PLOS ONE

RESEARCH ARTICLE

Risk factors for unfavorable clinical outcomes in patients with brain abscess in South Korea

Yun Suk Cho[1,2], Yu Jin Sohn[1,2], Jong Hoon Hyun[1,2], Yae Jee Baek[1,2], Moo Hyun Kim[1,2], Jung Ho Kim[1,2], Jin Young Ahn[1,2], Su Jin Jeong[1,2], Nam Su Ku[1,2]*, Jun Yong Choi[1,2], Joon-Sup Yeom[1,2], Young Goo Song[1,2]

1 Department of Internal Medicine, Yonsei University College of Medicine, Seoul, South Korea, **2** AIDS Research Institute, Yonsei University College of Medicine, Seoul, South Korea

* smileboy9@yuhs.ac

Check for updates

OPEN ACCESS

Citation: Cho YS, Sohn YJ, Hyun JH, Baek YJ, Kim MH, Kim JH, et al. (2021) Risk factors for unfavorable clinical outcomes in patients with brain abscess in South Korea. PLoS ONE 16(9): e0257541. https://doi.org/10.1371/journal.pone.0257541

Editor: Miguel A. Barboza, Hospital Dr. Rafael A. Calderón Guardia, CCSS, COSTA RICA

Received: December 30, 2020

Accepted: September 6, 2021

Published: September 20, 2021

Copyright: © 2021 Cho et al. This is an open access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Data Availability Statement: All relevant data are within the paper.

Funding: The author(s) received no specific funding for this work.

Competing interests: The authors have declared that no competing interests exist.

Abstract

Background

Brain abscess can be life-threatening and manifest various neurological findings, although the mortality rate has decreased recently. We investigated the risk factors for unfavorable outcomes of patients with brain abscess.

Methods

A retrospective cohort study examined patients with brain abscess seen from May 2005 to December 2018 in a tertiary care hospital in Seoul, South Korea. We reviewed the medical records for clinical findings, therapeutic modalities, and prognostic factors of brain abscess. Unfavorable clinical outcomes were defined as death, moderate to severe disability with neurological deficits, or vegetative state at 1 year or at the time of discharge from outpatient follow-up.

Results

The study enrolled 135 patients: 65.2% were males; the mean age was 56 years. 35.6% had unfavorable outcomes. In multivariate analysis, higher Sequential Organ Failure Assessment (SOFA) ($p < 0.001$), pre-existing hemiplegia ($p = 0.049$), and higher Charlson comorbidity index (CCI) ($p = 0.028$) were independently associated with unfavorable outcomes.

Conclusions

Higher SOFA, pre-existing hemiplegia and higher Charlson comorbidity index were significant risk factors for unfavorable clinical outcomes in patients with brain abscess.

Introduction

A brain abscess is a severe purulent infection of the brain, and its worldwide prevalence is 0.4–0.9 persons per 1,000 population [1–3]. Abscesses result from cerebritis, where a capsule forms

around the area of inflammation and has a pus-filled center composed of necrotic brain tissue and bacteria. Edema is also increased in the surrounding white matter [3–5].

In the past, brain abscess was invariably fatal. The mortality rate of brain abscess has decreased from 40% to 10% over the past 50 years with the introduction of computed tomography (CT), the development of neurosurgical techniques, and the use of broad-spectrum antibiotics [4, 6–8].

Brain abscess can be life-threatening and have severe neurological sequelae, such as motor weakness, aphasia, and epilepsy [9–11]. Thus, it is important to identify predictors of clinical outcomes of brain abscess. To our knowledge, however, few studies have done this. Therefore, we investigated the risk factors for unfavorable clinical outcomes of patients with brain abscess.

