FAST FACTS AND CONCEPTS #404
DEPRESSION IN END-STAGE RENAL DISEASE
Yara Moustafa MD, PhD1, Molly Kilpatrick MD2, Michael Schuh Pharm D2, Maisha T Robinson MD, MS2,4

Background: End-stage renal disease (ESRD) occurs when individuals have an estimated glomerular filtration rate (GFR) < 15 ml/min/1.73 m² body surface area or require long-term dialysis irrespective of GFR (1). Depression is common in patients with ESRD, with estimated prevalence rates between 20% and 40%, yet it is underdiagnosed and undertreated (1,2). Patients with ESRD and depression have longer hospital stays, poorer quality of life, and are twice as likely to die or require hospitalization within a year compared to those without depression (3-5). This Fast Fact reviews depression management considerations in ESRD. See Fast Facts #7, 273, and 309 for discussion about depression management in serious illness and #146 for information specific to depression screening in serious illness.

Non-pharmacologic therapy: Psychological interventions such as individual and group cognitive behavioral therapy (CBT) are considered to be efficient interventions for depression in patients with ESRD (6-8). Due to reluctance to attend appointments on non-dialysis days, non-pharmacologic interventions which take place on the dialysis unit such as chairside CBT therapy have been investigated in the hopes of improved long-term adherence (9,10). Mind-body techniques including guided imagery, breathing, and mindfulness provided in the hemodialysis unit via smart-phone apps have also been examined in early investigations (9,11).

Pharmacologic therapy: Despite the high prevalence of depression in patients with ESRD, supporting evidence for antidepressant pharmacologic therapy specific to this patient population is sparse (12). In general, data from meta-analyses suggest that antidepressants may reduce depression when compared to placebo, but their effect on quality of life, hospitalizations, survival, and suicide is unknown (12). Certain anti-depressants improve symptoms common to ESRD patients such as nausea, fatigue, constipation, pruritus, and restless leg syndrome (RLS), others exacerbate them. Therefore, the selection of a pharmacologic agent must be individualized (13). Indications for pharmacologic antidepressant therapy are severe or refractory depression, psychosis, or suicidal ideation (14). Clinicians should be aware of potential barriers to pharmacotherapy common to patients on dialysis including: attributing depression to an acute situational factor such as the initiation of dialysis itself, cost, polypharmacy, and to a lesser extent concern about side effects (15). Addressing these concerns is crucial before initiating pharmacotherapy to maximize adherence.

Selective serotonin reuptake inhibitors (SSRIs): These are the most commonly prescribed and studied anti-depressants for patients with ESRD (16). They are protein-bound, metabolized by the liver, and unlikely to be removed by dialysis (14). Therefore, all SSRIs can be considered in patients with ESRD. Most SSRIs require no renal dose adjustment, except for sertraline which should be reduced to 25 mg/day on initial dosing (17). Of note, common SSRI side effects (nausea, vomiting, diarrhea, sexual dysfunction) may mimic symptoms of ESRD (13) and SSRIs may worsen RLS in patients with uremia (18). Fluoxetine is the most activating SSRI followed by sertraline which may be beneficial for those with fatigue. Sertraline may reduce pruritus, while fluoxetine is most likely to exacerbate it (19).

Selective norepinephrine reuptake inhibitors (SNRIs): Painful neuropathy is common in patients with renal disease and SNRIs are effective in treating neuropathy and depression. They require renal dosing however. Venlafaxine should be dose-reduced 50% in ESRD patients (14). Duloxetine should be avoided when eGFR is less than 30 ml/min due to a theoretical concern of an increase in renally excreted metabolites (20). Both have been associated with new or worsening RLS (18).

Monoamine oxidase inhibitors (MAOIs) and Tricyclic antidepressants (TCAs): While known to be effective antidepressants, generally these medication classes are avoided in ESRD due to their side effect profile (e.g. RLS, orthostatic hypotension, and cardiac arrhythmias) (17, 18, 21). Of note, doxepin (which is commonly used to palliate pruritus), nortriptyline and amitriptyline do not require dose adjustment (14).
Other: Bupropion and mirtazapine can be used with dose adjustment. While the usual initial dose of bupropion is 75 mg daily and usual maximum dose is 150 mg daily (14); a study suggested that a dosing scheme of 150 mg every 3 days can be safe and effective in ESRD (22). Bupropion has less sexual dysfunction, somnolence and weight gain than SSRIs and is less likely to worsen RLS, but it can lower seizure threshold (23). The initial dose of mirtazapine is 7.5 mg in ESRD with a maximum dose of 15 mg per day (14); it may worsen RLS (18), fatigue, and constipation (24). St. John’s wort (hypericum perforatum) is not recommended in patients with ESRD due to potential drug interactions. For severe and/or treatment refractory depression, there may be a role for ECT or ketamine (see Fast Fact #384).

Summary: Non-pharmacologic interventions are recommended as first-line for patients with ESRD and mild-to-moderate depression, particularly if offered during dialysis. When pharmacotherapy is indicated, selecting an antidepressant with additional benefits is advised. Sertraline may improve pruritis and fatigue. Venlafaxine ER (starting dose 37.5 mg) has the potential benefit of reducing neuropathic pain. Bupropion fewer sexual side effects, weight gain, and RLS.

References
21. Eyler RF, Unruh ML, Quinn DK, Mary Vilay A, editors. Psychotherapeutic Agents in End-Stage Renal Disease. Seminars in dialysis; 2015: Wiley Online Library.

Authors' Affiliations: 
1 St. Elizabeths Hospital Department of Behavioral Health, Washington, DC.
2 Mayo Clinic, Department of Family Medicine, Jacksonville, Florida.
3 Mayo Clinic, Pharmacy, Jacksonville, Florida.
4 Mayo Clinic, Department of Neurology, Jacksonville, Florida.

Conflicts of Interest: No conflicts of interest to be disclosed.

Version History: first electronically published in August 2020; originally edited by Sean Marks MD