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Methods for assessment of cognitive failure and delirium in palliative care patients: implications for practice and research

Marianne J Hjermstad The Norwegian Cancer Society, Oslo and Department of Behavioral Sciences in Medicine, University of Oslo and Department of Clinical and Molecular Medicine, Faculty of Medicine, The Norwegian University of Technology and Science, Trondheim, and **Jon H Loge** Department of Behavioral Sciences in Medicine, University of Oslo and Department of Clinical and Molecular Medicine, Faculty of Medicine, The Norwegian University of Technology and Science, Trondheim and **Stein Kaasa** Palliative Medicine Unit, Department of Oncology, St. Olav's Hospital, Trondheim

The most commonly encountered clinical conditions presenting with cognitive failure (CF) are delirium, dementia and amnestic disorders. Of these, delirium is probably the most prevalent in palliative care, and it is potentially reversible. Thus, improvement in diagnostics seems warranted. The objectives of this review were to examine the methods for assessment of CF and delirium in palliative care.

Twenty-two studies were reviewed: 64% were published in 2000 or later. Twelve reports focused on delirium, six on CF, while the remaining four assessed confusion (2), hallucinations and general psychological morbidity. Median sample size was 100 (20–393). Ten different instruments were used: The Mini Mental State Exam was used in 13 studies. Five studies were validation reports of new or existing instruments.

The term CF is an imprecise description of a loss in one or more of the cognitive functions. The interchangeable use of CF as a description of specific diagnoses should be avoided, as this contributes to prevalence rates that are not representative. Assessment tools that discriminate between the different diagnostic entities presenting with CF should be used in future studies. *Palliative Medicine* 2004; **18:** 494–506

Key words: clinical practice; cognitive failure; delirium; palliative care

Introduction

Cognitive functions include: attention, concentration, intelligence, learning, judgment, memory, orientation, perception, problem solving and psychomotor ability.[1–3] The wide range of cognitive functions suggests that cognitive impairments are likely to have important implications for patients' quality of life (QOL) through the impact on the understanding of information, informed consent, participation in decision making, treatment compliance, and relationship with relatives and care givers.[3–5] Consequently, valid and reliable assessment of cognitive function is of great relevance for practice and research in palliative care.

Cognitive failure (CF) is reported as frequent in cancer patients. A wide variety of mechanisms such as direct cerebral tumour involvement, infections, metabolic disturbances, medications, drug interactions, age and other premorbid conditions might contribute to CF in this group of patients.[4,6,7] CF, particularly the acute onset of delirium, is associated with impending death in patients with advanced disease.[6–11] CF has been demonstrated to be an independent survival predictor[12] and a risk factor for longer hospitalization.[7,13]

The concept CF has not been used consistently in the literature. This is reflected by the many synonymous or overlapping terms such as: cognitive impairment, confusion, agitated confusional states, impaired mental status, cerebral insufficiency, acute brain failure and dementia. In the present paper CF denotes the loss of one or more of the cognitive functions. An alternative term: altered mental status, is perhaps preferable as an over-riding description because it refers to specific deviations observed in standard mental examination.[7] According to the most recent version of the Diagnostic and Statistical Manual of Mental Disorders Text Revision, the DSM-IV TR,[14] CF is an essential feature of three separate conditions: delirium, dementia and amnestic disorders. Each of these has additional, separate diagnostic characteristics. All three conditions present with impaired cognitive functioning in one or more areas (Table 1).

Delirium is due to a general medical condition and the CF is not accounted for by a pre-existing, established or

Address for correspondence: Marianne Jensen Hjermstad, Department of Behavioral Sciences in Medicine University of Oslo, Box 1111, N-0317 Oslo, Norway.
E-mail: m.j.hjermstad@basalmed.uio.no

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Table 1 Diagnostic criteria for the three separate conditions: amnestic disorder, dementia and delirium[1]

Amnestic disorder	
Memory impairment	Manifested by impairment in the ability to learn new information or the ability to recall previously learned information
Functional impairment	Significant impairment in social or occupational functioning, representing a significant decline from a previous level of functioning
Chronologic criteria	The memory disturbance does not only occur exclusively during the course of delirium or dementia
Organicity criteria	Evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of a general medical condition
Dementia	
Development of multiple cognitive deficits	Manifested by impairment in the ability to learn new information or the ability to recall previously learned information and THE presence of one or more of the following cognitive disturbances: aphasia, apraxia, agnosia, disturbance in executive functioning
Delirium due to a general medical condition	
Disturbance of consciousness	Reduced clarity of awareness of the environment, with reduced ability to focus, sustain or shift attention
Change in cognition	Memory deficit, disorientation, language or perceptual disturbance that is not better accounted for by a pre-existing, established or evolving dementia
Chronologic criteria	Develops over a short period of time (hours to days) and tends to fluctuate during the course of day
Organicity criteria	Evidence from the history, physical examination or laboratory findings of a general medical condition judged to be aetiologically related to the disturbance

According to and adapted from the DSM-IV TR[14] and DSM-IV.[23]

evolving dementia.[14,15] An agitated, a hypoactive and a mixed form (the most frequent) of delirium can be recognized.[7,14–16] Delirium differs from dementia by its abrupt onset (often within hours), and the fluctuation of symptoms during the day.[16] The amnestic syndrome is characterized by memory impairment that is a direct physiological consequence of a medical condition (Table 1).[14] The symptoms in amnestic syndrome should not be accounted for by delirium or dementia.