Methods

Study population and design

A retrospective cohort study examined patients with brain abscess from May 2005 to December 2018 in a 2,400-bed, tertiary care hospital in Seoul, South Korea. The patients enrolled met the following criteria: (1) aged 18 years or over; (2) symptoms including fever, headache and altered mental status, which are deemed the classical clinical findings of brain abscess [4, 12–15]; (3) brain CT or magnetic resonance imaging findings showing intracranial brain abscess; and (4) evidence of brain abscess seen on aspiration or in microbiological samples. Patients with fungal, mycobacterial, or parasitic infection, and those with other forms of intracranial abscess, such as an epidural abscess or subdural empyema, were excluded [9]. Demographic data, and data on neurological status on admission, clinical presentation, risk factors for an unfavorable outcome, microbiological profiles, neuroimaging findings, treatment modalities, and clinical outcomes were collected from the electronic medical records. Patients were divided into favorable and unfavorable outcome groups, at 1 year or at the time of discharge from out-patient follow-up if earlier. The study was approved by the Institutional Review Board (IRB) of Yonsei University Health System Clinical Trial Center (4-2020-0160). Because the study was retrospective and the data were anonymized, the IRB waived the requirement for consent.

Definitions

Unfavorable clinical outcomes were defined as death, moderate-to-severe disability with neurological deficits, or vegetative state at 1 year or at the time of discharge from outpatient follow-up. The outcome was assessed using the Glasgow Outcome Scale, a validated global scale used to measure the functional outcome following a brain injury, including brain abscess (Table 1) [16]. The neurological deficits included partial or complete paralysis, partial or complete loss of sensation, seizures, poor cognitive function, or visual defects and dysphasia [17–19]. The Charlson comorbidity index (CCI) [20–22] and Sequential Organ Failure Assessment (SOFA) scores were calculated. The SOFA score comprises six organ system function domains (respiratory, cardiovascular, renal, neurological, hepatic, and hematological) [23–25].

Laboratory tests

Tissue samples were obtained from inflammatory lesions of the frontal, sphenoid, and ethmoid sinuses. The microorganisms were identified using the ATB 32 GN System (bioMérieux, Marcy l'Étoile, France) and MALDI Biotyper (Bruker Daltonics, Bremen, Germany).

Table 1. The Glasgow outcome scales of the patients in this study.

Score	Clinical Meaning	Outcome	No. (%)
1	Death	unfavorable	14 (10.4)
2	Neurovegetative state; patient unresponsive and speechless for weeks or months	unfavorable	4 (3.0)
3	Severe disability; patients dependent for daily support	unfavorable	26 (19.2)
4	Moderate disability; patients independent in daily life	unfavorable	4 (3.0)
5	Good recovery; resumption of normal life with minor neurological and psychological deficits	favorable	87 (64.4)

https://doi.org/10.1371/journal.pone.0257541.t001

Statistical analysis

Independent *t*-tests were used to analyze continuous variables, and chi-square or Fisher's exact tests were used for analyzing categorical variables. A multivariate binary logistic regression analysis that included significant predictors in the univariate analysis ($p < 0.05$) was conducted to identify independent predictors of an unfavorable outcome. The Hosmer–Lemeshow test was used to determine goodness of fit for logistic regression models. Variables correlated linearly with other variables were excluded from the multivariate analysis. A p-value < 0.05 in the multivariate analysis was considered indicative of statistical significance. The analyses were performed using SPSS (ver. 25.0; IBM, Armonk, NY, USA).

Results

Baseline characteristics

The study initially investigated 180 patients, of whom 45 were excluded: 31 with epidural abscesses and 14 with subdural empyema. Finally, 135 patients were eligible for the analysis. Of these, 15 had brain abscesses in multiple lobes. There were 88 males (65.2%) and 47 females (34.8%). Their mean age was 56 years. Common clinical findings were focal neurological deficit (51.9%), headache (45.9%), and fever (29.6%). The most common focal neurological deficits were hemiparesis and dysarthria. The most common comorbidities were diabetes mellitus (17.8%) and solid tumor with or without metastasis (15.6%). Radiologically, 120 (88.9%) had a single lobe abscess and 15 (11.1%) had abscesses in multiple lobes. The underlying source of the brain abscess was identified in 46 patients (34.1%): 17 patients (12.6%) had hematogenous spread, 12 (8.9%) had sinusitis, and 9 (6.7%) had a dental infection. Table 2 shows the patients' demographic and clinical characteristics.

