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Renal disease rehabilitation and delaying dialysis

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ABSTRACT

A clinical decision report using:


for a patient with non-dialysis CKD interested in slowing the progression toward necessary dialysis.

Keywords: CKD, chronic kidney disease, kidney function, exercise therapy, physical activity, dialysis

Clinical-Social Context

Mrs. Molly Jann (pseudonym) is a 63 year old Caucasian woman with CKD stage 4 and eGFR of 17 mL/min secondary to Antineutrophilic Cytoplasmic Antibody (ANCA) and Anti-glomerular basement membrane diseases on a background of hereditary thin basement membrane disease. She has familial thin basement membrane inherited through the paternal side of her family; her father and paternal uncle had kidney disease with microscopic hematuria and nephrotic range proteinuria unrelated to ocular or hearing abnormalities. She also has an autoimmune phenotype and had Graves disease at a young age for which she has been on long-term thyroid replacement therapy.

In August 2020, she received a kidney disease diagnosis characterized by new-onset progressive azotemia, with an eGFR of 22 mL/min and accompanying nephrotic range proteinuria. Subsequent biopsy confirmation identified vasculitides, leading to a treatment regimen involving four rounds of cyclophosphamide 'pulse' therapy, along with six months of high-dose prednisone. An additional dose of rituximab was administered, resulting in reduced ANCA titers and subsequent disease remission. Her urine output (3/4 gallons/day), and proteinuria (5 g/day) are presently stable. Importantly, there are no present indications of gross hematuria, recurrent urinary tract infections, kidney stones, nocturia, urgency, or signs/symptoms indicative of obstructive or neurogenic bladder issues. Given her short vintage of kidney disease, the absence of additional chronic health conditions, and her normal BMI of 24.2, her cardiovascular risk profile is expected to be comparable to that of the general population.

During discussions with Mrs. Jann and her husband, she vividly described the profound upheaval her life has experienced since receiving her diagnosis. She states that she was previously very active, enjoying her job as a teacher while also volunteering in her church and working at a local winery on the side for pleasure. Although she has been able to maintain these commitments at a reduced level, she reports that she is now constantly tired with...
regular headaches and insomnia. Specifically, these changes have drastically decreased her ability to be present in the lives of her adult children and resulted in great difficulty caring for her elderly mother. She also has struggled with depression since her diagnosis due to a concern about her long-term outlook without a transplant. Per her husband, her family is increasingly concerned about her refusal to even discuss the possibility of dialysis treatment in the future. When asked, Mrs. Jann states that she is “really hoping to maintain her GFR for as long as possible,” and that she “does not think [she] wants to undergo dialysis” due to the lifestyle changes required. She previously worked at a dialysis center as a lab tech and stated that it “was too depressing and no way to live.” Despite these concerns, Mrs. Jann still describes how much fulfillment she receives from her family and her career and reports being happy that her GFR has remained stable since her first round of immunosuppressant therapy.

Mrs. Jann has an impressive health literacy and a strong understanding of her care. She is strictly compliant with her recommended treatment regimen and diet, has been approved for kidney transplantation, and continues to await this procedure. Nevertheless, at her most recent nephrology appointment, she expressed interest in ascertaining whether daily exercise could help her maintain her present renal function to delay her need for dialysis in the event of a prolonged wait for transplantation. Before her diagnosis, she attended studio cycling classes multiple times weekly but due to her disease and the pandemic she now only walks in her neighborhood infrequently for exercise. She states that she intends to purchase a Peloton to exercise at home and has been told that it would be safe to do so by a renowned specialist in anti-GBM disease at an outside hospital but wanted to know if this would specifically help her slow/halt the progression of her current kidney disease based on her GFR. Our team is interested in ascertaining if Mrs. Jann, in addition to her current treatment and regular monitoring, would see delayed disease progression from regular moderate exercise.

