Delirium screening in critically ill patients: A systematic review and meta-analysis

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Objective: Despite its frequency and impact, delirium in critically ill patients is poorly recognized. Our aim was to systematically review the accuracy of delirium screening instruments in critically ill patients.

Data Source: Systematic review and meta-analysis of publications between 1966 and 2011. The Medline and Embase databases were searched for studies on delirium in critically ill patients.

Study Selection: The meta-analysis was limited to studies in critically ill patients in intensive care units, surgical wards, or emergency rooms. The delirium screening tool had to be feasible in a clinical setting for use by a nonexpert. As the gold standard, delirium had to be diagnosed based on appropriate criteria by a delirium expert.

Data Extraction: The outcomes assessed were sensitivity, specificity, likelihood ratios, and summary receiver operating characteristics curves.

Data Synthesis: Sixteen studies covering 1,523 participants and five screening tools were included in the systematic review. The pooled sensitivities and specificities of Confusion Assessment Method for the Intensive Care Unit for detection of delirium in critically ill patients were 75.5% and 95.8%, and for Intensive Care Delirium Screening Checklist 80.1% and 74.6%, respectively. All but one study was performed in a research setting, and that one study suggested that with routine use of the Confusion Assessment Method for the Intensive Care Unit, half of the patients with delirium were not detected.

Conclusions: The Confusion Assessment Method for the Intensive Care Unit was the most specific bedside tool for the assessment of delirium in critically ill patients. However, there was significant heterogeneity of the results. These findings were largely obtained in research settings, and the low sensitivity of the Confusion Assessment Method for the Intensive Care Unit in routine, daily practice may limit its use as a screening test. (Crit Care Med 2012; 40:1946–1951)

Key Words: bedside; critical care; delirium; meta-analysis; review; screening

Delirium is a clinical syndrome characterized by acute or subacute onset of altered cognition or the development of a perceptual disturbance that is not better accounted for by a preexisting, established, or evolving dementia. It typically involves disturbance of consciousness with reduced ability to focus, sustain, or shift attention and may or may not include perceptual disturbances (1, 2). It affects a substantial proportion of hospitalized patients and increases their likelihood of unfavorable outcomes, such as a longer hospital stay (3), persistent cognitive dysfunction (4, 5), and mortality (3, 5, 6).

The occurrence of delirium is especially high in critically ill populations (3 ,7–9), in whom delirium is arguably the most prevalent form of organ dysfunction and is associated with complications such as accidental extubation (7), longer duration of mechanical ventilation (3), longer stay in the intensive care unit (ICU) (3), and increased mortality (3, 6, 10, 11).

Critical care physicians recognize fewer than half of delirium cases (12). The criterion standard for the diagnosis of delirium is based on the *Diagnostic and Statistical Manual of Mental Disorders IV* (13). Various delirium detection tools have been developed for use by nonpsychiatric personnel (14). Several studies have been conducted to test these different bedside tools, but these were all performed in small populations of critically ill patients. Thus, the aim of our study was to systematically review and summarize the current literature on delirium screening instruments in the ICU.

METHODS

Search Methods to Identify Studies. Studies were identified through a computerized search of the Medline (1966–2011) and Embase (1990–2011) databases using a sensitive search strategy combining Medical Subject Headings and keywords (see details in Supplemental Digital Content 1, http://links.lww.com/CCM/A432). The terms were combined with validated search filters for retrieving articles on the diagnosis of health disorders (15, 16). Finally, all review articles and cross-referenced studies from retrieved articles were screened for pertinent information. There was no language restriction.

Selection of Studies and Data Extraction. The cumulative analysis was limited to studies conducted in critically ill patients in ICUs, surgical wards, or emergency rooms. The delirium screening tool had to be feasible in a clinical setting for use by a nonexpert. The study needed to describe the use of appropriate reference criteria (*Diagnostic and Statistical Manual of Mental Disorders IV*) by a delirium expert (i.e., a geriatrician, psychiatrist, or neurologist). Furthermore, the study should apply the same index test to most patients (>80%), with and without delirium. Studies were excluded if the data were not extractable or were based

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on pediatric patients. In the case of republication of the same series after an update of cases, only the most recent article was included in the analysis. When necessary, additional data were obtained by contacting the study authors.

