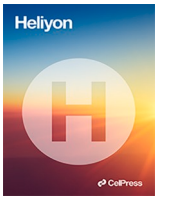
Heliyon 10 (2024) e25918

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon



Research article

Screening and differential diagnosis of delirium in neurointensive stroke patients

Lucia Bakošová [a,b,*], David Kec [a,b], Miroslav Škorňa [a,b], René Jura [a,b], Zdeněk Kundrata [a,b], Milena Košťálová [a,b], Josef Bednařík [a,b]

[a] Faculty of Medicine, Masaryk University, Kamenice 5, Brno, 62500, Czech Republic
[b] Department of Neurology, The University Hospital Brno, Jihlavská 20, Brno, 62500, Czech Republic

ARTICLE INFO

Keywords:
Delirium
Stroke
CAM-ICU
ICDSC
Nonconvulsive status epilepticus
Aphasia

ABSTRACT

Diagnosing delirium in neurointensive care is difficult because symptoms of delirium, such as inappropriate speech, may be related to aphasia due to primary brain injury. Therefore, validated screening tools are needed.

The aim of this study was to compare two Czech versions of already validated screening tools - the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) and the Intensive Care Delirium Screening Checklist (ICDSC) - in a cohort of acute stroke patients. We also aimed to assess the pitfalls of delirium detection in the context of non-convulsive status epilepticus (NCSE). We analysed 138 stroke patients admitted to the neurological intensive care unit (ICU) or stroke unit. According to expert judgement, which was used as the gold standard, 38 patients (27.54%) developed delirium. The sensitivity and specificity of the ICDSC were 91.60% and 95.33%, respectively, and the positive and negative predictive values were 76.76% and 98.54%, respectively. Similarly, the sensitivity and specificity of CAM-ICU were 75.63% and 96.74%, respectively, and the positive and negative predictive values were 79.65% and 95.93%, respectively. We did not detect an episode of NCSE mimicking delirium in any of our stroke patients who were judged to be delirious by expert assessment. Our results suggest that the ICDSC may be a more suitable tool for delirium screening than the CAM-ICU in patients with neurological deficit. NCSE as a mimic of delirium seems to be less common in the acute phase of stroke than previously reported.

1. Introduction

Delirium is a clinical syndrome represented by a combination of symptoms defined in the 5th edition of the American Psychiatric Association's Diagnostic and Statistical Manual (DSM-5) [1] and in the 11th edition of the International Statistical Classification of Diseases and Related Health Problems (ICD-11) [2]. It is an acute disorder of consciousness and cognition characterised by fluctuating mental status, inattention, altered level of consciousness and disorganised thinking, and is associated with acute encephalopathy [3].

Detection of delirium in the intensive care unit (ICU) can be problematic. It is even more challenging in the neurointensive care unit

* Corresponding author. Jihlavská 20, Brno, 62500, Czech Republic.
E-mail addresses: Bakosova.Lucia@fnbrno.cz (L. Bakošová), Kec.David@fnbrno.cz (D. Kec), Skorna.Miroslav2@fnbrno.cz (M. Škorňa), Jura.Rene@fnbrno.cz (R. Jura), Kundrata.Zdenek@fnbrno.cz (Z. Kundrata), Kostalova.Milena@fnbrno.cz (M. Košťálová), Bednarik.Josef@fnbrno.cz (J. Bednařík).

https://doi.org/10.1016/j.heliyon.2024.e25918
Received 28 July 2023; Received in revised form 9 January 2024; Accepted 5 February 2024
Available online 10 February 2024

because the symptoms of delirium may overlap with those of the primary brain injury. As a result, many cases of delirium may go underdiagnosed, or symptoms of brain injury may mimic delirium [4]. The incidence of delirium after stroke varies from 13% to 48% [5], which is higher than the 10%–25% incidence of delirium in patients admitted to general medical wards [6]. Delirium, which is associated with higher morbidity and mortality [7,8], has a high impact on stroke patients and therefore regular screening for the presence of delirium is recommended [9]. Two screening tools, The Confusion Assessment Method for the ICU and The Intensive Care Delirium Screening Checklist, show both high sensitivity and specificity in critically ill patients and can be used as screening tests for the diagnosis of delirium in the ICU [10]. Although studies that compared ICDSC against CAM-ICU in neurological patients preferred ICDSC [11,12], the ideal screening tool is still lacking. The ICDSC validation study included patients with neurological deficits [13], whereas the CAM-ICU validation study excluded all patients with neurological deficits [14]. Although the validation study for CAM-ICU in neurological patients after stroke showed promising results [15], it also did not include patients with severe neurological deficits. Structural impairment can lead to altered cognition [16], and tests of inattention and disorganised thinking can be affected by aphasia or reduced alertness, so the inclusion of neurological patients in validation studies results in lower sensitivity and specificity. Fluent aphasia may mimic delirium and may be difficult to a less skilled physicians to distinguish. Screening test results thus may be falsely positive [15]. Another diagnostic challenge is the differential diagnosis of delirium and non-convulsive status epilepticus (NCSE). Clinical features of NCSE can be difficult to distinguish from normal behaviour, as behavioural changes can be very discrete [17] and may be mistaken for the more common delirium. Diagnosis may also be influenced by the level of altered consciousness and neurological deficit. Electroencephalography (EEG) is the method of choice for confirming or rejecting the diagnosis of NCSE using the Salzburg criteria [18]. These criteria directly define the characteristics of the abnormalities recorded during the EEG examination and also include other relevant circumstances such as clinical correlates and response to therapeutic testing [18]. In our study, we screened a cohort of patients with acute stroke for delirium by comparing two screening tests with an expert assessment based on the DSM-5 delirium criteria and we focused on the differential diagnosis of delirium against aphasia and non-convulsive status epilepticus.

