

Chapter 5: Rate of Decline in eGFR and Clinical Evaluation of the Elderly With a Low eGFR

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AGE AND RATE OF DECLINE OF RENAL FUNCTION

In cross-sectional studies, levels of renal function are on average lower in older compared with younger participants.¹⁻³ However, the extent to which this phenomenon results from an age-associated decline in renal function *versus* a higher prevalence of comorbidities linked to chronic kidney disease (CKD) in the elderly is uncertain. Relatively few studies have explicitly examined rates of decline in renal function across age groups. Most of what we know about longitudinal changes in renal function comes from the Baltimore Longitudinal Study of Aging (BLSA).⁴⁻⁶ A subset of participants in this study underwent serial creatinine clearance measurements over time. Observations on these patients have provided some important insights into the effect of age on change in level of renal function. First, even in individuals without known comorbid conditions and without intrinsic renal disease or proteinuria, level of creatinine clearance declined on average by 0.75 ml/min per year.⁴ Second, renal function was stable and even improved in some subjects.⁴ Hemmelgarn *et al.*⁷ reported a similar phenomenon among community-dwelling elderly in Canada followed over a 2-yr period (Figure 1). Thus, these reports suggest that, on average, renal function declines with increasing age even in the absence of comorbidity. At the same time, decline in renal function does not seem to be an inevitable consequence of aging.

Among participants in the BLSA without CKD, the rate at which creatinine clearance declined over time was greater among older participants.⁶ Consistent with these results and with prior cross-sectional studies showing lower levels of renal function among older people, older age seems to be a risk factor for the development of CKD, defined as an estimated GFR (eGFR) <60 ml/min per 1.73 m².⁸ However, the relationship between age and rate of

change in eGFR seems to be somewhat complex and perhaps dependent on baseline level of eGFR. Among a national cohort of veterans with an eGFR <60 ml/min per 1.73 m², eGFR declined more rapidly for older than for younger patients at higher levels of eGFR (*i.e.*, ≥45 ml/min per 1.73 m²). However, the opposite was true at lower levels of eGFR (*i.e.*, <45 ml/min per 1.73 m²), where eGFR declined more slowly in older than in younger patients.⁹ Collectively, these data seem to suggest that, although older patients are more likely to develop CKD, those who survive long enough to reach more advanced stages of CKD are actually less likely than their younger counterparts to experience progressive loss of eGFR.

AGE AND RISK OF PROGRESSION TO END-STAGE RENAL DISEASE

Studies of rate of change in measured or estimated renal function can be difficult to interpret for a variety of reasons: (1) progression may not occur in a predictable and linear fashion; (2) the clinical significance of changes renal function, particularly within the normal range, is uncertain; and (3) it can be difficult to account for differences in survival and follow-up among participants. Thus, results of studies reporting change in level of renal function as an outcome are probably quite sensitive to the analytic approach selected. Progression to end-stage kidney disease (ESKD) often represents a more meaningful clinical outcome than change in level of renal function. This outcome is easily defined and identified, and the clinical significance of ESKD (de-

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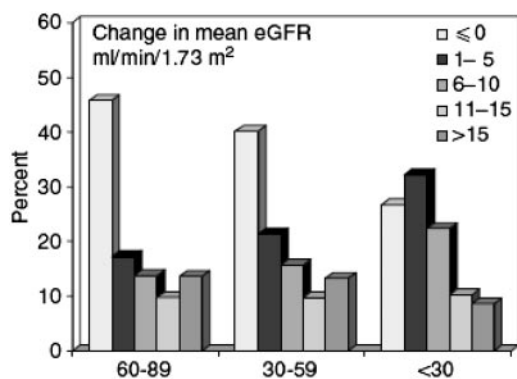


Figure 1. Change in eGFR over a 2-yr period among members of an elderly community cohort. (Source: Hemmelgarn BR, et al.: *Kidney Int.* 69: 2155–2161, 2006.) This material is copyrighted by the ISN.

