Primary Results of the Time to Reduce Mortality in End-Stage Renal Disease (TiME) Trial: A Pragmatic Trial Demonstration Project of the NIH Health Care Systems Research Collaboratory

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BACKGROUND

Observational studies of patients receiving maintenance hemodialysis suggest that mortality is lower with dialysis sessions longer than 4 hours but this hypothesis has not been evaluated in a randomized trial, and broad acceptability of longer treatments has not been established.

METHODS

Cluster-randomized trial fully embedded in clinical care delivery with no on-site research staff or primary data collection. 266 dialysis units operated by two US dialysis providers were randomized to Intervention or Usual Care. Intervention units were to adopt a default hemodialysis session duration of ≥4.25 hours (255 minutes) for incident patients. Usual Care units had no trial-driven approach to duration. The primary outcome was mortality. The major secondary outcome was hospitalization rate.

RESULTS

7035 incident patients highly representative of the US dialysis population were enrolled between 12/18/13 and 9/30/16. The trial was discontinued at a median follow-up of 1.1 years after an interim analysis showed a smaller than targeted group difference in session duration and no difference in outcomes. For the primary analysis population (patients with Watson V≤42.5L), per-patient mean session durations were 219 and 210 minutes for Intervention and Usual Care, respectively, and there was no difference in mortality (HR 0.97, 95% CI 0.84, 1.12; p=0.69) or hospitalization rate (204 vs 213 per 100 patient-yrs, p=0.44). Findings were similar for the full analysis population (all patients).

CONCLUSION

A partnership between academic investigators and multiple dialysis providers and a highly pragmatic design resulted in successful and efficient participant enrollment, data acquisition, and trial monitoring but uptake of the intervention was insufficient to determine whether longer hemodialysis sessions improve clinical outcomes. The TiME trial results demonstrate feasibility of several aspects of large-scale pragmatic trials in dialysis. However, effective strategies for engaging clinicians and patients are required to evaluate interventions fully incorporated into routine care delivery. [NCT02019225]

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