

GUEST EDITORIAL

Improving the outcomes of delirium in older hospital inpatients

Delirium is a cognitive disorder characterized by acute onset, fluctuating course and disturbances in consciousness, orientation, memory, thought, perception and behavior (American Psychiatric Association, 2000). It occurs in hyperactive, hypoactive or mixed forms in up to 42% of older hospital inpatients (Siddiqi *et al.*, 2006), many with pre-existing dementia (Fick *et al.*, 2002).

Notably, the occurrence of an episode of delirium in older hospital inpatients is associated with many poor outcomes, including increased cognitive impairment and functional disability (Inouye *et al.*, 1998; McCusker *et al.*, 2001), length of hospital stay (O’Keeffe and Lavan, 1997; Inouye *et al.*, 1998), rates of institutionalization (O’Keeffe and Lavan, 1997; Inouye *et al.*, 1998; McCusker *et al.*, 2001) and rates of death (Rockwood *et al.*, 1999; McCusker *et al.*, 2002). Interventions to address these poor outcomes would improve the lives of older people and probably reduce health care costs (Inouye, 2006). To date, however, trials of different interventions (i.e. systematic detection of delirium early in the course of hospitalization, multi-faceted interventions to reduce drug use, manage medical problems optimally, increase family and nursing support and increase sensory cues) have not demonstrated any substantial benefits (Cole, 2004). We propose that the poor outcomes associated with delirium in older hospital inpatients may be related, in large part, to the persistence of delirium in a substantial minority of these patients. Accordingly, interventions to identify this substantial minority and ensure full recovery from delirium may improve the poor outcomes.

Persistent delirium

Recovery from delirium refers to the sustained return to the pre-delirium level of mental function. Levkoff *et al.* (1992) and Rockwood (1993) were among the first investigators to assess recovery systematically and report that many older hospital inpatients had not recovered by the time of discharge. A more recent study assessed symptoms of delirium at enrolment, then at two, six and 12 months later (McCusker *et al.*, 2003). The frequencies of symptoms were greatest at enrolment but many symptoms persisted in many patients throughout

the entire 12-month follow-up period. This persistence of symptoms occurred in patients both with and without dementia. Moreover, using a diagnostic algorithm based on DSM-III-R criteria, 31% of the patients still met criteria for delirium at six months.

A systematic literature review to determine the frequency and prognosis of persistent delirium in older hospital patients located 18 reports (involving 1322 patients with delirium) that met the following seven inclusion criteria: original research published in English or French, prospective study design, study sample of at least 20 hospital patients, patients aged 50 years or more, follow-up of at least one week, acceptable definition of delirium at enrolment, and at least one assessment for persistent delirium at discharge or later (Cole *et al.*, 2009). The combined proportions with persistent delirium at discharge, and at one, three and six months were 44.7% (95% CI, 26.8–63.7), 32.8% (95% CI, 18.4–47.2), 25.6% (95% CI, 7.9–43.4) and 21% (95% CI, 1.4–40.6), respectively. When these rates are used to calculate rates of recovery from delirium, 55.3% of patients recover by two weeks and 67.2%, 74.4% and 79% recover by one, three and six months, respectively (Figure 1). Thus, the majority of patients appear to have recovered at each time point but a substantial minority has not recovered and, given the asymptotic slope of the curve after three months, a substantial minority may never recover.

Outcomes of persistent delirium

Three of the studies included in the systematic review compared the outcomes of patients who did or did not recover from delirium (Marcantonio *et al.*, 2000; McCusker *et al.*, 2003; McAvay *et al.*, 2006). These studies reported that the outcomes (cognition, function, nursing home placement, mortality) of patients who recovered were consistently better than the outcomes of patients who did not recover. One study reported that the outcomes of patients who recovered within 24 hours were better than those of patients who recovered by discharge (McCusker *et al.*, 2003).

None of the above studies compared the outcomes of patients who recovered with the outcomes of patients who did not have an index episode of delirium. The results of such a comparison would indicate whether or not the occurrence of an episode of delirium per se accounts

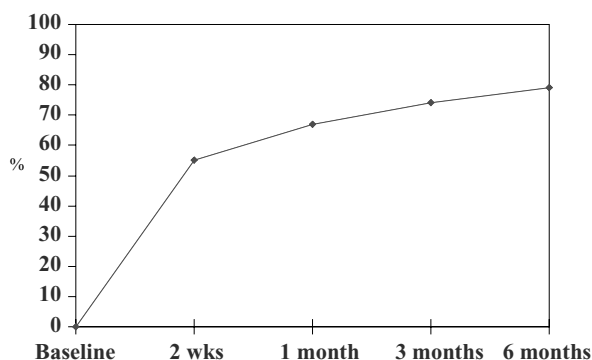


Figure 1. Proportion of older hospital inpatients who recover from delirium at each time point.