Surgery was performed in 109 patients (80.7%), of whom 74 underwent drainage, and 35 received open surgery. All patients were treated with systemic antibiotics and 26 patients were treated only with antibiotics (19.3%) (Table 2). Of these 26 patients, seven did not undergo surgical treatment because they had multiple brain abscesses, in six cases, surgery was not performed because the abscess was smaller than 1 cm, four patients had no surgery due to a critical medical condition, seven patients had abscesses that were difficult to access surgically, and two patients with a high risk of bleeding did not undergo surgery.

Microbiological characteristics

Causative pathogens were identified in 44 culture-positive brain abscess patients (32.6%). Gram-positive bacteria, particularly *Streptococcus* species, were the most frequently detected pathogens (Table 3).

Risk factors for unfavorable outcomes among patients with brain abscess

The outcomes were unfavorable in 48 patients (35.6%) (Table 1): 30 patients had a moderate-to-severe disability, four were in neurovegetative states, and 14 had died by 1 year. In

Table 2. Baseline characteristics of the patients with brain abscess.

Variables	Total	Favorable outcome	Unfavorable outcome	*p*-value
	(n = 135)	(n = 87)	(n = 48)	
Male (%)	88(65.2)	53(60.9)	35(72.9)	0.161
Age (year, mean±SD)	56±14	53.9±13.1	60.7±14.9	0.015
Presenting symptoms (%)				
headache	62(45.9)	54(62.1)	8(16.7)	< 0.001
fever (≥ 37.8˚C)	40(29.6)	29(33.3)	11(22.9)	0.205
seizure	26(19.3)	14(16.1)	12(25.0)	0.209
altered mental status	38(28.1)	15(17.2)	23(47.9)	< 0.001
Focal neurologic deficit (%)	70(51.9)	42(48.3)	28(58.3)	0.263
Concomitant meningitis (%)	14(10.4)	8(9.2)	6(12.5)	0.547
Cerebral hemorrhage (%)	8(5.9)	3(3.4)	5(10.4)	0.101
Source of infection (%)				
sinusitis	12(8.9)	7(8.0)	5(10.4)	0.643
dental infection	9(6.7)	5(5.7)	4(8.3)	0.564
eye infection	2(1.5)	2(2.3)	0(0)	0.290
otitis	1(0.7)	0(0)	1(2.1)	0.177
head injury	5(3.7)	2(2.3)	3(6.3)	0.245
hematogenous	17(12.6)	9(10.3)	8(16.7)	0.289
unknown	77(57.0)	55(63.2)	22(45.8)	0.051
Site of brain abscess (%)				
single lobe	120(88.9)	76(87.4)	44(91.7)	0.446
multiple lobes	15(11.1)	11(12.6)	4(8.3)	0.446
Comorbidity (%)				
CHF	6(4.4)	2(2.3)	4(8.3)	0.103
CVA	5(3.7)	2(2.3)	3(6.3)	0.245
peripheral vascular disease	2(1.5)	1(1.2)	1(2.1)	0.673
COPD	1(0.7)	1(1.1)	0(0)	0.456
chronic liver disease	13(9.6)	7(8.0)	6(12.5)	0.401
chronic renal disease	5(3.7)	3(3.4)	2(4.2)	0.832
diabetes mellitus	24(17.8)	12(13.8)	12(25.0)	0.103
non-metastatic solid tumor	19(14.1)	9(10.3)	10(20.8)	0.093
metastatic solid tumor	3(2.2)	1(1.1)	2(4.2)	0.255
hematologic malignancy	2(1.5)	1(1.2)	1(2.1)	0.673
pre-existing hemiplegia	11(8.2)	1(1.1)	10(20.8)	< 0.001
CCI (mean±SD	2.44±2.04	1.88±1.7	3.48±2.23	< 0.001
Laboratory data (mean±SD)				
WBC (× 10^3/μL)	10.9±14.6	11.4±17.5	10±5.4	0.721
PLT (× 10^3/μL)	272.9±120.3	281.9±120.6	255.3±119.2	0.100
BUN (mg/dL)	16.5 ± 14.3	15.1 ±12.2	19.3 ± 17.2	0.087
Cr (mg/dL)	0.9±0.6	0.9±0.7	0.9±0.6	0.633
SOFA (mean±SD)	1.8±2.0	1.2±1.5	3.0±2.2	< 0.001
Treatment modality (%)				
open surgery + antibiotics	35(25.9)	25(28.7)	10(20.8)	0.316
drainage + antibiotics	74(54.8)	44(50.6)	30(62.5)	0.183
antibiotics only	26(19.3)	18(20.7)	8(16.7)	0.570

