

# Suicidality in an older patient with chronic kidney disease

Paul G. Yang, MS, Clark W. Johnson, MD, and Kenneth H. Hicken, LCSW



## How would you handle this case?

Answer the challenge questions at [MDedge.com/psychiatry](https://www.mdedge.com/psychiatry) and see how your colleagues responded

Mr. J, age 72, has chronic kidney disease and major depressive disorder. He is brought to the ED with suicidal ideation. Is his depression to blame, or could it be something else?

### **CASE** Depressed, anxious, and suicidal

Mr. J, age 72, is brought to the emergency department by law enforcement at his wife's request due to worsening suicidal thoughts and anxiety. He has a history of major depressive disorder (MDD) and chronic kidney disease (CKD). Mr. J has been compliant with his medications, but they seem to no longer be effective. He is admitted to the geriatric psychiatry unit.

### **HISTORY** Increased debilitation

Over the past several years, Mr. J has experienced increasing debilitation at home, including difficulty walking and an inability to perform activities of daily life. Recently, he has begun to ask for multiple pills in an attempt to take his own life.

Mr. J has been previously treated in a psychiatric clinic with duloxetine 60 mg/d, mirtazapine 30 mg/d at bedtime, buspirone 15 mg 3 times a day, and trazodone 50 mg/d at bedtime. He is also taking amlodipine 5 mg twice daily for hypertension, lisinopril 2.5 mg/d for hypertension, furosemide 20 mg/d orally for CKD, and potassium chloride 10 mEq/d for hypokalemia secondary to CKD and furosemide use. Over the past year, his psychiatric medications have been steadily increased to target his MDD and anxiety.

### **EVALUATION** Disorientation and Stage 3A CKD

In the psychiatric unit, Mr. J describes panic, feelings of impending doom, and profound anxiety. He states he has increasing anxiety related to "being a burden" on his family and wife. Additionally, he describes decreased appetite, difficulty sleeping, low energy, difficulty concentrating, no interest in outside activities, and feelings of hopelessness.

Mr. J's temperature is 39.2° C; heart rate is 109 beats per minute; respiratory rate is 18 breaths per minute; blood pressure is 157/83 mm Hg; and pulse oximetry is 97%. Laboratory screening indicates a red blood cell count of 3.57, hemoglobin 11.2, hematocrit 33.8, red blood cell distribution width 17.5, blood urea nitrogen 45, creatinine 1.5 with no known baseline, and an estimated glomerular filtration rate (GFR) of 46 mL/min, indicating Stage 3A CKD (**Table 1, page 45**). Additional testing rules out other potential causes of delirium and psychosis.



Discuss this article at [www.facebook.com/MDedgePsychiatry](https://www.facebook.com/MDedgePsychiatry)



Mr. Yang is a 4th-year medical student, Rocky Vista University College of Osteopathic Medicine, Ivins, Utah. Dr. Johnson is Medical Director, Senior Behavior Health Unit, Salt Lake Regional Medical Center, Salt Lake City, Utah. Mr. Hicken is Clinical Supervisor, Senior Behavior Health Unit, Salt Lake Regional Medical Center, Salt Lake City, Utah.

#### **Disclosures**

Dr. Johnson has received income from Teva Pharmaceuticals. The other authors report no financial relationships with any companies whose products are mentioned in this article, or with manufacturers of competing products.

doi: 10.12788/cp.0322

Table 1

## Stages of chronic kidney disease

Stage	Glomerular filtration rate (mL/min/1.73 m <sup>2</sup> )	Description
1	≥90	Normal or high
2	60 to 89	Mildly decreased
3A	45 to 59	Mildly to moderately decreased
3B	30 to 44	Moderately to severely decreased
4	15 to 29	Severely decreased
5	<15	Kidney failure (add vitamin D if treated by dialysis)

Source: Reference 1

A physical exam reveals Mr. J has a fine tremor, myoclonus, muscle rigidity, and hyperreflexia. He is oriented to name, but not to date, place, or situation, and is easily confused. Mr. J uses a walker but has significant tremors while walking and immediately asks for assistance due to profound anxiety related to a fear of falling. Mr. J's mood and affect are labile with tearful and anxious episodes. His anxiety focuses on overvalued thoughts of minor or irrelevant concerns. Additionally, he has poor insight and judgment. When asked about the cause of his anxiety, Mr. J says, "I don't know why I'm anxious; I'm just a worrywart." His memory is impaired, and he does not know why he is in the hospital. Mr. J scores 24 on the Montreal Cognitive Assessment, which indicates mild impairment.