Mrs. Jann’ inquiry about the potential benefits of regular moderate exercise in slowing or halting the progression of her kidney disease is not only of personal significance but also holds broader implications in the ever-expanding realms of social determinants of health and patient-centered care. Her experience underscores the intricate interplay between balancing the demands of everyday life with the enormous changes in routine that are required for patients to best manage CKD. Her concerns encompass not only medical outcomes but also the social and emotional aspects of her well-being, showcasing the importance of a holistic approach to patient care. Her hesitation towards dialysis reflects the intricate balance between medical recommendations and patients’ values and preferences, highlighting the necessity of considering individual patients' desires and psychosocial contexts in medical decision-making. While her financial stability, car ownership, lack of children living as dependents, healthy husband, and robust family support are all optimal for the weekly demands of dialysis, continuing in her rewarding career while attending routine dialysis appointments would be exceedingly inconvenient, if not impossible. Of note, she states that retirement within the next two years would not be practical as it would affect her ultimate pension allocation. Furthermore, lengthy dialysis visits several times each week would jeopardize her ability to care for her mother who lives across town.

Similar social concerns and innumerable others not present in the case of Mrs. Jann, such as transportation limitations, childcare constraints, and poverty, factor into the personal decisions required of every patient confronted with ESRD (commonly defined as a GFR<15) and the resulting necessity of beginning dialysis treatment. Mrs. Jann’s pursuit of exercise as a potential avenue for maintaining renal function showcases the growing role of patients as active participants in their care, seeking interventions that align with their lifestyles and goals. Mrs. Jann’ case thus serves as a reminder that medical treatment exists within a broader framework, encompassing the patient’s lived experiences, aspirations, and the intricate web of health-related social determinants.

Clinical Question
Can regular physical activity in patients with established, non-dialysis CKD slow declines in renal function as measured by GFR and subsequently prolong progression to dialysis?
Research Article

Description of Related Literature
In our search for literature relevant to Mrs. Jann’s case, we utilized MeSH terms to enhance the precision of our query. At the time of this report’s literature evaluation, an initial query on PubMed using the MeSH terms “renal insufficiency, chronic” and “Disease Progression” with the advanced filter set to include instances where both of these terms appeared simultaneously produced 6,898 results. Narrowing this search by adding the MeSH term “Exercise” with the stipulation that the article includes all three terms yielded a reduced 33 results. Filtering this search to include only systematic reviews further refined these results down to three papers. Of these results, two were unrelated to Mrs. Jann’s case as they did not evaluate the effects of exercise on disease progression in patients at similar stages of CKD. Kelly et al. analyzed the efficacy of exercise, among other modifiable lifestyle factors, in primary prevention of CKD, while Martins et al. evaluated the relationship between physical activity and mortality in ESRD patients already on renal replacement therapy. In contrast, the third article by Evangelidis et al., discussed below, provided a robust, systematic review assessing the overall viability of numerous lifestyle modifications in preventing renal function deterioration to dialysis in patients with existing CKD regardless of disease staging.

To assess the effects of lifestyle interventions for preventing the progression of CKD, Evangelidis et al. performed a systematic review of 26 studies involving 4263 adult participants with CKD ranging from stages 1-5 and who were not presently requiring renal replacement therapy. Interventions evaluated included diet, physical activity, smoking, and alcohol consumption, among others.

Eight studies specifically evaluated the effects of regulated exercise routines in patients on outcomes ranging from subjective quality of life and depression levels to changes in peripheral endothelial function in these patients. While all of these studies offer additional insight into the effects that exercise may have in the care of Mrs. Jann and patients like her, only three studies evaluated by Evangelidis et al. directly assessed changes in eGFR following the initiation of exercise therapy: Aoike et al., Barcellos et al., and this report’s chosen article.

In the randomized control study by Aoike et al., the impact of home-based aerobic exercise on the physical capacity of overweight patients with non-dialysis-dependent chronic kidney disease (NDD-CKD) was evaluated. This study aimed to assess the influence of a home-based aerobic training program on both the cardiopulmonary and functional capacities of overweight NDD-CKD patients. The study included 29 sedentary patients, aged 55.1 ± 11.6 years, with a BMI of 31.2 ± 6.1 kg/m², and an estimated glomerular filtration rate (eGFR) of 26.9 ± 17.4 mL/min/1.73 m². Patients were randomly assigned to either a home-based exercise group (n = 14) or a control group (n = 15), which remained inactive. The exercise regimen comprised aerobic training conducted three times per week for 12 weeks. Cardiopulmonary exercise tests, assessments of functional capacity, and clinical parameter evaluations were conducted. Overall, the exercise group displayed significant improvements in cardiopulmonary capacity parameters, demonstrated simultaneous enhancements in multiple functional capacity tests, experienced reduced systolic and diastolic blood pressure, and showed reduced decline in eGFR (p=0.046). Nevertheless, given this study’s assessment of overweight patients the impact of these impressive findings for Mrs. Jann, who at the time of this report was of normal BMI, may be less applicable.

