



Original Article

Validity and reliability of the Persian version of the confusion assessment method for intensive care units

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ABSTRACT

Background & Aim: Delirium is prevalent in the intensive care unit, especially among mechanically-ventilated patients. Delirium is associated with a significant increase in adverse outcomes but it usually remains undiagnosed, making it necessary to develop and validate diagnostic tools. This study determined the validity and reliability of the Persian version of Confusion Assessment Method for Intensive Care Units in Iran.

Methods & Materials: This cross-sectional study was conducted in open-heart intensive care unit of three university hospitals of Tehran, Iran. After piloting the translated confusion assessment method for intensive care units on 10 patients and refining the translated scale accordingly, 40 ventilated patients were consecutively selected and screened for delirium by two independent evaluators, and one psychiatrist. Inter-rater reliability between the two evaluators was assessed by the Kappa coefficient. Validity indices (i.e., sensitivity and specificity) of the Persian-CAM-ICU and 95% confidence intervals were calculated, given the psychiatrists' diagnosis as reference standard. Data were analyzed in Stata software (v. 11).

Results: Of 40 selected patients, CAM-ICU detected delirium in 30%. The Persian-CAM-ICU had a sensitivity and specificity of 75% and 96%, and a positive and negative predictive value of 92% and 85%, respectively. The Youden's J statistic of the scale was 71%. Each of the four domains of the CAM-ICU showed a sensitivity and specificity of more than 69% and 90%, respectively, suggesting acceptable construct validity. There was good agreement between the two evaluators in terms of delirium diagnosis with the Persian-CAM-ICU (kappa coefficient = 0.74, $P < 0.0001$).

Conclusion: The Persian version of the CAM-ICU is an effective, valid and reliable diagnostic tool in critically ill ICU patients. Application of the scale is recommended for the promptly diagnosis and prevent potential delirium in ventilated patients.

Introduction

Delirium is a disturbance of consciousness characterized by an acute onset of fluctuating and impaired cognitive functions, in a way that patient's ability to receive, process, store, and recall information is severely impaired (1).

Delirium can be subdivided to three types based on the motoric symptoms: a) hyperactive (agitated) delirium with positive symptoms; b) hypoactive (quiet) delirium with negative symptoms; and c) mixed type, if an exchange between both subtypes appears alternately over time (2). Delirium is associated with poor outcomes in hospitalized patients, including higher mortality and

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morbidity rates, increased length of hospital stay, and the need for subsequent hospitalizations (3, 4). In a systematic review of delirium outcomes in critically ill patients, patients with delirium showed also longer durations of mechanical ventilation, elongated lengths of stay in the intensive care unit and higher mortality during admission (5).

The frequency of delirium varies from 18-35% in general medical inpatients to 50% among intensive care patients (6). Delirium rate is considerably higher among ICU patients. The rate becomes even higher (close to 80%) among mechanically-ventilated patients (1, 7, 8).

Despite the high prevalence of delirium among ICU patients, it is usually overlooked during routine checkups of nurses and other non-psychiatric caregivers. Studies show that reliance on clinical judgment, either by nurses or physicians, leaves a large number of delirious patients unrecognized. In this regard, hypoactive delirium is a type that is mostly remained undiagnosed (7). This is of utmost importance, because hypoactive delirium is the most common subtype and particularly associated with adverse effects such as increased length of hospital stay and higher rate of decubitus ulcers (4). As delirium has a fluctuating yet recurrent nature, its detection requires frequent visits (9).

Delirium assessment is also time-consuming especially in patients receiving mechanical ventilation (10). Therefore, in most health care settings, especially in those hospitals where the nurse-to-patient ratio is low, it is not possible to ensure that all delirious cases are properly detected.

Accurate diagnosis is limited in the absence of a validated delirium instrument. According to a qualitative study, development and/or integration of risk

assessment and screening tools is one of the enablers to better identification of delirium symptoms (11). In a systematically review of the instruments to diagnosis the delirium, among 11 instruments used by conducted studies, the Confusion Assessment Method (CAM) had the best results, considering the ease of use and test performance (12).

A number of delirium assessment tools have been introduced for hospitalized and ICU patients. These instruments, however, do not consider communication limitations of non-verbal and ventilated patients (13).

