Title

Residual Kidney Function and Cause-Specific Mortality among Incident Hemodialysis Patients: A Nationwide U.S. Cohort Study

Summary

A research group of Dr. Masaki Okazaki at Nagoya University Graduate School of Medicine, Professor Kamyar Kalantar-Zadeh and Dr. Connie Rhee at University of California Irvine, Dr. Yoshitsugu Obi and Professor Tariq Shafi at the University of Mississippi, and Professor Csaba Kovesdy at the University of Tennessee conducted an international collaborative study involving patients with end-stage renal disease. This study investigated the association between residual kidney function and the risk of cardiovascular and noncardiovascular mortality, including sudden cardiac death (SCD), in approximately 40,000 U. S. adults who started thrice-weekly in-center hemodialysis from 2007 to 2011.

Many patients starting hemodialysis for end-stage renal disease still have some remaining kidney function, referred to as residual kidney function or RKF. RKF is advantageous in maintaining electrolyte levels as well as removing body fluid that accumulates between hemodialysis treatments. Therefore, it is postulated that patients with preserved RKF would have lower risk of cardiovascular disease, the most common cause of death in end-stage kidney disease. However, such data comparing cardiovascular to other causes of death have been lacking. In this cohort study using nationwide data on hemodialysis patients in the United States, associations of lower RKF with higher mortality were consistently observed across all categories of causes of death, i.e., SCD, non-SCD cardiovascular death, and noncardiovascular death. Our findings emphasize the need for further clinical trials to demonstrate the benefits of interventions to preserve RKF and whether these interventions reduce the extraordinarily high mortality in patients undergoing hemodialysis.

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Key Points

- The survival benefit of residual kidney function (RKF) in hemodialysis patients is presumably due to enhanced fluid management and solute clearance.
- Lower baseline renal urea clearance showed the trends toward higher ultrafiltration rates (UFR), lower normalized protein catabolic rate (nPCR), and greater proportion of highest potassium levels.
- Associations of lower RKF with higher mortality were consistently observed across all categories of causes of death, i.e., sudden cardiac death (SCD), non-SCD cardiovascular death, and non-cardiovascular death.

Research Background

As of 2023, approximately 350,000 individuals with end-stage renal disease are undergoing maintenance hemodialysis in Japan. Despite of advances in dialysis technology, the 5-year mortality rates among dialysis patients is comparable to or lower than that for stomach cancer or malignant lymphoma. Further investigation of the specific factors underlying the cause of death may reveal potential mechanisms responsible for the extraordinary high risk of death among dialysis patients.

Research Results

Among 39,623 patients with data on baseline renal urea clearance and urine volume, there was a significant trend toward a higher mortality risk across lower RKF levels irrespective of cause of death in a case-mix adjustment model (Ptrend <0.05). Adjustment for ultrafiltration rate slightly attenuated the association between low renal urea clearance and high cause-specific mortality, while adjustment for highest potassium did not have substantial effect. Among 12,169 patients with data on change in RKF, a 6-month decline in renal urea clearance showed graded associations with SCD, non-SCD cardiovascular death, and non-cardiovascular death risk, while the graded associations between faster 6-month decline in urine output and higher death risk were clear only for SCD and non-cardiovascular death.

Research Summary and Future Perspective

In summary, in our collaborative nationwide cohort study, lower RKF and loss of RKF were associated with higher cause-specific mortality among incident hemodialysis patients. Future clinical trials are warranted to demonstrate the benefits of interventions to preserve RKF and whether these interventions improve high mortality in patients undergoing hemodialysis.

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