Likewise, Barcellos et al. studied exercise therapy in patients with CKD and comorbidities that were not present in the case of Mrs. Jann. This study investigated the effects of exercise on patients with both hypertension and chronic kidney disease (CKD) through a randomized controlled trial. Non-diabetic adult patients with hypertension and CKD stages 2-4 were randomized into either an intervention group receiving 16 weeks of combined aerobic and resistance training or a control group receiving usual care. The primary outcome measure was the change in estimated glomerular filtration rate (eGFR). Secondary outcomes included changes in systolic and diastolic blood pressure (BP), body weight, fasting blood glucose, lipid profile, high-sensitivity C-reactive protein (hs-CRP), and functional capacity. The analysis followed an intention-to-treat approach, utilizing linear mixed-effects models for repeated measurements over time. The study enrolled 150 patients, with 76 in the intervention group and 74 in the control group. While no significant differences were observed in eGFR, BP, body weight, or lipid profile changes between the two groups, the exercise group showed notable decreases in hs-CRP and fasting blood glucose. Additionally, the exercise group demonstrated an
improvement in functional capacity on a variety of tests. While the exercise intervention did not significantly impact kidney disease progression in this study, these findings still underscore the potential benefits of exercise for individuals with CKD and the inclusion of patients with HTN makes this study less applicable to the present case.

Although the study that was eventually selected for this clinical decision report was discussed in Evangelidis et al., the relatively limited literature found in our initial search that addressed the impact of exercise on GFR decline in non-dialysis CKD patients with similarly few comorbidities as Mrs. Jann, the decision was made to perform a secondary search without MeSH criteria to expand the search results. At the time of this subsequent literature evaluation, an initial query on PubMed using the advanced filter for "CKD AND progression" produced 10,715 results. Adding the search criteria of "((physical activity) OR (Exercise))" yielded a reduced 256 results. Filtering this search for systematic reviews yielded 19 results; however, most of these articles were unrelated to the present clinical question due to patient criteria not specific for non-dialysis CKD patients and/or a focus on the effects of physical activity on variables less specific for functional renal decline, such as cardiovascular health or overall exercise tolerance.

Consequently, the rule "AND ((non-dialysis) OR (nondialysis))" was added to the search query. This refinement yielded 19 results, which were reduced to three upon filtering for systematic reviews. Of these results, two were unrelated to Mrs. Jann’s case, with one not assessing renal function as its dependent variable for evaluating the impact of physical activity on nondialysis CKD patients and the others centering on the role of weight loss in CKD progression. The third article involved the analysis of broader lifestyle interventions for patient self-management, thus not isolating the effects of exercise intervention alone on renal function. Lastly, the fourth article by Villanego et al. provided a robust meta-analysis of studies investigating potential positive health outcomes for exercise in CKD patients that was more current than Evangelidis et al. Of note, the chosen article by Greenwood et al. was also found by filtering this same PubMed search query for randomized control trials (RCTs) instead of systematic reviews. This yielded three results, including the chosen article and two additional reports that investigated dependent variables unrelated to the present case.

Villanego et al. performed a systematic review and meta-analysis regarding the impact of physical activity in patients with chronic kidney disease using the databases PubMed, Scopus, Embase, Ovid (MEDLINE), and PEDro. This paper examined RCTs written in both English and Spanish published between 2007 and 2008 that compared a physical activity/exercise intervention with a control group in non-dialysis CKD patients. Analysis of grouped data for 429 patients across 12 studies suggested that physical activity produced no observed differences in the estimated glomerular filtration rate between exercise intervention and control groups. While this paper did not conclusively demonstrate a correlation between physical activity and slower declines in GFR across all non-dialysis CKD patients, the greatest limitation in applying these overall results to the current case involves the inclusion of numerous studies centering on patients with CKD alongside other existing conditions not present in Mrs. Jann, such as obesity and diabetes, and the evaluation of imprecise exercise regimens.

