Depression and dementia or Alzheimer’s disease often go together. The presence of dementia may also increase the odds of depression. What can clinicians do to treat these two often comorbid conditions?

Depression and dementia are common in older people and their association is very complex. Major and minor depression occur often in patients with dementia and can be associated with deterioration in cognitive functioning. Many clinicians have difficulty determining whether dementia, depression or both are the underlying disease for their patients’ apathy, psychomotor retardation, concentration deficit and short-term memory impairment. Moreover, depression in dementia brings additional disability to patients who are demented and their caregivers, and a previous history of depression may be associated with an increased risk for the subsequent development of a dementing illness. In this article, we review the literature to address the interaction between depression and dementia and provide clinicians with information to improve the care of their patients who are demented.

Prevalence
The aging of the U.S. population has been accompanied by a dramatic rise in the prevalence of both depression and dementia. Among community-dwelling older adults, 3% to 11% have dementia (Boustani et al., 2003) and 2% to 14% have depression (Beekman et al., 1999). In long-term care settings, 44% to 53% of the residents have dementia (Magaziner et al., 2000) and 9% to 30% have depression (Parmelee et al., 1989; Payne et al., 2002; Rovner et al., 1991; Watson et al., 2003). Depending on the threshold used to define depression, the different scales and methods implemented to measure depressive symptoms, and various clinical settings, numerous studies in dementia estimate that depression occurs in 30% to 50% of patients (Olin et al., 2002). Approximately 24% of community-dwelling older adults with dementia (Lyketsos et al., 2000), 24% of residents in assisted living with dementia and 27% of those in nursing homes suffer from depression (Gruber-Baldini et al., 2003). Dementia leads to a high burden of suffering for patients, their families and for the entire society, with an annual cost of approximately $100 billion (Boustani et al., 2003). Furthermore, depression is independently related to poor outcomes, including greater medical morbidity, increased health care services use, functional decline and death (Charney et al., 2003). Having both dementia and depression increases the risk of mortality and disability and leads to higher health care utilization and costs (Kopetz et al., 2000; Lyketsos et al., 1999, 1997).

Does depression increase the risk for the future development of dementia? History of depression in early, mid- or late life has been associated with an increased risk for the future development of dementia. In a meta-analysis of seven case-controlled and six prospective cohort studies, Jorm (2001) found that history of depression approximately doubled the risk of developing dementia. More recently, a retrospective cohort study found a significant association between dementia and a history of depression symptoms that first reported within one year or more than 25 years before the onset of dementia (Green et al., 2003). Another longitudinal study found that 43% to 89% of elderly patients with depression who presented with cognitive impairment developed dementia within the following three to eight years (Table 1) (Schweitzer et al., 2002). Numerous hypotheses have been suggested to explain the previous association between depression and the increased risk for developing dementia. These hypotheses included that: 1) pharmacological treatment of depression might be a risk factor for dementia; 2) depression and dementia share common risk factors such as cerebrovascular disease; 3) depression is an early stage of dementia; 4) depression occurs as a reaction to the early cognitive decline of dementia; 5) depression hastens the clinical manifestation of dementia; and 6) depression-related glucocorticoid effects lead to hippocampal injuries and damage (Green et al., 2003; Jorm, 2001; Wilson et al., 2003). Nevertheless, recent data suggest that the association of depressive symptoms with Alzheimer’s disease (AD) and cognitive impairment appears to be independent of cortical plaques and tangles and, therefore, depression may be a risk factor for dementia more than being early sign of its symptoms (Wilson et
Depression in Dementia

The diagnosis of depression in dementia is not an easy task. Although the majority of patients with dementia do not develop major depression (Olin et al., 2002), more than half suffer from one or more depressive symptoms such as anxiousness, sadness, irritability, agitation or psychomotor retardation, sleep problems, diminished social activity, or loss of interest (Gruber-Baldini et al., 2003). There is an overlap between dementia and depressive symptoms and behaviors, and it is difficult to determine whether the dementing illness or depression is the underlying pathology. Although apathy is often associated with depression, approximately 60% of patients with dementia with apathy have no depression and 44% of patients with dementia with depression have no apathy (Lyketsos et al., 2001).

Diminished social activity, loss of interest and apathy may be responses to a cognitive deficit, or they may be manifestations of major depression. Moreover, memory problems in early stages of dementia might compromise patients' self-report of depressive symptoms. Language and communication difficulties in later stages of dementia might change the expression of depressive symptoms. These atypical presentations often lead to lower rates of clinician recognition and diagnosis of depression (Gallo and Rabins, 1999).

In one study that used the DSM-III criteria to diagnose major depression among patients with dementia, 14% of the sample met the criteria for major depression based on patient interviews, and 50% met the diagnostic criteria on the basis of caregiver interviews (Mackenzie et al., 1989). This discrepancy might be due to the inability of the caregivers to distinguish between depressive symptoms and apathy, or to the caregivers' own depression.