SD, standard deviation; CHF, congestive heart failure; CVA, cerebrovascular attack; COPD, chronic obstructive pulmonary disease; CCI, Charlson comorbidity index; SOFA, Sequential Organ Failure Assessment; WBC, white blood cells; PLT, platelets; BUN, blood urea nitrogen; Cr, creatinine.

https://doi.org/10.1371/journal.pone.0257541.t002

Table 3. Bacteria isolated from patients with culture-positive brain abscesses.

Causative Organism	No. of Cases (%) (n = 44)
Gram-positive	29 (65.9)
α-Streptococcus	8
Streptococcus anginosus group	5
Coagulase-negative *Staphylococcus* sp.	5
Staphylococcus aureus	5
Bacillus sp.	1
Lactobacillus	1
Enterococcus faecium	1
Parvimonas mica	1
Clostridium bifermentans	1
Nocardia sp.	1
Gram-negative	15 (34.1)
Klebsiella pneumoniae	8
Escherichia coli	2
Enterobacter cloacae	2
Haemophilus aphrophilus	1
Pseudomonas aeruginosa	1
Fusobacterium nucleatum	1

https://doi.org/10.1371/journal.pone.0257541.t003

univariate analyses, age ($p = 0.018$), headache ($p = 0.001$), altered mental status ($p < 0.001$), pre-existing hemiplegia ($p = 0.004$), higher SOFA ($p < 0.001$), and higher CCI ($p < 0.001$) were significantly associated with unfavorable outcomes. In the multivariate analysis, higher SOFA [$p < 0.001$, odds ratio (OR) 1.523, 95% confidence interval (CI) 1.206–1.925], pre-existing hemiplegia ($p = 0.049$, OR 7.652, 95% CI 1.850–68.919), and higher CCI ($p = 0.028$, OR 1.279, 95% CI 1.027–1.594) were independent risk factors for unfavorable clinical outcomes in patients with brain abscess (Table 4).

Discussion

We found that independent risk factors for unfavorable clinical outcomes in patients with brain abscess were higher SOFA, pre-existing hemiplegia, and higher CCI. Previous studies have reported some prognostic factors for brain abscess. Zhang *et al.* reported that female gender was associated with a poor outcome, while Larsen *et al.* reported that a low Glasgow coma scale score on admission and comorbidities were related to a poor outcome [2, 26].

Table 4. Uni- and multivariate analysis of risk factors for unfavorable clinical outcomes in patients with brain abscess.

Variables	Univariate			Multivariate		
	OR	95% CI	p-value	OR	95% CI	p-value
Age (per 1-year increase)	**1.034**	**1.006–1.063**	**0.018**	**1.003**	**0.960–1.048**	**0.905**
Headache	**0.525**	**0.999–1.002**	**0.001**	**1.000**	**0.998–1.001**	**0.648**
Altered mental status	**4.416**	**1.997–9.767**	**<0.001**	**2.384**	**0.734–7.739**	**0.121**
Pre-existing hemiplegia	**22.368**	**2.764–181.011**	**0.004**	**7.652**	**1.850–68.919**	**0.049**
CCI (per 1 increase)	**1.652**	**1.299–2.102**	**<0.001**	**1.279**	**1.027–1.594**	**0.028**
SOFA (per 1 increase)	**1.578**	**1.253–1.987**	**<0.001**	**1.523**	**1.206–1.925**	**<0.001**

OR, odds ratio; CI, confidence interval; CCI, Charlson comorbidity index; SOFA, Sequential Organ Failure Assessment.

