AJKD
Original Investigation

# Initial Session Duration and Mortality Among Incident Hemodialysis Patients

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**Background:** The association of dialysis session duration with mortality in patients undergoing maintenance hemodialysis is unclear. We compared mortality rates of patients treated in dialysis facilities that used initial session durations of either ≥ 4 versus 3 hours for all incident patients.

**Study Design:** Retrospective cohort study.

**Settings & Participants:** Patients with end-stage renal disease beginning maintenance hemodialysis therapy in January 2006 to December 2010 and followed up through December 2012, including 39,172 patients in 852 facilities who initiated treatment for ≥ 4 hours and 47,721 patients in 631 facilities who initiated treatment for 3 hours.

**Predictor:** Initial session duration of ≥ 4 hours versus 3 hours.

**Outcome:** 2- and 1-year mortality rates.

**Results:** Total numbers of deaths observed within 2 years after initiating dialysis therapy were 8,945 in the ≥ 4-hour group and 15,624 in the 3-hour group. The corresponding numbers of deaths observed within 1 year were 5,492 and 10,372, respectively. The 2-year adjusted HR in the ≥ 4-hour versus 3-hour group was 0.79 (95% CI, 0.73-0.86). The corresponding 1-year adjusted HR was 0.77 (95% CI, 0.70-0.84). Results were robust when analyses were restricted to specific subgroups of patients classified by age, sex, race, and select clinical characteristics.

**Limitations:** We did not observe hemodialysis duration in sessions subsequent to initiation. We only included patients treated in facilities with uniform session length (at initiation) for all their patients. Furthermore, we lacked information for dialysis dosage and patients' baseline residual kidney function.

**Conclusions:** Patients in facilities routinely initiating hemodialysis therapy for ≥ 4 hours may have substantially lower mortality as compared with patients in facilities initiating for only 3 hours of treatment.
*Am J Kidney Dis.* 70(1):69-75. 

***INDEX WORDS:*** Renal hemodialysis; treatment time; session length, dialysis duration, dialysis facilities; death; mortality rate; facility-level analysis; quasi-experimental design; end-stage renal disease (ESRD).

Since the Medicare program extended coverage to patients with end-stage renal disease 4 decades ago, the average number of hours per hemodialysis session has declined from 6 hours in 1973 to 3.5 to 4 hours in 2010.[1] Although this decline may be partly explained by the improved efficiency of dialyzers,[1] the clinical consequences of shorter session durations for this high-risk cohort remain unclear.

The National Cooperative Dialysis Study (NCDS) remains the only randomized controlled clinical trial to have tested the relationship between session length and hospitalization.[2] The relationship between longer session length and lower risk for hospitalization in this study did not reach statistical significance. The landmark Hemodialysis (HEMO) trial found no evidence that more intensive dialysis, as compared with regimens recommended under accepted practice guidelines, reduce mortality.[3] However, the study was not designed to assess the independent effect of longer session length. Observational studies of the association of dialysis session duration with mortality have not produced consistent findings. Some studies[4-7] found evidence that longer session duration was associated with lower mortality, whereas others report that longer session duration was associated with higher mortality[8] and that the relationship between session length and mortality varied across countries.[9]

The primary challenge of observational studies is that providers may assign patients to shorter or longer dialysis session durations according to their clinical risk.[10] We address this problem by focusing our primary analysis on the many dialysis centers in the United States that prescribe the exact same session duration to all patients initiating maintenance hemodialysis therapy (either ≥4 or 3 hours) and therefore do

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*Received November 23, 2015. Accepted in revised form November 9, 2016. Originally published online February 21, 2017.*

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*0272-6386*
*http://dx.doi.org/10.1053/j.ajkd.2016.11.017*

not appear to select their incident patients for varying session lengths.

## METHODS

### Data Source and Study Population

We examined data from the Renal Information Management System (REMIS), available from the data repository at the Centers for Medicare & Medicaid Services (CMS). The data include information for patient demographic and clinical characteristics, facility-level characteristics, date of first maintenance hemodialysis treatment and length of each hemodialysis session (hours), and date of death. Brown University's Institutional Review Board approved the study and waived the requirement for informed consent (approval # 1107000452).

From the REMIS data and, more specifically, data entered from the Medical Evidence Form, we identified 463,288 patients who initiated dialysis therapy during January 1, 2006, to December 31, 2010, and who were aged 20 to 90 years at the time of initiation. These data, entered around the time of initiation, also include a question that asks the number of hours that a patient is undergoing hemodialysis (response to question 23 in the form), as well as information for the number of dialysis sessions per week. The data for hemodialysis hours are reported in integer values (ie, 3, 4, or 5 hours). The Medical Evidence Form, including the report on hemodialysis hours, is expected to be submitted within 45 days of the patient initiating dialysis therapy. Because we focused on patients who were undergoing in-center hemodialysis exactly 3 times per week and reported nonmissing hemodialysis hours on the Medical Evidence Form, we excluded 11,451 patients who did not receive exactly 3 dialysis sessions per week, and a further 90,472 patients were excluded because no information for hemodialysis hours was provided. In addition, we excluded patients who were not in facilities that were uniformly treating patients to either ≥ 4 hours or 3 hours (269,251 patients), although sensitivity analysis included these individuals as described in the Statistical Analysis section. We excluded those with missing observations for any of the individual-level variables shown in Table 1 (2,443 observations dropped). In addition, 2,778 observations could not be matched to the facility-level database in REMIS. Thus, our final analytic sample included 86,893 patients (see Fig 1 for flow chart). Of this sample, 39,172 patients were in one of 852 facilities that initiated treatment for all patients for ≥ 4 hours while 47,721 patients were undergoing hemodialysis in one of 631 facilities that initiated treatment for all patients for 3 hours.

