

Physical Resilience in Older Patients Incident to Hemodialysis: Can Following Trajectories Improve Our Ability to Intervene on Functional Decline?

Anoop Sheshadri^{1,2,3} and Jessica R. Elia¹

¹University of California San Francisco, San Francisco, California, USA; ²San Francisco VA Health Care System, San Francisco, California, USA; and ³Kidney Health Research Collaborative, University of California, San Francisco, San Francisco, California, USA

Kidney Int Rep (2022) **7**, 1927–1929; https://doi.org/10.1016/j.ekir.2022.07.172 Published by Elsevier Inc. on behalf of the International Society of Nephrology. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/ licenses/by-nc-nd/4.0/).

See Clinical Research on Page 2006

railty is a well-known state of physiological vulnerability which carries a high burden of morbidity in end-stage kidney disease (ESKD).^{1,2} Prior research has established that patients with ESKD who meet the criteria for frailty have substantially worse outcomes and higher mortality than those who are nonfrail.² Furthermore, most older dialysis patients irrespective of frailty status report low physical functioning^{\$1,\$2} low and physical activity, ^{\$3,\$4} both of which are components of frailty and independent risk factors for mortality. In contrast, physical resilience is a multidimensional construct related to but distinct from frailty, defined as the ability of an individual to either recover from a health stressor or continue a stable trajectory

despite this stressor.^{3,4} In contrast to frailty, there are relatively few studies which incorporate the concept of physical resilience in the ESKD population.

A key element distinguishing analyses of physical resilience from those of frailty and its components is that measurement of physical resilience requires observing an individual or cohort across a span of time, ideally charting a trajectory from prestressor to poststressor response. The ability to respond to any individual stressor may be limited by one's physiological reserve (i.e., frail or nonfrail), but physical resilience is not determined by frailty alone. As many of our patients and their caregivers can attest, physical resilience is not simply the amalgamation of one's physical components; it is influenced by mental health (MH), social support, and the environment in which the stressor occurs.^{5,S5} This holistic view of physical resilience may aid our understanding of why some individuals are more resilient than



others, irrespective of their baseline level of physiological reserve.³

In this issue of KIR, Hladek et al.⁶ have extended the concept of physical resilience to older patients treated with dialysis. The authors leveraged data from 485 older adults $(\geq 55$ years of age) incident to hemodialysis and enrolled in the Choices for Health Outcomes In Caring for End-stage renal disease study,^{S6} categorizing trajectories of physical resilience into "Declining," "Stable," and "Improving" trajectories. The study examined the associations of these trajectories with post-12-month survival after dialysis initiation as a preliminary step toward better risk assessment. Physical resilience trajectories were derived from scores from the Physical Function (PF), MH, Vitality (VT), and General Health scales of the SF-36 Short Form Health survey. The authors hypothesized that these measures represent phenotypes that are both related to physical resilience and affected by the complex biological changes following the stressor of hemodialysis initiation. Their study results showed that a substantially higher mortality (hazard ratio 1.32, 95% confidence interval 1.05-1.66) for those in the Declining versus Stable category of PF. Conversely, risk of mortality was lower in those with Improving versus Stable VT (hazard ratio 0.73, 95% confidence interval 0.53-1.00). These associations remained intact despite multivariable adjustment, including the baseline characteristics. The authors conducted sensitivity analyses, which showed an interaction such that patients with higher baseline PF had a survival benefit from improving PF trajectory, and that those with lower MH to start with had a considerably higher mortality associated with declining MH.

Correspondence: Anoop Sheshadri, Division of Nephrology, Department of Medicine, University of California, San Francisco San Francisco, California 94131-3204, USA. E-mail: anoop.sheshadri@ucsf.edu

Taken as a whole, these early findings suggest that following the trajectory of an individual across domains of PF and VT may provide greater insight into risk for mortality than relying on baseline characteristics alone. It should be acknowledged that there are several limitations of the study that constrain its immediate clinical application. First, there is a significant amount of mortality within the first year after starting dialysis. The data here only applies to post-12-month mortality. Second, the physical resilience trajectories do not capture prestressor characteristics, which are required for formal testing of resilience. Third, although the Shor Form-36 PF dimension covers a broad range of PFs, self-reported measures of PF vary considerably from performance-based measures and may not be adequate for planning rehabilitation.^{7,S7} Finally, despite the number of sociodemographic covariates being adjusted for, it is

difficult to capture all environmental factors crucial to recovery.³ For example, most older patients treated with dialysis rely on caregivers for some portion of their daily activities.^{S8} Therefore, in order to be actionable, any intervention triggered by declining physical resilience merits some assessment of caregiver status. Nevertheless, the rigorous methodology, the large sample size, and the length of follow-up lend support to ability of physical resilience trajectories to improve risk assessment in ESKD.

With our current understanding, the findings of the study could perhaps best be used to triage patients for comprehensive interdisciplinary evaluation. Indeed, the authors themselves suggest that an individual's overall declining trajectory could trigger a more indepth examination from the primary nephrologist with or without adjunctive evaluations by physical therapy, registered dietitians, and social workers. Older adults treated with dialysis and reporting low PF or VT scores should be referred for more in-depth physical therapy evaluation upon initial assessment, and those found to have declining trajectories at subsequent timepoints referred upon reassessment (Figure 1). Periodic reassessment and establishment of physical resilience trajectories would therefore allow for identification of both patients with baseline physical impairments and those who initially appear robust but fail to compensate for the stress of dialysis initiation. Such patients could be formally assessed by physical therapists and started on individualized programs to help maintain or improve PF and quality of life over time. The timely provision of adjunctive physical therapy and other services may also allow reconsideration of patients who were initially deemed unsuitable for transplantation but who subsequently show improvement.