One of the most applicable studies examined in Villanego, Pechter et al., conducted a randomized controlled trial with a 10-year follow-up comparing water aerobic exercise as an intervention compared to baseline exercise levels in non-dialysis CKD patients evaluating the initiation of dialysis or all-cause mortality as final measures. Notably, this study included a very small sample size with only seven patients assigned to the intervention group and nine in the control. Nevertheless, after the study period, they found that no one assigned to the intervention group reached the endpoints while 55% of the control group either required hemodialysis or passed away. While these results may elucidate a potential long-term benefit of exercise in patients seeking to avoid the onset of dialysis, as in Mrs. Jone’s case, on analysis the results were not statistically significant and thus only suggest more research is required to assess progression to dialysis over long-term exercise treatments in non-dialysis CKD patients. Furthermore, without access to a pool at home, having to attend regular water aerobic exercises would present further lifestyle and scheduling difficulties for Mrs. Jann.

Hirakii et al., also included in Villanego et al., conducted a randomized control trial evaluating the effects of physical activity on kidney function and muscle strength in non-dialysis CKD patients with stable kidney function. Aerobic exercises (walking quickly) and resistance exercises (grip strength building, squats, and heel raises) were performed by patients at home thrice weekly for 30 minutes each session. Following 12 months, no differences were found in the eGFR between patients prescribed the exercise treatment or no intervention. Although this study excluded participants with underlying uncontrolled hypertension and cardiac failure, motor disorders, and dementia, to avoid sex-based differences in its exploration of muscle strength women were excluded making this study less directly applicable to Mrs. Jann’s case. Additionally, despite the random allocation of participants to each group (n=14 for treatment and control), eliminating bias in patient intervention assignment, the authors note that their control
group was significantly more active at baseline. Even with increases in exercise levels only observed in the treatment group, by the end of the recording period the overall time spent on exercise was nearly equal between both groups making the lack of variability in GFR difficult to directly apply to the present case.

The chosen study by Greenwood et al. analyzed the effects of a moderate-intensity physical activity program on renal function and cardiovascular risk indices in non-dialysis CKD patients in both men and women, which was directly relevant to Mrs. Jann’s situation. The study evaluated 18 patients with a control group (n=10) and an intervention group (n=8) assigned to aerobic exercise on a stationary bike at moderate intensity, similar to Mrs. Jann’s expressed intentions for exercise, and resistance exercise (bicep curl, leg press, knee extension, etc.) at a frequency of three times weekly for 20-40 minutes. Less deterioration of eGFR in the intervention group was demonstrated, as well as other improved secondary endpoints (eg. pulse wave velocities, BMI, weight, and waist circumference), were noted after 12 months. Unlike other papers assessed, this study involved treatment conducted under partial supervision to ensure compliance, a significant increase in exercise levels for the treatment group vs. control, and a patient sample most closely matching the sex, age, and medical history of Mrs. Jann. This body of evidence indicates a B-level Strength of Recommendation and an overall Level II categorization according to the Strength of Recommendation Taxonomy (SORT).

Critical Appraisal
The selected publication utilized a randomized, single-blind, controlled parallel panel. As previously stated, this study design can be categorized as Level II evidence using SORT criteria. The purpose of the study was to determine the impact of moderate-intensity exercise on kidney function and indexes of cardiovascular risk in individuals with chronic kidney disease stages 3-4 not requiring dialysis.

20 participants were identified from a renal patient database (17 male, 3 female). The small study sample and very skewed gender representation are not ideal for Mrs. Jann’s case. Participants were included if they were 18 years or older, confirmed to have CKD stages 3 to 4 (GFR 20-60 mL/min/1.73m²) as well as evidence of a decline in kidney function (≥2.9 mL/min/1.73m²) in the year prior to the study. Patients were excluded if they were pregnant, required support for ambulation, had unstable medical conditions, were participants in structural exercise programs within the last 3 months, had a known neurological disorder, uncontrolled diabetes, severe orthopedic conditions, psychiatric illness, or infection or course of antibiotics within the prior month. Although Mrs. Jann’s current eGFR is 17 mL/min/1.73m², it is assumed to be close enough to the researcher’s chosen 20-60 mL/min/1.73m². Mrs. Jann fits all of the other inclusion criteria and only satisfies one exclusion criterion given her current mild depression.