The confusion assessment method for the intensive care unit (CAM-ICU), however, has been developed in English for the assessment of delirium in ventilated patients (7) and is commonly used in the studies carried out on these patients (14, 15). A distinct advantage of this tool is that it suits mechanically ventilated patients as patients must show a response to mild or moderate stimulation and it does not require the patient to speak (16). It is also a fast and simple tool which can be used as a routine assessment tool in the daily practice of nurses.

The instrument has been adapted to numerous languages (17-25) showing high sensitivity and specificity to identify delirium in ICU patients. For example, the Arabic CAM-ICU appeared to be valid and reliable tool for diagnosing delirium in Geriatric, Emergency and Surgical intensive care units with a sensitivity of 81% (60%-93%) and specificity of 81% (62%-92%). Sensitivity and specificity measures for mechanically ventilated patients were 100% (21).

However, to the best of our knowledge, there are no published reports on the validity and reliability of the CAM-ICU in the Persian language. Therefore, the aims of the present study were to: a) develop a Persian

version of the CAM-ICU and make it available to the Iranian non-psychiatric clinicians, as well as to the scientific community for research purposes; and b) investigate the psychometric properties of the Persian-CAM-ICU on a sample of open-heart ICU patients due to the high prevalence of delirium in these patients.

Methods

Sampling

This was a cross-sectional study. The sensitivity of the English CAM-ICU has been reported to range from 70% to 90% (7, 10, 26). Considering a minimum acceptable sensitivity of 75%, a delirium prevalence of 40% for ICU (10), and an alpha level of 5%, the minimum sample size was calculated as 40 patients. To collect study samples, we consecutively included all patients admitted to open-heart ICUs after heart surgery in three university hospitals of Tehran, Iran. Participants should be mechanically ventilated and post-surgery patients for no more than 10 days. To recruit individuals with minimum level of consciousness, we included those patients who had a Richmond Agitation Sedation Score (RASS) (27) of more than -3, could react to vocal stimuli (calling patient's name), and were able to make eye contact and obey simple tasks. They should not suffer audiovisual complications (which was assessed through observation) with no background history of cerebrovascular disease, psychosis and other mental disorders (checked in patient's medical record).

The RASS score is a standard method for scoring patients' agitation level, and was used by the psychiatrist to include individuals with a minimum level of consciousness who could fulfill the CAM-ICU assessment. In this system, calm

patients receive a score of Zero, while the scores of -1 to -4 are given to patients with different levels of sedations. On the other hand, the more the patient gets agitated, the higher scores (in a range of +1 to +4) he/she will receive (27).

As delirium has a fluctuating nature and is more prominent in the second half of the day, all participants went under delirium assessment between 4-6 PM. The time interval between the two assessments should not take more than 1 hour. In average, about three patients were assessed each day by the two evaluators. Informed consent was verbally obtained from all patients.

The questionnaire

The CAM-ICU was originally developed and validated by Ely, et al. (7, 28) to screen delirium in intubated patients. Compared with the reference standard for identifying delirium, using the CAM-ICU showed sensitivities of 100% and 93% and specificities of 98% and 100% for 2 study nurses and high interrater reliability ($\kappa=0.96$) (7) CAM-ICU comprises four features, including: a) acute onset of change or fluctuation in mental status; b) inattention; c) altered level of consciousness; and d) disorganized thinking. Under each feature, a number of symptoms presenting that feature are checked, and its presence/absence is determined.

For feature a, the scores included in the 10-point Richmond Agitation-Sedation Scale (RASS), range from a high of 4 to a low of -5. For feature b, the visual or auditory components of the Attention Screening Examination (ASE) are examined and difficulty focusing attention is evidenced by a score of less than 8 correct answers in each examination. Delirium is

considered positive when features a and b, with either feature c or d is present (7).

Linguistic validation

The Persian CAM-ICU was translated according to the Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient Reported Outcomes (PRO) Measures into Persian language (29). After obtaining the agreement of CAM-ICU developers, the English CAM-ICU was translated into Persian language by two professional English translators (forward-translation). The translated version was revised by a psychiatrist who was blind about the original version of the questionnaire, and then “back-translated” into English by a third qualified English translator, who was unaware of the original version. The back-translated version was then reviewed by two professional English translators for its consistency with the original version, based on which necessary modifications were made on the Persian version. The Persian version of the CAM-ICU is provided in Supplementary File 1.

