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See related article, "Infection Risk with Bolus versus Maintenance Iron Supplementation in Hemodialysis Patients," on pages 1151–1158.

Ideal Cardiovascular Health and Progression of CKD: Perhaps not so "Simple"

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CKD is a global public health challenge. More than 13 million adults in the United States have moderate to severe CKD.[1] The prevalence of CKD has increased over time, in part due to the higher prevalence of diabetes and hypertension and the aging population.[2,3] Importantly, elderly adults with CKD are 13-fold more likely to die than reach advanced CKD requiring renal replacement therapy (CKD 5D), with cardiovascular disease being the leading cause of death.[4] Identifying health behaviors and health factors that lower the risk of progressive kidney dysfunction and death in the CKD population is paramount to optimizing health and longevity. In 2010, the American Heart Association (AHA) published "Defining and Setting National Goals for Cardiovascular Health Promotion and Disease Reduction: The American Heart Association's Strategic Impact Goal Through 2020 and Beyond," wherein the concept of ideal cardiovascular health was defined.[5] Ideal cardiovascular health is a conceptual framework that includes favorable health behaviors and health factors such as abstinence from smoking, an ideal body mass index (BMI), routine physical activity, a healthy diet, an untreated cholesterol <200 mg/dl, an untreated BP <120/80 mmHg, and the absence of diabetes mellitus. Although these health behaviors and factors define ideal cardiovascular health, these metrics correlate with general health, longevity, and prevention of other chronic diseases including CKD.[5] The AHA has developed Life's Simple 7 and the My Life Check,[6] which focus on optimizing these key modifiable health behaviors and factors.

In this issue of *JASN*, Muntner *et al.*[7] examined the association between the AHA's Life's Simple 7 and the incidence of CKD 5D in Reasons for Geographic and Racial Differences in Stroke (REGARDS) study participants with an estimated GFR (eGFR) <60 ml/min per 1.73 m^2. All-cause death was examined in secondary analyses. REGARDS participants' BP, total cholesterol, serum glucose, cigarette smoking, physical activity, diet, and BMI were each classified as poor, intermediate, or

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ideal health. The proportion of participants classified as ideal health varied substantially by health behavior or factor, with <1% of participants classified as ideal for diet and 89% classified as ideal for cigarette smoking. The vast majority of participants (84%) had 1–3 ideal health behaviors or factors, whereas only 3% of participants had ≥5 ideal health components. During a median follow-up of 4 years, 160 participants (5%) developed CKD 5D and 610 participants (20%) died. The incidence of CKD 5D ranged from 0 to 22.5 per 1000 person-years, with the lowest incidence in those with ≥5 ideal components of Life's Simple 7. In adjusted analyses that accounted for demographics, geographic region, income, education, prevalent stroke, and coronary heart disease, a graded association between the number of ideal factors and the risk of CKD 5D was observed. Participants with 4 ideal health components had an almost 50% lower risk of CKD 5D compared with those with 0–1 ideal health behaviors or factors. However, once eGFR was accounted for in statistical analyses, the association between the number of ideal health components and CKD 5D was attenuated and no longer significant. The association was also attenuated by the inclusion of urine albumin and the direction of the effect changed (*i.e.,* higher hazard ratio with higher number of ideal components), albeit the association was not statistically significant. Interestingly, when only health behaviors (*e.g.*, BMI, cigarette smoking, physical activity, and diet) were examined, no statistically significant association between the number of ideal health behaviors and the risk of incident CKD 5D was observed; however, the direction of the effect was generally protective or neutral. When the association between the number of ideal Life's Simple 7 components and the risk of death was examined, inclusion of eGFR and urine albumin largely attenuated any observed association, similar to the findings with CKD 5D.

The study by Muntner *et al.*[7] is interesting because Life's Simple 7 represent modifiable health behaviors and factors that have been linked to cardiovascular health and to CKD. Therefore, examining whether Life's Simple 7, a public health campaign by the AHA, are associated with important outcomes in CKD is inherently appealing. The study by Muntner *et al.* provides a thoughtful examination of the association between ideal cardiovascular health and CKD 5D and death in older adults with established CKD. As perhaps expected, the higher the number of ideal cardiovascular health behaviors or factors, the lower the observed incidence of CKD 5D. However, the association between ideal cardiovascular health behaviors and factors and the incidence of CKD 5D was completely attenuated by kidney function and albuminuria, suggesting that kidney function and albuminuria mediate or confound the association between Life's Simple 7 and the incidence of CKD 5D. Given these findings, should we not take the time to encourage our patients living with CKD to engage in a healthier lifestyle? Before drawing any conclusions, we should delineate what we can learn from this study and highlight important findings. First, we note that a large percentage of participants were classified as poor health with respect to specific components of Life's Simple 7: 46% for physical activity, 40% for BMI, 29% for BP, 15% for glucose, and 82% for diet (with the caveat that 33% had missing dietary data). These observations identify potential areas for intensified efforts and care in the CKD population. Second, the findings with respect to health behaviors are particularly interesting. Although not statistically significant, the direction of effect was generally protective. Perhaps these findings should reinvigorate our interest in health behaviors and stimulate further study of the relation between health behaviors and kidney disease progression. Other important considerations include the older age of participants in this study (72 years) and the mean eGFR of 47 ml/min per 1.73 m^2—the observations may have differed in younger cohorts or those with less advanced kidney disease. Furthermore, with respect to the ideal classification for cigarette smoking (defined as none in the last year) and BMI (defined as <25 kg/m^2), some participants classified as ideal health may actually have had advanced chronic disease or illness. For example, smoking cessation may occur as a result of occult malignancy or declining health, and a low BMI may be due to unintentional weight loss or malnutrition; if poor health resulted in ideal classification for these health behaviors, then the relation between cardiovascular health and progressive kidney disease or death may be obscured. Finally, this observational study cannot inform our understanding of what would have happened with intervention or modification of health behaviors and factors.

The study by Muntner *et al.*[7] identifies important opportunities to address and improve health behaviors, especially when considering the large percentage of participants with poor health behaviors. Despite a dearth of definitive data from controlled trials, there are strong arguments for optimizing health behaviors in the CKD population.[8,9] A review by Johansen and Painter on exercise in patients with CKD provided a clear rationale for exercise and a practical approach to implementing exercise, despite the limitations of the existing literature.[10] Likewise, clear-cut data on smoking cessation and its effectiveness in slowing CKD progression are limited, despite the significant association between smoking and cardiovascular disease in CKD.[11,12] However, available information suggests that smoking cessation may have positive effects on kidney function.[13–15]

In conclusion, the study by Muntner *et al.* found that eGFR and albuminuria attenuated the association of Life's Simple 7 with CKD 5D and death. As nephrologists, we can view these findings with either a "glass half full" or a "glass half empty" perspective. We feel that this study provides an opportunity to reconsider and reevaluate our approach to modifying health behaviors and factors in individuals living with CKD. Whether a combination of health behavior changes (*e.g.*, routine exercise, healthy eating, smoking cessation, and attaining ideal body weight) in conjunction with optimal management of health factors (*e.g.*, BP, cholesterol, and glucose) alters the progression of CKD remains a topic worthy of continued study. In the meantime, we suggest taking the optimistic viewpoint and advocating for a healthy lifestyle in our patients living with CKD.

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DISCLOSURES

None.

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