Data were independently extracted from each report by two of the authors using a data record form developed for this purpose. After extraction, the data were reviewed and compared by the first author. Instances of disagreement between the two other data extractors were resolved by consensus among the investigators. The quality of each study was evaluated by the Quality Assessment of Diagnostic Accuracy Studies tool (see details in Supplemental Digital Content 1, http://links.lww.com/CCM/A432) (17).

Statistical Analysis. The data from each of the studies were summarized in two-by-two tables. From these, we conducted our primary analysis, computing sensitivity (true positive rate), specificity (true negative rate), and positive and negative likelihood ratios (LR+: the ratio of the sensitivity to 1 − specificity; and LR−: the ratio of the 1 − sensitivity to specificity, respectively) (15). All results were reported with 95% confidence intervals. As part of the assessment for heterogeneity between studies, the relationship between sensitivity and specificity was explored using a graphical approach (a plot of sensitivity and specificity in a receiver operating characteristics curve). In addition, we used the Mantel-Haenszel computation method to check whether the differences between studies were due to random chance and whether there was an association between sensitivity and specificity. Where feasible, we used cumulative analysis to pool results for each test separately. Interrater reliability was determined by comparing the number of studies included by author 1 with author 2 in each stage of the search using the kappa coefficients.

Meta-DiSC software was used to generate pooled sensitivities and specificities and summary receiver operating characteristics plots. In this fixed effects modeling approach, each study was assigned a weight depending on the number of patients analyzed in that study. The degree of heterogeneity between studies was reported using the Cochran chi square (Cochrane Q) statistic. When this value was divided by the degrees of freedom (number of studies minus 1), a result >1 was indicative of heterogeneity. When this value was found to be statistically significant, the causes of heterogeneity were explored statistically (by the random effects mode) and clinically (by sensitivity analyses). A receiver operating characteristics curve for an inconclusive test will have a flatter slope and will lie close to the diagonal line, whereas the receiver operating characteristics line of a perfect diagnostic test will have an extremely steep ascent, because both the sensitivity and the specificity approach 100%. In clinical practice, it is suggested that a positive LR >10 or a negative LR <0.1 supports high diagnostic accuracy for the test in question.

RESULTS

The comprehensive literature search yielded 1,396 references published between 1968 and 2011. Of these, 1,339 articles were excluded during the first screening, which was based on abstracts or titles, leaving 57 articles for the full text review. During this review, 41 articles were excluded (the reasons for exclusion are exposed in Supplemental Digital Content 1, http://links.lww.com/CCM/A432). Finally, 16 articles (1,523 participants) were included in the final cumulative analysis (Fig. 1). For the comparisons of interrater reliability in each stage of the search, the kappa coefficient was 0.94 in the citation stage (p = .002), 0.81 in the abstract stage (p = .01), and 0.88 in the full text stage (p = .006). The quality of each study is shown in Supplemental Digital Content 1, http://links.lww.com/CCM/A432.

The included studies ranged in size from 29 to 181 participants, and five bedside delirium instruments were evaluated (Table 1). The average age of all the patients across the studies was 61.0 ± 6.2 years (mean ± SD). All the studies used as a reference the *Diagnostic and Statistical Manual of Mental Disorders IV* criteria, assessed by a psychiatrist in 11 studies (10, 18–27), a neurologist, psychiatrist, or geriatrician in two (12, 28), a neurologist or psychiatrist in two (29, 30), and a neurologist or geriatrician in one (31). Twelve studies evaluated the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU) (10, 12, 18–22, 27–31), five evaluated the Intensive Care Delirium Screening Checklist (ICDSC) (12, 23, 24, 26, 30), and one evaluated the Nursing Delirium Screening Scale (Nu-DESC) (20), the Delirium Detection Score (DDS) (20), or the Neelon and Champagne Confusion Scale (20). It is important to note that only the CAM-ICU and the ICDSC have been validated for use in critically ill patients.