defined as treatment with chronic dialysis or transplant) is beyond dispute. Rates of progression to ESKD among patients with different levels of eGFR vary substantially with age.^{9,10} Although eGFR is an excellent predictor of who will progress to ESKD among patients of all ages, there are large differences in the absolute risk of ESKD among patients of different ages with similar levels of eGFR, with older patients being less likely to progress to ESKD at any given level of eGFR.^{9–11} This phenomenon likely reflects a number of different factors including a greater competing risk of mortality in older patients, slower rates of progression among older patients with advanced CKD, and age differences in acceptance or receipt of chronic dialysis when indications arise.

Mortality rates among elderly people with CKD are much higher than among their younger counterparts.^{2,3} Consequently, many older patients with CKD will not survive long enough to progress to the point where they need dialysis. Furthermore, as described above, CKD is often either slowly progressive or non-progressive in the elderly. Thus, at any given level of renal function, there are large differences between younger and older patients in the most common clinical outcomes. For example, among younger members of a national cohort of VA patients, progression to ESKD was a more likely outcome than death among those with relatively high levels of eGFR (e.g., <45 ml/min per 1.73 m² for those 18 to 44 yr of age). However, among older patients, death was a more likely outcome than ESKD even among those with very low levels of eGFR (e.g., <15 ml/min per 1.73 m² for those 65 to 84 yr of age) (Figure 2). Patients 85 yr and older were more likely to die than to reach ESKD at all levels of eGFR. Thus, among the vast majority of older persons with CKD, even when this is quite advanced (i.e., eGFR 15 to 29 ml/min per 1.73 m²), death is a more common outcome than progression to ESKD.

RISK FACTORS FOR PROGRESSION IN THE ELDERLY

Although older patients are less likely to progress to ESKD than their younger counterparts with similar levels of renal function, most patients who progress to the point of needing dial-

ysis are nevertheless elderly.⁹ In fact, patients 75 yr and older currently represent one of the fastest growing contingents of the ESKD population, most likely reflecting both population aging and the high overall prevalence of CKD in the elderly.¹² Thus, a critical challenge for health systems and providers caring for older patients with CKD lies in identifying the relatively small proportion, but large absolute number, of older patients with CKD who are at greatest risk for progressive loss of renal function and ultimate need for dialysis.

In general, relatively little is known about what predicts more rapid loss of renal function in elderly patients with CKD and whether risk factors are similar in older and younger patients. Male gender is a strong risk factor for progression of kidney disease in the general population, and this may also be the case in the elderly. For example, among an elderly Canadian cohort, rate of progression was greater in men than in women.⁷ African-American race is a strong risk factor for progression of renal disease in the general population. However, a study of patients with incident ESKD suggested that the risk of ESKD related to African-American race may be greatest in middle age.¹³ To date, the effect of age on the relationship between race and progression has not been studied prospectively. Similarly, although hypertension is a prototypical risk factor for progression of renal disease in the overall population, the association of hypertension with progression of renal disease may be attenuated at older ages.¹⁴ Diabetes seems to be a risk factor for progression of CKD in older patients as it is in younger patients, although it is unclear whether the strength of this association is the same in patients of different ages.⁷

Level of proteinuria shows some promise as a marker for clinically significant outcomes in elderly patients with CKD. The presence of microalbuminuria and macroalbuminuria has been shown to be associated with mortality in a variety of different populations, including patients with and without diabe-

