Psychiatric illness in adults receiving maintenance dialysis

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INTRODUCTION

Psychiatric illness is common among patients with chronic general medical disorders, including end-stage kidney disease (ESKD) [1-3]. This topic focuses upon the diagnosis and treatment of psychiatric disorders in patients with ESKD who are treated with maintenance dialysis. Other aspects of dialysis are discussed separately. (See "Indications for initiation of dialysis in chronic kidney disease" and "Dialysis disequilibrium syndrome".)

OVERVIEW

Epidemiology — Psychopathology is common in patients who are treated with maintenance dialysis. In a prospective study that enrolled 70 dialysis patients (mean age 53 years) and assessed them for psychiatric disorders using a semistructured interview and standardized diagnostic criteria, the point prevalence of any current psychiatric diagnosis was 71 percent [4].

Psychiatric disorders that are common in end-stage kidney disease (ESKD) include [1,4-7]:

- Anxiety disorders, such as generalized anxiety disorder or panic disorder (see 'Anxiety disorders' below)
- Depressive disorders, such as unipolar major depression (major depressive disorder) and persistent depressive disorder (dysthymia) (see "Depression in adults receiving

maintenance dialysis")

- Neurocognitive disorders, such as delirium and dementia (see 'Neurocognitive disorders' below)
- Substance-related and addictive disorders, such as alcohol use disorder (see 'Other disorders' below)

One review reported that the prevalence of depression, dementia, and substance-related and addictive disorders was each greater in dialysis patients than the general population [8].

Potential adverse consequences — Psychiatric comorbidity in ESKD may lead to poor adherence with dialysis and disruptive behavior on dialysis units [3,6,9]. As an example, depressive symptoms are independently associated with missed hemodialysis treatments, as well as abbreviated treatments that are shortened by patient request [10].

Comorbid psychiatric disorders in patients on maintenance dialysis are also associated with significant morbidity [3]. In a retrospective study that examined patients who initiated dialysis and were followed during the first year of dialysis, the primary findings included the following [7]:

- Among patients age 22 to 64 years (n = approximately 400,000), hospitalization with a primary or secondary psychiatric diagnosis occurred in 2 and 25 percent.
- Among patients age ≥65 years (n >600,000), hospitalization with a primary or secondary psychiatric diagnosis occurred in 2 and 19 percent.

Among patients who initiate dialysis, mortality is greater in those who develop psychiatric illnesses [3]. A retrospective study used a national registry dedicated to chronic kidney disease and ESKD to identify patients who were hospitalized within the first year of starting dialysis, either with a psychiatric diagnosis (n >11,000) or a nonpsychiatric diagnosis (controls, n >300,000) [7]. The most common psychiatric disorders leading to hospitalization included depression, neurocognitive disorders, and substance-related and addictive disorders, and the mean duration of follow-up was approximately three years. After controlling for potential confounding factors such as sociodemographic variables and general medical comorbidities, the analyses found that all-cause mortality was nearly 30 percent greater in patients with psychiatric disorders than controls (hazard ratio 1.29, 95% CI 1.26-1.32).

Psychiatric disorders in dialysis patients are also associated with suicide [3]. (See 'Suicide' below.)

Diagnosis and treatment — Among patients who are treated with maintenance dialysis, the diagnostic criteria for psychiatric disorders are identical to those used in the general population [11].

Psychiatric disorders in patients receiving maintenance dialysis are often underdiagnosed [3]. One reason may be that symptoms of psychiatric disorders overlap with symptoms of inadequate dialysis, complications of ESKD, and medication adverse effects [7,8].

In addition, psychiatric illnesses in patients with ESKD are undertreated and relatively few studies have examined how to treat these comorbidities [3]. Thus, the efficacy of therapeutic interventions for comorbid psychiatric conditions is often not clear, and treatment recommendations are generally based upon the general population of patients with psychiatric disorders. The combination of pharmacotherapy and psychotherapy is likely to be successful, and may be cost effective [12].

Referral — Although some nephrologists have the requisite training and experience to diagnose and manage specific psychiatric disorders (eg, unipolar major depression), most patients are referred to psychiatrists and other mental health clinicians if these specialists are available [8]. Indications for referral include:

- Suicidal ideation and behavior (see "Suicidal ideation and behavior in adults")
- Psychotic features (eg, auditory hallucinations commanding patients to kill themselves) (see "Psychosis in adults: Epidemiology, clinical manifestations, and diagnostic evaluation", section on 'Clinical manifestations')
- Catatonia – Prominent psychomotor disturbances, such as immobility, mutism, and posturing, which occur during most of the mood episode (see "Catatonia in adults: Epidemiology, clinical features, assessment, and diagnosis" and "Catatonia: Treatment and prognosis")
- Impulsive and dangerous behavior (eg, significant aggression)
- Fluctuating symptoms
- Functional impairment (eg, chronic marital conflicts or unemployment)
- Multiple comorbid psychiatric disorders (eg, depressive disorder plus a substance-related and addictive disorder)
- Administering psychotherapy

- Prior history of recurrent episodes of the psychiatric disorder
- Poor adherence with psychiatric treatment
- Discontinuing psychiatric treatment following a period of stability, or with no clear precipitant
- Recalcitrant psychiatric symptoms despite appropriate treatment, or poor tolerance to multiple treatments

In addition, referral to social work is often appropriate; indications include problematic social circumstances, such as intimate partner violence or other trauma, poverty, or homelessness. Social workers may also facilitate treatment uptake.