Participants were identified using a renal patient database and were contacted via telephone or during in-person pre-dialysis clinics. Patients consenting to the study had baseline assessments conducted before being randomly assigned to either rehabilitation care or regular care. A researcher was blinded to the patient groups and conducted all patient assessments. Patients were asked to not reveal their group allocation. The exercise intervention group received an exercise program for 12 months including both aerobic and resistance exercises. Patients worked towards two 20-minute sessions and eventually one 40-minute session 3 times a week. Resistance training was also prescribed at 80% of one repetition maximum, with monthly reassessments and adjustments as needed. Participants received free exercise classes twice a week, a stationary cycle, and free weights to use at home. Given Mrs. Jann’s desire to increase her activity level, she would most likely enjoy and benefit from this form of conservative treatment. Mrs. Jann also intends to buy a peloton bike for at-home workouts, which would eliminate the concern of the treatment implementing a financial burden on the patient.

18 participants completed the study, and 2 participants from the exercise group dropped out of the trial. The adherence to the exercise program was defined as the total number of exercise sessions attended compared to the total possible exercise sessions and was found to be 79.2% ± 13.2%. The mean age of the exercise group was 53.8, with the majority being of white ethnicity, which benefits Mrs. Jann’s case. When it comes to the causes of the participants’ kidney disease, none matched Mrs. Jann.

The mean change in eGFR was -9.7 ± 7.2 mL/min/1.73m² for the pre-intervention assessment and -3.8 ±2.8 mL/min/1.73m² post-therapy in the exercise rehab group. The usual care group pre-intervention assessment was -6.6 ± 4.7 mL/min/1.73m² and -8.5 ± 6.4 mL/min/1.73m² post interventional. The alterations in eGFR from the exercise rehab group may show the potential to slow CKD progression in specific individuals. However, given the small study sample and limited data, it is unsure if this form of rehab would be beneficial to the population of interest.
Some limitations of the study include the very small sample size as well as the overwhelming male-to-female participant ratio. Having more females in the study, as well as more participants in general would have allowed for stronger and more applicable data. Within the rehab group, there were not many differing causes of kidney disease noted. Hypertensive nephrosclerosis, obstructive neuropathy, polycystic kidney disease, and medullary sponge kidney disease were the only causes identified. A larger study sample size would have helped increase the odds of observing more causes of kidney disease within the experimental group. Lastly, the measurements of primary and secondary kidney function were found to be inconsistent and may impact reliability.

Clinical Application

It is well known that a sedentary lifestyle and reduced physical activity are common in dialysis and chronic kidney disease patients and are associated with an increased risk of morbidity and mortality in this patient population. This can be due to many factors including the presence of concomitant diseases such as diabetes, heart disease, hypertension, and others that can be both associated causes and consequences of chronic kidney disease. What is less well understood is the effect that exercise can have on disease progression for patients with existing CKD stages 3 and 4 not on current hemodialysis. Observational research has suggested an association between higher levels of baseline physical activity and decreased rates of GFR loss in these patients. Although several studies with experimental interventions to improve kidney function in non-dialysis CKD patients have not consistently demonstrated renal protective effects, animal models have demonstrated that long-term exercise training treatments may preserve renal functioning relative to controls. Thus, exercise has the potential to reduce the decline rate in renal functioning through a variety of mechanisms. Therefore, it is pertinent to investigate if Mrs. Jann could have success in maintaining her current renal functioning by incorporating an exercise regimen alongside her current treatment regimen.

Mrs. Jann came to clinic with the specific question of whether there could be renal protective effects from increasing her levels of home exercise. Motivated by her desire to avoid the progression of her Stage 4 CKD to dialysis and to restore her prior baseline of exercise levels, she was willing to pursue a moderate home workout regimen using structured classes through Peloton. It was concluded that while the current evidence regarding the degree to which regular exercise may play a renal protective role in CKD patients not presently on dialysis needs further expansion, there is at least moderate evidence to conclude that Mrs. Jann would benefit from an exercise regimen. Additionally, given Mrs. Jann’s presently stable GFR on her current medications, the additional evidence that exercise can have physical and mental health benefits for similar patients without worsening renal function, and her past tolerance of regular exercise we recommend that she begin her desired workout routines as tolerated regardless of whether it will significantly preserve her current GFR. This advice is also likely to benefit or prevent other common comorbid conditions common in Mrs. Jann or similar patients.