for the adverse outcomes associated with delirium. A recent study comparing the outcomes of these two groups reported that most of the outcomes at six and 12 months (cognition, function, rates of institutionalization) of patients who recovered by eight weeks and survived were similar to the outcomes of patients who did not have an index episode (Cole *et al.*, 2008a). Moreover, a study comparing the outcomes (cognition, function, rates of institutionalization or death) of patients who recovered from subsyndromal delirium (SSD) by eight weeks with the outcomes of patients who did not recover or did not have an index episode reported that most of the six- and 12-month outcomes of patients who recovered from SSD and survived were better than the outcomes of patients who did not recover and, for the most part, intermediate between the outcomes of patients who did not recover or did not have an index episode (Cole *et al.*, 2008b). These findings suggest that it is not the occurrence of episodes of delirium or SSD per se but the failure to recover that accounts, in large part, for the adverse cognitive, functional and institutional status outcomes associated with these conditions.

In both of the above studies, there were clinically important increases in the six-month mortality rates of patients who had recovered from episodes of delirium or SSD, compared to those who did not have an index episode. This increase, independent of many demographic and clinical variables, is difficult to explain but may be related to uncontrolled confounding or effect modification by some unidentified factor related to the medical illness or patient vulnerability.

Persistent partial delirium

To this point in the paper, recovery has been considered as an “all or none” phenomenon: either patients recover fully from delirium or they do not. However, most studies of delirium have defined recovery as “not meeting accepted criteria for delirium.” Many patients may have not met criteria

for delirium but had only partial recovery. Rates of partial recovery range from 20% to 42% at the time of discharge and appear to remain high for many months (Levkoff *et al.*, 1992; O’Keeffe and Lavan, 1997; McAvay *et al.*, 2006). If these rates of partial recovery are subtracted from the rates of recovery in Figure 1, the resulting curve of *full* recovery from delirium (i.e. no symptoms of delirium) is probably much shallower than the one presented. To date, there have been no studies of the outcomes of patients with partial recovery but, given the prognostic significance of the presence of even one symptom of delirium among patients with subsyndromal delirium (Cole *et al.*, 2003), partial recovery is probably associated with poorer outcomes than *full* recovery.

Of note, current approaches to studying the course of delirium and SSD may not be adequate to understand the recovery status and outcomes of these complex conditions. An exploratory study of repeated delirium severity scores over a two-week period, using principal factor analysis and cluster analysis, revealed five patterns: “Steady,” “Fluctuating,” “Worsening,” “Fast improvement,” and “Slow improvement” (Sylvestre *et al.*, 2006). The “Fast improvement” and “Worsening” groups experienced a high death rate during the first two weeks (adjusted relative risks of approximately 3 and 6, respectively), but that risk decreased rapidly thereafter. Use of serial measures of delirium symptoms may allow for a more reliable classification of the course (and recovery status). Also needed are good measures of the pre-morbid cognitive status (including dementia), severity of medical illness, and perhaps other factors that are likely to be associated with the course. For example, in the above study, patients with dementia were more likely to be in the “Steady” or “Slow improvement” groups; patients with more severe physical illness were more likely to be in the “Fast improvement” group.

Improving outcomes of delirium

In summary, we propose that the majority of older hospital inpatients may recover fully from delirium but a substantial minority of patients will not recover or will recover only partially. Patients who recover fully appear to have good outcomes but patients who do not recover fully have poor outcomes. Thus, identification and treatment of patients who do not recover fully may be a key to improving many of the poor outcomes associated with delirium.

What are the implications of this proposal for research? First, it is unknown whether most of the patients who have not recovered by three months can ever recover, even with intervention. There should be efforts to identify these patients in order to explore the usefulness of different types of interventions. Such interventions might involve the

use of protocols to detect and manage putative causes of incomplete recovery such as unresolved medical illness or unrecognized drug toxicity. The goal of these interventions would be to ensure full recovery from delirium.

If any of the above interventions are successful, the optimal time for screening and intervention must be determined. On the one hand, an examination of the rates of recovery in Figure 1 indicates that half of the patients who have not recovered by discharge appear to have recovered by three months (without any special intervention); thereafter, the proportion of patients who recover is small. These findings suggest that patients should probably be screened for persistent delirium at three months. On the other hand, one study (McCusker *et al.*, 2003) reported that even when recovery was delayed to the time of discharge (i.e. at two weeks), this delayed recovery was associated with poorer outcomes than rapid recovery (i.e. within 24 hours). These findings suggest that patients should be screened for recovery as early as possible. Ultimately, randomized clinical trials will be needed to determine if and when screening and intervention should be conducted to increase rates of full recovery and improve the outcomes of delirium.

In the meantime, incomplete recovery from delirium may have two implications for clinical practice. First, it is probably important to monitor the course of delirium in older hospital inpatients, especially at discharge and beyond, with a view to ensuring full recovery. Second, it is probably important for clinicians to recognize that the persistence of symptoms of delirium after discharge and the associated cognitive impairment may interfere with patients' self-management of chronic medical conditions (e.g. poor compliance with diet or medication) which may, in turn, contribute to poor outcomes.

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