Nephrologists who refer patients on dialysis to psychiatric specialists are encouraged to remain involved in management. The nephrologist often knows the patient's personal situation and can help educate patients and families about psychotropics and psychotherapy, reinforce the need for adherence, and typically collaborates in monitoring treatment effectiveness by virtue of frequent interactions with patients.

Psychopharmacology — For patients treated with maintenance dialysis, the dose of most psychotropic medications does not need to be adjusted because they are metabolized in the liver [6]. However, the metabolites are often excreted by the kidney and some drugs may require a dose adjustment. Dosing recommendations that are specific for hemodialysis and peritoneal dialysis can be found in the Lexicomp drug information topic for that drug, in the section on dosing in renal impairment. Some of the dose recommendations are based upon the European Renal Best Practice guideline [13]. The Lexicomp drug information topics are included in UpToDate.

If uncertainty exists regarding the dose of a psychotropic to use in patients on dialysis, it is prudent to start at a lower dose (eg, one-half) than that used for the general population of patients [14]. In addition, dose titration should also proceed more slowly than the standard rate.

The therapeutic dose of some drugs is determined by their serum concentrations; one example is valproate, which may be indicated for bipolar disorder. However, in patients with ESKD, total serum concentrations of drugs that are highly protein bound may be misleading because uremic toxins may displace the drug from serum proteins and increase the unbound fraction of the drug [14]. If feasible, it is preferable to monitor the free concentration of the drug rather than the total concentration.

It is unlikely that dialysis will remove meaningful amounts of antidepressants, antipsychotics, and benzodiazepines [1-3,14]. These medications typically undergo hepatic metabolism, are highly bound to plasma proteins, and are lipophilic and have a large volume of distribution.

However, lithium, which may be indicated for bipolar disorder and unipolar major depression, is completely dialyzed [14]. After each hemodialysis session, patients generally receive a single supplemental dose of 300 mg. At least two to three hours should elapse after dialysis before lithium serum concentrations are assayed because the drug re-equilibrates and is released from tissue stores immediately following dialysis.

For patients who are treated with hemodialysis, clinicians should try to avoid drugs that can prolong the QT interval because these patients are at increased risk of adverse cardiac events due to comorbid cardiovascular disease and electrolyte shifts during dialysis [15]. Psychotropic drugs that can cause QT prolongation include citalopram, thioridazine, and tricyclics. (See "Selective serotonin reuptake inhibitors: Pharmacology, administration, and side effects", section on 'Citalopram' and "Tricyclic and tetracyclic drugs: Pharmacology, administration, and side effects", section on 'Cardiac' and "First-generation antipsychotic medications: Pharmacology, administration, and comparative side effects", section on 'QT interval prolongation and sudden death'.)

We also try to avoid drugs that can cause orthostatic hypotension (eg, tricyclic antidepressants and trazodone) in patients on hemodialysis [14]. Fluid shifts during the dialysis session can cause intradialytic hypotension as well as symptoms that persist for several hours after the treatment ends and can render patients more vulnerable to orthostasis.

In addition, drug-drug interactions can occur between psychotropic medications and other medications that may be prescribed for patients with ESKD [1,6,14]. Interactions of a specific drug with other medications may be determined using the Lexicomp drug interactions tool (Lexi-Interact Online) included in UpToDate.

ANXIETY DISORDERS

Anxiety disorders include acute procedure anxiety, agoraphobia, generalized anxiety disorder, panic disorder, and social anxiety disorder [11]. Another disorder that may arise in patients on hemodialysis is specific phobia, due to a fear of needles, the sight of blood, and vascular access cannulation.

Anxiety disorders and clinically significant symptoms frequently occur in patients treated with maintenance dialysis [14,16]. Meta-analyses of observational studies found that the prevalence

was as follows [17]:

- Anxiety disorders (9 studies, n >1000 patients) – 19 percent
- Elevated anxiety symptoms (52 studies, n >10,000 patients) – 43 percent

These results, when compared with studies in the general population, suggest that anxiety may be greater in dialysis patients than the general population. (See "Generalized anxiety disorder in adults: Epidemiology, pathogenesis, clinical manifestations, course, assessment, and diagnosis", section on 'Prevalence'.)

Risk factors associated with elevated anxiety symptoms in dialysis patients include concomitant depression, increased duration of hospitalization, and reduced quality of life [17].

Symptoms of anxiety such as fatigue or impaired concentration may overlap with symptoms of inadequate dialysis [9]. In addition, anxiety may manifest with somatic symptoms such as dyspnea, palpitations, and gastrointestinal distress, which can overlap with general medical illnesses (eg, cardiovascular and pulmonary disorders). Somatic anxiety symptoms are associated with an increased number and severity of dialysis symptoms [18].