We thus felt that a further comparative study of these screening tools in a larger, more homogeneous stroke population and focusing on some of the pitfalls in detecting delirium, such as aphasia and NCSE, is needed.

2. Methods

2.1. Study sample

This prospective single-centre observational study was conducted at the Department of Neurology, University Hospital Brno from January to October 2021, and from January to September 2022. All patients admitted to the neuro-ICU or stroke unit with ischaemic or haemorrhagic stroke, with the first assessment within 24 h of admission and expected stay of 48 h or more, were screened for inclusion criteria. We excluded patients with pre-existing brain injury including previous stroke, head injury, arteriovenous malformation and hydrocephalus. We used information from relatives and from medical records available in our hospital's data system. Patients whose first language was not Czech, patients who remained comatose during their hospital stay and mechanically ventilated patients were excluded. We also excluded patients with severe brain injury after stroke who had a palliative care treatment plan. The evaluation was carried out every day except weekends and holidays.

2.2. Setting

All included patients were initially admitted to Neuro-ICU or Stroke unit with the possibility of 24-h monitoring of vital functions. We continued with the evaluation even after moving patients to the ward until the end of hospitalisation. During the monitoring, we applied the ABCDEF bundle [9] as a possible delirium prevention. We also assessed daily Sequential Organ Failure Assessment (SOFA), including the level of consciousness using the Glasgow Coma Scale (GCS). We also screened for Systemic Inflammatory Response Syndrome (SIRS) and classified as "positive" those patients (n = 32, 23.2%) who met at least two criteria (body temperature above 38 or below 36 °C, heart rate above 90 beats per minute, respiratory rate above 20 breaths per minute or partial pressure of CO2 less than 32 mmHg, leukocyte count greater than 12,000 or less than 4000 per microlitre or greater than 10% immature form) for at least one day during the follow up [19]. In addition, we completed the Blessed Dementia Rating Scale [20] based on information from relatives to determine probable dementia.

2.3. Data collection

2.3.1. Expert assessment

We performed daily assessment of delirium conducted by neurology specialists with over 10 years of experience (RJ, SP, MŠ), who applied the criteria for delirium presented in the DSM-5. The expert obtained information from nurses, hospital charts and experienced examination of the patients in the morning hours, usually around 8 a.m. The expert labelled the patient as either delirium negative, positive or unable to assess (UTA). The evaluation was performed independently from the screening evaluation.

2.3.2. Screening tests

For the delirium screening CAM-ICU and ICDSC screening tests were used. The Czech version of the CAM-ICU [14] was already available and validated in the cohort of neurological patients [15]. The validation study was performed by the team in our Department of Neurology. The ICDSC was translated into Czech and back into English by the authors, using forward-backward translation. The

translated version was then approved by the author of the instrument (Y. Skrobik) [13]. As the ICDSC contains items which can be usually detected during a longer period of time, the nurses' cooperation was necessary. The nurses were instructed and given the list of items concerning delirium to detect during their 12-h shift. They were instructed to write these items, including the Richmond agitation sedation scale (RASS) in the chart when present. We screened daily for delirium in patients in our study using both screening tests during their whole hospitalisation at the Department of Neurology, we continued screening also when the patients were moved to the ward. The screening was performed by the junior physician (LB) daily within 2 h apart from the expert delirium assessment. The young physician was blinded to the result of the expert evaluation until after screening was performed.

2.3.3. Aphasia

Every admitted patient with a stroke was screened for aphasia by a skilled neurointensivist. Patients with suspicion of aphasia were then examined by a skilled speech therapist (MK, NL) and the Mississippi aphasia screening test (MAST) [21] was performed to evaluate the level of speech disturbance.

2.3.4. Nonconvulsive status epilepticus

In patients who were diagnosed by the expert as "delirium positive", a 10-min native electroencephalogram (EEG) was performed to rule in /out NCSE. Every electroencephalography result was then evaluated by Salzburg criteria for NCSE [22]. According the Salzburg criteria scoring rules, the therapeutic test by intravenous application of anti-seizure medication would be performed, when statements "possible NCSE" or definitive "NCSE" were considered.

2.4. Statistical analysis

Standard descriptive statistics were used for patient characteristics. Categorical variables were compared between groups of patients with delirium or without delirium using the Chi-square test or Fisher Exact test, as appropriate. Differences between continuous variables were analysed by the Mann-Whitney *U* test. The performance of ICDSC and CAM-ICU was compared with the expert diagnosis, which was considered as the reference standard. Using a two-by-two frequency table, we calculated sensitivity, specificity, positive and negative predictive value and overall accuracy. We used two different methods to calculate sensitivity and specificity, the first being to evaluate each day separately. At the same time, we calculated sensitivity and specificity on a patient-by-patient basis, considering even one true delirium-positive day as a true delirium-positive patient. The same parameters were then calculated