The prevalence of delirium ranged from 14% to 87%. The highest prevalence was found in a study with a higher proportion of older patients (>65 yrs) and with some patients with possible dementia (22). The prevalence of delirium among patients admitted to a mixed ICU ranged from 16% to 87% (12, 18, 19, 22, 24–26, 28, 30), from 22% to 48% among mechanically ventilated patients (10, 18, 19, 22), and from 14% to 46% among patients admitted to surgical wards (20, 21).

For all tests, a positive finding had a LR of at least 2.0. Only the studies that evaluated CAM-ICU and ICDSC were included in the meta-analysis, because the other tools were all investigated in one study only. The CAM-ICU showed a higher specificity and a higher LR of a positive score than the ICDSC (Table 2 and Figs. 2 and 3). These results were maintained when stratified according to the setting where patients were treated (mixed, surgical, or stroke unit).

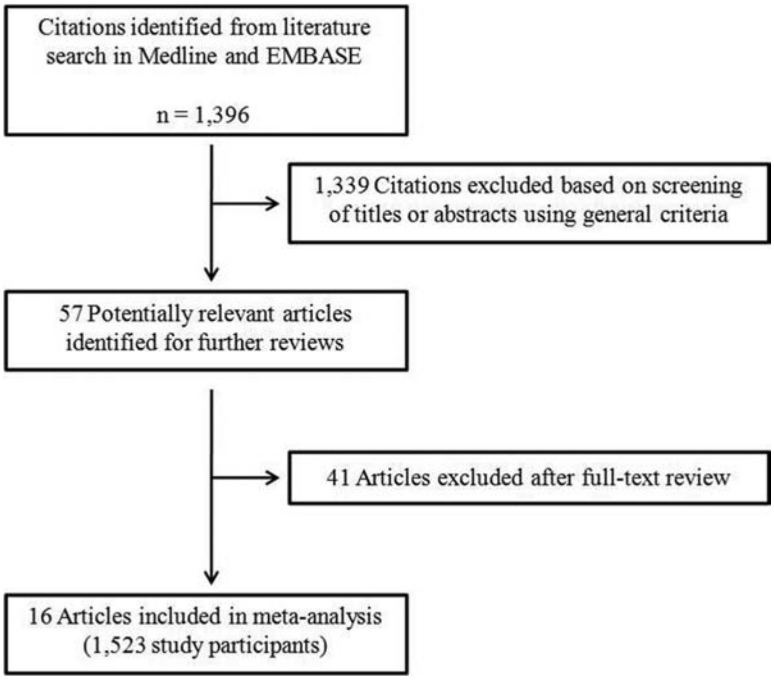

Figure 1. Literature search strategy.