Dementia and amnestic disorders are reported less frequently than delirium in palliative care, with prevalence rates of 11% and 3% respectively.[11] CF, in particular delirium, is reported as commonly encountered, especially towards end of life.[3] The frequencies of CF in various samples of palliative care cancer patients range from 14% to 44%,[6,7,11,17–19] while up to 90% of patients show impairment before death.[4,6,19] The reported prevalence rates for delirium among palliative care patients range from 28% to 52%, and up to 85% develop delirium at some stage before the end of life.[2,4,10,11,18–20] A median duration of six days was reported for nonreversed delirium before death.[2]

The differences in prevalence rates across studies are probably due to various factors such as sampling procedures, sample sizes, sample characteristics such as age, study designs, methods of assessment, time to death and the revisions of the classification criteria, such as the DSM-III,[21] DSM-III-R,[22] DSM-IV,[23] and DSM-IV TR.[14] A study undertaken to determine the prevalence of delirium in a general patient sample of older, hospitalized patients yielded a variation in prevalence from 9% to 38% i.e., 9% as assessed by the ICD-10 research criteria,[24,25] 33% by DSM-III-R and 38% DSM-III.[26]

CF is often underdiagnosed, misdiagnosed as depression[27–31] or simply overlooked and hence untreated by nurses and clinicians.[4,5,30] Clinically, the standard mental examination, if conducted properly, should reveal impairment in central cognitive functions such as attention, consciousness, memory and orientation. For screening, research or as a supplement to the clinical examination, specific instruments for assessment of cognitive functioning might be warranted. Given the high prevalence of CF, the selection of appropriate instruments is important in most patient populations including palliative care patients.

Several instruments for assessing cognitive functions are available. Some QOL questionnaires such as the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30),[32] the Functional Assessment of Cancer Therapy Scale (FACT)[33] and the Rotterdam Symptom Checklist (RSCL)[34] incorporate questions on cognitive function, but these are insufficient for screening purposes. Additionally, there is low correlation between patients' self-reporting of CF, often conceptualized as memory and/or concentration difficulties, and objective testing.[35,36] The diagnostic classification systems; the DSM-system,[14,21–23] and the ICD classifications: ICD-9[24] and ICD-10,[25] yield the relevant diagnoses for conditions presenting with CF. The operationalization of the DSM-III-R criteria in the Structured Clinical Interview for DSM-III-R (SCID)[37] and other diagnostic interviews such as the Delirium Symptom Interview (DSI)[38] and the Confusion Assessment Method (CAM)[39] are most relevant for palliative care. The Delirium Rating Scale (DRS),[40,41] the Confusion Rating Scale (CRS),[42] the Saskatoon Delirium Checklist (SDC)[43] and the MDAS (Memorial Delirium Assessment Scale)[20] all specifically assess delirium. There are also a

number of cognitive screening instruments: the Short Portable Mental Status Questionnaire (SPMSQ),[44] the Cognitive Capacity Screening Examination (CCSE),[45] the Blessed Orientation Memory Concentration test (BOMC)[46] and the MMSE (Mini-Mental State Exam).[47] A thorough review of the different instruments is provided by Smith *et al*.[48]

The major objectives of the present report were therefore to examine how CF or delirium was assessed in studies on cancer patients in palliative care with the aim of answering the following questions:

1) Are studies undertaken that specifically assess CF and/or delirium in cancer patients receiving palliative care?
2) What are the reported prevalence rates of these conditions?
3) Which assessment tools were used, and how were they validated?

Methods

Literature search

We selected three main criteria that had to be fulfilled for inclusion in this report:

1) The assessment of CF, confusion or delirium by specific assessment tools should be one of the main outcomes.
2) The patient sample should be described as having advanced cancer and be receiving palliative care, for example at a palliative care unit (PCU) or in a hospice.
3) The study design should be described, there should be a quantitative approach and the sample size should be at least 20 patients.

The following electronic databases were searched: *Pubmed*, *Cancerlit* and *PsychInfo* (from 1966 to May 2003); *Embase* (from 1980 to April 2003), *Cinahl* (from 1982 to April 2003); and the *Cochrane Library* (from 1970 to April 2003). All searches proceeded from the first to the most recent issue. The following Medical Subject Heading (MeSH) search terms were used: 'cognitive function' or 'CF' or 'delirium', combined with 'palliative care' or 'palliative care research' or 'palliative medicine' or 'hospice'. The reference lists of all publications that were classified as relevant were searched manually.

