Depression in End-Stage Renal Disease

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ABSTRACT
The occurrence of depression within the population of patients with renal disease may be underrecognized and undertreated in practice. Furthermore, depression in the presence of end-stage renal disease may be resistant to treatment or require multiple modes of treatment and coordination of care across settings and providers for symptom relief. Improved assessment and diagnosis of depression could permit earlier psychotherapeutic intervention and improve the quality of life for patients with renal disease.

Against a background of a general understanding and recognition of mental illness concurrent with chronic disease, medical knowledge regarding the comorbidity of mental illness and renal disease, in particular, has grown considerably during the past 5 years. Emerging data regarding the presence of mental illness in patients with renal disease are becoming sufficiently clear to support application of this new level of understanding into practice. Specific areas in which mental health practice may be improved include earlier and more detailed assessment and diagnosis and, consequently, earlier and more directed psychotherapeutic intervention. The purpose of this article is to describe the physiological and psychosocial implications of end-stage renal disease (ESRD) compounded by depression and to address the challenges to assessment and treatment in this population.
BACKGROUND AND SIGNIFICANCE

Chronic kidney disease (CKD) is a progressive disease categorized according to its severity, ranging from Stage I to Stage V, depending on various measures of kidney function. CKD is defined as a patient having at least 3 months of functional or structural kidney abnormality, as indicated by criteria such as glomerular filtration rate and albuminuria. The prevalence of CKD in the United States is estimated to be close to 20 million; of those, between 400,000 and 500,000 have Stage V disease—also known as ESRD—and experience complete or nearly complete loss of kidney function (Coresh et al., 2007). Patients with ESRD typically require hemodialysis (HD) or renal transplant in order to survive.

Nearly all mental illnesses that affect the general population are also found in patients with renal disease; major depression and anxiety are the most frequently observed (Cukor, Coplan, et al., 2007). The coincidence of renal disease and mental illness can be characterized as comorbidity, or, alternatively, as a mental illness compounding the renal disease. The term compounding refers more to an interrelationship between the diseases—each worsening the other—in contrast to their mere side-by-side co-occurrence. More specifically, compound depression is generally more treatment resistant than depression occurring without another comorbid medical or mental illness (Cohen, Norris, Acquaviva, Peterson, & Kimmel, 2007; Kimmel & Peterson, 2005). The focus of this article is on depression compounding ESRD.

Renal disease occurs across a spectrum, and patients with less severe forms of the disease may experience few or no physical symptoms, but patients with ESRD experience a host of physical symptoms arising from their renal impairment. They also face considerable disruptions in their daily life in the management of an illness that demands a significant commitment to dietary and HD prescriptions. Studies have found that between 20% and 30% of the population with ESRD also experience depression (Cukor, 2007) with considerable variation in estimates owing in part to the challenges of assessment and diagnosis of depression in the context of such a medically complex and burdensome disease. Other comorbid mental and physical illnesses such as anxiety, substance abuse, diabetes, cardiovascular disease, and chronic pain further complicate efforts at specific diagnostic and therapeutic intervention (Cukor, Cohen, et al., 2007).

AFFECED POPULATIONS AND ASPECTS OF PATHOPHYSIOLOGY

Several aspects of renal disease compounded by mental illnesses such as anxiety and depression can provide an informative perspective for practitioners who deliver medical and psychiatric care to patients with renal disease. First, renal disease is increasingly prevalent in the U.S. population and is likely to increase in the future. Renal disease can be a secondary consequence of the primary diseases of diabetes and hypertension, and these diseases themselves are growing in prevalence (Abdel-Kader, Unruh, & Weisbord, 2009). Subpopulations at higher risk for developing diabetes and hypertension, such as African American and Native American groups, are also more highly represented in the population with CKD (Coresh et al., 2007).

Another consideration relates to the independent influence of renal disease on the stress-related responses seen in depression and anxiety. Cukor, Coplan, et al. (2007) discussed similarities between the effects of renal disease by itself and the effects of stress arising from any source. Physiological mechanisms of handling stress include achieving an overall state of stability or homeostasis by way of adjusting the dynamics within the hypothalamic-pituitary-adrenal (HPA) axis, in major part to maintain blood pressure and electrolyte balance through complex regulation of hormones and pro-inflammatory cytokines. Renal disease by itself, even uncomplicated by stress, also directly affects aspects of the same HPA axis. The kidneys are responsible for the metabolism of peptide and steroid hormones acting on the HPA axis, so kidney impairment contributes to a biochemical milieu similar to that of chronic stress (Cukor, Cohen, et al., 2007). Furthermore, there is considerable overlap between the symptoms of uremia and depression. These include fatigue and lethargy, sleep disturbance, decreased concentration, decreased appetite, and decreased libido. Cukor, Cohen, et al. (2007) proposed a mechanism of a vicious cycle in ESRD compounded by depression whereby allostatic dysregulation exacerbates either or both illnesses, leading to poor dietary and HD treatment adherence. This, in turn, cycles back to disease progression.