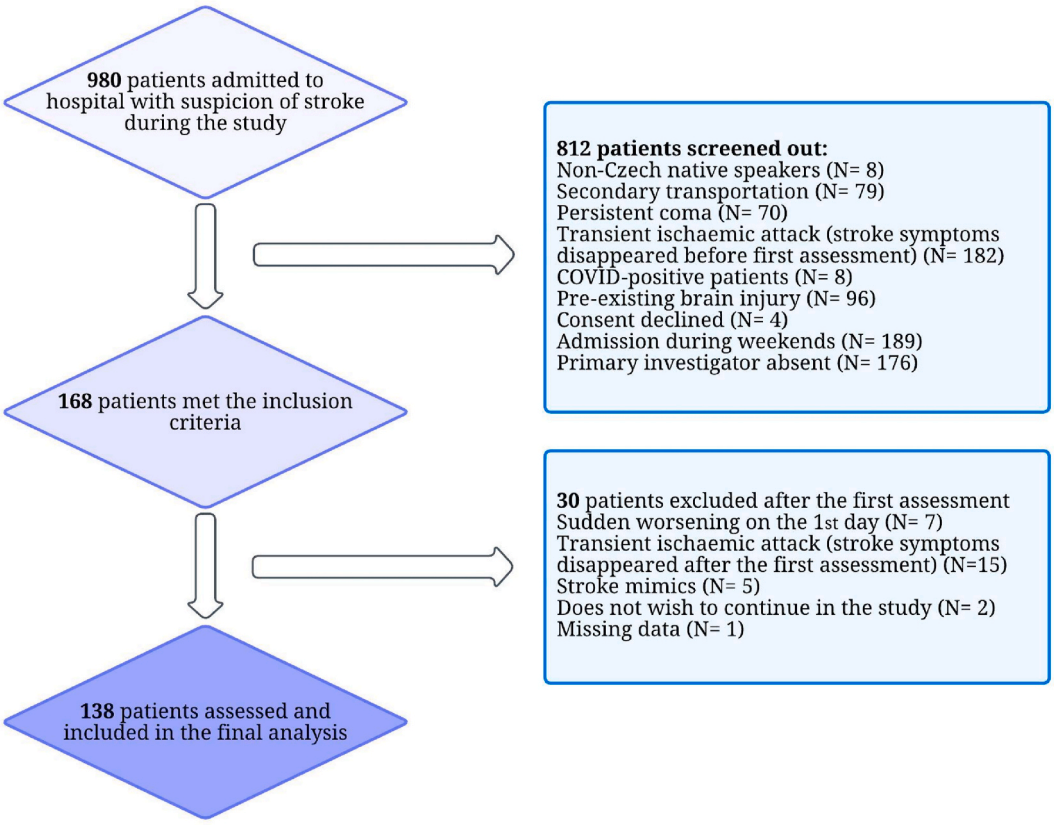


Fig. 1. Patient flow chart.

separately for the cohort of patients with aphasia. All hypotheses testing was two-sided, and the threshold of significance was set at 0.05. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 28.

2.5. Ethics

The study was approved by the Ethics Committee of the University Hospital Brno, and also by the Ethics Committee of the Faculty of Medicine, Masaryk University. The written consent was obtained from each patient directly, or in the case of inability of decision-making, we addressed the closest relative, in accordance with the Ethics Committee approval.

3. Results

During the data collection period of 19 months (1–10/2021 and 1–9/2022), 980 patients were admitted to our Neuro-ICU or Stroke unit with stroke symptoms. We enrolled 168 patients, who met the inclusion criteria, of whom 30 were excluded, leaving 138 (82.14%) for the final analysis (Fig. 1).

All of the remaining patients in our study cohort were white, the mean age was 74.56 years (SD, 11.5 years), and 55.1% were male. Ischemic aetiology was the cause of 89.9% (n = 124) of strokes and the mean National Institute of Health Stroke Scale (NIHSS) at admission was 6.72 (SD, 5.16) (Table 1).

Other collected data included possible risk factors of delirium and risk factors of stroke, such as SOFA, GCS, SIRS.

Aphasia was present in 37 patients (26.8%) and all patients with confirmed aphasia were evaluated by a skilled speech therapist using the Mississippi aphasia screening test (MAST). The median MAST value at the admission was 46.00 (range 0–94) and the median value at the end of the follow-up was 79.00 (range 0–98). Of these thirty-seven patients, 16 developed delirium (42.10%) according to expert evaluation.

According to DSM-5 criteria and expert evaluation, 38 patients (27.54%) developed delirium at some point of their hospitalisation (Fig. 2).

The final number of screening evaluation days performed was 846. Twenty-one evaluation days were reported as “unable to assess” (UTA) due to low level of arousal (RASS -4 or −5). Evaluation days rated as UTA were excluded from the final analysis. In four of our patients we had to stop the assessment due to sudden worsening, which led to the need of ventilation support (brainstem stroke, sepsis, heart failure, pulmonary embolism). None of these patients presented with delirium.

The sensitivity and specificity of the ICDSC, when evaluated each day separately, were 91.60% (CI 85.09%–95.90%) and 95.33% (CI 93.50%–96.76%), respectively, and the positive and negative predictive values were 76.76% (CI 70.21%–82.24%) and 98.54% (CI

Table 1
Patient characteristics.