The search was restricted to publications from English-language journals. Case reports, editorials, letters, commentaries, reviews and overviews were excluded, as were reports on children. The decision on whether or not to include the publications identified through the search was made by examining all titles and abstracts in relation to the inclusion criteria. This was conducted by MJH. If there was uncertainty as to whether a paper fulfilled the criteria, the entire paper was read, and one of the other reviewers, JHL, was consulted. Because our population of interest was cancer patients receiving palliative care, publications concerning other diagnostic groups were excluded.

Results

A total of 1411 citations were retrieved from the literature searches, with 978 being duplicates.

A close examination of the identified hits revealed that of the remaining 433 hits, only 22 publications met our criteria for inclusion, because they were actual studies in palliative care. The majority of the excluded studies failed to meet two or more of the inclusion criteria. The most frequent reasons for exclusion were that the publication was not a clinical study (17%) or that CF or delirium was not a specified study outcome (8%).

Study objectives

Of the 22 studies, six were specifically aimed at screening for CF.[4,6,10,35,49,50] The assessment of delirium was the main objective in 12 reports,[2,8,9,18,20,31,51–56] defined as 'agitated impaired mental status' in one[55] and 'acute confusional states' in another.[56] Four studies evaluated the assessment of psychological morbidity,[11] confusion[57,58] or visual hallucinations in relation to CF,[59] respectively. The majority of the studies, 64%, i.e., 14 of 22 were published in 2000 or later, indicating that research on cognitive function in palliative care is a relatively new field.

All of these studies are described in Table 2. The 22 studies covered 24 samples, with sample sizes varying from 20 to 393 patients (mean: 123, median: 100).

Design

Seventeen studies were performed in PCUs, while a validation study of the MDAS was undertaken in a general cancer ward where the treatment intention was not reported.[20] However, based on the poor performance status – with a median Karnofsky score of 30 – we decided to include this study. Four studies were undertaken in patients who were undergoing a hospice program, with one of these studies also including patients receiving palliative care at home.[58] The reasons for being admitted to the PCU were described in nine studies as symptom management for advanced or incurable disease, where chemotherapy was no longer viable. Terminal cancer was used as a descriptor in six reports, while two studies were undertaken during the patients' last week of life.[53,56] Life expectancy was defined as less than six months in the studies by Klepstad *et al.* and

Table 2 Overview of selected studies, objectives, instruments and conclusions

First author, publication year	Sample size	Study design[a]	Study objectives	Instruments	No. of assessments	Prevalence of CF	Conclusion
Breitbart, 1997[20]	I: 33	I: Cross-sectional	To perform reliability and validity testing of the MDAS	I: Initial, independent psychiatric evaluation, MDAS assessed during stay by two other psychiatrists	I: Psychiatric evaluation before weekly MDAS	I: 52% with delirium, 24% with other CF	MDAS is a brief, reliable and stable instrument for assessment of severity of delirium. It correlated highly with other tools for cognitive impairment and delirium. It is beneficial for repeated measures, particularly in clinical research. Further research necessary to determine validity and cut-offs for diagnostic purposes, and properties in other patient groups.
	II: 51	II: Cross-sectional		II: MDAS assessed by one clinician compared with DRS, MMSE and the Clinician's Global Rating of Delirium severity assessed by another clinician	II: Psychiatric evaluation before clinicians' ratings	II: All met DSM-IV criteria for delirium	
Bruera, 1992[4]	61	Prospective	To determine the prevalence and clinical course of CF in patients with terminal cancer	MMSE	Three times a week before discharge or death	83% before death	CF is extremely prevalent in the last week of life; informed consent is unreliable.
Bruera, 1992[10]	61	Prospective	To estimate survival through medical examination and nursing assessments	MMSE, symptom registration. Medical examination first day	Once upon admission	Not specified, included as part of the prognostic indicator	Three simple determinations: weight loss, MMSE <24 and dysphagia can predict survival as more or less than four weeks, as good as physicians exams.
Bruera, 1995[55]	I: 117 (1988–89)	Retrospective	To compare the prevalence of impaired mental status (IMS) after routine cognitive assessment, regular hydration and opioid rotation	I: Chart reviews for records of clinical examinations	I: Not regular, based on clinical observation	I: IMS: 31%, agitated IMS: 26%	The incidence of agitated impaired mental status may be reduced after routine cognitive assessment, hydration and opioid rotation in terminal cancer patients.
	II: 162 (1991–92)			II: Chart reviews for records of clinical examinations including MMSE	II: MMSE twice a week until death	II: IMS: 40%, agitated IMS: 10%	
Bruera, 1996[50]	120	Prospective	To assess withdrawal symptoms after rapid discontinuation of hypnotics, and the effect on insomnia and CF	Four visual analogue scales for intensity of insomnia, restedness and difficulty falling asleep, MMSE	Days 1, 4 and 7 during discontinuation	Prevalence rates not reported, MMSE scores expressed as normal with mean >80%	Rapid withdrawal of hypnotics can be safely administered, achieving improved CF.
Caraceni, 2000[8]	393	Consecutive series	To assess the impact of delirium on survival	CAM, PaP	Once upon study entry	28% with delirium	The diagnosis of delirium worsens life expectancy. Median survival time in delirious patients were 21 days, compared with 39 in nondelirious patients. Assessment of CF may help in predicting survival together with the PaP score.