Onset of anxiety in dialysis patients may occur prior to or at commencement of dialysis and persist during dialysis. A prospective study enrolled 182 patients who were starting dialysis and followed them for a median of 20 months; assessments included a self-report questionnaire at baseline and during follow-up [19]. Clinically significant symptoms of anxiety, which were present at baseline in 24 percent, did not improve during the first year of follow-up and dialysis.

Quality of life among dialysis patients is worse in those with comorbid anxiety disorders [7,20,21].

Among patients who are treated with maintenance dialysis, the diagnostic criteria for anxiety disorders are the same as those used in the general population [9,11]. In addition, treatment of anxiety in dialysis patients typically includes the standard lifestyle modifications, psychotherapies, and pharmacotherapies that are used for anxiety in the general population. If a benzodiazepine is indicated, we prefer lorazepam because it does not have an active metabolite [14]. The diagnosis and treatment of anxiety disorders are discussed in separate topics.

MAJOR DEPRESSION

Major depression is common in patients treated with maintenance dialysis. (See "Depression in adults receiving maintenance dialysis".)

NEUROCOGNITIVE DISORDERS

Neurocognitive disorders include cognitive impairment, dementia, and delirium [11].

Cognitive impairment — Cognitive impairment encompasses a spectrum of persistent cognitive and functional deficits that range from mild to severe [11].

It is not clear to what degree cognitive impairment in patients treated with dialysis is related to dialysis per se, uremic toxins and electrolyte disturbances that occur in end-stage kidney disease (ESKD), comorbid general medical disorders such as cardiovascular disease and diabetes that are common in ESKD, toxicity of medications excreted by the kidney, or to neurodegenerative disease [14,22].

Epidemiology — Several studies in patients treated with maintenance dialysis indicate that cognitive impairment across multiple domains of neuropsychological functioning is common [6,23]. As an example, one review found that among patients older than age 55 years, moderate to severe chronic cognitive impairment is present in up to 70 percent [14]. Another review estimated that the point prevalence of impairment is three to five times greater in dialysis patients than the general population [24]. In addition, cognitive impairment occurs more frequently in dialysis patients age 21 to 54 years, compared with individuals in the general population over 65 years.

In prospective, cross-sectional studies of dialysis patients, cognitive impairment was identified in approximately 30 to 85 percent, and was often not recognized [25]:

- One study included 458 dialysis patients (mean age 52 years) who were screened with a modified version of the Mini-Mental State Examination, and found that global cognitive function was impaired in 28 percent [26].

- A third study administered a battery of nine cognitive tests to assess executive function, language, and memory in 338 hemodialysis patients aged 55 years and older [27]. A documented history of cognitive impairment was present in 3 percent. However, based upon the test results, patients were classified as follows:

    - No impairment – 13 percent
    - Mildly impaired – 14 percent
      Moderately impaired – 36 percent

- Severely impaired – 37 percent

Severe impairment was correlated with a history of stroke, a Kt/V (dialysis dose) greater than 1.2, and education ≤12 years [27].

Using the same battery of tests, the investigators compared a random sample of 101 hemodialysis patients drawn from the 338 patients with 101 controls drawn from general medicine clinics [27]. After controlling for potential confounding factors such as age, depression, and diabetes, the analyses found that the likelihood of severe cognitive impairment was three and a half times greater in hemodialysis patients than controls (odds ratio 3.5, 95% CI 1.3-9.8).

Cognitive function among all dialysis patients may vary in relation to the timing of the dialysis procedure. As an example, one study found that global cognitive function was worst during dialysis and best just prior to dialysis and the day between dialysis sessions [28].

Risk factors for cognitive dysfunction that are often present in dialysis patients include advanced age (eg, ≥75 years), depression, comorbid general medical disorders (eg, cardiovascular disease, diabetes, dyslipidemia, and hypertension), reduced serum albumin, hypoxemia, large fluid and osmolar shifts, and unidentified uremic toxins [26,29,30].

It remains unclear whether the prevalence of cognitive impairment differs between hemodialysis and peritoneal dialysis. The results of one meta-analysis (42 observational studies, total n >3500 study participants) indicate that cognitive functioning is generally comparable in patients who are treated with either hemodialysis or peritoneal dialysis [29]. However, a subsequent meta-analysis of 15 observational studies (sample size not reported) found that the risk of neuropsychological deficits was greater with hemodialysis than peritoneal dialysis [31].

Specific deficits — Evidence regarding the specific cognitive domains that are impaired includes a meta-analysis of 42 studies that examined neuropsychological test performance in dialysis patients and in various control groups (total n >3500 study participants; mean age 51 years) [29]. Eight cognitive domains were assessed, including global cognition, attention and orientation, concept formation and reasoning, construction and motor performance, executive functioning (eg, planning, problem solving, and sequencing actions), language, memory, and perception. The primary findings included the following:

- Test scores in each domain (except perception) were lower for hemodialysis patients lower than individuals with no known kidney disease (general population), and the clinical differences were generally moderate to large; however, heterogeneity across studies was also moderate to large. Scores for perception in the two groups did not differ statistically.