Characteristics	All patients (n = 138)	Delirium present (n = 38)	Delirium not present (N = 100)	P value[d]
Age, mean (SD) median (range)	74.56 (11.5)	77.61 (11.66)	73.40 (11.30)	0.042[c]
	76.00 (37–96)	79.50 (44–96)	75.50 (37–92)	
Male, n (%)	76 (55.1%)	17 (44.7%)	59 (59.0%)	0.180[a]
Comorbidities				
Prior stroke (no clinics) n (%)	61 (44.2%)	25 (65.8%)	36 (36.0%)	0.002[a]
Cognitive impairment, n (%)	27 (19.6%)	13 (34.2%)	14 (14.0%)	0.01[a]
SOFA score ≥2, n (%)	45 (32.6%)	19 (50.0%)	26 (26.0%)	0.009[a]
Hypertension, n (%)	118 (85.5%)	32 (84.2%)	86 (86.0%)	1.00[a]
Diabetes, n (%)	39 (28.7%)	11 (28.9%)	28 (28.0%)	1.00[a]
Atrial fibrilation, n (%)	48 (34.8%)	20 (52.6%)	28 (28.0%)	0.009[a]
Overweight, n (%)	81 (58.7%)	18 (47.4%)	63 (63.0%)	0.122[a]
BMI, median (range)	25.95 (16.2–42.8)	24.90 (16.2–35.6)	26.25 (16.4–42.8)	0.258[c]
History of smoking, n (%)	50 (36.2%)	13 (34.2%)	37 (37.0%)	0.844[a]
Heavy alcohol use, n (%)	44 (31.9%)	11 (28.9%)	11 (11.0%)	0.688[a]
Stroke characteristics				
NIHSS median (range)	5.00 (0–22)	8.50 (0–22)	4.00 (0–20)	0.002[c]
Hemispheral lesion				0.691[a]
The left hemisphere, n (%)	56 (40.6%)	18 (13.0%)	38 (27.5%)	
Right hemisphere, n (%)	65 (47.1%)	18 (13.0%)	47 (34,0%)	
Primary lesion				0.022[b]
Ischemic stroke, n (%)	124 (89.9%)	30 (78.9%)	94 (94.0%)	
Hemorrhagic stroke, n (%)	14 (10.1%)	8 (21.1%)	6 (6.0%)	
Aphasia, n (%)	37 (26.8%)	16 (42.1%)	21 (21.0%)	0.018[a]
SIRS criteria present, n (%)	32 (23.2%)	20 (52.6%)	12 (12.0%)	<0.001[a]

Abbreviations: SOFA, Sequential Organ Failure Assessment; BMI, Body Mass Index; NIHSS, National Institutes of Health Stroke Scale; SIRS, Systemic Inflammatory Response Syndrome.

[a] Chi-square test.

[b] Fisher’s test.

[c] Mann-Whitney *U* test.

[d] p values for the comparison between groups of patients with delirium and without delirium.

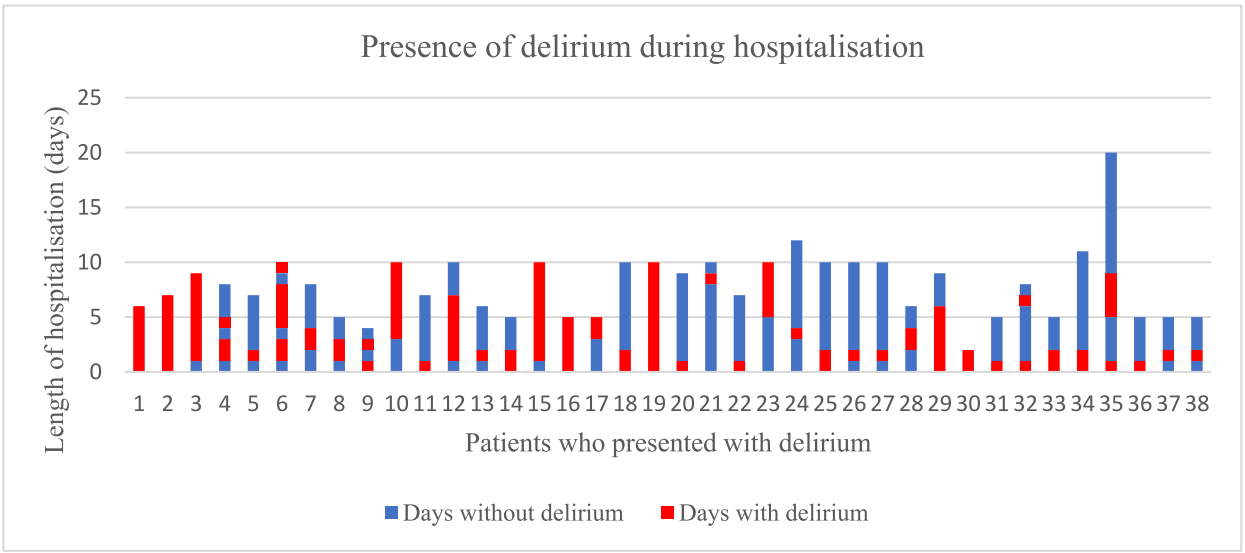


Fig. 2. Presence of delirium during hospitalisation.