Table 1. Characteristics of the included studies

Source	n	Delirium Prevalence, %	Type of Patient	Standard Reference	% (95% Confidence Interval) Sensitivity	Specificity	Likelihood Ratio (95% Confidence Interval) Positive	Negative
CAM-ICU								
van Eijk et al (12)	125	34	Mixed ICU	P, G, or N[a]	64.0 (49.0–77.0)	88.0 (79.0–93.0)	5.33 (2.33–11.0)	0.40 (0.24–0.64)
Toro et al (19)	129	26	Mixed ICU	Psychiatrist	79.4 (63.2–89.7)	97.9 (92.6–99.4)	37.7 (9.47–150)	0.21 (0.11–0.41)
Tobar et al (18)	29	48	MV[b]	Psychiatrist	92.9 (68.5–98.7)	86.7 (62.1–96.3)	6.96 (1.90–25.5)	0.08 (0.01–0.55)
Lin et al (10)	102	22	MV[b]	Psychiatrist	93.0 (ND[c])	98.0 (ND[c])	46.5 (ND[c])	0.07 (ND[c])
Luetz et al (20)	156	40	Mixed ICU	Psychiatrist	79.0 (ND[c])	97.0 (ND[c])	24.6 (8.02–75.4)	0.21 (0.13–0.34)
Guenther et (21)	54	46	Surgical ICU	Psychiatrist	90.0 (71.5–98.5)	100 (88.0–100)	∞ (5.95–∞)	0.10 (0.01–0.32)
Ely et al (31)	96	39	MV[b]	G or N[a]	96.5 (86.0–99.5)	99.0 (92.0–100)	96.5 (10.7–∞)	0.03 (0.00–0.15)
Ely et al (22)	38	87	Mixed ICU	Psychiatrist	97.0 (78.3–100)	91.6 (62.3–100)	11.5 (2.07–∞)	0.03 (0.00–0.34)
van Eijk et al (28)	181	41	Mixed ICU	P, G, or N[a]	47.0 (35.0–58.0)	98.0 (93.0–100)	24.7 (6.10–100)	0.50 (0.40–0.80)
Heo et al (27)	22	73	Mixed ICU	Psychiatrist	83.6 (54.4–96.0)	74.1 (28.6–98.1)	3.25 (0.79–13.2)	0.25 (0.08–0.76)
Mitasova et al (29)	129	43	Stroke Unit	P or N[a]	76.0 (54.9–90.6)	98.1 (93.2–99.8)	47.2 (26.8–83.0)	0.21 (0.17–0.26)
Gusmão-Flores et al (30)	119	39	Mixed ICU	P or N[a]	72.5 (55.9–84.9)	96.2 (88.5–99.0)	17.4 (5.68–53.6)	0.29 (0.18–0.46)
ICDSC								
van Eijk et al (12)	118	34	Mixed ICU	P, G, or N[a]	43.0 (29.0–58.0)	95.0 (87.0–98.0)	8.60 (2.23–29.0)	0.60 (0.42–0.81)
George et al (23)	59	34	Non-MV[b] ICU	Psychiatrist	90.0 (ND[c])	61.5 (ND[c])	2.33 (ND[c])	0.16 (ND[c])
Radtke et al (24)	68	69	Mixed ICU	Psychiatrist	89.0 (ND[c])	57.0 (ND[c])	2.06 (ND[c])	0.19 (ND[c])
Bergeron et al (26)	93	16	Mixed ICU	Psychiatrist	99.0 (ND[c])	64.0 (ND[c])	2.75 (ND[c])	0.02 (ND[c])
Gusmão-Flores et al (30)	119	39	Mixed ICU	P or N[a]	96.0 (81.5–99.8)	72.4 (58.6–83.0)	3.49 (2.39–5.09)	0.06 (0.01–0.23)
Nu-DESC								
Luetz et al (20)	156	40	Mixed ICU	Psychiatrist	82.0 (ND[c])	83.0 (ND[c])	4.79 (ND[c])	0.21 (ND[c])
DDS								
Luetz et al (20)	156	40	Mixed ICU	Psychiatrist	25.0 (ND[c])	89.0 (ND[c])	2.36 (ND[c])	0.83 (ND[c])
NEECHAM								
Immers et al (25)	123	29	Mixed ICU	Psychiatrist	97.2 (ND[c])	82.8 (ND[c])	5.65 (ND[c])	0.03 (ND[c])

CAM-ICU, Confusion Assessment Method for Intensive Care Unit; ICDSC, Intensive Care Delirium Screening Checklist; Nu-DESC, Nursing Delirium Screening Scale; DDS, Delirium Detection Score; NEECHAM, Neelon and Champagne Confusion Scale; ND, not defined.

[a]Psychiatrist, geriatrician, or neurologist; [b]mechanical ventilation; [c]not described.