Mr. J continues to endorse suicidal ideation but denies homicidal thoughts. Based on these symptoms, the differential diagnosis includes serotonin syndrome, MDD with suicidal ideation, generalized anxiety disorder, and panic disorder.

#### What laboratory values are used to monitor chronic kidney disease?

- Creatinine
- Creatinine clearance
- GFR
- Potassium

#### The authors' observations

GFR is used to determine the level of renal impairment. Mr. J's GFR of 46 mL/min indicates Stage 3A CKD (*Table 1*). Additionally, he displayed anemia and increased creatinine due to CKD. Twenty percent of patients with CKD also experience MDD.<sup>2</sup> In a prospective observational cohort study, Hedayati et al<sup>3</sup> found that Stage 2 to Stage 5 CKD with MDD leads to an increased risk of death, hospitalization, or progression to dialysis. It is important to properly manage Mr. J's MDD and CKD to prevent future comorbidities. Renal impairment is common in people age >65.<sup>4</sup> Even when GFR is normal, it is recommended to decrease dosing of medications in older adults due to age-related decreased renal excretion. As kidneys decrease in function, their ability to excrete normal amounts of medications also decreases, leading to increased serum levels and potential toxicity.

A combination of 4 serotonergic psychotropic medications may not be unusual to address treatment-resistant depression in a healthy, nongeriatric adult. However, Mr. J displayed signs of serotonin toxicity, such as hyperthermia, tachycardia, increased blood pressure, increased tremors, myoclonus, hyperreflexia, and muscle rigidity. These are classic signs of serotonin toxicity. For Mr. J, serotonin toxicity can be treated with the removal of serotonergic medications and

#### Clinical Point

Approximately 20% of patients with chronic kidney disease also experience major depressive disorder

**Clinical Point**

It is recommended to decrease medication dosages in older adults due to age-related decreased renal excretion

**Table 2**

**Recommended starting dose of antidepressants for MDD<sup>a</sup>**

Medication	Recommended starting dose to treat MDD	Comments
Fluoxetine <sup>8</sup>	20 mg/d	
Paroxetine <sup>9</sup>	20 mg/d	
Citalopram <sup>10</sup>	20 mg/d	Caution use with changes in CYP2C19, CYP2D6, CYP3A4 metabolism <sup>10,11</sup> May be affected in hepatic impairment <sup>12</sup>
Escitalopram <sup>12</sup>	10 to 20 mg/d	Caution use with changes in CYP2C19, CYP2D6, CYP3A4 metabolism <sup>10,11</sup> May be affected in hepatic impairment <sup>12</sup>
Sertraline <sup>13</sup>	50 mg/d	Caution use with changes in CYP3A4, CYP2B6, CYP2C19, CYP2D6 metabolism <sup>11,14</sup>
Venlafaxine <sup>15</sup>	75 mg/d	Decrease dose in renal impairment <sup>16</sup>
Desvenlafaxine <sup>16</sup>	50 mg/d	Decrease dose in renal impairment <sup>16</sup>
Duloxetine <sup>17</sup>	20 to 30 mg twice daily	Use with caution based on Beers Criteria <sup>4</sup> Discontinue or decrease dose in renal impairment <sup>4</sup> Caution use with fluvoxamine <sup>17</sup>
Mirtazapine <sup>18</sup>	15 mg/d	Caution use with changes in CYP1A2, CYP2D6, and CYP3A4

<sup>a</sup>For all selective serotonin reuptake inhibitors, the Beers Criteria<sup>4</sup> suggest use with caution in older adults due to risk of hyponatremia  
CYP: cytochrome P450; MDD: major depressive disorder

lorazepam for symptom relief. If symptoms persist, cyproheptadine, a serotonin antagonist, can be used. Mr. J's psychotropic medications were increased in an outpatient setting and he was unable to renally excrete higher doses of these serotonergic agents, which lead to chronic serotonin toxicity.