https://doi.org/10.1371/journal.pone.0257541.t004

In this study, a higher SOFA was an independent risk factor for an unfavorable outcome. The SOFA is used to assess organ dysfunction and failure. Several studies have addressed the relationship between unfavorable outcomes of central nervous system (CNS) infection and the SOFA score [27–29]. An early change in SOFA is a useful early prognostic marker for sepsis and mortality. Nakashima *et al*. found that a high SOFA score was associated with mortality in patients with critical illness, including CNS infection [30, 31]. In a meta-analysis of 25 studies, De Grooth *et al*. revealed a strong association between the SOFA and unfavorable outcomes [25, 32, 33]. Ferreira *et al*. showed that serial evaluation of the SOFA during the first 48 hours could predict the outcome of critically ill patients [34]. The SOFA is a good prognostic measure in patients with severe illness, including brain abscess.

Pre-existing hemiplegia was also an independent risk factor for an unfavorable outcome. Patients with hemiplegia as a result of traumatic accidents, strokes, or brain tumors prior to brain abscess have impaired mobility. McLean *et al*. reported that less mobile patients had low lean mass, reduced physical strength, and an elevated mortality rate [35–37]. If damaged brain tissue is exposed to an infectious agent, the damage is exacerbated, thus increasing the severity of neurological deficits [38–40]. It is not clear why patients with impaired mobility are more susceptible to neurological deficits after brain abscess. However, it is likely that their low stamina and damaged brain tissue increase the probability of sequelae after treatment for brain abscess.

A higher CCI was an independent risk factor for an unfavorable outcome in this study. The CCI is a widely validated simple measure of the prognosis in numerous medical conditions, with significant relationships between the CCI and prognosis in multiple diseases [41–44]. A recent large study reported that the CCI predicted mortality in patients with brain abscess in Denmark from 1982 through 2016 [45].

This study had several limitations inherent to its retrospective design. As with any observational study, unmeasured confounders may have influenced the findings. Also, the single-center design (one tertiary referral hospital) led to the selection of severe cases only. A multicenter study including a large patient sample is needed.

In conclusion, in this study, a higher SOFA, pre-existing hemiplegia, and higher CCI were significantly associated with unfavorable treatment outcomes in patients with brain abscess. Therefore, we need to consider treatment carefully in patients with brain abscess who have these predictors.

Author Contributions

Conceptualization: Yun Suk Cho, Nam Su Ku.

Data curation: Yun Suk Cho, Nam Su Ku.

Formal analysis: Yun Suk Cho, Nam Su Ku.

Funding acquisition: Nam Su Ku.

Investigation: Yun Suk Cho, Nam Su Ku.

Methodology: Yun Suk Cho, Nam Su Ku.

Project administration: Yun Suk Cho, Nam Su Ku.

Resources: Yun Suk Cho, Nam Su Ku.

Software: Nam Su Ku.

Supervision: Yu Jin Sohn, Jong Hoon Hyun, Yae Jee Baek, Moo Hyun Kim, Jung Ho Kim, Jin Young Ahn, Su Jin Jeong, Nam Su Ku, Jun Yong Choi, Joon-Sup Yeom, Young Goo Song.

Validation: Nam Su Ku.

Visualization: Nam Su Ku.

Writing – original draft: Yun Suk Cho.

Writing – review & editing: Yun Suk Cho, Nam Su Ku.