Figure 1. Hypothetical clinical workflow to operationalize physical resilience trajectories in dialysis.

Clinical adoption of physical resilience trajectories in management of ESKD would require further study on assessment timing, effect on quality of life, potentially incorporation of objective measures of physical performance, integration of a multidisciplinary care team, and inclusion of the caregiver perspective. Given the age-accelerating nature of ESKD,^{S9} assessing patients earlier in their trajectories may help to ultimately reduce morbidity and mortality.⁸ Therefore, although the data in this study can only directly be applied after 12 months, we think it is reasonable to begin assessment at time of dialysis initiation. Firmly establishing the appropriate timing and cadence of assessment will be necessary because the development of frailty or frank disability may affect the ability of patients to benefit from targeted interventions. Similarly, although only PF and VT had associations with mortality in the primary analysis, assessment of multiple domains of health-related quality of life and subsequent multidisciplinary evaluation may identify support opportunities that would be missed by focusing on PF and VT alone. For example, although trajectories of MH were not shown to influence mortality in the primary analysis, declining MH is likely to affect other aspects of quality of life^{\$10} and clinicians should consider prompt referral to appropriate services.

Physical resilience trajectories may ultimately be more clinically relevant if self-reported measures such as the Short Form-36 are administered alongside relatively easy to perform objective physical performance measures such as the $5 \times$ -chair stand and gait speed components of the Short Physical Performance Battery,^{S11} Timed Up and Go,^{\$12} and grip strength.^{\$13} The use of both subjective and objective screening measures would potentially allow for more individualized exercise programs along with providing the clinician a window into the patient's own perspective of their physical abilities, which is important not only for adherence and engagement with interventions,^{9,S14} but also as a starting point for understanding patients' goals for and barriers toward their physical functioning. Performance assessment at the point of dialysis may also allow for better integration of physical therapists into routine dialysis practice. Similarly, working with social workers and dieticians to account for neighborhood poverty, food deserts, and access to resources to ease economic hardship may add needed nuance to bolster patient's ability to engage constructively in interventions and nutritional counseling, a program component critical to successful physiologic adaptation and PF advancement.^{S15} Finally, whenever possible, assessment should also include discussion with the caregiver (if one exists) to understand their perspective on the patient's trajectory. Such discussion may include caregiver burdens or challenges, leading to adjunctive interventions such as caregiver education or respite.

Hladek *et al.*⁶ have provided a potential framework for future research that may lead to clinical use of physical resilience in ESKD. We hope future studies will continue to provide much needed insights into these complex multifactorial relationships and operationalize physical resilience trajectories in ESKD management.

DISCLOSURE

Both the authors declared no competing interests.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF) Supplementary References.

REFERENCES

- Fried LP, Tangen CM, Walston J, et al. Frailty in older adults: evidence for a phenotype. A Biol Sci Med Sci. 2001;56:M146–M156. https://doi.org/ 10.1093/gerona/56.3.m146
- Johansen KL, Chertow GM, Jin C, Kutner NG. Significance of frailty among dialysis patients. J Am Soc Nephrol. 2007;18:2960–2967. https:// doi.org/10.1681/ASN.2007020221
- Whitson HE, Duan-Porter W, Schmader KE, et al. Physical resilience in older adults: systematic review and development of an emerging construct. *A Biol Sci Med Sci*. 2016;71: 489–495. https://doi.org/10.1093/gerona/glv202
- Whitson HE, Cohen HJ, Schmader KE, Morey MC, Kuchel G, Colon-Emeric CS. Physical resilience: not simply the opposite of frailty. *J Am Geriatr Soc.* 2018;66:1459– 1461. https://doi.org/10.1111/jgs. 15233
- Moore RC, Eyler LT, Mausbach BT, et al. Complex interplay between health and successful aging: role of perceived stress, resilience, and social support. Am J Geriatr Psychiatry. 2015;23:622–632. https://doi.org/10. 1016/j.jagp.2014.08.004
- Hladek MD, Zhu J, Crews DC, et al. Physical resilience phenotype trajectories in incident hemodialysis: characterization and mortality risk assessment. *Kidney Int Rep.* 2022;7: 2006–2015. https://doi.org/10.1016/j. ekir.2022.06.009
- Johansen KL, Dalrymple LS, Glidden D, et al. Association of performance-based and selfreported function-based definitions of frailty with mortality among patients receiving hemodialysis. *Clin J Am Soc Nephrol.* 2016;11:626– 632. https://doi.org/10.2215/CJN. 03710415
- Fried LP, Cohen AA, Xue QL, Walston J, Bandeen-Roche K, Varadhan R. The physical frailty syndrome as a transition from homeostatic symphony to cacophony. *Nat Aging*. 2021;1:36–46. https://doi.org/ 10.1038/s43587-020-00017-z
- Bennett PN, Breugelmans L, Barnard R, et al. Sustaining a hemodialysis exercise program: a review. Semin Dial. 2010;23:62–73. https:// doi.org/10.1111/j.1525-139X.2009. 00652.x