97.38%–99.19%), respectively. Similarly, the sensitivity and specificity of the CAM-ICU were 75.63% (CI 66.91%–83.03%) and 96.74% (CI 95.15%–97.92%), the positive and negative predictive values were 79.65% (CI 72.10%–85.56%) and 95.93% (CI 94.49%–97.00%) (Table 2). The same parameters were then calculated separately for patients with aphasia (Table 3). We also calculated sensitivity and specificity on a patient-by-patient basis. In this case, the sensitivity and specificity of the ICDSC were 97.37% (CI 86.19%–99.93%) and 95.00% (CI 88.72%–98.36%), respectively, and the positive and negative predictive values were 88.10% (CI 74.37%–96.02%) and 98.96% (CI 94.33%–99.97%), respectively. Similarly, the sensitivity and specificity of the CAM-ICU were 86.84% (CI 71.91%–95.59%) and 98.00% (CI 92.96%–99.76%), and the positive and negative predictive values were 94.29% (CI 80.84%–99.30%) and 95.15% (CI 89.03%–98.41%), respectively (Table 4). We also used this method to calculate these parameters in patients with speech disorders (Table 5).

Both screening tests displayed high specificity and negative predictive value. We identified two patients with a single false positive ICDSC and one patient with a single false positive ICDSC and CAM-ICU. Only one patient was reported to be repeatedly falsely positive for delirium on both screening tests despite remaining negative on expert evaluation. This patient had severe aphasia.

The sensitivity of ICDCS was high (91.6%) compared to the moderate sensitivity of CAM-ICU (75.6%). The ICDSC enables to distinguish so-called “subsyndromal delirium” when patients scored positive in 3 features, close to the cut-off value of 4. We detected 43 (5.2%) days of possible subsyndromal delirium, which were assessed as delirium-negative in our final analysis (Table 6). If the positivity of subsyndromal delirium were included, the sensitivity of ICDCS increased to 93.28% (CI 87.18%–97.05%), while specificity remained high, 89.38% (CI 86.87%–91.55%).

We disclosed no episode of NCSE in any of our patients with delirium.

4. Discussion

Despite the known pitfalls of diagnosing delirium in the neuro-ICU, our study demonstrated that the two commonly used screening tests - CAM-ICU and ICDSC - can be used in stroke patients including those with aphasia, with slightly better performance of the ICDCS.

Table 2
Performance characteristics of CAM-ICU and ICDSC in all patients, on daily basis assessment (N = number of screened days).

	CAM-ICU	ICDSC
Sensitivity (95% CI)	75.63% (66.91–83.03)	91.60% (85.09–95.90)
Specificity (95% CI)	96.74% (95.15–97.92)	95.33% (93.50–96.76)
Positive predictive value (95% CI)	79.65% (72.10–85.56)	76.76% (70.21–82.24)
Negative predictive value (95% CI)	95.93% (94.49–97.00)	98.54% (97.38–99.19)
Accuracy (95% CI)	93.70% (91.82–95.26)	94.79% (93.04–96.20)
Reference-standard	Delirium positive	Delirium negative
CAM-ICU (N = 825)		
CAM-ICU positive	90 (True positive)	23 (False positive)
CAM-ICU negative	29 (False negative)	683 (True negative)
ICDSC (N = 825)		
ICDSC positive	109 (True positive)	33 (False positive)
ICDSC negative	10 (False negative)	673 (True negative)

Table 3
Performance characteristics of CAM-ICU and ICDSC in patients with aphasia, on daily basis assessment (N = number of screened days).

	CAM-ICU	ICDSC
Sensitivity (95% CI)	73.17% (57.06–85.78)	82.93% (67.94–92.85)
Specificity (95% CI)	90.05% (85.05–93.82)	89.05% (83.90–93.01)
Positive predictive value (95% CI)	60.00% (48.75–70.28)	60.71% (50.43–70.13)
Negative predictive value (95% CI)	94.27% (90.83–96.47)	96.24% (92.86–98.05)
Accuracy (95% CI)	87.19% (82.31–91.13)	88.02% (83.24–91.83)
Reference-standard	Delirium positive	Delirium negative
CAM-ICU (N = 252)		
CAM-ICU positive	30 (True positive)	20 (False positive)
CAM-ICU negative	11 (False negative)	181 (True negative)
ICDSC (N = 252)		
ICDSC positive	34 (True positive)	22 (False positive)
ICDSC negative	7 (False negative)	179 (True negative)

Table 4
Performance characteristics for CAM-ICU and ICDSC in all patients, on a per-patient basis assessment (N = number of patients).

	CAM-ICU	ICDSC
Sensitivity (95% CI)	86.84% (71.91–95.59)	97.37% (86.19–99.93)
Specificity (95% CI)	98.00% (92.96–99.76)	95.00% (88.72–98.36)
Positive predictive value (95% CI)	94.29% (80.84–99.30)	88.10% (74.37–96.02)
Negative predictive value (95% CI)	95.15% (89.03–98.41)	98.96% (94.33–99.97)
Accuracy (95% CI)	94.93% (89.83–97.94)	95.65% (90.78–98.39)
Reference-standard	Delirium positive	Delirium negative
CAM-ICU (N = 138)		
CAM-ICU positive	33 (True positive)	2 (False positive)
CAM-ICU negative	5 (False negative)	98 (True negative)
ICDSC (N = 138)		
ICDSC positive	37 (True positive)	5 (False positive)
ICDSC negative	1 (False negative)	95 (True negative)

Table 5
Performance characteristics of CAM-ICU and ICDSC in patients with aphasia, on a per-patient basis assessment (N = number of patients).