- Across the eight cognitive domains, test scores were comparable for patients on hemodialysis and patients on peritoneal dialysis, with the exception that hemodialysis patients scored lower on tests of executive function. In addition, one study found that language skills were worse in hemodialysis patients.

- Cognitive functioning in each domain was comparable in hemodialysis patients and nondialysis-dependent chronic kidney disease patients, except for memory, which was worse in hemodialysis patients.

One review concluded that in dialysis patients, the most commonly impaired cognitive domain is executive functioning [24].

Screening and assessment — Screening patients on maintenance dialysis for cognitive impairment can be useful, provided services are in place to ensure appropriate diagnosis, treatment, and follow-up [24]. Several studies in patients treated with dialysis indicate that although impairment across multiple domains of neuropsychological functioning is common, it is often unrecognized [23,24,27]. Periodic screening (eg, every 12 months) is important for recognizing cognitive impairment in ESKD that develops or progresses over time and may uncover subtle symptoms that are not obvious when the patient is being observed during dialysis. (See 'Course of illness' below.)

Patients on maintenance dialysis are screened for cognitive impairment with the same instruments that are used in the general population [23,24]. Widely used instruments include either the clinician administered Mini-Mental State Examination or the Montreal Cognitive Assessment, which can each be completed in 5 to 15 minutes. Other reasonable choices include the Saint Louis University Mental Status Examination and the Clock-Drawing Test. No scale has been validated in ESKD. Information about these instruments and other available scales is described separately. (See "Mental status scales to evaluate cognition".)

Screening for cognitive impairment typically occurs the day before or after a hemodialysis session, rather than the day of dialysis [23]. The reason is that dialysis involves hemodynamic shifts that may induce cerebral hypoperfusion and transient cognitive impairment [32].

The potential benefits of screening for cognitive impairment include identifying causes that may be reversible such as delirium and depression, and possibly mitigating some effects of dementia [23]. In addition, cognitive deficits impair decision making and are associated with poor adherence; thus, recognizing these deficits may enable clinicians to improve these aspects of care. Recognition of relatively mild impairment, prior to progression to dementia, is key to the assessment of decision making capacity as needed for advanced care planning [24].

Clinicians should interview patients who screen positive for cognitive impairment to establish or rule out a diagnosis (eg, mild or major vascular dementia) because screening is not sufficient for case-finding. In addition, patients who screen positive may require neuropsychological testing to establish a diagnosis, especially in complicated cases, such as differentiating a neurodegenerative disorder (eg, vascular dementia) from unipolar major depression [23]. Testing can also be used to assess capacity for decision-making.

Assessing cognitive function in dialysis patients is often difficult because of patient limitations. In a prospective study of cognitive function in 767 patients on dialysis, data were missing in 48 percent [33]. The reasons included visual impairment, lack of motivation, and motor impairment. Patients with missing cognitive testing data were more likely to have depression than patients with complete data.

Information about assessing cognition and cognitive deficits in the general population is discussed separately. (See "Mild cognitive impairment: Epidemiology, pathology, and clinical assessment", section on 'Evaluation' and "Evaluation of cognitive impairment and dementia", section on 'Evaluation'.)

Potential adverse consequences — In patients who are treated with maintenance dialysis, cognitive impairment may be related to poor outcomes, including hospitalization and increased mortality:

- A retrospective study included more than 140,000 patients age ≥65 years who initiated dialysis and were hospitalized during the first year of dialysis with a primary or secondary psychiatric diagnosis [7]. Hospitalization with a primary diagnosis of a neurocognitive disorder (eg, delirium or dementia) occurred in 3 percent.

- Cognitive impairment is associated with an increased risk of mortality in dialysis patients. A seven-year prospective study assessed attention, concentration, learning and verbal memory, and psychomotor speed at baseline in dialysis patients (patients with dementia were excluded) [25]. Testing determined that cognitive impairment was present in 98 patients and absent in 47. After controlling for potential confounding factors such as sociodemographic and clinical features (eg, comorbidities and depression), the analyses found that all-cause mortality was two and a half times greater in dialysis patients with cognitive impairment than unimpaired patients (hazard ratio 2.53, 95% CI 1.03-6.22).

One possible explanation for the association between cognitive dysfunction and increased mortality in dialysis patients is that dialysis is a complex treatment and cognitive deficits may interfere with one’s ability to follow treatment recommendations and may lead to poor

adherence [6,25]. Alternatively, impaired cognition may reflect general physical deterioration or a specific disease process such as vascular disease.