Face and content validity

To assess face and content validity, two focus group discussions (FGD) were conducted by the research team. The members of the FGD included the research team (two nurses, one general practitioner, and one psychiatrist), four psychiatrists and two open-heart ICU nurses. The objective of the first FGD was to ensure the content, wording and appearance of the scale makes it acceptable and comprehensible for the users in Iran. Minor disagreements about the wording were resolved through consensus between FGD members. Then, one trained nurse applied the Persian CAM-ICU to 10 ventilated patients, and in the second FGD session, shared her experience about CAM-

ICU application. Required modifications were made by the research team to improve the applicability of the Persian scale.

Concurrent validity and inter-rater reliability

For the accuracy and validity studies, DSM-IV criteria applied by a psychiatrist were considered as the reference standard. CAM-ICU was applied independently by two evaluators, who were trained nurses. For each study participants, the evaluators classified the delirium status as “present” or “absent”. They also documented the duration of performing CAM-ICU assessment. The same patient underwent clinical assessment by a psychiatrist who used DSM-IV diagnostic criteria for delirium diagnosis and also classified patient’s delirium status as “present” or “absent”. The time interval between the two assessments should not take more than one hour. The nurses and the psychiatrist were blind to the classification results of the other raters. To evaluate concurrent validity, ratings of one evaluator were compared to the reference standard. To evaluate inter-rater reliability, pair assessments by the two evaluators were compared.

Construct validity

CAM-ICU has four domains including: a) acute onset or fluctuating course, b) inattention, c) altered level of consciousness, and d) disorganized thinking, all of which requiring a yes/no answer. To evaluate the construct validity of the CAM-ICU, sensitivity and specificity of each constructs in detecting the targeted feature was evaluated given DSM-IV criteria applied by a psychiatrist as the reference standard, following the standard formula proposed for sensitivity and specificity (30-32).

Ethical considerations

The study protocol was reviewed and approved by the Ethics Committee of Tehran University of Medical Sciences (Ethical Code: 10251-28-01-89). Informed consent was verbally obtained from all patients.

Data analysis

Validity indices including sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), accuracy, and Youden's J statistics were calculated using a simple 2 by 2 table. Ninety-five percent confidence intervals (CI) were calculated using exact score interval for these proportions. Values less than 0.7 was considered as 'undesirable' validity. Values between 0.7 and 0.8 were considered as acceptable validity. Values greater than 0.8 were considered as excellent validity (33). Inter-rater reliability was evaluated by calculating Kappa statistics. All data were analyzed using Stata software (v. 11). Statistical tests were considered as significant at 0.05 levels.

Results

A total of 40 mechanically-ventilated patients were included in this study. Most participants were male (n=33; 82.5%) and married (n=36; 90%), with a mean age of 56.9±12.3 yr. Participants were mainly hospitalized for coronary artery bypass graft (CABG) surgery (n=27; 67.5%). Other reasons included heart transplantation (n=5; 12.5%), aneurysm surgery (n=3; 7.5%), aortic valve surgery (n=3, 7.5%), pericardial effusion (n=1; 2.5%), and atrial septal defect (n=1; 2.5%). The prevalence of delirium based on psychiatrist's decision and the

CAM-ICU was 40% and 30%, respectively. Most participants (n=26, 65%) had a RASS score of zero, and least of them (n=4, 10%) had a score of $\geq +1$, suggesting some levels of agitation (Table 1).

Table 1. Demographic and clinical characteristics of study participants (n= 40)

Demographic characteristics	n (%)
Age (Mean \pm SD)	56.9 \pm 12.3
Sex	
Male	33 (82.5)
Female	7 (7.5)
Residential area	
Tehran	31 (77.5)
Other	9 (22.5)
Educational status	
Illiterate	13 (32.5)
Some school	12 (30)
Diploma	9 (22.5)
University-level	6 (15)
Marital status	
Married	17 (42.5)
Single	3 (7.5)
Divorced	7 (17.5)
Widow	13 (32.5)
Insurance	
Yes	27 (67.5)
No	13 (32.5)
Living with family member(s)	
Yes	35 (87.5)
No	5 (12.5)
Clinical characteristics	n (%)
Reason for hospitalization	
CABG*	27 (67.5)
Heart transplant	5 (12.5)
Aneurysm surgery	3 (7.5)
Aortic valve surgery	3 (7.5)
Pericardial effusion	1 (2.5)
Atrial septal defect	1 (2.5)
RASS score**	
Zero (normal)	26 (65)
-1 to -4 (sedation)	10 (25)
+1 to +4 (agitation)	4 (10)
Delirium status***	
None	24 (60.0)
Mild	1 (2.5)
Severe	15 (37.5)
Delirium prevalence	
DSM-IV	16 (40)
CAM-ICU****	12 (30)

* CABG: Coronary artery bypass graft; **RASS: Richmond Agitation-Sedation Scale; ***Delirium status reported here is based on psychiatrist's diagnosis, who used DSM-IV criteria for his diagnosis. ****CAM-ICU does not categorize delirium cases into mild/severe categories.