	CAM-ICU	ICDSC
Sensitivity (95% CI)	100.00% (79.41–100.00)	100.00% (79.41–100.00)
Specificity (95% CI)	90.48% (69.62–98.83)	85.71% (63.66–96.95)
Positive predictive value (95% CI)	88.89% (65.29–98.62)	84.21% (60.42–96.62)
Negative predictive value (95% CI)	100.00% (82.35–100.00)	100.00% (81.47–100.00)
Accuracy (95% CI)	94.59% (81.81–99.34)	91.89% (78.09–98.30)
Reference-standard	Delirium positive	Delirium negative
CAM-ICU (N = 37)		
CAM-ICU positive	16 (True positive)	2 (False positive)
CAM-ICU negative	0 (False negative)	19 (True negative)
ICDSC (N = 37)		
ICDSC positive	16 (True positive)	3 (False positive)
ICDSC negative	0 (False negative)	18 (True negative)

Table 6
ICDSC positive features.

Features positive	Frequency (n)	Percent
0	535	64.8 %
1	53	6.4 %
2	52	6.3 %
3	**43**	5.2 %
4	24	2.9 %
5	47	5.7 %
6	40	4.8 %
7	17	2.1 %
8	14	1.7 %
Screened days total	825	

Surprisingly, we showed that NCSE, which can mimic delirium, is rare in the acute phase of first-ever stroke patients. Strengths of our study include the fact that all patients with expertly confirmed delirium were screened for NCSE to exclude it as a possible differential diagnosis. In addition, patients with aphasia were assessed by a speech and language therapist, as aphasia may affect the performance of screening tests as well as the diagnosis of delirium.

The incidence of delirium in our group was 27.54%, which is within the expected range in stroke patients [5], but significantly lower, than in neurological populations in similar studies [11,12]. This may be due to our exclusion criteria (including patients with preexisting stroke) and the lower mean NIHSS score in our cohort. We also excluded patients on mechanical ventilation because they were mostly comatose, either due to stroke or sedation, and even if assessable on some days, aphasia could not be reliably evaluated. The incidence of delirium would probably have increased, if these patients had been included. Another factor contributing to the lower delirium rate is the implementation of the ABCDEF bundle in our neuro-ICU. As expected, a higher SOFA score was associated with the development of delirium.

Two methods were used to calculate sensitivity and specificity because of the different methods used in the variable articles. This allows the results to be compared with other studies. However, the assessment of delirium-positive days is more accurate and important for the daily assessment of delirium. Both screening tests showed good performance in terms of sensitivity and specificity when calculated on a daily basis, while sensitivity increased for both tests when calculated on a per-patient basis. On the other hand, the specificity increased only in the CAM-ICU and decreased slightly in the ICDSC.

The CAM-ICU is commonly used as a screening tool in general ICUs, where it has shown very good specificity and sensitivity, as well as being reliable and very easy to use. Although the CAM-ICU was originally developed for use in non-verbal patients presumed to be on mechanical ventilation, many validation studies have excluded patients with aphasia [16]. Aphasia is a common consequence of stroke and is a major neurological deficit with a reported prevalence of 30–34% [23]. The prevalence of aphasia in our cohort was slightly lower (26.8%), which may be due to the exclusion of patients with severe neurological deficit and severe brain injury on admission, who had a palliative treatment plan. Aphasia is an obstacle to the diagnosis of delirium and a challenge even for experienced clinicians. In terms of screening tests, false-positive results might be expected in patients with aphasia. However, both tests retained high specificity even in patients with aphasia. Regarding the comparison between the two tests, our findings support the results of other studies comparing CAM-ICU and ICDSC in neurological patients [11,12]. We verified that the ICDSC may be a more suitable tool for screening in patients with language disorders, probably due to the fact, that it is not based on verbal communication with a patient. Only one patient in our cohort was repeatedly reported as positive on both screening tests but negative on expert judgement. This may have been due to severe aphasia. On detailed examination by a qualified speech and language therapist, the patient showed poor performance in the ability to follow instructions, which may have led to a lack of cooperation during the screening and therefore a false positive assessment. When only the group of patients with aphasia was analysed, the prevalence of delirium increased (42.10%). Apart from the fact that aphasia may mimic delirium, there is also the possibility of misinterpretation by experts due to severe language impairment, which may exceptionally lead to a false positive for delirium even by experts. However, in line with the review by Rhee et al. we found no significant association between the side of stroke and the development of delirium [24].

Although both screening tests can be used in the neuro-ICU, sensitivity and specificity decrease in patients with severe neurological deficits [25]. The ideal screening tool for this challenging patient population is lacking. Adaptation of one of the existing screening tools may be an option. Boβelmann et al. suggest increasing the cut-off value of the ICDSC to $\geq$5 when assessing the neurological population [26]. However, when we applied this approach to our cohort, the sensitivity decreased to 73.12% (CI 57.06%–85.78%) and the specificity remained stable at 90.05% (CI 85.05%–93.82%). Our results, therefore, do not support this view.

Although it is thought to be underdiagnosed [27], we did not detect any episodes of NCSE in our cohort of patients in the acute phase of stroke. This may be due to the smaller cohort of patients, as the prevalence may be much lower than previously described [28]. Also, due to our exclusion criteria, patients with a neurological deficit prior to the current admission were not included in our study. Stroke lesions are a risk factor for the development of epileptic activity, but this is a late complication [27]. This may explain the lack of NCSE disclosure, as we enrolled patients with first-ever clinical stroke. The detection of NCSE may have been erroneously reduced by our design of the EEG evaluation, as we used a 10-min evaluation in patients who were actually judged to be delirious. However, we diagnosed 5 cases in our neuro-ICU during our study, but they were not admitted to the neurology department with a primary diagnosis of stroke but with acute changes in behaviour, cognition or consciousness and therefore with a high suspicion of NCSE in the first place.