Course of illness — Studies of patients with chronic kidney disease suggest that a decline in cognitive function probably begins with early kidney disease, prior to onset of ESKD, and progresses over time [24,34,35]:

- In a nationally representative survey of United States adults aged 45 years and older (n >23,000), chronic kidney disease (estimated glomerular filtration less than 60 mL/min per 1.73 m^2) was associated with an increased prevalence of cognitive impairment (odds ratio 1.2, 95% CI 1.1 to 1.4) [36]. Each 10 mL/min per 1.73 m^2 decrease in glomerular filtration rate below 60 mL/min per 1.73 m^2 was associated with an 11 percent increase in the prevalence of cognitive impairment.

- A study of hemodialysis patients (n = 314; average age 63 years) found that during a mean follow-up of two years, patients suffered a yearly decline in global cognitive function and executive function [37]. Older age was associated with greater declines.

Management — Management of cognitive impairment in patients treated with dialysis depends upon the severity of impairment and whether a specific diagnosis is established:

- Mild cognitive impairment (see "Mild cognitive impairment: Prognosis and treatment")

- Dementia (see 'Prevention and treatment' below)

- Delirium (see 'Treatment' below)

Dementia — Dementia is marked by a significant decline in at least one cognitive domain such as executive function (eg, planning, problem solving, and sequencing actions), learning and memory, language, and social cognition (eg, identifying basic emotions such as happiness, sadness, and fear in others) [11]. In addition, the deficits interfere with independence in activities of daily living to the extent that others need to assume responsibility for tasks that were previously completed by the patient.

The major dementia syndromes in patients treated with maintenance dialysis include [38]:

- Vascular dementia
- Alzheimer disease
- Dementia with Lewy bodies
- Frontotemporal dementia

Patients with ESKD may be more susceptible to vascular dementia than other dementias [14,24,38]. Multiple reviews have found that the incidence of stroke is greater in dialysis patients than the general population [39-41]. In addition, leukoaraiosis and other white matter hyperintensities on brain magnetic resonance imaging, which are associated with vascular dementia, appear to be more prevalent in dialysis and predialysis patients, compared with controls [40-43]. A high incidence of vascular dementia in dialysis patients relative to the general population is likely because of the high number of older patients with diabetes, hypertension, and vascular disease who start dialysis [14]. (See "Etiology, clinical manifestations, and diagnosis of vascular dementia".)

Dementia secondary to aluminum toxicity is now uncommon because aluminum is removed from water used for dialysis. In addition, phosphate binders that do not contain aluminum are the standard of care. (See "Aluminum toxicity in chronic kidney disease".)

Epidemiology — Patients treated with maintenance dialysis are at increased risk of developing dementia [23,44]. Dementia appears to affect up to 20 percent of patients on dialysis, and the prevalence of dementia appears to be approximately two times greater in dialysis patients than the general population:

- A retrospective study used a national (United States) registry dedicated to chronic kidney disease and ESKD to identify patients age 66 years and older who initiated dialysis (n >350,000) and did not have dementia [45]. After accounting for competing risks such as kidney transplantation or death, the proportion of patients diagnosed with dementia at various times during follow-up were approximately as follows:
  - 1 year – 5 percent
  - 5 years – 15 percent
  - 10 years – 20 percent
- A 12-year, retrospective study of a national (Taiwan) administrative health care database included hemodialysis patients and controls without ESKD (n >63,000 each group), as well as peritoneal dialysis patients and controls (n >9000 each group) [38]. Dialysis patients and controls were matched for the propensity (probability) of receiving dialysis, using baseline demographic and clinical characteristics. After adjusting for potential confounding factors (eg, age, sex, and general medical comorbidities such as diabetes), the analyses found that dementia occurred more often in:
  - Hemodialysis patients than controls – Hazard ratio 1.64 (95% CI 1.58-1.71)
  - Peritoneal dialysis patients than controls – Hazard ratio 2.21 (95% CI 1.87-2.62)

- For both groups of dialysis patients, the subtype of dementia that occurred from most to least often was unspecified dementia, vascular dementia, and Alzheimer disease.

Risk factors for dementia in dialysis patients include older age (≥75 years), female sex, non-White race/ethnicity, and institutionalization [23,45].

It remains unclear whether the prevalence of dementia differs between hemodialysis and peritoneal dialysis. A meta-analysis of three studies compared patients treated with either hemodialysis (n >165,000) or peritoneal dialysis (11,000), and found that the likelihood dementia was greater with hemodialysis (odds ratio 1.6, 95% CI 1.2-2.3) [31]. However, the results of the study from Taiwan described immediately above, which was not included in the meta-analysis, suggest that dementia may be greater with peritoneal dialysis than hemodialysis, given the lack of overlap in the confidence intervals [38].

Potential adverse consequences — Dementia in patients treated with maintenance dialysis is associated with increased hospitalization and dialysis withdrawal [23,24]. In addition, the risk of all-cause mortality is increased by a factor of two to three:

- A retrospective study used a national registry dedicated to chronic kidney disease and ESKD to identify patients who initiated dialysis (n >270,000), including those with dementia at baseline (n >1700); all patients were followed for at least two years [46]. After controlling for potential confounding factors such as sociodemographics, smoking, and general medical comorbidities, the analyses showed that life expectancy was reduced in patients with dementia. As an example, the two-year survival was approximately three-fold less in dialysis patients with dementia than those without dementia (24 versus 66 percent).