References

1. Nicolosi A, Hauser WA, Musicco M, Kurland LT. Incidence and prognosis of brain abscess in a defined population: Olmsted County, Minnesota, 1935–1981. Neuroepidemiology. 1991; 10:122–31. https://doi.org/10.1159/000110257 PMID: 1922645
2. Helweg-Larsen J, Astradsson A, Richhall H, Erdal J, Laursen A, Brennum J. Pyogenic brain abscess, a 15 year survey. BMC Infect Dis. 2012; 12:332. https://doi.org/10.1186/1471-2334-12-332 PMID: 23193986
3. Brouwer MC, van de Beek D. Epidemiology, diagnosis, and treatment of brain abscesses. Curr Opin Infect Dis. 2017; 30:129–34. https://doi.org/10.1097/QCO.0000000000000334 PMID: 27828809
4. Brouwer MC, Tunkel AR, McKhann GM, 2nd, van de Beek D. Brain abscess. N Engl J Med. 2014; 371:447–56. https://doi.org/10.1056/NEJMra1301635 PMID: 25075836
5. Adukauskiene D, Bivainyte A, Radaviciūte E. Cerebral edema and its treatment. Medicina (Kaunas). 2007; 43:170–6. PMID: 17329953
6. Carpenter JP, Lane JS 3rd, Trani J, Hussain S, Healey C, Hashemi H, et al. Proper technical procedures improved outcomes in a retrospective analysis of EVAS FORWARD IDE trial 3-year results. J Vasc Surg. 2020; 72:918–30. https://doi.org/10.1016/j.jvs.2019.11.039 PMID: 32035772
7. Sharma R, Mohandas K, Cooke RP. Intracranial abscesses: changes in epidemiology and management over five decades in Merseyside. Infection. 2009; 37:39–43. https://doi.org/10.1007/s15010-008-7359-x PMID: 19139814
8. Menon S, Bharadwaj R, Chowdhary A, Kaundinya DV, Palande DA. Current epidemiology of intracranial abscesses: a prospective 5 year study. J Med Microbiol. 2008; 57:1259–68. https://doi.org/10.1099/jmm.0.47814-0 PMID: 18809555
9. Amornpojnimman T, Korathanakhun P. Predictors of clinical outcomes among patients with brain abscess in Thailand. J Clin Neurosci. 2018; 53:135–9. https://doi.org/10.1016/j.jocn.2018.04.059 PMID: 29716805
10. Buonaguro A, Colangelo M, Daniele B, Cantone G, Ambrosio A. Neurological and behavioral sequelae in children operated on for brain abscess. Child's Nerv Syst. 1989; 5:153–5. https://doi.org/10.1007/BF00272117 PMID: 2758427
11. Nielsen H, Harmsen A, Gyldensted C. Cerebral abscess. A long-term follow-up. Acta Neurol Scand. 1983; 67:330–7. https://doi.org/10.1111/j.1600-0404.1983.tb03150.x PMID: 6613520
12. Sonneville R, Ruimy R, Benzonana N, Riffaud L, Carsin A, Tadié JM, et al. An update on bacterial brain abscess in immunocompetent patients. Clin Microbiol Infect. 2017; 23:614–20. https://doi.org/10.1016/j.cmi.2017.05.004 PMID: 28501669
13. Mathisen GE, Johnson JP. Brain abscess. Clin Infect Dis. 1997:763–79. https://doi.org/10.1086/515541 PMID: 9356788
14. Brouwer MC, Coutinho JM, van de Beek D. Clinical characteristics and outcome of brain abscess: systematic review and meta-analysis. Neurology. 2014; 82:806–13. https://doi.org/10.1212/WNL.0000000000000172 PMID: 24477107
15. Tattevin P, Bruneel F, Clair B, Lellouche F, de Broucker T, Chevret S, et al. Bacterial brain abscesses: a retrospective study of 94 patients admitted to an intensive care unit (1980 to 1999). Am J Med. 2003; 115:143–6. https://doi.org/10.1016/s0002-9343(03)00292-4 PMID: 12893401
16. Teasdale GM, Pettigrew LE, Wilson JT, Murray G, Jennett B. Analyzing outcome of treatment of severe head injury: a review and update on advancing the use of the Glasgow Outcome Scale. J Neurotrauma. 1998; 15:587–97. https://doi.org/10.1089/neu.1998.15.587 PMID: 9726258
17. Carey ME, Chou SN, French LA. Long-term neurological residua in patients surviving brain abscess with surgery. J Neurosurg. 1971; 34:652–6. https://doi.org/10.3171/jns.1971.34.5.0652 PMID: 5090943
18. Rousseaux M, Lesoin F, Destee A, Jomin M, Petit H. Long term sequelae of hemispheric abscesses as a function of the treatment. Acta Neurochir (Wien). 1985; 74:61–7. https://doi.org/10.1007/BF01413280 PMID: 3976448

19. Harris LF, Maccubbin DA, Triplett JN Jr., Haws FP. Brain abscess: recent experience at a community hospital. South Med J. 1985; 78:704–7. https://doi.org/10.1097/00007611-198506000-00022 PMID: 4002002