There are some limitations to this study that should be acknowledged. Firstly, our study is conducted as a single-centre study, so there is no external validation. Second, the sample size is moderate for this type of study. Thirdly, screening for delirium was only done once a day, so we may have missed some episodes of delirium. To overcome this limitation, we tried to communicate as much as possible with the nursing staff present on the night shift. Fourth, the screening tools were administered by only one examiner, so there was no way to test for interrater variability. Finally, we used a 10-min EEG evaluation in delirious patients only which may have erroneously decreased the detection of NCSE.

5. Conclusions

Delirium in the neurointensive care is challenging because delirium symptoms may overlap with those of a primary brain injury. Both commonly used screening tests – CAM-ICU and ICDCS - are useful in the diagnosis of delirium, but ICDSC appears to be slightly more accurate when used in neurological patients, particularly in those with aphasia. The development of a specific screening tool or appropriate modification of an existing tool may be warranted. NCSE may be less common in the acute phase of stroke, but our results may be influenced by the composition of our cohort and further studies are needed to verify our findings.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon request.

Funding

The project was supported by the Ministry of Health of the Czech Republic project for conceptual development in research organisations, ref. No. 65269705 (University Hospital Brno, Brno, Czech Republic), by Specific Research Project ref. MUNI/A/1186/2022 and by the Internal Grant Agency of the Masaryk University MUNI/IGA/1309/2020.

Ethics approval and conflicts of interests statement

I confirm that our Institution Ethics Review Board (Etická komise Fakultní nemocnice Brno) (n134/20) and the Ethics Committee of the Faculty of Medicine, Masaryk University (n71/2020) approved this study. Also, on behalf of all authors I deny any potential conflicts of interests and sources of funding.

CRediT authorship contribution statement

Lucia Bakošová: Writing – original draft, Project administration, Investigation, Formal analysis. **David Kec:** Writing – review & editing. **Miroslav Škorňa:** Writing – review & editing. **René Jura:** Writing – review & editing. **Zdeněk Kundrata:** Writing – review & editing. **Milena Košťálová:** Writing – review & editing. **Josef Bednařík:** Writing – review & editing, Methodology, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