In addition to the intrapatient characteristics of this population, an enormous influence of social, cultural, and economic variables potentially contribute to stress load. Patients undergoing HD treatment deal with role changes. They often must rely on family and social supports with their attendant conflicts and dynamics for basic assistance in disease management and activities of daily living. They may face issues of access to treatment and financial constraints, in addition to coping with the reality of end-of-life issues (Cukor, Cohen, et al., 2007; Tossani, Cassano, & Fava, 2005).

Health care providers working with patients who have both ESRD and depression may have a medical or psychiatric orientation that aligns with either contributor to this comorbid situation, but clearly these two orientations must
collaboratively find common ground in terms of treating dysregulation in the HPA axis. The relationship between stress and renal disease mandates careful communication, particularly in regard to the pharmacotherapeutic approaches to treating separate aspects of this complex, metabolism-compromising, comorbid condition.

Impact on Patient Lives and an Opportunity for Health Care Providers

Underrecognition of the prevalence of mental illness in patients with renal disease, particularly its early onset, represents a missed opportunity for psychotherapeutic intervention that could improve quality of life for these patients. Cohen et al. (2007) commented that the single largest barrier to providing psychotherapeutic intervention is medical staff’s absence of inquiry into the state of patients’ mental health. Most patients with ESRD compounded by depression do not seek specific psychiatric care for their mood disorder. They are overwhelmed by their physical illness and receive most of their medical care from nephrology specialists, dialysis teams, and primary care physicians (Cohen et al., 2007). It is not surprising that these providers, owing to a perceived lack of time or expertise, would be hesitant in diagnosing and treating a psychiatric illness in complex patients. However, although present data cannot support a conclusion that psychotherapeutic intervention can decrease mortality in the renal disease population, some data have linked interventions to quality-of-life indicators and to improved medical outcomes (Cohen et al., 2007; Cukor, Cohen, et al., 2007). It is imperative that those caring for this population are alert to the signs and symptoms of depression and take appropriate interventional action.

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**DIAGNOSIS AND MEASUREMENT OF DEPRESSION SEVERITY**

Assessment of depression in patients with ESRD is complicated by the considerable overlap of the symptoms of depression and uremia and by complex patient characteristics and social factors (Cukor, Cohen, et al., 2007). Additionally, assessments may be time variable, with patients experiencing different symptoms early in HD treatment than they do after years of HD treatment or even before and after a single treatment. Well-controlled research studies have identified the Beck Depression Inventory®-II (BDI®-II) and the Patient Health Questionnaire™ (PHQ-9) as valid and reliable tools for assessing depression in ESRD compared with the Structured Clinical Interview for DSM-IV (SCID-I), the gold standard in depression assessment (Cohen et al., 2007). The severity of depressive affect, as measured by greater BDI-II scores, has been clearly correlated with increased morbidity, decreased treatment adherence, and decreased quality of life, and less clearly but nevertheless compellingly associated with increased mortality (Cukor, Cohen, et al., 2007). Cohen et al. (2007) argued for the screening of all patients with ESRD with the BDI-II and initiating depression treatment for those with scores >14. Clearly, this represents a considerable burden to both patients and providers, as the authors acknowledged. Research focused on the development and validation of brief assessments in this population is sorely needed.

Interestingly, primary nursing staff may play a key role in establishing a depression diagnosis. Wilson et al. (2006), nurses identified depression in 74.6% of patients with ESRD who met criteria for depression in a separately administered interview. Nephrologists identified only 24.2%. The authors were cautious in interpreting these results but clearly viewed the nursing role as vital to the collaborative interdisciplinary treatment of this population.

A considerable amount of data suggests that depression manifests early in renal disease. Abdel-Kader et al. (2009) reported that little difference exists between the prevalence of depression in patients with severe renal disease not yet warranting HD and patients with ESRD. If prevalence of mental illness increased in close association with advancement through stages of renal disease, a higher prevalence of depression among patients with ESRD, compared with patients with earlier stages of the disease, would be expected. Cukor, Coplan, Brown, Peterson, et al. (2008) observed that the single strongest predictor of depression in advanced cases of renal disease is the occurrence of depression at an earlier time point. This exemplifies the importance of earlier assessment and treatment interventions as a potential means to improve disease course.

**Suicide and Treatment Withdrawal**

The suicide rate among patients with ESRD on dialysis is 84% higher than that of the general population (Cohen et al., 2007). Suicide in this population is strongly associated with alcohol and substance abuse as well as
hospitalization for a psychiatric illness, thus screening for substance abuse and depression may help identify those at greatest risk for suicide and afford opportunities for intervention.

Treatment withdrawal is also associated with depression (Cukor, Cohen, et al., 2007). However, the decision to withdraw from HD is complex. Many patients with ESRD who are not depressed may, after careful consideration, arrive at the decision to withdraw from dialysis. It is important for mental health providers to be part of any conversation regarding treatment withdrawal and to advocate for treatment of underlying mental illness when warranted, allowing patients and their families to make these difficult decisions in the best and most supportive environment possible.