It is important to rule out other causes of psychosis or delirium in geriatric patients. A study by Marcantonio et al<sup>5</sup> found that >40% of patients referred to a consulting psychiatrist for depression ultimately had delirium, and this was more likely in geriatric patients.

**TREATMENT Adjustments to the medication regimen**

The treatment team decides to taper and discontinue duloxetine, buspirone, and trazodone and reduce mirtazapine to

15 mg/d at bedtime. Additionally, oral lorazepam 1 mg as needed is prescribed to alleviate agitation and correct vital signs. Mr. J's vital signs improve, with decreased temperature and normal cardiac and respiratory rhythms.

Mr. J's Stage 3A CKD is treated with oral fluids, and his hypertension is managed with an increase of lisinopril from 2.5 mg/d to 10 mg/d. After 10 days on the psychiatric unit, he shows improvement, decreased anxiety, and remission of suicidal ideation.

**In addition to duloxetine, dosages of which other antidepressants (not mentioned in the Beers Criteria) need to be adjusted in patients with impaired kidney function?**

- a) Sertraline
- b) Venlafaxine
- c) Fluoxetine
- d) Mirtazapine

### The authors' observations

In 2019, the American Geriatric Society (AGS) updated the Beers Criteria for potentially inappropriate medication use in older adults.<sup>4</sup> The Beers Criteria were created to educate clinicians about the use of potentially inappropriate medications that have an unfavorable balance of benefits and risks compared to alternative treatments. The AGS lists medications that should be avoided or have their dosage reduced with varying levels of kidney function in older adults. Duloxetine is one of the medications listed with the recommendation to avoid for patients with a creatinine clearance <30 mL/min. Creatinine clearance is an estimation of GFR.

Although duloxetine is mentioned in the Beers Criteria, many other antidepressants have metabolites excreted by the kidneys.<sup>6</sup> Potential adverse effects include increased bleeding, nausea, vomiting, and serotonin toxicity symptoms.<sup>7</sup> Mr. J has Stage 3A CKD and takes 4 psychotropics, which will additively increase the serum concentration of serotonergic medications. In terms of treatment for serotonin toxicity, it is important to remove the causative medications. After discontinuing serotonergic medications, lorazepam can be administered as needed. If a patient continues to have symptoms, cyproheptadine is an option.

For patients with impaired renal function, adding nonpharmacologic options should be considered, such as cognitive-behavioral therapy, electroconvulsive therapy, and transcranial magnetic stimulation. *Table 2*<sup>4,8-18</sup> (page 46) lists the minimum effective doses for well-known medications for treating MDD.

## Bottom Line

Older patients are more sensitive to psychotropic medications, regardless of any comorbidities. It is important to review each patient's glomerular filtration rate to better understand their renal function and adjust medications accordingly.

### Related Resources

- Whittaker P, Vordenberg SE, Coe AB. Deprescribing in older adults: an overview. *Current Psychiatry*. 2022;21(5):40-43. doi:10.12788/cp.0246
- Gibson G, Kennedy LH, Barlow G. Polypharmacy in older adults. *Current Psychiatry*. 2020;19(4):40-46.
- Barr R, Miskle B, Thomas C. Management of major depressive disorder with psychotic features. *Current Psychiatry*. 2021;20(2):30-33. doi:10.12788/cp.0092

#### Drug Brand Names

Amlodipine • Norvasc	Furosemide • Lasix
Bupirone • BuSpar	Lisinopril • Zestril
Citalopram • Celexa	Lorazepam • Ativan
Cyproheptadine • Periactin	Mirtazapine • Remeron
Desvenlafaxine • Pristiq	Paroxetine • Paxil
Duloxetine • Cymbalta	Sertraline • Zoloft
Escitalopram • Lexapro	Trazodone • Desyrel
Fluoxetine • Prozac	Venlafaxine • Effexor

### OUTCOME Improvement and discharge

Mr. J's confusion improves, his heart rate decreases, and his feelings of panic and doom improve. He continues to have depressive symptoms, but his suicidal ideation stops. At discharge, Mr. J is receiving mirtazapine 15 mg/d, potassium chloride 10 mEq/d orally, lisinopril 20 mg/d orally at bedtime, furosemide 20 mg/d orally, and amlodipine 5 mg orally twice a day. Additionally, the treatment team recommends psychotherapy to Mr. J to address his anxiety and depression.