### Measures

Our outcomes were 2- and 1-year mortality following initiation of hemodialysis therapy. Our primary independent variable was an indicator variable of whether the patient initiated hemodialysis therapy in a facility that treated all incident patients with ≥ 4 hours per session of hemodialysis or in facilities that treated all incident patients with 3 hours of per session of hemodialysis. Of note, patients who switched their hemodialysis facility during the study period were retained in the analysis and assigned to their session duration at the initiation of dialysis therapy.

Individual-level covariates included age, sex, race (ie, indicator variables for black and other race groups), laboratory variables at initiation of dialysis therapy reported on Medical Evidence Form 2728 (estimated glomerular filtration rate derived using the isotope-dilution mass spectrometry–traceable 4-variable MDRD [Modification of Diet in Renal Disease] Study equation, central venous catheter as vascular access, albumin level ≥ 3.5 g/dL, hemoglobin level (in grams per deciliter), body mass index, primary cause of end-stage renal disease (hypertension, diabetes, and other), history of cancer, and history of heart disease. Facility-level covariates included ownership status of the facility, number of dialysis stations, and indicator variables denoting whether the facility was free standing, accepted transient patients, had evening dialysis sessions, reused dialyzers, offered only hemodialysis, and had isolation dialysis stations. All of the mentioned individual-level variables were reported as of the date when the individual initiated dialysis therapy. We also include indicator variables to denote the calendar year of incidence.

**Table 1.** Characteristics of Patients at Initiation of Hemodialysis by Facility's Initial Hemodialysis Session Duration

| Characteristic | ≥4-h Facilities | 3-h Facilities |
|---|---|---|
| Sample size | 39,172 | 47,721 |
| Age, y | 61 ± 15 | 64 ± 16 |
| Male sex | 21,545 (55) | 26,724 (56) |
| Race | | |
| White | 22,719 (58) | 32,927 (69) |
| Black | 15,277 (39) | 10,022 (21) |
| Other/unknown | 1,176 (3) | 4,772 (10) |
| eGFR, mL/min/1.73 $m^2$ | 10.5 ± 5.5 | 10.4 ± 5.6 |
| Central venous catheter | 31,337 (80) | 39,130 (82) |
| Albumin ≥ 3.5 g/dL | 10,185 (26) | 12,407 (26) |
| Initial hemoglobin, g/dL | 9.8 ± 1.7 | 9.9 ± 1.7 |
| Body mass index, kg/$m^2$ | 29.2 ± 7.3 | 28.2 ± 7.3 |
| Cause of ESRD | | |
| Diabetes | 19,194 (49) | 21,950 (46) |
| Hypertension | 9,793 (25) | 11,930 (25) |
| Other | 10,185 (26) | 13,841 (29) |
| History of cancer | 2,350 (6) | 2,863 (6) |
| History of heart disease | 18,018 (46) | 21,472 (45) |

*Note:* Values for categorical variables are given as number or number (percentage); for continuous variables, as mean ± standard deviation.

Abbreviations: eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease.

### Statistical Analysis

#### *Primary Analysis*

In our main analysis, we modeled 2- and 1-year mortality among incident patients undergoing maintenance hemodialysis in ≥ 4-hour and 3-hour facilities. We censored 5,094 patients who received kidney transplants at the date of their transplantation.

We estimated Cox proportional hazards models for 2- and 1-year mortality, with hemodialysis session duration (≥4 vs 3 hours) as the main independent variable, adjusting for the mentioned covariates. For each analysis (2- and 1-year Cox model), follow-up time was censored at the respective time (ie, 730 and 365 days).

We plotted Kaplan-Meier survival curves (using inverse probability weights) for patients treated in the 2 groups of facilities (ie, ≥4 vs 3 hours) and calculated the 75th percentile on survival probabilities in each of the 2 groups. Finally, we estimated the proportional hazard model for 1-year mortality separately by age, sex, race, and the presence or absence of heart disease, diabetes, and hypertension. All models are estimated using STATA/SE, version 12.0 (StataCorp LP).[11]

Our primary analysis uses inverse probability weights calculated from the propensity scores to reweight the data.[12] We first estimate a logit model in which the outcome is equal to 1 if the patient was treated in a ≥ 4-hour facility and the outcome is equal to 0 if the patient was treated in a 3-hour facility. Independent variables were all those included in Tables 1 and 2 (individual and facility