**Distinguishing Depression from Anxiety**

It is also important to distinguish between depression and anxiety in patients with renal disease. Cukor, Coplan, Brown, Friedman, et al. (2008) reported that anxiety is often misperceived as depression and demonstrated that results from both the SCID-I and Hospital Anxiety and Depression Scale show distinctness and substantial nonconcordance of depression and anxiety in patients with ESRD undergoing HD. Although this is not a surprising finding, it does underscore the importance of skilled assessment; however, many health care providers caring for patients with ESRD lack formal education and experience in mental health assessment. Effective psychotherapeutic treatment can only be provided if the diagnosis is correct.

**TREATMENT INTERVENTIONS**

It is widely accepted that the treatment of depression in the general medical population is best achieved through a combination of psychotherapy and pharmacological treatment. Many antidepressant agents have demonstrated efficacy in patients with ESRD, but the selection and dosing of medication in this population require careful consideration of the patient's complex medical makeup. Drugs and drug metabolites excreted by the kidneys accumulate in patients with ESRD, and doses need to be adjusted accordingly. Pharmacological approaches to treating depression are reviewed by Cohen et al. (2007) and Cukor, Coplan, et al. (2007). Selective serotonin reuptake inhibitors (SSRIs) are generally favored, as they have more tolerable side effect profiles; however, they can exacerbate the sexual dysfunction and sleep disturbance symptoms of renal disease. Additionally, they may cause gastrointestinal distress, in turn negatively affecting adherence to the strict dietary regimens essential for treatment of renal disease. Some agents, such as tricyclic antidepressant drugs, monoamine oxidase inhibitors, and St. John's wort are contraindicated for dialysis patients. Possible consequences of the use of these drugs include exacerbation of common adverse events in dialysis, such as drug-drug interactions, arrhythmias, and orthostatic hypotension. Because of the high rates of diabetes and cardiovascular disease in this population, approved and off-label use of second-generation antipsychotic agents should be approached with appropriate caution.

Research on psychotherapy interventions for depression in ESRD is limited, but the data have been encouraging. According to Cukor's (2007) study of the perspective of patients with ESRD and depression, two overarching beliefs emerge: the belief that depression is part of the disease "package" and that their disability prevents enjoying life. However, in view of the fact that many patients with ESRD are not depressed, it can be understood that depression is not an inevitable condition and that the belief in its inevitability is a dysfunctional thought. Cognitive-behavioral therapy (CBT), with its symptom-reduction focus and time-limited nature, has been shown to restructure these views in a manner that is helpful for patients. In his study of 16 ESRD patients with major depression, Cukor (2007) reported that all patients showed a significant decrease in BDI-II score, which was sustained at 3-month follow up. The author considered and piloted several ways to provide psychotherapy and concluded that in practical terms, it was best delivered in conjunction with dialysis treatment itself—within the dialysis center—in a "chair-side" manner.

In a study of 41 patients in Brazil undergoing HD, Duarte, Miyazaki, Blay, and Sesso (2009) found that 3 months of weekly group CBT yielded significant and sustained improvements in BDI score and quality of life measures when compared to a no-intervention control group. The authors also found a significant decrease in suicide risk in the treatment group, which is important because depression symptoms are predictors of both suicide and withdrawal from dialysis in this population (Duarte et al., 2009). Social support group therapy intervention and an exercise therapy intervention also demonstrated improved outcomes compared with no-intervention controls (Duarte et al., 2009). Larger, randomized controlled studies of all these interventions are required to determine their potential effects on depression, mortality, and quality of life in patients with depression and renal disease (Cohen et al., 2007).

**NURSING IMPLICATIONS AND ROLES**

Nursing education teaches a holistic model of care. As such, nurses view patient health as being composed not only of their physiological well-being, but also as influenced by their beliefs and emotions and as existing in a complex social and environmental context. This orientation makes nurses especially well suited to care for the biopsychosocial complexities seen in patients with ESRD and depression. Advanced nursing practice should respond to the data demonstrating high prevalence of depression in ESRD. Advanced practice
KEYPOINTS

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1. Individuals with end-stage renal disease (ESRD) are at a higher risk for depression than the general population.

2. Depression in ESRD is often undiagnosed and untreated.

3. Depression may exacerbate ESRD symptoms, affect treatment adherence, and increase morbidity.

4. Treating depression in individuals with ESRD poses challenges for providers, but effective pharmacological and nonpharmacological treatments are available.

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CONCLUSION

Patients with ESRD contend with multiple psychosocial stressors related to their illness, its treatment, and the realities of their prognosis. They must also cope with a significant physical symptom burden. Many people with renal disease develop depression at some point during the course of their disease progression. ESRD compounded by depression results in reduced quality of life and may increase mortality in this population. Research suggests that appropriate screening, diagnosis, and treatment of this population improves outcomes. Coordinated care across medical and psychiatric disciplines is essential for safe and effective treatment in this population.

REFERENCES


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