Table 2 (*Continued*)

First author, publication year	Sample size	Study design[a]	Study objectives	Instruments	No. of assessments	Prevalence of CF	Conclusion
Fainsinger, 2000[53]	150	Three consecutive series, in hospices and two PCUs	To assess the prevalence of symptoms requiring sedation at the end of life	MMSE, ESS, screening questions for alcohol abuse	Data collected as close to death as possible	80% in all settings developed delirium prior to death, 40% requiring sedation in the acute care setting, 80% in the tertiary pall. unit	The prevalence of delirium and other symptoms requiring sedation was relatively low. Improved management in palliative and terminal care have probably resulted in fewer distressing symptoms at the end of life.
Fountain, 2001[59]	100	Consecutive series	To screen for CF and visual hallucinations	MMSE and semi-structured interview on visual hallucinations	Once upon study entry	25% were too drowsy or delirious to complete the MMSE	47% of the patients had experienced visual hallucinations in the previous month. No association between hallucinations and CF was found.
Gagnon, 2000[18]	89	Prospective	To determine delirium frequency and outcome in terminal care	CRS, CAM	Daily until death	20% (CI 12–29%) prev. of delirium symptoms on admission, 13% (CI 6–21%) confirmed, 52% (CI 41–64%) prev. of delirium symptoms during follow-up in those negative on admission, 33% (CI 12–29%) confirmed	Delirium is a frequent and serious complication in terminal cancer. Significant symptom improvement occurred in 50%, indicating that delirium might be reversed. Integration of daily assessments of cognitive status enhances the awareness of CF among staff.
Gagnon, 2002[51]	124 care givers	Consecutive, voluntary recruitment of caregivers. Comparative, nonrandomized design	To develop, implement and assess the impact of a psychoeducational intervention on the knowledge and coping with delirium in family care givers	CRS for assessment of delirium in patients	CRS on admission	Delirium in patients	Family care givers only had a slight benefit from the specific psychoeducational intervention in the terminal phase. A specific intervention on delirium might be more beneficial if delivered earlier in the course of disease.
				Psychoeducational intervention for care givers, then interview on mood, competence and knowledge	Interview of care givers 2–3 weeks after death		
Klepstad, 2002[35]	29	Cross-sectional	To assess the relationship between self-reports and observers' ratings on cognitive function and sedation	MMSE, EORTC QLQ-C30 (cognitive function), OAA/S, verbal rating scale of sedation	Once, twice for seven patients who were readmitted to palliative care	29% of CF, on the MMSE	Self-reports are not related to objective assessment of cognitive function and sedation.
Lawlor, 2000[31]	104	Prospective	To assess the clinical utility, factor structure and validity of the MDAS	DSM-IV, MMSE, MDAS	Clinical assessment twice daily, MMSE twice weekly, +when needed, DOCS during shifts, MDAS when clinical signs were observed	68%: at least one episode of delirium in 71 patients of 104	MDAS is representative of the multifaceted delirium, and demonstrates ability to differentiate between the different types of delirium. Because pro-rating of scores might be necessary, the MDAS less well suited for research, but offers a clinical advantage for assessment in patients with advanced cancer.

Table 2 (*Continued*)