Table 2. Meta-analysis of CAM-ICU and ICDSC

Test	n	Diagnostic OR (95% Confidence Interval)	AUC (± SE)	p^a	% (95% Confidence Interval) Sensitivity	Specificity	Likelihood Ratio (95% Confidence Interval) Positive	Negative
CAM-ICU	1180	60.6 (39.4–93.2)	0.946 ± 0.00		75.5 (71.3–79.4)	95.8 (94.0–97.1)	16.3 (11.5–23.0)	0.26 (0.22–0.31)
ICDSC	457	20.7 (11.2–38.2)	0.889 ± 0.02	0.0044	80.1 (73.3–85.8)	74.6 (69.1–79.5)	3.06 (2.47–3.79)	0.28 (0.21–0.38)

CAM-ICU, Confusion Assessment Method for Intensive Care Unit; ICDSC, Intensive Care Delirium Screening Checklist; OR, odds ratio; AUC, area under the curve.

[a]AUC of CAM-ICU vs. AUC of ICDSC.

There was significant heterogeneity among the CAM-ICU studies ($p < .0001$ for sensitivity and negative LR, $p = .01$ for specificity, and $p = .01$ for positive LR). Besides the possible differences among studies in quality and experience, we found that by excluding the studies of Luetz et al (20) and van Eijk et al (12, 28), the heterogeneity disappeared ($p = .143$ for sensitivity, $p = .120$ for specificity, $p = .323$ for positive LR, and $p = .113$ for negative LR). In the ICDSC analyses, the heterogeneity identified was also explained in the study by van Eijk et al (12) ($p < .001$ for sensitivity before and $p = .86$ after, $p < .001$ for specificity before and $p = .63$ after, $p = .09$ for positive LR before and $p = .49$ after, and $p < .001$ for negative LR before and $p = .77$ after). We recalculated the results stratified by quartiles of prevalence of delirium and did not find improvement in heterogeneity.

DISCUSSION

This systematic review and meta-analysis on the diagnostic properties of delirium screening tools is the first to summarize recent validation studies. We found 16 studies with 1,523 patients; however, only the CAM-ICU and the ICDSC were evaluated in more than one study and could be summarized in the meta-analysis. Our main finding is that in critically ill patients, the ICDSC had a higher sensitivity than CAM-ICU for delirium diagnoses. The CAM-ICU appears to be a useful tool to exclude delirium because of its high specificity.

However, there was significant heterogeneity of the results. Heterogeneity could be explained by differences in the type of patients (neurological vs. nonneurological) and, primarily, the setting (in routine, daily practice vs. research setting). The study by van Eijk et al (28), was the only one that tested the CAM-ICU in routine, daily practice, instead of a research