#### References

1. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Am J Kidney Dis*. 2002;39(2 Suppl 1):S1-S266.
2. Shirazian S, Grant CD, Aina O, et al. Depression in chronic kidney disease and end-stage renal disease: similarities and differences in diagnosis, epidemiology, and management. *Kidney Int Rep*. 2017;2(1):94-107.
3. Hedayati SS, Minhajuddin AT, Afshar M, et al. Association between major depressive episodes in patients with chronic kidney disease and initiation of dialysis, hospitalization, or death. *JAMA*. 2010;303(19):1946-1953.

continued

### Clinical Point

The Beers Criteria recommend avoiding duloxetine in patients with a creatinine clearance <30 mL/min

### Clinical Point

**Adding nonpharmacologic options might be particularly helpful for patients with impaired renal function**

- 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *J Am Geriatr Soc.* 2019;67(4):674-694.
- Marcantonio E, Ta T, Duthie E, et al. Delirium severity and psychomotor types: their relationship with outcomes after hip fracture repair. *J Am Geriatr Soc.* 2002;50(5):850-857.
- Cukor D, Cohen, SD, Peterson RA, et al. Psychosocial aspects of chronic disease: ESRD as a paradigmatic illness. *J Am Soc Nephrol.* 2007;18(12):3042-3055.
- Cohen SD, Norris L, Acquaviva K, et al. Screening, diagnosis, and treatment of depression in patients with end-stage renal disease. *Clin J Am Soc Nephrol.* 2007;2(6):1332-1342.
- Sommi RW, Crismon ML, Bowden CL. Fluoxetine: a serotonin-specific, second-generation antidepressant. *Pharmacotherapy.* 1987;7(1):1-15.
- Jenner PN. Paroxetine: an overview of dosage, tolerability, and safety. *Int Clin Psychopharmacol.* 1992;6(Suppl 4):69-80.
- Montgomery SA. Selecting the optimum therapeutic dose of serotonin reuptake inhibitors: studies with citalopram. *Int Clin Psychopharmacol.* 1995;10(Suppl 1):23-27.
- Milosavljevic F, Bukvic N, Pavlovic Z, et al. Association of CYP2C19 and CYP2D6 poor and intermediate metabolizer status with antidepressant and antipsychotic exposure: a systematic review and meta-analysis. *JAMA Psychiatry.* 2021;78(3):270-280.
- Rao N. The clinical pharmacokinetics of escitalopram. *Clin Pharmacokinet.* 2007;46(4):281-290.
- Preskorn SH, Lane RM. Sertraline 50 mg daily: the optimal dose in the treatment of depression. *Int Clin Psychopharmacol.* 1995;10(3):129-141.
- Huddart R, Hicks JK, Ramsey LB, et al. PharmGKB summary: sertraline pathway, pharmacokinetics. *Pharmacogenet Genomics.* 2020;30(2):26-33.
- Furukawa TA, Cipriani A, Cowen PJ, et al. Optimal dose of selective serotonin reuptake inhibitors, venlafaxine, and mirtazapine in major depression: a systematic review and dose-response meta-analysis. *Lancet Psychiatry.* 2019;6(7):601-609.
- Norman TR, Olver JS. Desvenlafaxine in the treatment of major depression: an updated overview. *Expert Opin Pharmacother.* 2021;22(9):1087-1097.
- Knadler MP, Lobo E, Chappell J, et al. Duloxetine: clinical pharmacokinetics and drug interactions. *Clin Pharmacokinet.* 2011;50(5):281-294.
- Anttila SA, Leinonen EV. A review of the pharmacological and clinical profile of mirtazapine. *CNS Drug Rev.* 2001;7(3):249-264.