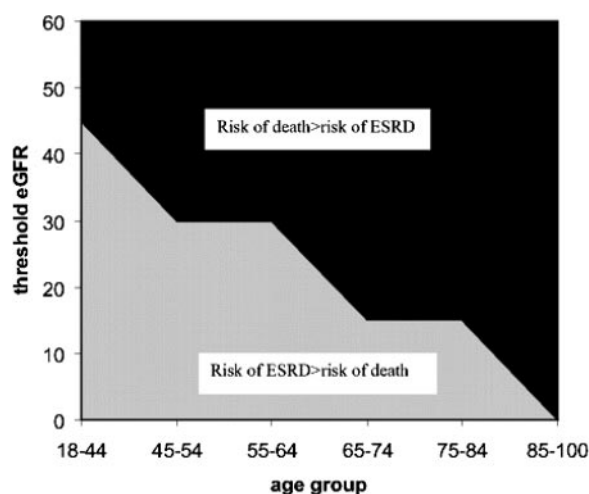


Figure 2. Relationship between age, eGFR, and risk of death in relation to risk of ESKD. (Source: O'Hare AM, et al.: *J Am Soc Nephrol* 18: 2758–2765, 2007.) Copyright ©2007 American Society of Nephrology.

tes.^{15–25} Several recent studies have shown an additive risk of death among those with microalbuminuria and a low eGFR.^{26–29} One of these studies specifically confirmed the presence of this association in the elderly.²⁶ Hallan *et al.*²⁶ described the relationship between eGFR and urinary albumin-to-creatinine ratio among 9709 participants in the Hunt II study, a large-scale Norwegian general health survey. Among patients with a similar level of eGFR, mortality risk increased with increasing level of urinary albumin excretion. However, mortality risk increased with falling eGFR only in those with microalbuminuria and not among those with lower levels of urinary albumin excretion. Of note, these associations were present both among those younger and older than 70 yr. These findings suggest that urinary albumin measurement may be helpful in identifying the subset of older persons with very moderate reductions in eGFR (*e.g.*, 45 to 60 ml/min per 1.73 m²) who are at greatest risk for mortality. To date, no information is available on the prognostic significance of urinary protein excretion for progression to ESKD in the elderly, but numerous studies in younger cohorts have identified proteinuria as a risk factor for progression of renal disease.

Perhaps more valuable than knowing whether an older person with CKD has traditional risk factors for progressive renal disease may be an understanding of what the course of that person's renal functional decline has been to date (Figure 1). Regardless of the underlying etiology and presence or absence of known risk factors for progression, information on a patient's past trajectory of renal function may help to predict how their renal function will change in the future, whether this is likely to occur in a predictable fashion, and under what circumstances progression is most likely to occur (*e.g.*, hospitalization). Even if the course of an older patient's prior trajectory of renal function is found to be variable, making it difficult to accurately predict future trends, it may still be helpful for the patient and provider to be aware of this uncertainty.

CLINICAL ASSESSMENT OF THE OLDER PATIENT WITH CKD

Because heterogeneity increases with age, perhaps the only statement that can be made with any certainty about the assessment and management of older patients with CKD is that a single approach is unlikely to be appropriate for all older patients. However, there may be some general differences in the ideal emphasis of the assessment of CKD in older and younger patients related to general differences in the expected course of CKD at different ages.

The cornerstone of the evaluation of all patients with CKD is assessment of risk for future adverse events (*e.g.*, progression of renal disease, mortality, cardiovascular events, complications of CKD). Because so many older patients with CKD do not progress to the point of needing dialysis, assessment of each patient's risk for progressive disease and likelihood for requiring dialysis in relation to the competing risk of death can

be very important in shaping future management decisions. However, making this distinction represents one of the major challenges to clinicians caring for older patients with CKD. As discussed earlier, although traditional risk factors such as diabetes, hypertension, and black race are potentially important predictors of progression in the elderly as they are in younger patients with CKD, few studies have examined the importance of these risk factors in the elderly. While not specifically studied, if prior records exist, it may simply be more helpful in many instances to review each patient's prior trajectory of renal function to determine whether their CKD is rapidly progressive, slowly progressive, or nonprogressive.