References

[1] American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders, fifth ed., American Psychiatric Association, Arlington, 2013.
[2] International Statistical Classification of Diseases and Related Health Problems, 11th Revision, World Health Organization, 2019.
[3] A.J.C. Slooter, W.M. Otte, J.W. Devlin, R.C. Arora, T.P. Bleck, J. Claassen, et al., Updated nomenclature of delirium and acute encephalopathy: statement of ten Societies, Intensive Care Med. 46 (5) (2020) 1020–1022, https://doi.org/10.1007/s00134-019-05907-4.
[4] M.M. van Eijk, M. van den Boogaard, R.J. van Marum, P. Benner, P. Eikelenboom, M.L. Honing, et al., Routine use of the confusion assessment method for the intensive care unit: a multicenter study, Am. J. Respir. Crit. Care Med. 184 (3) (2011 Aug) 340–344, https://doi.org/10.1164/rccm.201101-0065OC.
[5] A.W. Oldenbeuving, P.L.M. de Kort, B.P.W. Jansen, G. Roks, L.J. Kappelle, Delirium in acute stroke: a review, Int. J. Stroke 2 (4) (2007 Nov) 270–275, https://doi.org/10.1111/j.1747-4949.2007.00163.x.
[6] N. Siddiqi, A.O. House, J.D. Holmes, Occurrence and outcome of delirium in medical in-patients: a systematic literature review, Age Ageing 35 (4) (2006 Jul 1) 350–364, https://doi.org/10.1093/ageing/afl005.
[7] T.T. Hshieh, S.K. Inouye, E.S. Oh, Delirium in the elderly, Clin. Geriatr. Med. 36 (2) (2020 May) 183–199, https://doi.org/10.1016/j.cger.2019.11.001.
[8] K.M. Fiest, A. Soo, C. Hee Lee, D.J. Niven, E.W. Ely, C.J. Doig, et al., Long-term outcomes in ICU patients with delirium: a population-based cohort study, Am. J. Respir. Crit. Care Med. 204 (4) (2021 Aug 15) 412–420, https://doi.org/10.1164/rccm.202002-0320OC.
[9] A. Marra, E.W. Ely, P.P. Pandharipande, M.B. Patel, The ABCDEF bundle in critical care, Crit. Care Clin. 33 (2) (2017) 225–243, https://doi.org/10.1016/j.ccc.2016.12.005.
[10] D. Gusmao-Flores, J.I.F. Salluh, R. Chalhub, L.C. Quarantini, The confusion assessment method for the intensive care unit (CAM-ICU) and intensive care delirium screening checklist (ICDSC) for the diagnosis of delirium: a systematic review and meta-analysis of clinical studies, Crit. Care 16 (4) (2012) R115, https://doi.org/10.1186/cc11407.
[11] L.K. Larsen, V.G. Frøkjaer, J.S. Nielsen, Y. Skrobik, Y. Winkler, K. Møller, et al., Delirium assessment in neuro-critically ill patients: a validation study, Acta Anaesthesiol. Scand. 63 (3) (2019) 352–359, https://doi.org/10.1111/aas.13270.
[12] M.E. Reznik, J. Drake, S.A. Margolis, S. Moody, K. Murray, S. Costa, et al., Deconstructing poststroke delirium in a prospective cohort of patients with intracerebral hemorrhage, Crit. Care Med. 48 (1) (2020) 111–118, https://doi.org/10.1097/CCM.0000000000004031.
[13] N. Bergeron, M.J. Dubois, M. Dumont, S. Dial, Y. Skrobik, Intensive care delirium screening checklist: evaluation of a new screening tool, Intensive Care Med. 27 (5) (2001 May) 859–864, https://doi.org/10.1007/s001340100909.
[14] E.W. Ely, S.K. Inouye, G.R. Bernard, S. Gordon, J. Francis, L. May, et al., Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU), JAMA 286 (21) (2001 Dec 5) 2703, https://doi.org/10.1001/jama.286.21.2703.
[15] A. Mitasova, M. Kostalova, J. Bednarik, R. Michalcakova, T. Kasparek, P. Balabanova, et al., Poststroke delirium incidence and outcomes: validation of the confusion assessment method for the intensive care unit (CAM-ICU), Crit. Care Med. 40 (2) (2012 Feb) 484–490, https://doi.org/10.1097/CCM.0b013e318232da12.
[16] G. Carin-Levy, G.E. Mead, K. Nicol, R. Rush, F. van Wijck, Delirium in acute stroke: screening tools, incidence rates and predictors: a systematic review, J. Neurol. 259 (8) (2012) 1590–1599, https://doi.org/10.1007/s00415-011-6383-4.
[17] M. Holtkamp, H. Meierkord, Nonconvulsive status epilepticus: a diagnostic and therapeutic challenge in the intensive care setting, Ther Adv Neurol Disord 4 (3) (2011 May) 169–181, https://doi.org/10.1177/1756285611403826.
[18] S. Beniczky, L.J. Hirsch, P.W. Kaplan, R. Pressler, G. Bauer, H. Aurlien, et al., Unified EEG terminology and criteria for nonconvulsive status epilepticus, Epilepsia 54 (2013) 28–29, https://doi.org/10.1111/epi.12270.
[19] R.C. Bone, R.A. Balk, F.B. Cerra, R.P. Dellinger, A.M. Fein, W.A. Knaus, et al., Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis, Chest 101 (6) (1992 Jun) 1644–1655, https://doi.org/10.1378/chest.101.6.1644.
[20] G. Blessed, B.E. Tomlinson, M. Roth, The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects, Br. J. Psychiatry 114 (512) (1968) 797–811, https://doi.org/10.1192/bjp.114.512.797.
[2][1] R. Nakase-Thompson, E. Manning, M. Sherer, S.A. Yablon, S.L.T. Gontkovsky, C. Vickery, Brief assessment of severe language impairments: initial validation of the Mississippi aphasia screening test, Brain Inj. 19 (9) (2005 Aug 20) 685, https://doi.org/10.1080/02699050400025331, 91.

[22] M. Leitinger, E. Trinka, G. Zimmermann, S. Beniczky, Salzburg criteria for nonconvulsive status epilepticus: details matter, Epilepsia 60 (11) (2019) 2334–2336, https://doi.org/10.1111/epi.16361.
[23] H.L. Flowers, S.A. Skoretz, F.L. Silver, E. Rochon, J. Fang, C. Flamand-Roze, et al., Poststroke aphasia frequency, recovery, and outcomes: a systematic review and meta-analysis, Arch. Phys. Med. Rehabil. 97 (12) (2016 Dec) 2188–2201.e8, https://doi.org/10.1016/j.apmr.2016.03.006.
[24] J.Y. Rhee, M.A. Colman, M. Mendu, S.J. Shah, M.D. Fox, N.S. Rost, et al., Associations between stroke localization and delirium: a systematic review and meta-analysis, J. Stroke Cerebrovasc. Dis. 31 (3) (2022 Mar) 106270, https://doi.org/10.1016/j.jstrokecerebrovasdis.2021.106270.
[25] J. von Hofen-Hohloch, C. Awissus, M.M. Fischer, D. Michalski, J.J. Rumpf, J. Classen, Delirium screening in neurocritical care and stroke unit patients: a pilot study on the influence of neurological deficits on CAM-ICU and ICDSC outcome, Neurocritical Care 33 (3) (2020) 708–717, https://doi.org/10.1007/s12028-020-00938-y.
[26] C. Boßelmann, J. Zurloh, M.I. Stefanou, V. Stadler, Y. Weber, H. Lerche, et al., Delirium screening in aphasic patients with the intensive care delirium screening checklist (ICDSC): a prospective cohort study, Front. Neurol. 10 (2019), https://doi.org/10.3389/fneur.2019.01198.
[27] S. Dupont, K. Kinugawa, Nonconvulsive status epilepticus in the elderly, Rev. Neurol. 176 (9) (2020 Nov) 701–709, https://doi.org/10.1016/j.neurol.2019.12.007.
[28] E. Özaydın Göksu, F. Genç, N. Atiş, Y. Bıçer Gömceli, Early and late-onset nonconvulsive status epilepticus after stroke, Arq. Neuro. Psiquiatr. 79 (5) (2021 May) 384–389, https://doi.org/10.1590/0004-282X-ANP-2020-0018.