Furthermore, the experiences of Mrs. Jann also underscore the intricate interplay between CKD and the broader social determinants that shape her circumstances and clinical question. Despite her impressive health literacy and strict adherence to her recommended treatment regimen, her case reminds us that medical decisions are often influenced by factors beyond that which can be addressed by any prescription. Mrs. Jann’s commitment to her career, responsibilities as a caregiver, and concerns about the emotional toll of renal replacement therapy highlight the profound impact of social determinants on healthcare choices. In her situation, the energy and time required to participate in exercise therapy at home, though notable, do not rival the personal and professional sacrifices that would be required of Mrs. Jann if she were to be placed on dialysis. In patients at similar stages of CKD who possess even less social support than Mrs. Jann or who fundamentally lack the financial or practical means to attend regular dialysis, the potential for individualized physical activity to allow patients to go longer without requiring renal replacement therapy could have even more profound benefits. Even if exercise only provides a small delay in the progression of CKD to dialysis in some patients, since patients can choose when and where to exercise this inarguably provides far more agency, independence, flexibility, and ability to live fulfilling lives than they would experience attending dialysis for several hours multiple times a week during that same period.
While Mrs. Jann was disappointed to learn that exercise is not a guaranteed measure to preserve renal functioning in her condition, she was pleased with our team’s recommendations to proceed with regular at-home exercises and the potential for long-term benefit. She did mention concerns about returning to her pre-diagnosis levels of exercise immediately and was advised to ensure that she gradually built up her levels of exercise as tolerated to avoid overexertion. Ultimately, it is concluded that in Mrs. Jann’s case beginning a low-to-moderate level of regular exercise will, in addition to the normal health benefits of exercise, have the potential to reduce the rate of progression of her renal disease.

New Knowledge Related to Clinical Decision Science

Patients with chronic kidney disease often face reduced exercise capacities, leading to sedentary lifestyles and disease progression. The study conducted by Greenwood et al. gathered data focused on whether or not implementing exercise rehabilitation slows declining renal function when compared to usual CKD treatment. While the outcomes of this study remain inconclusive regarding exercise therapy’s long-term effectiveness in slowing renal function decline in the population of interest, no negative side effects were apparent from increasing exercise levels in patients with non-dialysis CKD. Additionally, the investigation highlights several vital considerations for patient care related to clinical decision science in patients with CKD.

Central to Mrs. Jann’s inquiry is the concept of individualized treatment approaches. Her preference to sustain renal function while avoiding the constraints of dialysis demonstrates the importance of aligning treatment plans with patients’ priorities. Greenwood et al.’s investigation of exercise as a supplemental therapy for CKD helps illuminate the intricate balance between evidence-based practices and patient autonomy to control their health outcomes in their day-to-day lives. The study’s findings offer an additional layer of information for Mrs. Jann, similarly motivated patients, and their healthcare teams to consider when engaging in collaborative shared decision-making to establish treatments that fit within the lifestyle goals of the patient.

Similarly, this study also underscores the holistic approach to patient-centered care, central to both Clinical Decision Science and modern medical practice as a whole. Acknowledging the multifaceted nature of patient well-being, the case of Mrs. Jann considers not only medical outcomes but also social, emotional, and lifestyle dimensions, exemplifying the integration of medical decisions with patient experiences. Contemplating exercise as an intervention in diseases thought to previously be largely unrelated to physical activity, empowers patients to play an active role in their care while harmonizing medical evidence and patient preferences.

Although clinicians are widely familiar with concepts such as cardiac rehabilitation, pulmonary rehabilitation, and post-stroke care, little evidence is available for “Renal Failure Rehabilitation”. Yet, as this case demonstrates, this subgroup of patients has unique challenges for mobility and functional status. A demonstration project to collect data on outcomes related to a significant healthcare expense (renal replacement therapy) would be a great step forward in this field and could even be accomplished in the setting of “group visits” in a primary care office, similar to the expansive literature on group visits for diabetes, etc. Ultimately, further research is needed to identify what benefits are accessible for patients with CKD by undergoing exercise rehab but granting these patients the autonomy to use exercise as a safe and possibly effective strategy to delay progression to dialysis has social benefits that cannot be measured simply by eGFR.

Conflict Of Interest Statement

The author declares no conflicts of interest.

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