Although primary renal disease processes can manifest at all ages (*e.g.*, glomerulonephritis, polycystic kidney disease, lupus nephritis), in many elderly people, CKD may function more as a marker for a variety of other comorbid conditions (*e.g.*, atherosclerosis, diabetes, and hypertension). Furthermore, the presence of CKD in an older person may reflect the cumulative end result of a variety of different known and unknown processes that have occurred during the course of that patient's lifetime. Thus, in many elderly patients, the future course of CKD may have more to do with that person's overall health, level of comorbidity, and level of renal reserve than with progression of a single underlying renal disease process (as is more likely to be the case in younger people with CKD). Related to this, it may be more difficult to predict the future trajectory of renal functional decline in older compared with younger patients if this will primarily reflect events and disease processes that impact the kidney only indirectly.

Although, in general, identifying the underlying etiology of CKD is often viewed as a critical first step in patient assessment, in many older patients, it may not be possible to come up with a single etiology for their CKD. However, much depends on the clinical presentation. In older as in younger patients, an aggressive diagnostic work up to uncover the underlying etiology of CKD has the potential to provide important information on prognosis and help guide management when a single dominant renal process is suspected. For example, if an older patient experiences rapid loss of renal function in the setting of heavy proteinuria and active urinary sediment, the results of a renal biopsy and serologic work up might provide critical information that could change management and alter prognosis. However, for many older patients with CKD, particularly in the absence of proteinuria, active urinary sediment, and rapid progression, a single unifying diagnosis may not be possible. In these situations, rather than trying to come up with a definitive diagnosis, it may be more helpful to view the diagnostic evaluation of CKD as an opportunity to rule out potentially reversible processes that are common at older ages (*e.g.*, obstructive uropathy, renal artery stenosis, medication-induced interstitial nephritis).

Because the burden of comorbidity is so high in many older patients with CKD, it is also critically important in managing older patients with a low eGFR to weigh the clinical significance of this finding in relation to other comorbid conditions that might be present in a given patient.^{7,9} If these other co-

morbid conditions are more likely to impact overall health and quality of life, interventions to slow progression of CKD should perhaps not be prioritized to the same extent as these other comorbid conditions. On the other hand, if the patient has few comorbid conditions and CKD is their primary clinical problem, a stronger focus on efforts to diagnose and manage progressive CKD may be very appropriate, particularly if their CKD is clearly progressive or they have risk factors for progression such as proteinuria.

CONCLUSION

Among patients with similar levels of eGFR, clinical outcomes vary substantially by age. In general, older patients are more likely than their younger counterparts to have a low eGFR but are less likely to experience progression to ESKD. At the same time, older patients represent the largest and fastest growing contingent of the ESKD population. Therefore, the main challenge in managing older patients with CKD is to identify the small proportion but large number who are most likely to progress to ESKD and who may benefit the most from aggressive efforts to diagnose and treat their underlying renal disease.

TAKE HOME POINTS

- A growing number and proportion of all patients initiating chronic dialysis are 75 yr and older
- Most older patients who meet criteria for CKD are much more likely to die before they reach ESKD; this is true even for older patients with severe reductions in eGFR
- It is often difficult to know which subset of older patients with CKD will progress to ESKD
- Most older patients who meet the criteria for CKD have other health conditions
- The importance of interventions to slow progression of CKD should be weighed against other, perhaps competing, health priorities

DISCLOSURES

None.