20. Bodilsen J, Dalager-Pedersen M, van de Beek D, Brouwer MC, Nielsen H. Incidence and mortality of brain abscess in Denmark: a nationwide population-based study. Clin Microbiol Infect. 2020; 26:95–100. https://doi.org/10.1016/j.cmi.2019.05.016 PMID: 31158518

21. Thygesen SK, Christiansen CF, Christensen S, Lash TL, Sørensen HT. The predictive value of ICD-10 diagnostic coding used to assess Charlson comorbidity index conditions in the population-based Danish National Registry of Patients. BMC Med Res Methodol. 2011; 11:83. https://doi.org/10.1186/1471-2288-11-83 PMID: 21619668

22. Lange N, Berndt M, Jörger AK, Wagner A, Wantia N, Lummel N, et al. Clinical characteristics and course of primary brain abscess. Acta Neurochir (Wien). 2018; 160:2055–62. https://doi.org/10.1007/s00701-018-3633-6 PMID: 30069602

23. Vincent JL, de Mendonça A, Cantraine F, Moreno R, Takala J, Suter PM, et al. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. Crit Care Med. 1998; 26:1793–800. https://doi.org/10.1097/00003246-199811000-00016 PMID: 9824069

24. Lambden S, Laterre PF, Levy MM, Francois B. The SOFA score-development, utility and challenges of accurate assessment in clinical trials. Crit Care. 2019; 23:374. https://doi.org/10.1186/s13054-019-2663-7 PMID: 31775846

25. de Grooth HJ, Geenen IL, Girbes AR, Vincent JL, Parienti JJ, Oudemans-van Straaten HM. SOFA and mortality endpoints in randomized controlled trials: a systematic review and meta-regression analysis. Crit Care. 2017; 21:38. https://doi.org/10.1186/s13054-017-1609-1 PMID: 28231816

26. Zhang C, Hu L, Wu X, Hu G, Ding X, Lu Y. A retrospective study on the aetiology, management, and outcome of brain abscess in an 11-year, single-centre study from China. BMC Infect Dis. 2014; 14:311. https://doi.org/10.1186/1471-2334-14-311 PMID: 24903315

27. Karakike E, Kyriazopoulou E, Tsangaris I, Routsi C, Vincent JL, Giamarellos-Bourboulis EJ. The early change of SOFA score as a prognostic marker of 28-day sepsis mortality: analysis through a derivation and a validation cohort. Crit Care. 2019; 23:387. https://doi.org/10.1186/s13054-019-2665-5 PMID: 31783881

28. Oda S, Hirasawa H, Sugai T, Shiga H, Nakanishi K, Kitamura N, et al. Comparison of Sepsis-related Organ Failure Assessment (SOFA) score and CIS (cellular injury score) for scoring of severity for patients with multiple organ dysfunction syndrome (MODS). Intensive Care Med. 2000; 26:1786–93. https://doi.org/10.1007/s001340000710 PMID: 11271086

29. Gholipour Baradari A, Sharifi H, Firouzian A, Daneshiyan M, Aarabi M, Talebiyan Kiakolaye Y, et al. Comparison of Proposed Modified and Original Sequential Organ Failure Assessment Scores in Predicting ICU Mortality: A Prospective, Observational, Follow-Up Study. Scientifica (Cairo). 2016; 2016:7379325. https://doi.org/10.1155/2016/7379325 PMID: 28116220

30. Nakashima T, Miyamoto K, Shimokawa T, Kato S, Hayakawa M. The Association Between Sequential Organ Failure Assessment Scores and Mortality in Patients With Sepsis During the First Week: The JSEPTIC DIC Study. J Intensive Care Med. 2018: 35:656–62. https://doi.org/10.1177/0885066618775959 PMID: 29764273

31. Nakashima T, Miyamoto K, Shimokawa T, Kato S, Hayakawa M. The Association Between Sequential Organ Failure Assessment Scores and Mortality in Patients With Sepsis During the First Week: The JSEPTIC DIC Study. J Intensive Care Med. 2020; 35:656–62. https://doi.org/10.1177/0885066618775959 PMID: 29764273