- Another study used the same registry and identified patients age 66 years and older who did not have dementia and initiated dialysis (n >350,000) [45]. Patients were followed for up to 13 years, during which time dementia occurred in 18 percent. After adjusting for potential confounding factors such as sociodemographics, smoking, and general medical comorbidities, the analyses found that the risk of all-cause mortality was twice as high in dialysis patients with dementia than in patients without dementia (hazard ratio 2.14, 95% CI 2.07-2.22).

Evaluation — Dementia is often not recognized in patients on maintenance dialysis, and assessing patients for dementia is complicated by the overlap between symptoms of dementia and symptoms related to kidney failure and medication adverse effects [7,23]. The evaluation of dementia in dialysis patients is generally the same as in nondialysis patients. (See "Evaluation of cognitive impairment and dementia".)

A screening tool for dementia that is specific for dialysis patients utilizes the patient's age and the presence of 10 particular comorbidities, including Parkinson disease, depression, stroke, diabetes mellitus, and traumatic brain injury [47].

Prevention and treatment — Some nephrologists have the requisite training and experience to manage dementia in patients on maintenance dialysis. However, there may be uncertainty about the diagnosis, or these clinicians may not be comfortable treating dementia and thus refer patients to psychiatrists or other mental health clinicians if these specialists are available; referrals are also made if requested by patients or families.

The literature describing the prevention and treatment of dementia in dialysis patients is limited to low quality studies [48,49]; thus, interventions for ESKD patients generally follow the approaches utilized in the general population of patients who are at risk for or have dementia:

- Prevention (see "Prevention of dementia")
- Overview (see "Management of the patient with dementia")
- Early-onset dementia (see "Early-onset dementia in adults")
- Vascular dementia (see "Treatment of vascular cognitive impairment and dementia")
- Alzheimer disease (see "Treatment of Alzheimer disease")
- Dementia with Lewy bodies (see "Prognosis and treatment of dementia with Lewy bodies")
- Frontotemporal dementia (see "Frontotemporal dementia: Epidemiology, pathology, and pathogenesis")
- Agitation and aggression, as well as depressive syndromes (see "Management of neuropsychiatric symptoms of dementia")
- Sleep disorders (see "Sleep-wake disturbances and sleep disorders in patients with dementia")
- Palliative care for advanced dementia (see "Care of patients with advanced dementia")

Delirium — Delirium is a disturbance of attention and awareness that develops over a short period of time (usually hours to days) and is accompanied by additional cognitive impairment (eg, memory deficits) [11]. In addition, the history, physical examination, and laboratory findings indicate that the disturbance is caused by a general medical condition, substance

intoxication or withdrawal, or medication side effect. Patients treated with maintenance dialysis, especially older patients (eg, ≥65 years), are susceptible to delirium.

Pathogenesis — Many of the common causes of delirium are similar in patients with and without ESKD. (See "Diagnosis of delirium and confusional states", section on 'Pathogenesis'.)

Causes of delirium that are specifically relevant for patients on maintenance dialysis include the following [1,23]:

- Uremic encephalopathy – The central nervous system dysfunction that is universally observed among patients with severe untreated uremia is termed uremic encephalopathy. Central nervous system dysfunction should abate within days to weeks after the initiation of adequate renal replacement therapy. (See "Acute toxic-metabolic encephalopathy in adults", section on 'Uremic encephalopathy' and "Indications for initiation of dialysis in chronic kidney disease".)

- Dialysis disequilibrium syndrome – The syndrome is characterized by acute symptoms, including headache, nausea, disorientation, restlessness, blurred vision, and asterixis, which develop during or immediately after hemodialysis. The etiology is thought to be primarily cerebral edema. (See "Dialysis disequilibrium syndrome".)

- Electrolyte disorders – Examples include hypercalcemia, hypocalcemia, hypoglycemia, hyperglycemia, hyponatremia, and hypernatremia. (See "Acute complications during hemodialysis".)

- Drugs – Medications can accumulate due to lack of renal excretion. Thus, exposure to agents (including illicit drugs) cleared by the kidney that affect central nervous system function must be excluded (see 'Psychopharmacology' above). In addition, delirium may arise as an adverse effect of medications such as anticholinergics, benzodiazepines, corticosteroids, and opioids.

- Foods – Dialysis patients may experience delirium by ingesting the star fruit (Averrhoa carambola) [50] or the mushroom Sugihiratake [51].

- Infections – Examples include catheter-related bacteremia and abscess.

- Hemodynamic instability (either hypotension or hypertension). (See "Intradialytic hypotension in an otherwise stable patient" and "Hypertension in patients on dialysis" and "Moderate to severe hypertensive retinopathy and hypertensive encephalopathy in adults".)