REFERENCES

*Key References

1. Coresh J, Selvin E, Stevens LA, Manzi J, Kusek JW, Eggers P, Van Lente F, Levey AS: Prevalence of chronic kidney disease in the United States. *JAMA* 298: 2038–2047, 2007*
2. O'Hare AM, Bertenthal D, Covinsky KE, Landefeld CS, Sen S, Mehta K, Steinman MA, Borzecki A, Walter LC: Mortality risk stratification in chronic kidney disease: one size for all ages? *J Am Soc Nephrol* 17: 846–853, 2006*
3. Raymond NT, Zehnder D, Smith SC, Stinson JA, Lehnert H, Higgins RM: Elevated relative mortality risk with mild-to-moderate chronic kidney disease decreases with age. *Nephrol Dial Transplant* 22: 3214–3220, 2007*
4. Lindeman RD, Tobin J, Shock NW: Longitudinal studies on the rate of decline in renal function with age. *J Am Geriatr Soc* 33: 278–285, 1985
5. Lindeman RD, Tobin JD, Shock NW: Association between blood pressure and the rate of decline in renal function with age. *Kidney Int* 26: 861–868, 1984
6. Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW: The effect of age on creatinine clearance in men: a cross-sectional and longitudinal study. *J Gerontol* 31: 155–163, 1976
7. Hemmelgarn BR, Zhang J, Manns BJ, Tonelli M, Larsen E, Ghali WA, Southern DA, McLaughlin K, Mortis G, Culleton BF: Progression of kidney dysfunction in the community-dwelling elderly. *Kidney Int* 69: 2155–2161, 2006*
8. Fox CS, Larson MG, Leip EP, Culleton B, Wilson PW, Levy D: Predictors of new-onset kidney disease in a community-based population. *JAMA* 291: 844–850, 2004
9. O'Hare AM, Choi AI, Bertenthal D, Bacchetti P, Garg AX, Kaufman JS, Walter LC, Mehta KM, Steinman MA, Allon M, McClellan WM, Landefeld CS: Age affects outcomes in chronic kidney disease. *J Am Soc Nephrol* 18: 2758–2765, 2007*
10. Eriksen BO, Ingebreetsen OC: The progression of chronic kidney disease: a 10-year population-based study of the effects of gender and age. *Kidney Int* 69: 375–382, 2006
11. Evans M, Fryzek JP, Elinder CG, Cohen SS, McLaughlin JK, Nyrén O, Forel CM: The natural history of chronic renal failure: results from an unselected, population-based, inception cohort in Sweden. *Am J Kidney Dis* 46: 863–870, 2005
12. Collins AJ, Foley R, Herzog C, Chavers B, Gilbertson D, Ishani A, Kasiske B, Liu J, Mau LW, McBean M, Murray A, St Peter W, Xue J, Fan Q, Guo H, Li Q, Li S, Li S, Peng Y, Qiu Y, Roberts T, Skeans M, Snyder J, Solid C, Wang C, Weinhandl E, Zaun D, Zhang R, Arko C, Chen SC, Dalleska F, Daniels F, Dunning S, Ebben J, Frazier E, Hanzlik C, Johnson R, Sheets D, Wang X, Forrest B, Constantini E, Everson S, Eggers P, Agodoa L: Excerpts from the United States Renal Data System 2007 annual data report. *Am J Kidney Dis* 51: S1–S320, 2008
13. Lopes AA, Hornbuckle K, James SA, Port FK: The joint effects of race and age on the risk of end-stage renal disease attributed to hypertension. *Am J Kidney Dis* 24: 554–560, 1994
14. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, Shulman NB, Stamler J: Blood pressure and end-stage renal disease in men. *New Engl J Med* 334: 13–18, 1996
15. Yuyun MF, Khaw KT, Luben R, Welch A, Bingham S, Day NE, Wareham NJ; European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study: Microalbuminuria independently predicts all-cause and cardiovascular mortality in a British population: The European Prospective Investigation into Cancer in Norfolk (EPIC-Norfolk) population study. *Int J Epidemiol* 33: 189–198, 2004
16. Romundstad S, Holmen J, Hallan H, Kvenild K, Ellekjaer H: Microalbuminuria and all-cause mortality in treated hypertensive individuals: does sex matter? The Nord-Trøndelag Health Study (HUNT). *Norway Circulation* 108: 2783–2789, 2003
17. Klausen K, Borch-Johnsen K, Feldt-Rasmussen B, Jensen G, Clausen P, Scharling H, Appleyard M, Jensen JS: Very low levels of microalbuminuria are associated with increased risk of coronary heart disease and death independently of renal function, hypertension, and diabetes. *Circulation* 110: 32–35, 2004
18. Jager A, Kostense PJ, Ruhé HG, Heine RJ, Nijpels G, Dekker JM, Bouter LM, Stehouwer CD: Microalbuminuria and peripheral arterial disease are independent predictors of cardiovascular and all-cause mortality, especially among hypertensive subjects: five-year follow-up of the Hoorn Study. *Arterioscler Thromb Vasc Biol* 19: 617–624, 1999
19. Hillege HL, Janssen WM, Bak AA, Diercks GF, Grobbee DE, Crijs HJ, Van Gilst WH, De Zeeuw D, De Jong PE; PREVEND Study Group: Microalbuminuria is common, also in a nondiabetic, nonhypertensive population, and an independent indicator of cardiovascular risk factors and cardiovascular morbidity. *J Intern Med* 249: 519–526, 2001
20. Gerstein HC, Mann JF, Yi Q, Zinman B, Dinneen SF, Hoogwerf B, Hallé