First author, publication year	Sample size	Study design[a]	Study objectives	Instruments	No. of assessments	Prevalence of CF	Conclusion
Lawlor, 2000[2]	113	Prospective	To assess the occurrence, duration, precipitating factors and reversal rates of delirium and patient survival	DSM-IV, MMSE, MDAS, DOCS (ad hoc delirium observational checklist)	Clinical assessment twice daily, MMSE twice weekly, +when needed, DOCS during shifts, MDAS every 72 hours in delirious patients	42% had delirium on admission, 45 of those who were not diagnosed developing it later. Terminal delirium in 88%. Reversal occurred in 49%	Delirium is reversible in 50% of terminal cancer patients through change or dose reduction of opioids, hydration, discontinuation of other medication.
Minagawa, 1996[11]	93	Consecutive series	To determine the rate of psychiatric disorders in patients with terminal cancer	MMSE, SCID (for DSM-III-R)	Once within the first week of admission	54% met the DSM III-R criteria for psychiatric morbidity, 42% with CF, 28% with delirium	Above 50% of the patients were diagnosed with a psychiatric disorder, delirium being most common. Prospective trials are necessary to establish appropriate treatment modalities.
Morita, 2001[52]	30	Cross-sectional	To assess the validity of two new scales for quantification of communication capacity and agitated behaviour in delirium	Communication scale, Agitation scale, MDAS, DRS, Sedation scale	Once within the first 24 hours of diagnosis	All diagnosed with delirium according to the DSM-IV	The Communication and Agitation scales are useful for evaluation of terminal delirium in palliative care. They are brief, simple, suited for repeated measures and showed acceptable reliability and validity in terminally ill cancer patients.
Morita, 2001[9]	237	Prospective	To identify precipitating factors and their association with features of delirium	MDAS, DRS, PPS, KPS, clinical parameters	At least twice a day, MDAS and DRS within 24 hours after clinical signs of delirium	Delirium was an inclusion criteria, 245 episodes were identified in 213 patients	Precipitating factors were identified in 93%, two or more factors in 52%. Standard examinations can confirm contributing factors, thus aid in prediction of the severity of delirium.
Nowels, 2002[58]	299	Cross-sectional	To describe the prevalence and severity of confusion and estimate the prevalence of delirium	DSM-IV criteria checklist and demographics	Registration by nurses of episodes during the preceding week	50% were confused, 36% of those were severely confused or disabled by confusion, 14% met criteria for delirium	Confusion among hospice patients was frequent, causing a problem for the patients or others 79% of the time.
Pereira, 1997[6]	348	Retrospective	Assessment of the frequency and clinical course of CF	MMSE	Upon admission, then once or twice weekly (4.7 in average)	44% had abnormal MMSE on admission, 55% at discharge or before death, 68% prior to death	CF is reversible in a significant number of cases. Reduced cognitive function is a poor prognosticator for discharge; cognitive screening should be performed on admission.
Radbruch, 2000[49]	123	Consecutive series	To test a new assessment for sufficient pain and symptom information with minimal burden to patients and staff	MIDOS, MMSE, SF-12, BPI, ECOG	On admission, then 2–4 weekly intervals (not included)	42% had CF on the MMSE (cut-off 23/24, 35% with cut-off 20/21, 28% with cut-off 18/19	Only a minority of the patients were able to use numerical scales for symptoms other than pain. Symptom assessment in clinical practice in palliative care should provide simple categorical rating scales, and also be administered by interview.

Table 2 (*Continued*)

First author, publication year	Sample size	Study design[a]	Study objectives	Instruments	No. of assessments	Prevalence of CF	Conclusion
Sarhill, 2001[54]	50	Prospective	To evaluate the use of the BCS in detecting delirium in advanced cancer. To determine prevalence, precipitating factors and treatment of delirium	BCS, information on predisposing factors for delirium	Once upon admission	32% (13/41) were delirious, 10 of 41 (24%) were classified as borderline	BCS is simple, portable valid and easy to use by the health care providers. Delirium is common in advanced cancer patients, with brain metastatis and drugs being the most predisposing factors.
Stiefel, 1992[56]	100	Retrospective	To assess the need for medication for delirium	Chart reviews for records of clinical examinations	Last week of life	39% suffered from delirium during last week of life, all requiring medication	Symptoms were controlled in 23 patients (60%) by haloperidol, lorazepam or both. A combination treatment of neuroleptics and benzodiazepines is often utilized in palliative care to control symptoms and alleviate side effects.
Stillman, 2000[57]	31	Consecutive series	To develop a simple, sensitive bedside test for confusion and validate it against the established CAM	BCS, CAM, KPS	As part of the routine medical examination	58% confused on the CAM 65% on the BCS	The BCS possessed high sensitivity and might be useful for screening, due to its ease of operation. It showed satisfactory correlation with the CAM.

[a]To be labelled as prospective, the recruitment of patients should be described as consecutive, they should be followed to a specified study outcome and the study should preferably employ repeated measures.

Agitation scale: Agitation Distress Scale; BCS: Bedside Confusion Scale; BPI: Brief Pain Questionnaire; CAM: Confusion Assessment Method; Communication scale: Communication Capacity Scale; DOCS: Delirium Observational Checklist Scale; DRS: Delirium Rating Scale; DSM-III-R: Diagnostic and Statistical Manual for Mental Disorders, third edition, revised; ECOG: Eastern Cooperative of Oncology Groups performance status; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Core Questionnaire; ESAS: Edmonton Symptom Assessment Scale; ESS: Edmonton Staging System for cancer pain; KPS: Karnofsky Performance Status Scale; MDAS: Memorial Delirium Assessment Scale; MIDOS: Minimal Symptom Documentation System; MMSE: Mini-Mental State Examination; OAA/S: Observer's Assessment of Alertness /Sedation Scale; PaP: Palliative Prognostic; PPS: Palliative Performance Scale; SCID: Structured Clinical Interview for DSM-III-R.