- Cerebrovascular disease – Examples include infarction, hemorrhage, and subdural hematoma [39,52]; the frequency of these events may be increased during or shortly after the dialysis procedure [53]. (See "Overview of the evaluation of stroke" and "Stroke: Etiology, classification, and epidemiology" and "Definition, etiology, and clinical manifestations of transient ischemic attack" and "Subdural hematoma in adults: Etiology, clinical features, and diagnosis".)

- Vitamin deficiencies – Thiamine deficiency may give rise to delirium [54]. (See "Overview of water-soluble vitamins".)

- Alcohol withdrawal. (See "Management of moderate and severe alcohol withdrawal syndromes".)

- Seizure – Seizures are relatively common in dialysis patients. (See "Seizures in patients undergoing hemodialysis".)

  Rarely, nonconvulsive status epilepticus is the cause of acute confusional states [55]. (See "Nonconvulsive status epilepticus: Classification, clinical features, and diagnosis".)

- Aluminum toxicity – This may rarely cause an acute encephalopathy. (See "Aluminum toxicity in chronic kidney disease".)

Evaluation — The evaluation of delirium in the dialysis patient is generally the same as in the nondialysis patient. (See "Diagnosis of delirium and confusional states".)

However, the clinician must consider causes of delirium that are specific to dialysis patients (see 'Pathogenesis' above). In addition, symptoms of delirium can overlap with symptoms of uremia from underdialysis and medication adverse effects [7].

Treatment — For patients on maintenance dialysis, treatment of delirium rests upon identifying and managing the underlying cause (see 'Pathogenesis' above). In addition, agitation and behavioral disturbances that arise as part of delirium need to be managed to provide safe dialysis. Treatment of delirium, including agitation, is discussed in separate topics. (See "Delirium and acute confusional states: Prevention, treatment, and prognosis" and "Assessment and emergency management of the acutely agitated or violent adult".)

If pharmacotherapy is used for treating delirium in patients on dialysis, the need to adjust doses is discussed elsewhere in this topic. (See 'Psychopharmacology' above.)

OTHER DISORDERS

Other psychiatric disorders that are observed in patients with end-stage kidney disease (ESKD) include schizophrenia and substance-related and addictive disorders.

- Schizophrenia
  - A study enrolled 70 patients receiving dialysis who were assessed for schizophrenia and other psychotic disorders using a semistructured interview and standardized diagnostic criteria [20]. The point prevalence of schizophrenia and other psychotic disorders was 10 percent, which may exceed the rate in the general population. (See "Schizophrenia in adults: Epidemiology and pathogenesis", section on 'Epidemiology'.)
  - A retrospective study included more than 100,000 patients age 22 to 64 years who initiated dialysis and were hospitalized during the first year of dialysis with a primary or secondary psychiatric diagnosis [7]. Hospitalization with a primary diagnosis of schizophrenia occurred in 1 percent.
  - A study of an administrative health care dataset included patients with schizophrenia (n >27,000) and a control group matched at a 1:1 ratio on age and sex [56]. After controlling for potential confounding factors (eg, age, general medical illnesses, and smoking), the analyses found that the risk of chronic kidney disease was greater in patients with schizophrenia than controls (odds ratio 1.6, 95% CI 1.5-1.8). In addition, chronic kidney disease patients with schizophrenia were less likely to receive dialysis or kidney transplantation than chronic kidney disease patients without schizophrenia.
- Substance-related and addictive disorders
  - A study enrolled 70 patients receiving dialysis who were assessed for substance-related and addictive disorders using a semistructured interview and standardized diagnostic criteria [20]. The point prevalence of alcohol use disorder was 18 percent and the prevalence of nonalcohol use disorders was 19 percent. It is not known if the prevalence of these disorders is greater in ESKD than the general population. (See "Risky drinking and alcohol use disorder: Epidemiology, clinical features, adverse consequences, screening, and assessment", section on 'DSM-5 alcohol use disorder'.)
  - A retrospective study included more than 100,000 patients age 22 to 64 years who initiated dialysis and were hospitalized during the first year of dialysis with a primary or secondary psychiatric diagnosis [7]. Hospitalization with a primary diagnosis of an alcohol-related disorder occurred in 1 percent. In addition, hospitalization with a primary diagnosis of a substance-related disorder not involving alcohol occurred in 1 percent.

- Sleep disorders (see "Sleep disorders in end-stage kidney disease")
- Restless leg syndrome (see "Clinical features and diagnosis of restless legs syndrome and periodic limb movement disorder in adults", section on 'Uremia')

REQUEST TO WITHDRAW FROM DIALYSIS

Psychiatric disorders that may lead patients to discontinue dialysis include unipolar major depression, dementia, and toxic-metabolic (uremic) encephalopathy [2,6]. In assessing patients who make this request, clinicians should determine that the patient wants no further interventions to treat psychiatric disorders that may be associated with the request for withdrawal of dialysis. In addition, clinicians must establish that the patient has decision making capacity and fully comprehends the consequences, including imminent death (eg, within one to two weeks) and the symptoms of the dying process. Psychiatrists and/or other mental health professionals are often consulted.