32. Garbero RF, Simões AA, Martins GA, Cruz LVD, von Zuben VGM. SOFA and qSOFA at admission to the emergency department: Diagnostic sensitivity and relation with prognosis in patients with suspected infection. Turk J Emerg Med. 2019; 19:106–10. https://doi.org/10.1016/j.tjem.2019.05.002 PMID: 31321343

33. Song JU, Sin CK, Park HK, Shim SR, Lee J. Performance of the quick Sequential (sepsis-related) Organ Failure Assessment score as a prognostic tool in infected patients outside the intensive care unit: a systematic review and meta-analysis. Crit Care. 2018; 22:28. https://doi.org/10.1186/s13054-018-1952-x PMID: 29409518

34. Ferreira FL, Bota DP, Bross A, Mélot C, Vincent JL. Serial evaluation of the SOFA score to predict outcome in critically ill patients. JAMA. 2001; 286:1754–8. https://doi.org/10.1001/jama.286.14.1754 PMID: 11594901

35. McLean RR, Shardell MD, Alley DE, Cawthon PM, Fragala MS, Harris TB, et al. Criteria for Clinically Relevant Weakness and Low Lean Mass and Their Longitudinal Association With Incident Mobility

Impairment and Mortality: The Foundation for the National Institutes of Health (FNIH) Sarcopenia Project. J Gerontol A Biol Sci Med Sci. 2014; 69:576–83. https://doi.org/10.1093/gerona/glu012 PMID: 24737560

36. Fried LP, Ferrucci L, Darer J, Williamson JD, Anderson G. Untangling the Concepts of Disability, Frailty, and Comorbidity: Implications for Improved Targeting and Care. J Gerontol A Biol Sci Med Sci. 2004; 59:255–63. https://doi.org/10.1093/gerona/59.3.m255 PMID: 15031310

37. Sinn CJ, Heckman G, Poss JW, Onder G, Vetrano DL, Hirdes J. A comparison of 3 frailty measures and adverse outcomes in the intake home care population: a retrospective cohort study. CMAJ Open. 2020; 8:E796–E809. https://doi.org/10.9778/cmajo.20200083 PMID: 33262118

38. Sveinsson OA, Asgeirsson H, Olafsson IH. Brain abscess—overview. Laeknabladid. 2013; 99:25–31. https://doi.org/10.17992/lbl.2013.01.478 PMID: 23341403

39. Yen JK, Rhodes GR, Bourke RS, Powers SR Jr., Newell JC, Popp AJ. Delayed impairment of arterial blood oxygenation in patients with severe head injury: preliminary report. Surg Neurol. 1978; 9:323–7. PMID: 675490

40. Kim HJ, Tsao JW, Stanfill AG. The current state of biomarkers of mild traumatic brain injury. JCI Insight [Internet] 2018 Jan [cited 2020 Dec 30]; 3. Available from: https://doi.org/10.1172/jci.insight.97105 PMID: 29321373

41. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987; 40:373–83. https://doi.org/10.1016/0021-9681(87)90171-8 PMID: 3558716

42. D'Hoore W, Sicotte C, Tilquin C. Risk adjustment in outcome assessment: the Charlson comorbidity index. Methods Inf Med. 1993; 32:382–7. PMID: 8295545

43. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. J Clin Epidemiol. 1994; 47:1245–51. https://doi.org/10.1016/0895-4356(94)90129-5 PMID: 7722560

44. Poses RM, McClish DK, Smith WR, Bekes C, Scott WE. Prediction of survival of critically ill patients by admission comorbidity. J Clin Epidemiol. 1996; 49:743–7. https://doi.org/10.1016/0895-4356(96)00021-2 PMID: 8691223

45. Bodilsen J, Dalager-Pedersen M, van de Beek D, Brouwer MC, Nielsen H. Incidence and mortality of brain abscess in Denmark: a nationwide population-based study. Clin Microbiol Infect. 2020; 26:95–100. https://doi.org/10.1016/j.cmi.2019.05.016 PMID: 31158518