Morita.[9,35] Two studies did not specify the reason for admission to the PCU. Precise cancer diagnoses of the patients were provided in 16 studies. Over 54% of the patients in all studies suffered from cancer.

Six studies could be labelled as 'prospective' according to the following criteria (Table 2):

1) The patients were recruited consecutively.
2) The course of their illness was followed up to a defined clinical outcome (manifestation of delirium, death or discharge).
3) Repeated measures were performed.

Two other studies described their design as 'prospective' in their methods sections[10,54] and were also labelled as such in Table 2, although they failed to meet criterion 3. Repeated measures were performed in two of the three retrospective studies.[6,55] Four studies employed a cross-sectional design, while the publication by Gagnon *et al.* employed a comparative, nonrandomized design.[51] This was an intervention study that evaluated the effect of a general psychoeducational program on the knowledge of the disease and coping strategies of family care-givers of patients with delirium.

As in the prospective studies, the enrolment of patients was based on consecutive admissions in the remaining eight studies. It is noteworthy that the exclusion criteria for the patients who were potentially eligible were described in only nine of the 22 studies.

Prevalence

The reported prevalence rates in the evaluated studies ranged from 10% to 83% for general cognitive impairment, from 20% to 88% for delirium and from 50% to 68% for confusion. Only one study provided confidence intervals (CI) for estimates of the prevalence of delirium.[18] Fifteen of the 22 studies showed the standard deviations while four studies provided CIs of the mean scores of the various outcome measures such as MMSE scores and survival.

Instruments

The MMSE was the most frequently used assessment tool and was employed in 13 studies.[47] In six of these studies the MMSE was employed in combination with other specific instruments for assessment of CF/delirium. The MDAS was used in five studies,[20] together with the MMSE in three, while the CAM was used in three studies.[39] The DSM criteria were applied in four studies.[23]

Four publications focused on testing the reliability and validity of new assessment tools and instrument development of the Communication and Agitation Scales,[52] the Minimal Documentation System,[49] the Bedside Confusion Scale[54] and the Memorial Delirium Assessment Scale,[20] respectively. One study aimed at a further evaluation of the clinical utility, reliability and validity of the MDAS.[31]

Ten validated assessment tools that were used in the selected studies are outlined in Table 3. The ad hoc checklist DOCS[2] and the categorical scale for clinicians' rating of delirium[20] were omitted, due to poor information on their validation and properties. The DSM criteria (III, III-R or IV) were incorporated into four tools (SCID, DRS, CAM and CRS). In the selected studies as a whole, the psychometric properties of all instruments have been validated for the assessment of CF, confusion or delirium, by means of correlation with other instruments or tests (Table 3). According to the review by Smith *et al.*, the validity of these instruments with respect to screening, diagnostic and severity rating varied from poor to excellent depending on the purpose of the instrument.[48] Specific validation reports for use in palliative care were found for the MDAS,[2] the BCS[54] and the Agitation and Communication Scales.[52] The information on sensitivity and specificity yielded a variation from 68 to 100 and 82 to 97 respectively (Table 3). Nine of ten tools were observer rated and intended for use by clinicians. Only the MMSE and the BCS were suited for use by lay interviewers, the MDAS and DRS were intended for scoring by psychiatrists, while the remaining instruments required various amounts of training before administration. The duration of administration varied from two minutes for the BCS to 10–15 minutes for the MMSE/MDAS. Normative data exist for six instruments, but patients' scores were not compared against these or against other reference groups in any reports.

Discussion

Systematic studies with validated tools for the assessment of CF and/or delirium in a palliative care setting are sparse, as can be inferred from this report. However, a major problem concerning this research is related to definitions of study outcomes with the interchangeable use of terms such as confusion, CF, agitated confusional states etc. Many reports still use the term CF, even though the study outcome might be dementia, delirium or cerebral insufficiency of various kinds. Because the concept CF is not related to one or a few specific diagnostic criteria, but is merely a description of impairment in one or more of the cognitive functions, a precise definition of study outcomes is warranted for future studies. This will aid in the selection of the appropriate assessment tools and as such make the results more useful in clinical practice and research.