The average time to assess delirium for each patient using CAM-ICU was 4.2 ± 1.8 minutes. The overall inter-rater reliability was found to be 'very good' (kappa statistics: 0.74, $P < 0.0001$). Sensitivity and specificity of CAM-ICU features were as follows: a) acute onset or fluctuating course (0.71 and 0.97); b) inattention (0.69 and

0.94); c) altered level of consciousness (0.74 and 0.97); and d) disorganized thinking (0.71 and 0.97). The Youden's J statistic, as a way of summarizing the performance of a diagnostic test, was 0.71 (0.61-0.80). The results showed good accuracy as 0.87 (0.80–0.93). Table 2 provides further details about validity and reliability indices of CAM-ICU.

Table 2. Results obtained for CAM-ICU after comparing with the reference standard*

CAM-ICU	Reference standard*			Validity indices		
	Mild delirium	Severe delirium	Non-delirious	Point estimate	SE	95% CI
Delirious	0	12	1	-	-	-
Non-delirious	1	3	23	-	-	-
Validity indices						
Sensitivity	-	-	-	0.75	0.04	0.65 – 0.83
Specificity	-	-	-	0.96	0.02	0.90 – 0.99
Positive Predictive Value	-	-	-	0.92	0.03	0.85 – 0.96
Negative Predictive Value	-	-	-	0.85	0.04	0.76 – 0.91
Youden's J statistic	-	-	-	0.71	0.05	0.61 – 0.80
Accuracy	-	-	-	0.87	0.03	0.80 – 0.93
Kappa	-	-	-	0.74	0.15	$P < 0.0001$ **

* Reference standard was DSM-IV criteria, applied by a Psychiatrist. ** Indicates the P value for the Kappa test, and shows that the raters' agreement is beyond the chance-agreement. **SE:** Standard Error.

Discussion

This study aimed to adopt CAM-ICU in Persian language to assist ICU staff in delirium detection during their routine practices. Applying both CAM-ICU and DSM-IV criteria, our results also pointed to a high prevalence of delirium in investigated cardiovascular ICUs. Validity and reliability measures reported in this study showed that the Persian version of this scale has a high validity and reliability.

The development and validation of diagnostic and decision-support tools is important for proper diagnosis of clinical disorders. The CAM-ICU has been translated and adapted to many languages and has become the most frequently used instrument for diagnosing delirium in ICU patients. The CAM-ICU, an adopted version of the CAM to diagnose delirium in

mechanically-ventilated patients, was firstly validated by Ely, et al. on 38 patients. In addition to a high specificity and sensitivity, they observed an excellent inter-rater reliability (7). Later they published a second study, where they included 111 mechanically ventilated patients. Their study again resulted in a high inter-rater reliability (kappa statistic: 0.99, 95% CI: 0.92 – 0.99), as well as a sensitivity and specificity of approximately 100% (7).

Our study differs in some respects from these studies. First, we did not observe as high sensitivity for the CAM-ICU as reported by Ely et al. In our study, the sensitivity of the CAM-ICU was 75%. Although there is not a clear justification, the discrepancy is not likely related to the implementation of the CAM-ICU in Persian language, as similar results have been

observed in other settings and languages (17, 24). For example, Akinci, et al., observed a sensitivity and specificity of 65% and 69% for the Turkish version of CAM-ICU, respectively (25). Testing the validity of CAM-ICU in a mixed population of critically ill patients in Portugal, Gusmao-Flores, et al. reported a sensitivity of 72.5% and a specificity of 96.2% (24). The variation of the instrument's sensitivity in different settings should be considered and adjusted while the aim is to estimate delirium incidence and prevalence among ICU patients using CAM-ICU. A common feature of most validation studies, however, has been the high specificity and accuracy of the CAM-ICU (7, 17-19, 25, 26).