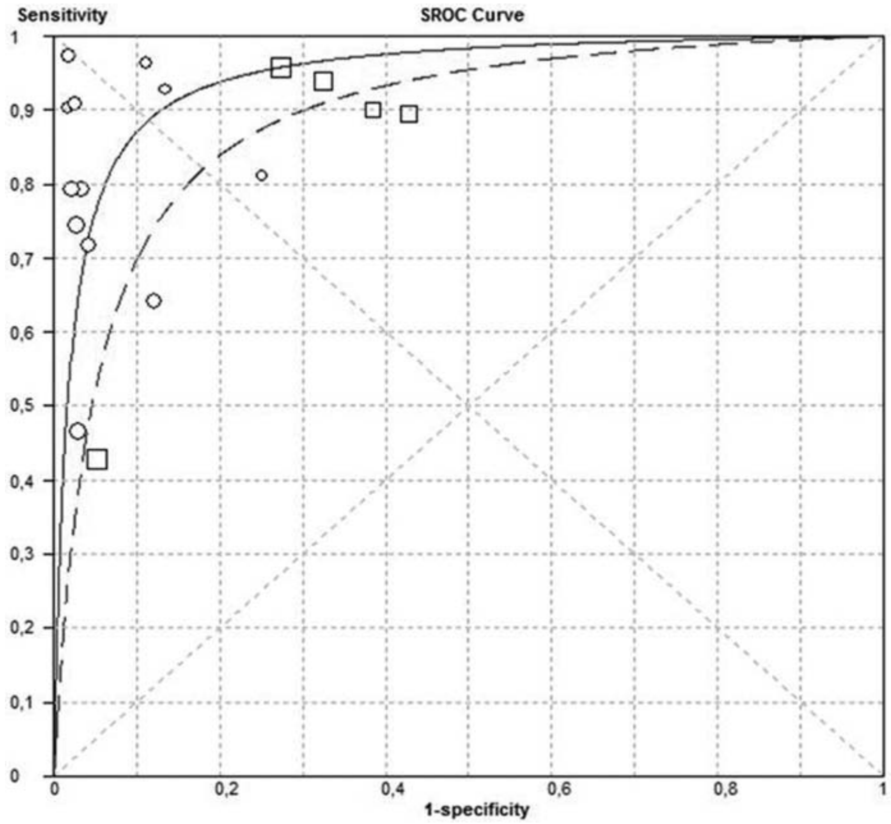

Figure 2. Summary receiver operating characteristics (*SROC*) curves for detection of delirium by Confusion Assessment Method for Intensive Care Unit (*solid line* and *circles*) or Intensive Care Delirium Screening Checklist (*dashed line* and *squares*).

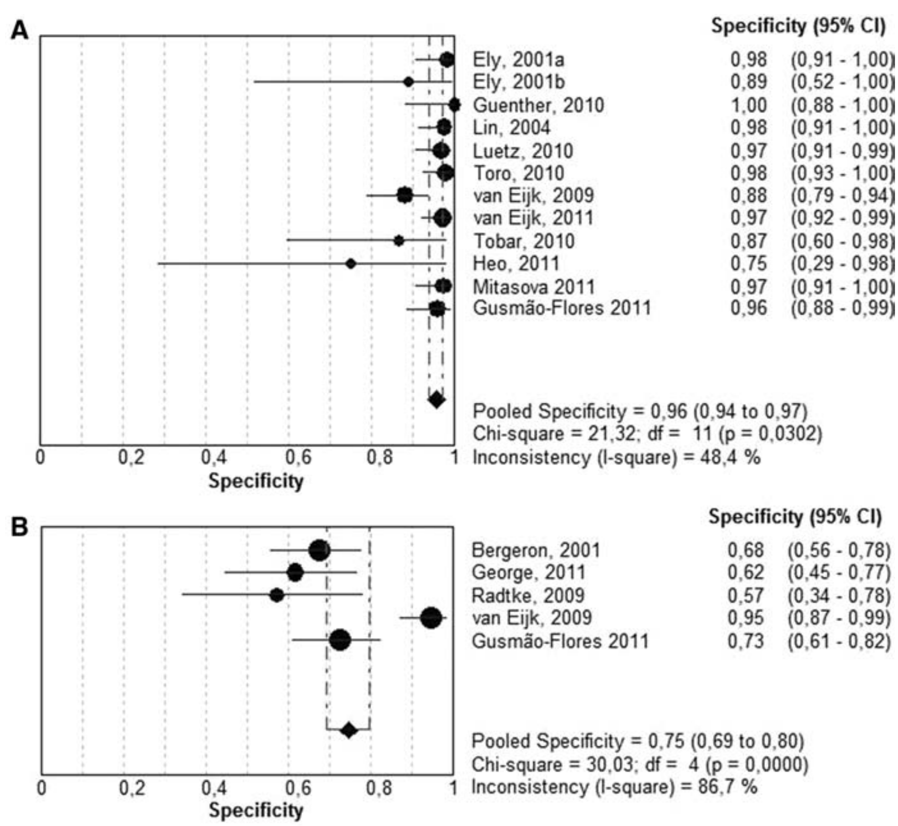

Figure 3. Pooled specificities for Confusion Assessment Method for Intensive Care Unit (*A*) and Intensive Care Delirium Screening Checklist (*B*). CI, confidence interval.

setting with a limited number of investigators. Furthermore, when we excluded the studies by van Eijk et al (12, 28) and Luetz et al (20), the remainder were almost all from the same research group, which may explain the homogeneity.