- JP, Young J, Rashkow A, Joyce C, Nawaz S, Yusuf S; HOPE Study Investigators: Albuminuria and risk of cardiovascular events, death, and heart failure in diabetic and nondiabetic individuals. *JAMA* 286: 421–426, 2001
21. Arnlöv J, Evans JC, Meigs JB, Wang TJ, Fox CS, Levy D, Benjamin EJ, D'Agostino RB, Vasan RS: Low-grade albuminuria and incidence of cardiovascular disease events in nonhypertensive and nondiabetic individuals: the Framingham Heart Study. *Circulation* 112: 969–975, 2005
 22. Ljungman S, Wikstrand J, Hartford M, Berglund G: Urinary albumin excretion—a predictor of risk of cardiovascular disease. A prospective 10-year follow-up of middle-aged nondiabetic normal and hypertensive men. *Am J Hypertens* 9: 770–778, 1996
 23. Dinneen SF, Gerstein HC: The association of microalbuminuria and mortality in non-insulin-dependent diabetes mellitus. A systematic overview of the literature. *Arch Intern Med* 157: 1413–1418, 1997
 24. Damsgaard EM, Froland A, Jorgensen OD, Mogensen CE: Microalbuminuria as predictor of increased mortality in elderly people. *BMJ* 300: 297–300, 1990
 25. Agewall S, Wikstrand J, Ljungman S, Fagerberg B: Usefulness of microalbuminuria in predicting cardiovascular mortality in treated hypertensive men with and without diabetes mellitus. Risk Factor Intervention Study Group. *Am J Cardiol* 80: 164–169, 1997
 26. Hallan S, Astor B, Romundstad S, Aasarod K, Kvenild K, Coresh J: Association of kidney function and albuminuria with cardiovascular mortality in older vs younger individuals: the HUNT II study. *Arch Intern Med* 167: 2490–2496, 2007
 27. Foster MC, Hwang SJ, Larson MG, Parikh NI, Meigs JB, Vasan RS, Wang TJ, Levy D, Fox CS: Cross-classification of microalbuminuria and reduced glomerular filtration rate: associations between cardiovascular disease risk factors and clinical outcomes. *Arch Intern Med* 167: 1386–1392, 2007
 28. Astor BC, Hallan SI, Miller ER III, Yeung E, Coresh J: Glomerular filtration rate, albuminuria, and risk of cardiovascular and all-cause mortality in the US population. *Am J Epidemiol* 167: 1226–1234, 2008
 29. Brantsma AH, Bakker SJ, Hillege HL, de Zeeuw D, de Jong PE, Gansevoort RT: Cardiovascular and renal outcome in subjects with K/DOQI stage 1–3 chronic kidney disease: the importance of urinary albumin excretion. *Nephrol Dial Transplant* 23: 3851–3858, 2008