Adding to the complexity of depression diagnosis in dementia, 60% to 70% of depressive symptoms in community-dwelling patients with dementia disappear within six months and 85% recur within one year (Lee and Lyketsos, 2003). Furthermore, patients with dementia might suffer from depressive disorders that are not related to dementia per se, such as adjustment disorder with depressed mood, recurrence of early and midlife major and minor depression, late-onset depression, and vascular depression (Lee and Lyketsos, 2003).

Due to the previous complexity and the absence of consensus on how to diagnose depression in patients who are demented, a panel of 21 experts in dementia and depression were assembled by the National Institute of Mental Health and suggested specific criteria for diagnosing depression in AD (Table 2) (Olin et al., 2002). Impact of Depression

In addition to decreasing functional and cognitive status, depression in dementia interacts with other behavioral and psychological symptoms (such as agitation, delusions and hallucinations, and wandering). In one clinical trial, improvement in depressive symptoms among community-dwelling patients with AD with major depression was associated with a decrease in the behavioral and psychological symptoms (Lyketsos et al., 2003).

Various cross-sectional studies conducted in long-term care have found that depression in dementia was associated with higher prevalence of wandering and verbal agitation (Dwyer and Byrne, 2000; Gruber-Baldini et al., 2003). Nursing home residents with dementia who manifested physical or verbal aggression had an approximately threefold increase in the prevalence of depression than those without such behaviors (Lyketsos et al., 1999; Menon et al., 2001). Finally, in a study of 303 community-dwelling patients with AD, the presence of depression was associated with an almost twofold increase in the risk of delusions (Bassiony et al., 2002). Treating Depression

The goal of antidepressant treatment for depressive symptoms in dementia is to alleviate depressive suffering, improve cognitive performance and decrease the contribution of depression to the other health outcomes of dementia, such as behavioral and psychological symptoms and caregiver burden.

Pharmacological interventions, electroconvulsive therapy, and caregiver or care-recipient-based behavioral interventions are currently available for clinicians to manage depression among older adults. There is concern, however, that some of the antidepressants (such as the tricyclic antidepressants) and ECT might exacerbate the cognitive impairment of patients with dementia with depression. Furthermore, few data are available to confirm the efficacy of the previous interventions among this selected group of vulnerable older adults.

Two reviews of the literature have identified nine randomized, placebo-controlled trials that evaluated the efficacy of pharmacological interventions in reducing depression among patients with dementia (Bains et al., 2002; Olin et al., 2002). Five trials evaluated selective serotonin reuptake inhibitors (sertraline [Zoloft], fluoxetine [Prozac] and citalopram [Celexa]), three evaluated TCAs (clomipramine [Anafranil], imipramine [Tofranil] and maprotiline [Ludiomil]), and one trial evaluated moclobemide (Aurorix), a monoamine oxidase inhibitor not approved in the United States (Fuchs et
al., 1993; Olin et al., 2002). These trials suggested that citalopram, sertraline, clomipramine, maprotiline and moclobemide might help in the management of depression in patients with dementia. The findings from the Olin et al. (2002) study are summarized in Table 3. However, patients enrolled in these trials were selected from both long-term care and community settings and had a spectrum of depressive disorders that ranged from major depression to mild depressive symptoms. Not surprisingly, the impact of medications was greater when treating major depression. None of the previous trials demonstrated any positive effects of antidepressants on cognition. Citalopram and sertraline appeared to be helpful in reducing the other behavioral and psychological symptoms related to dementia, and sertraline had some positive effect on the functional deficit of dementia.

In addition to pharmacological interventions, randomized, controlled trials also show that exercise and behavioral management reduce depressive symptoms in community-dwelling patients with dementia (Teri et al., 2003, 1997). More recently, Brodaty et al. (2003) conducted a 12-week, randomized, controlled trial in 11 Australian nursing homes. They found no efficacy differences among psychogeriatric case management, general practitioners with psychogeriatric consultation and standard care in managing 86 residents with dementia with depression, psychosis or both.

**Clinical Implications**

Due to the aging of the U.S. population, coexisting depression and dementia present a significant public health problem. Depending on the severity of dementia, using both caregiver and care-recipient-based depression screening instruments will help increase the recognition of depression in dementia. Treating depression adequately in mid- or late life may decrease the risk of the future development of dementia. Verbal agitation and physical aggression might be symptoms of depression among patients with severe dementia. Sertraline and citalopram improve major depression in those with dementia but their efficacy in milder depression is uncertain. Finally, behavioral interventions decrease depressive symptoms in community-dwelling patients with mild-to-moderate dementia. For clinicians treating patients with dementia, the most important message is to routinely assess for depression and to treat it, because successful treatment can improve many dementia-related outcomes.

**References: References**


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