Delirium is common in critically ill patients and has been associated with poor outcome, including increased morbidity and mortality, prolonged length of stay, institutionalization, and functional decline (3, 5). This tremendous negative impact of delirium may be modified by using multicomponent interventions with proven efficacy in wards (32) and strategies that have been shown to be associated with a decreased incidence of delirium, such as the early mobilization of patients on mechanical ventilation (33) and the use of dexmedetomidine instead of benzodiazepines for sedation (34). However, the first step for any intervention is to recognize the problem. A diagnosis of hyperactive delirium is easier; however, hypoactive delirium, which manifests as decreased mental activity and inattention, is more common but frequently overlooked by ICU physicians. A bedside tool for the detection of delirium could help in detection and, consequently, may improve prognosis by earlier treatment (35).

The original CAM is commonly used to detect and monitor delirium; however, mechanically ventilated patients have been excluded from these investigations (32, 36). The development of the CAM-ICU enabled the evaluation of mechanically ventilated patients by alternative methods of evaluating attentiveness and disorganized thinking with visual and auditory assessment components (picture recognition and vigilance A random letter tests, respectively) (22, 31). Some training is recommended for optimal use, and the performance of the CAM-ICU is linked to the quality of training (31). Although there are several clinical features of delirium, the CAM diagnostic algorithm is based on only four cardinal elements: 1) an acute onset of mental status changes of fluctuating course; 2) inattention; 3) disorganized thinking; and 4) an altered level of consciousness. The patient is diagnosed as delirious if he has both features 1 and 2, and either feature 3 or 4. Before assessing delirium with the CAM-ICU, it is necessary to assess the level of consciousness with the Richmond Agitation Sedation Scale. Only critically ill patients with a Richmond Agitation Sedation Scale ≥ -3 can be assessed with the CAM-ICU. This could explain some of the variation in sensitivity of the CAM-ICU, particularly in assessments of hypoactive, delirious patients. The use of CAM-ICU in mechanically ventilated patients incorporates the use of nonverbal, objective assessment instruments (22, 31).

The ICDSC is an eight-item scoring system based on observations during routine patient care; no patient cooperation is required. The items are scored over a period of 24 hrs, whereas the CAM-ICU provides an indication of the state of the patient at one moment in time (12). Different cutoffs in different studies emphasize the need for the validation of such screening tools in local settings before their use (23). In the studies evaluated, four used the cutoff of 4 (12, 24, 26, 30), and one the cutoff of 3 (23).

Delirium may be difficult to diagnose in intubated and mechanically ventilated patients in whom cognitive testing is a challenge. The majority of delirium patients, particularly those with predominantly hypoactive episodes, are not recognized by ICU physicians[12]. An evaluation by a neurologist, neurophysiologist, psychiatrist, or clinical geriatrician is regarded as the "gold standard" for a diagnosis of delirium but usually requires active consultation by an intensivist. Furthermore, in the majority of the studies, the delirium screening tools were administered by a limited number of research nurses. The diagnostic value of these instruments as administered by clinically assigned nurses is estimated by many intensivists to be much lower.

The results of this review should be interpreted within the context of the included studies. Systematic reviews are subject to publication bias and may exaggerate the summary estimate of the test accuracy if publication is related to the strength of the results. In addition, there were insufficient studies to look for funnel plot asymmetry. A limitation of a meta-analysis on a screening tool is that results from different groups are averaged. The publication of many of the evaluated studies by a single research group increased the homogeneity of the findings but limited their external validity.

CONCLUSIONS

There is a substantial under recognition of delirium in critical care, and the bedside tools reviewed here have emerged as candidate instruments. The CAM-ICU was the most specific instrument for the assessment of delirium in critically ill patients. However, these findings were obtained in a research setting, and the low sensitivity of the CAM-ICU in routine, daily practice may limit its use as a screening test.

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