One possible explanation for diverse sensitivity indices of the CAM-ICU, is patient-related factors. In our study, most patients had a RASS score of zero (65%), which may represent the lower degree of severity in our sample. This finding may also be indicative of a trend toward less sedation in ICU patients in recent years (34). Luetz, et al. demonstrated an association between CAM-ICU sensitivity and RASS score, in a way that patients with a RASS score of higher than 0.25 provide a higher sensitivity for the CAM-ICU.

Another explanation might be the fluctuating nature of delirium, especially during the first day after extensive surgeries, like CABG. In our study, the patients' cognitive status might have fluctuated from the time of CAM-ICU implementation to the time of psychiatrist visit. Although we have minimized the time lag between the two assessments, this issue may still be a reason for discrepant results in our study. A time lag of about one hour between two evaluators was similarly chosen by previous

studies who also reported the same sensitivity values (17, 18, 24, 26). This can further highlight the role of timing in this regard. In our study, four cases with discordant results for the two assessments were CABG patients that were assessed at their first day after surgery.

The last delirious patient, who was classified as non-delirious in our study, was a mild case of delirium. McNicoll, et al. has noted that CAM-ICU is less sensitive to mild cases of delirium (26). In a comprehensive review on assessment scales for delirium, Grover, et al. have noted that CAM-ICU is mostly applicable to the diagnosis of delirium rather than delirium severity rating (35). The more the time it takes to assess the delirium, the more mild and sub-clinical delirium cases are identified (36, 37). Therefore, for relatively conscious patients that might suffer from mild delirium, the use of standard CAM-ICU is preferred to the short form CAM-ICU (i.e., the flowchart).

Our results showed a very good inter-rater reliability. The value of Kappa statistics was also statistically significant suggesting that the observed agreement between the two rater was beyond the chance agreement. This is consistent with the results of previous studies in USA (7), Spain (17), Czech republic (18), Turkey (25), and Portugal (24).

Our study has some notable limitations. First, most patients included in our study were older than 65 years. This can limit the generalizability of our results to other age groups. This gap should lay a foundation for future studies in this area. Second, we restricted our samples to open-heart ICU patients. The reason for this was that delirium prevalence is considerably high among these patients. So we could ensure

that we can efficiently reach to the specified sample size. This may limit the generalizability of our results to other kinds of ICU patients. However, we believe that the effect of our sampling on the generalizability of our results would be negligible because there is no clear factor associated with open-heart ventilated patients that can significantly affect the results. All in all, we recommend similar studies to be conducted on other types of ventilated patients in future. Third, while assessing a patient for delirium, there are some differential diagnoses that should be ruled out, such as dementia, depression, schizophrenia, mania, and anxiety disorders. These disorders are not common among ICU patients but some are prevalent among elderly patients.

Therefore, while employing CAM-ICU to older adults, it is recommended to rule out the abovementioned conditions, although the abovementioned conditions put elderly at higher risk to develop delirium. Forth, in this study, only one case of mild-delirium was diagnosed by the psychiatrist. So, the sample size was not enough for performing discriminant validity analyses on mild cases. It is recommended that future studies perform this analysis for the Persian CAM-ICU questionnaire, indeed in a large sample size.

Our study also has some notable strengths. We measured the performance of the CAM-ICU against the DSM-IV criteria, using two independent evaluators (a nurse and a psychiatrist, respectively), who were also blind to assessment results of the other investigator. Therefore, the assessment results of the CAM-ICU in this study do not imply an evaluation bias. Not only was our study the first one to validate the CAM-ICU for Iranians, but also it was performed as a multicenter evaluation in three different

referral hospitals of Iran, admitting candidates for critical cardiovascular surgeries from across the country.

Our results suggest that the CAM-ICU is a valid tool that can be used in Persian-language countries with acceptable sensitivity and a high degree of accuracy. The instrument is an appropriate tool for developing a diagnostic profile. It can be used by Iranian non-psychiatric clinicians (e.g. nurses) to assist their routine patient assessment. This tool can also be used by researcher in relevant research works, as it helps to accurately detect delirium in a time-efficient manner. The instrument can also be used to promptly assess patients' cognitive status while drug therapy is performed with analgesics and sedatives. This way, nurses can efficiently control the drug dosage and monitor drug overdose and adverse effects.

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