Additional information about discontinuing dialysis, including the indications, legal and ethical issues, and clinical approach to withdrawing dialysis is discussed separately. (See "Kidney palliative care: Withdrawal of dialysis".)

SUICIDE

Suicide is approximately two times greater in dialysis patients than the general population; however, the absolute rate is relatively low:

- A study of administrative health care datasets included patients on maintenance dialysis (n >400,000) and found that during a six-year period, suicide was nearly twice as likely in the patients than the general population (standardized mortality ratio 1.8, 95% CI 1.5-2.3) [57]. During the six years, there were 264 suicides. Independent predictors included male sex, White or Asian race, recent hospitalization with psychiatric disorder, and substance-related and addictive disorders.
- A national registry study identified nearly 64,000 patients on maintenance dialysis and found that during a six-year period, suicide was more than twice as likely in the patients than the general population (standardized mortality ratio 2.4, 95% CI 2.0-2.8) [58]. During the six years, there were 133 suicides; the highest rate of suicides was in the first year of dialysis. In many cases, suicide occurred by cutting the vascular access for hemodialysis.

In addition, a study of national registry and survey data examined patients on maintenance dialysis (n >270,000), and found that during a two-year period, suicide/refusal of treatment was nearly three-fold greater in dialysis patients than the general population (standardized mortality ratio 2.9, 95% CI 2.6-3.1) [59]. During the two years, there were 480 suicides/refusals. However, suicides and deaths due to refusal of dialysis are distinct entities and aggregating the two makes it impossible to assess the prevalence of either suicide or refusal among these dialysis patients [1,6].

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or email these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Beyond the Basics topics (see "Patient education: Delirium (Beyond the Basics)")

SUMMARY

- **Overview**
  - Epidemiology – Among patients who are treated with maintenance dialysis, the prevalence of any psychopathology may be as high as 70 percent. Relatively common illnesses include anxiety disorders, depressive disorders, neurocognitive disorders, and substance-related and addictive disorders. (See 'Epidemiology' above.)
  - Potential adverse consequences – Psychiatric comorbidity in end-stage kidney disease (ESKD) may sometimes lead to poor adherence with dialysis and increased rates of hospitalization, suicide, and all-cause mortality. (See 'Potential adverse consequences' above and 'Suicide' above.)

- **Diagnosis and treatment** – Among patients who are treated with maintenance dialysis, the diagnostic criteria for psychiatric disorders are identical to those used in the general population. In addition, treatment recommendations for comorbid mental disorders are generally based upon patients in the general population of patients with psychiatric disorders. (See 'Diagnosis and treatment' above.)

  - Referral – Nephrologists may have the requisite training and experience to diagnose and manage psychiatric disorders; however, most patients are referred to psychiatrists and other mental health clinicians if these specialists are available. (See 'Referral' above.)

  - Psychopharmacology – Although the dose of most psychotropic medications does not need to be adjusted for patients on dialysis, some drugs may require a dose adjustment. Clinicians should try to avoid drugs that can prolong the QT interval or cause hypotension. (See 'Psychopharmacology' above.)

- **Anxiety disorders** – Among patients treated with maintenance dialysis, anxiety disorders and clinically significant symptoms occur in approximately 20 to 45 percent, which may be greater than the rate in the general population. (See 'Anxiety disorders' above.)

- **Major depression** – Major depression is common in patients treated with maintenance dialysis. (See "Depression in adults receiving maintenance dialysis".)

- **Cognitive impairment**

  - Specific deficits – The specific cognitive domains that are impaired in dialysis patients include attention, executive functioning, and language. (See 'Specific deficits' above.)

  - Screening and assessment – Screening dialysis patients for cognitive impairment can be useful, provided services are in place to ensure appropriate diagnosis, treatment, and follow-up. Widely used instruments include either the clinician administered Mini-Mental State Examination or the Montreal Cognitive Assessment. (See 'Screening and assessment' above.)

  - Management – Management of cognitive impairment in patients treated with dialysis depends upon the severity of impairment and whether a specific neurocognitive disorder diagnosis is established. (See 'Management' above.)

- **Dementia** – Dementia is marked by a significant decline in one or more cognitive domains, and the deficits interfere with independence in activities of daily living. Dementia appears to affect up to 20 percent of patients on maintenance dialysis, and the prevalence

of dementia may be approximately two times greater in dialysis patients than the general population. Dialysis patients appear to be more susceptible to vascular dementia than other dementias. (See 'Dementia' above.)

- **Delirium** – Delirium is a disturbance of attention and awareness that develops over a short period of time and is accompanied by additional cognitive impairment. The disturbance is caused by a medical condition, substance intoxication or withdrawal, or medication side effect. (See 'Delirium' above.)

  - Pathogenesis – Causes of delirium that are specifically relevant for patients on maintenance dialysis include uremic encephalopathy, dialysis disequilibrium syndrome, and electrolyte disorders. (See 'Pathogenesis' above.)

  - Treatment – Treatment of delirium rests upon identifying and managing the underlying cause. (See "Delirium and acute confusional states: Prevention, treatment, and prognosis".)

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