REVIEW QUESTIONS: RATE OF DECLINE IN EGFR AND CLINICAL EVALUATION OF THE ELDERLY WITH A LOW EGFR

1. An 86-yr-old woman in good health with no comorbidities is found to have an eGFR of 54 ml/min per 1.73 m² on routine testing. Three months later, her eGFR is 55 ml/min per 1.73 m². Urine testing shows an albumin to creatinine ratio of 12 mg/g, and her urinalysis is bland. Her primary care physician asks you whether a renal consultation is needed. Which of the following do you think is the most appropriate response to his or her question?
 - a. At this point, probably little to gain from renal consultation; however, would make sure all her medications are appropriately dosed and reasonable to follow serum creatinine to make sure her eGFR does not fall markedly
 - b. Would recommend seeing the patient for thorough review of possible causes for her chronic kidney disease and appropriate management
 - c. Would recommend checking for complications of chronic kidney disease and seeing the patient at least annually in nephrology for management of any complications of chronic kidney disease she might develop
 - d. Would recommend referral to nephrology with consideration for renal biopsy to identify the underlying cause of this patient's chronic kidney disease
2. A 72-yr-old woman has an eGFR of 25 ml/min per 1.73 m² that has been stable for 5 yr. Her albumin to creatinine ratio is 21 mg/g and her urinalysis is bland. Her hematocrit is 35, her calcium is 9 mEq/L, phosphorus is 4 mEq/L, and parathyroid hormone is 120 mEq/L. Her serum potassium is 5.0 mEq/L. Every day she takes Lisinopril 40 mg, amlodopine 10 mg, lasix 40 mg, and a multivitamin. In the past, she used nonsteroidal agents heavily but discontinued these about 5 yr ago when she found out about her kidney disease. Which of the following do you regard the most appropriate next step?
 - a. Make sure that all her medications are appropriately dosed and advise her to consult her pharmacist any time a new medication is started to make sure it is not nephrotoxic and is appropriately dosed
 - b. Discuss dialysis treatment modality with a view for sending her for vascular access placement if she starts hemodialysis
 - c. See her back monthly for surveillance for the complications of chronic kidney disease
 - d. Avoid potassium-containing foods
3. An 85-yr-old man has an eGFR of 25 ml/min per 1.73 m², an albumin to creatinine ratio of 9000 mg/g, hematuria with dysmorphic red blood cells, normal complements, negative ANCA, anti-GBM, hepatitis serologies, UPEP and SPEP, and an ANA of 1:80. In the last year, his eGFR has gone from 65 to 25 ml/min per 1.73 m². In the past and as recently as 1 yr ago, his urinalyses showed no proteinuria on dipstick. He is feeling very fatigued and listless compared with usual and has not been able to do his usual daily 3-mile walk. Which do you think is the most appropriate next step?
 - a. Refer the patient for a renal biopsy to identify the underlying cause of his renal disease
 - b. Start the patient on an ACE inhibitor
 - c. Discuss dialysis modality and send the patient for vascular access placement if they choose hemodialysis
 - d. Discuss end of life issues and hospice placement given the patient's poor prognosis
4. A new patient comes to see you. She is a 78-yr-old nondiabetic woman with an eGFR of 30 ml/min per 1.73 m² that has decreased from 40 ml/min per 1.73 m² in the last year. She has an albumin to creatinine ratio of 1000 mg/g. She is on amlodopine for hypertension. Her BP today is 170/80 mmHg. She comes into your office quite upset because she got lost on her way to clinic and actually forgot where she was. This is the first time this has ever happened to her. Her vital signs are otherwise stable and her blood sugar is 110 mg/dl. What should be the first priority for her care?
 - a. Review her urinalysis to determine whether she needs a biopsy
 - b. Obtain a serologic work up to identify the cause of her proteinuria
 - c. Talk with her primary care provider and review her medical record to determine whether she has any underlying cognitive issues to determine whether she needs an acute neurologic evaluation
 - d. Start her on an ACE inhibitor