A problem of the existing instruments for assessment of CF is related to the lack of portability and simplicity,

Table 3 Instruments used for assessment of cognitive function, confusion or delirium in the 22 studies

Name	Type and population	Items	Score	Answer categories	Dimensions	Reports on validity	Sensitivity/ specificity
Agitation Distress Scale[52]	Quantification of agitation distress in terminal cancer patients with delirium	6	0–4, obs[a]	No to severe motor anxiety, no hallucinations to presence of hallucinations, adequate sleep to inability to sleep	Behavioural/emotional hyper-activity, physical restlessness, psychological instability	Sign. Correlations with DRS and MDAS	na
Bedside Confusion Scale (BCS)[54]	Screening test for delirium, developed in cancer patients in palliative care	2	0–1, 0–4, obs	Normal to affected	Level of alertness, test of attention	Validated against the CAM	na
Communication Capacity Scale (CAP)[52]	Quantification of communication capacity in terminal cancer patients with delirium	5	0–3/0–5, obs	Awake, coherent, clear to not awake, inability to reply, incoherence	Comprehension, express oneself, conscious level, ability to answer	Sign. correlations with DRS and sedation scale, items on DRS and MDAS	na
Confusion Assessment Method (CAM)[39]	Diagnostic interview. Operationalized DSM-IIIR. Developed in hospitalized patients >65 years. Normative data	9	obs	No numerical score, positive diagnosis based on the dimensions assessed. A 4-point simplified scoring algorithm available for rapid identification of delirium	Acute onset, fluctuating course, inattention, and altered level of consciousness, disorganized thinking	Validated against the MMSE, GARS[b] and clinicians' ratings	68–100/90–97
Confusion Rating Scale (CRS)[42]	Confusion screening and rating. Developed in the elderly. Normative data	4	0–2, obs	None to severe	Disorientation, behaviour, communication, hallucinations	Sign. Correlations with SPMSQ[c]	na
Delirium Rating Scale (DRS)[40,41]	Generation of a delirium diagnosis, quantification of severity. Intended for hospitalized confused patients. Normative data	10	0–32, obs	Operationalized DSM-III-R criteria	Orientation, concentration, memory, perception, mood, sleep/wake cycle	Sign. Correlations with MMSE	94/82
EORTC QLQ-C30[32], CF scale	QOL instrument, developed in cancer patients. Normative data	2	1–4, self	Not at all, a little, quite a bit, very much	Concentration, memory	Low correlation with objective, neuropsychological tests, high on fatigue, anxiety/depression	
Memorial Delirium Assessment Scale (MDAS)[20]	Diagnostic interview reflecting the DSM-IIIR and -IV criteria for delirium in medically ill. Normative data	10	0–30, obs	None, mild, moderate, severe	Cognitive performance, memory, attention, orientation, disturbances in thinking	Highly correlated with DRS, MMSE, Clinicians Global Rating of Severity	71/93 with cut-off 13
Mini-Mental State Exam (MMSE)[47]	Screening tool for cognitive impairment in adults. Normative data	21	0–30, obs	Worst possible to perfect	Orientation, recall, naming reading, writing, copying, etc	Good correlation with the MDAS, BOMC[d], Cognitive Capacity Screening Exam, CAM, WAIS.[e] Mostly tested in organic brain disorders	52–87/76–82
Structured Clinical Interview for DSM-III-R (SCID)[37]	Diagnostic, structured interview and checklist for DSM-III-R disturbances (new version DSM-IV)	NA	obs	Modular approach to general medical condition, diagnostic criteria and psychiatric symptoms: absence to presence and severity	Psychotic symptoms, hallucinations, perceptions, behaviour, affective disorders	na	na

[a]obs: observer-rated questionnaire.
[b]GARS: Global Accessibility Rating Scale.[47,60]
[c]SPMSQ: Short Portable Mental Status Questionnaire.[44]
[d]BOMC: Blessed Orientation-Memory-Concentration Test.[46]
[e]WAIS: Wechsler Adult Intelligence Scale.[61]

and that many tools require the patient to respond orally or in writing to verbal or mathematical tasks, to answer direct questions, or to perform tests of psychomotor skills which restricts their clinical utility in severely ill patients. Many have been validated in the aged population and could not possess the necessary sensitivity for detecting the initial or minor deficits frequently observed in palliative settings. For the recognition of early stages of delirium, one might want to look for cognitive changes as a first step to identify patients who would need more detailed assessment. The MMSE is widely used in this respect and has become a reference against which other instruments have been judged, although it should not be used as a validation instrument for delirium assessment. Furthermore, its validity and reliability in a palliative setting are not well documented, which we find surprising, in contrast to the DRS[40,41] and the MDAS[20] among others. Despite favourable documentation in the literature, our impression is that the MMSE is regarded as quite cumbersome by clinicians. Furthermore, as a broad screening tool it is insensitive to mild cognitive changes and does not discriminate between different types of conditions presenting with CF.[3,4] In our opinion it has utility for routine cognitive assessment, but because of its high rates of false negatives and false positives, individual scores should be interpreted with caution and followed by more detailed assessments.

