, and melanoma cancers were 9.6%, 0.3%, and 1.1%, respectively; such tumours may require extra surveillance in the years following initial cancer treatment. Non-small cell lung cancer made up the majority of lung cancer SBM IP, at 13.4%, and small-cell lung cancer made up the majority of lung cancer - lifetime brain metastases at 23.1%. The most frequent spinal metastases (60%) are from breast, lung, or prostate cancer (61). The chance that an elderly patient (60–79 years old) is affected by bony metastases is four times higher in men and three times higher in women than a middle-aged patient (40–59 years old). Pain, neural compression with motor deficits, pathological fracture, and instability are the most common surgery indication. For cervical area: the occipito-cervical junction can generally be treated by posterior resection and stabilization, in the middle and lower cervical spine the anterior approach with anterior decompression and anterior column reconstruction; in the thoraco-lumbar spine a posterior decompression and postero-lateral vertebral body resection through a posterior approach only, with a concomitant reconstruction and stabilization. There are also for paleative cases different treatment modalities—irradiation, chemotherapy, steroids, biphosphonates, morphine pump. Since prospective randomized studies comparing different treatment modalities for spinal metastases including surgery are not available and are ethically difficult to achieve, each case remains an interdisciplinary, shared decision-making process for what is considered best for a patient or elderly patient. However, whenever surgery is an option, it should be planned before irradiation since surgery after irradiation has a significant higher complication rate.

Glioblastoma multiforme are at old age a high incidence, also most significant associated with poor prognosis, even after the introduction of temozolomide (TMZ) in 2006, without any clear borderline (62). After published statistics from the Japan Brain Tumour Registry from 2001 to 2004 (63), patients aged > 65 years and > 75 years accounting for 42% and 11.4%, respectively; the most frequent age group of patients was 65–69 years, which accounted for 17% of the cases, median overall survival was 15 months. GBMs are subdivided according to their molecular phenotype see WHO classification of central nervous system (CNS)

tumour 2016 (64), namely, CpG island methylator phenotype (G-CIMP) and isocitrate dehydrogenase (IDH) mutation: IDH wild type and IDH mutant - absence of IDH mutation, is the most predominant GBM in the elderly. Also MGMT promoter methylation is independent of age, with 47% in the elderly, epidermal growth factor receptor - EGFR, p53, CDKN2A, PTEN were not prognostic factors (65), vascular endothelial growth factor (VEGF) was higher in GBM in the elderly than in young patients, also the prognostic value of telomerase reverse transcriptase (TERT) promoter mutation in GBM has been debated (66). Although age is a poor prognostic factor, old age alone is suggested to have no association with poor prognosis, an aggressive treatment should not be withheld because of old age (67). Multimodal treatment in elderly patients with GBM aged > 65 years should include:

-surgical resection: achieving maximal tumour cytoreduction within the safety margin, brain decompression, histopathological and genetic diagnosis especially for *IDH* mutation and *MGMT* methylation status. Such aggressive attitude may prolonge survival by 2.8 times than biopsy (median OS: 171 days after the craniotomy versus 85 days after the biopsy), also for aged patients ≥ 75 years may extend survival by 2 months, delayed tumour progression and improved functional prognosis (68-76).

-radiotherapy - hypofractionated radiotherapy (Hypo-RT 40 Gy/15 Fr) alone can be considered if the tumour has an unmethylated *MGMT* promoter (77-80)

-with concurrent and adjuvant TMZ - in elderly patients with *MGMT* methylated tumours monotherapy with TMZ can expect prolonged survival (78-82); clinical benefits of bevacizumab use in remain unclear (83)(84), also lack of evidence regarding the efficacy of carmustine wafer (85)(86). *another cerebral tumor: schwannoma, pituitary adenoma* (87)

-*spinal pathology* means for old patients a wide range of neurosurgical procedures to solve: spinal degenerative myeloradiculopathy, mielopathy with cervical canal stenosis, lumbar spinal stenosis (it's important to clarify that surgery will not give

another spine, also surgery is better to be done in a only surgical procedure); spinal tumours: extra/intra dural, intramedullary and more frequent vertebral metastasis in lung, breast or prostate cancers; spinal instability and osteoporotic vertebral changes.

-chronic geriatric pain defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage", is a longstanding pain that persists beyond the usual recovery period or occurs along with a chronic health condition, for greater than 3 months is a more frequent neuropathic, persistent, recurrent, underreported; much more difficult to treat especially for those with long-lasting pain compared to young people, justified by pain corticalisation (88). Such condition is impairing activities of daily living, ambulation, quality of life; more difficult to be understood especially to those patients with cognitive or language impairments; also may generate polypharmacy with concomitant medication, but also responsive for poor health, accidents, gait abnormalities, cognitive decline, denial, depression, psychosocial concerns, with direct and indirect estimated treatments costs close to \$50 billion a year (89). There are several types of chronic pain, complex, multifactorial in older population, very debilitating and painful: trigeminal neuralgia, atypical facial pain, occipital neuralgia, postherpetic neuralgia, headache, stroke and phantom limb pain, failed spinal surgery, referred or pain related to cancer; also pain perception is more difficult to be treated. For such patients a multidisciplinary approach needs to be conceived: pharmacotherapy, psychological support, psychological support, also interventional procedures. A wide range of procedures (88) should be wisely proposed taking into account life expectancy, comorbidities, the patient's desire focusing on neuromodular rather than lesional techniques, also risks for each procedure: microvascular decompression, chemical neurolysis, radiofrequency and glycerol rhizotomy, stereotactic radiation, deep brain & spinal cord stimulation, motor cortex stimulation and neuraxial drug delivery.

-tremor (Parkinson's syndrome & disease and dystonic movements) treated especially by medication, DBS, motor cortex stimulation (90).

-neuro-infections especially to immunocompromise

patients: diabetes, TB, HIV, etc.

-multiple sclerosis

-dementia

CONCLUSIONS

This study is a plea argue that in elderly patients, which is likely to continue to grow (6), risk factors should be adequately managed even in emergency (3), with correct preoperative evaluation, appropriate perioperative care (8), titrated anesthetic management, efficient surgical skills. Planned postoperative management may improve neurological status (30)(91), outcomes, reduce mortality rates, reduce length of intensive care stay, improved resource utilisation, fiscal benefits (7)(9). Further studies in the elderly are mandatory to be performed to improve clinical decisions on risk benefit ratios pending on new technologies.

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