Delirium is often assessed as a dichotomous outcome, but is in reality a clinical syndrome, which also necessitates an assessment of severity. Screening tests for delirium have primarily been developed to identify cases, although the MDAS also might be used for rating of severity. Lengthy tools, such as the SCID or the DRS that require specific rater training are impractical to use for screening. While most screening tools for delirium incorporate some of the different DSM criteria for delirium, primarily orientation and memory, only the CAM encompasses all four diagnostic criteria. Responsiveness to cognitive change is of particular relevance to delirium with its typically abrupt onset and rapidly fluctuating course. The DRS for example, includes two symptoms that are constant for the clinical course of delirium: speed of onset and physical disease,[41] while the MDAS and the CAM have proven excellent for repeated measures.[20,39] Thus, in order to screen for delirium, the CAM instrument is promising, due to its brevity (the four-question algorithm), the high sensitivity and specificity and its validation for use in palliative care, although it requires some rater training. The Communication and Agitation scales probably needs further evaluation, because they have only been used in the evaluation of terminal delirium so far.[52]

The choice of a particular type of instrument will often be a compromise between optimizing psychometric properties, the brevity of the instrument, minimizing patient burden and easing administration, and the level of detailed measurement required. Thus, computerized data processing and Item Response Theory (IRT) technique based on a stepwise registration to differentiate between CF and delirium and to quantify the severity might be a powerful approach to generating evidence-based knowledge in this area.[62]

Research into palliative care is challenging from a methodological point of view, but it is possible to overcome these obstacles. Future studies designed with specifically defined outcome measures would be a significant step forward, in that the need for specific interventions would be more apparent. Even if randomized trials might not be feasible, it is possible to adhere to the generally recommended research guidelines encompassing adequate sample size, relevant, operationalized hypotheses and the use of well validated, observer-rated assessment tools with sufficient sensitivity and specificity and with a repeated-measures design. Although Stromgren *et al.* concluded that self-report questionnaires were feasible to administer to patients with advanced cancer,[63] their validity has been questioned, particularly when cognitive function is a study outcome.[49] That study concluded that CF prevents completion of instruments such as the SF-12,[64] and that there were more missing data on the numerical scales than on the categorical scales in the assessment of symptom intensity. Klepstad *et al.* found a poor association between self-reports and objective assessments of cognitive function and sedation in palliative patients being treated with morphine,[35] consistent with reports that measures of cognitive function from QOL questionnaires are insufficient for the assessment of higher mental functions.[36]

The reviewed studies varied with respect to sample size, methodology and design, which imply a huge variation in the prevalence figures. The reported figures are not necessarily representative of the prevalence of CF and delirium in palliative care patients, partly because there were no consistent definitions of categories of palliative care patients with respect to survival. It is also reasonable to assume that the sampling was biased, for example, due to CF and its consequences. Yet the characteristics of the study samples in those studies have clear relevance for their results, depending on whether the target population is defined according to specific criteria such as type of tumour, expected survival time, the type of treatment and performance status. For example, a classification system based on expected survival has been proposed: primary palliation (>6 months), early palliation (2–3 months), late palliation (<1 month) and imminently dying (<1–2 weeks).[65] Most studies were undertaken in PCUs, where a large proportion of the patients were in the terminal stages of disease. Terminal delirium requires a different medical approach from a situation in which the life

expectancy is longer. It could also be that early signs of CF might have led to earlier hospital admission than was strictly necessary for the alleviation of physical symptoms. The prevalence rates for CF and delirium in the 22 studies were reduced to around 50% if the rates from terminal care were excluded. Nevertheless, they were high compared with samples of general medical in-patients (CF 40%, delirium 15–16%).[29,66]

It is noteworthy that only one of the 22 studies presented CIs for the estimate of the prevalence. With a median sample size of 100, a 95% CI around an estimated prevalence of delirium of 40% would be 20 percentage points, representing a range from 30% to 50%. Thus, the high prevalence rates of CF in patients with advanced cancer, the aetiology of such comorbidity and the poor prognosis related to CF, emphasize the necessity of greater awareness among clinicians, particularly because there are potentially successful treatment strategies available. Delirium is a psychiatric syndrome that is mainly seen by nonpsychiatric clinicians,[56] which might be one of the reasons that it is reported as misdiagnosed or overlooked in 32–67% of cases.[15,29,30] Many researchers suggest that the assessment of cognitive function should be routine on admission to a palliative unit.[6,9,18,55] As such, early signs of cognitive impairment might be identified and predisposing factors for delirium revealed. A reduction in the incidence of agitated impaired mental status has been reported after routine screening,[55] consistent with a reduced incidence of delirium.[18]

Based on the results of this review, we support this strategy, but we think that a higher level of precision regarding assessment methods is warranted. The use of imprecise terms such as CF should be avoided. Further refinement and validation of observer-rated, simple and sensitive assessment tools that discriminate between the different diagnostic entities presenting with CF should be undertaken for screening and research purposes.

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