Eric Weinhandl, MS,[1] Jiannong Liu, PhD,[1] David Gilbertson, PhD,[1] Thomas Arneson, MD,[1] Allan Collins, MD, FACP[1,2]
[1]Minneapolis Medical Research Foundation, [2]University of Minnesota-Twin Cities

CDRG
Chronic Disease Research Group

# Relative Mortality in Daily Home and Matched, Thrice-weekly In-center Hemodialysis Patients

## Introduction

- Daily home hemodialysis (DHHD) is a rapidly growing alternative to thrice-weekly, in-center hemodialysis (3xIHD).
- DHHD is likely to improve fluid control and better control hypertension, plausibly potentiating lower risk of cardiovascular morbidity. The inherent flexibility of DHHD may also improve quality of life.
- Whether these mechanisms ultimately lower the risk of death is unclear.
- Previous studies have concluded that daily hemodialysis (either home or in-center) is associated with a much lower mortality rate than 3xIHD.[1,2,3]
  - [1]Blagg CR *et al*, *Hemodialysis Int*, 2006
  - [2]Kjellstrand CM *et al*, *Neph Dial Transplant*, 2008
  - [3]Miller BW *et al*, *American Soc Nephrology* abstract, 2009
- However, these studies have uniformly adjusted for only demographical factors and primary cause of ESRD.
- Residual confounding by disease severity is likely, because home dialysis (whether DHHD or peritoneal dialysis) typically attracts relatively healthier patients.
- Linking a provider registry with the United States Renal Data System (USRDS) database, we compared mortality between DHHD and 3xIHD patients in a matched cohort.

## Methods

- Exposed patients included those initiating DHHD (NxStage System One) in 2005-2007, as indicated by provider registry data.
- Patient data were linked to the USRDS database. We retained those patients who either had Medicare as the primary payer for ≥3 months before DHHD initiation or began renal replacement therapy (RRT) ≤6 months before initiation.
- For each DHHD patient, we selected 5 controls from the USRDS database.
- Each control underwent 3xIHD on the exposed patient's DHHD initiation date.
- Controls were matched according to an ordered set of covariates: age, hospital days during preceding 3 months, epoetin alfa dose during preceding 3 months, body mass index, transplant waiting list status, congestive heart failure, RRT duration, race, cancer, primary end-stage renal disease cause, stroke, peripheral vascular disease, other cardiac disease, diabetes, ischemic heart disease, gender, and dual eligibility for Medicare and Medicaid.
- We performed intention-to-treat analysis in all patients and as-treated analysis in only Medicare patients, with follow-up through December 31, 2008.

## Results

- The cohort included 1,873 DHHD patients.
- Compared to the 3xIHD population alive on January 1, 2007, DHHD patients were much younger, more likely to be male and non-African American, and were healthier (*i.e.*, had less comorbidity, received less epoetin alfa, and were hospitalized less frequently).
- Matching successfully balanced all measured covariates except dual eligibility (which did not independently predict death [adjusted hazard ratio = 1.03, $P = 0.57$]).
- In intention-to-treat (ITT) analysis, mean follow-up was 1.71 and 1.75 years in DHHD and matched 3xIHD patients, respectively.
- At 1, 2, and 3 follow-up years, ITT survival estimates (DHHD *vs.* matched 3xIHD) were 89.4 *vs.* 87.4%, 80.1 *vs.* 77.8%, and 72.9 *vs.* 69.8%, respectively. The overall hazard ratio (HR) was 0.87 (95% CI: 0.78-0.97).
- ITT HRs over 6-month intervals attenuated toward the null, but the trend was not statistically significant ($P = 0.92$).
- In as-treated (AT) analysis, the overall HR was 0.84 (95% CI: 0.73-0.96).
- There was no significant evidence of HR heterogeneity across strata, although HRs were larger in magnitude in patients with ASHD, CVA/TIA, PVD, and diabetes.

***Baseline characteristics of (1) all thrice-weekly, in-center HD (3xIHD) patients alive on January 1, 2007; (2) matched 3xIHD patients; and (3) daily home hemodialysis (DHHD) patients***

| | | | All 3xIHD (on 01.01.07) | Matched 3xIHD | DHHD | Standardized Difference |
|---|---|---|---|---|---|---|
| Sample Size | N | | 262,249 | 9,365 | 1,873 | |
| Age | Years | Mean (SD) | 62.4 (15.2) | 53.2 (14.7) | 52.2 (14.8) | 6.8 |
| | | Median | 64.0 | 53.1 | 52.3 | |
| Gender | % | Female | 45.3 | 37.7 | 35.8 | 3.9 |
| | | Male | 54.7 | 62.3 | 64.2 | 3.9 |
| Race | % | Black | 38.8 | 28.3 | 26.5 | 4.1 |
| | | Other | 61.2 | 71.7 | 73.5 | 4.1 |
| Primary Cause of ESRD | % | Diabetes | 44.1 | 30.3 | 27.3 | 6.7 |
| | | Hypertension | 28.9 | 20.6 | 19.3 | 3.4 |
| | | GN/PKD | 12.6 | 28.4 | 30.3 | 4.3 |
| | | Other | 14.4 | 20.7 | 23.1 | 5.9 |
| ESRD Duration | years | Mean (SD) | 4.0 (4.5) | 5.1 (5.8) | 5.5 (6.3) | 5.7 |
| | | Median | 2.7 | 3.3 | 3.2 | |
| Body Mass Index | kg/m² | Mean (SD) | 27.5 (7.0) | 27.9 (6.7) | 28.1 (7.0) | 2.4 |
| | | Median | 26.3 | 26.6 | 26.9 | |
| Comorbidity | % | ASHD | 34.6 | 22.7 | 24.0 | 3.2 |
| | | CHF | 44.6 | 27.1 | 26.9 | 0.4 |
| | | CVA/TIA | 16.4 | 8.1 | 8.3 | 1.0 |
| | | PVD | 32.0 | 20.5 | 20.9 | 0.9 |
| | | Other CVD | 25.8 | 17.9 | 20.0 | 5.2 |
| | | Cancer | 8.7 | 7.3 | 9.1 | 6.7 |
| | | Diabetes | 59.0 | 42.1 | 40.6 | 2.9 |
| Dual Eligibility | % | | 42.4 | 35.4 | 23.2 | 27.0 |
| Epoetin Alfa Dose (during preceding 3 months) | 1000s IU | Mean (SD) | 198.9 (227.0) | 180.6 (226.6) | 184.0 (237.4) | 1.5 |
| | | Median | 132.6 | 113.1 | 110.7 | |
| Hospitalization (during preceding 3 months) | Days | Mean (SD) | 4.0 (9.6) | 2.3 (7.7) | 2.3 (7.7) | 0.0 |
| | | Median | 0.0 | 0.0 | 0.0 | |
| On Transplant Wait List | % | | 14.2 | 34.8 | 35.0 | 0.5 |

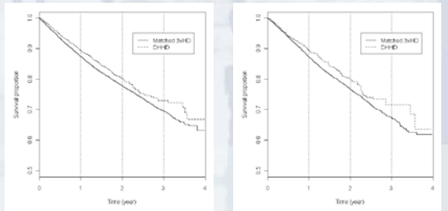
All patients in the prevalent cohort alive on 01.01.2007 had Medicare for ≥3 months before 01.01 or had begun renal replacement therapy ≤6 months before 01.01.

Standardized differences between matched 3xIHD and DHHD are displayed as percentage of one standard deviation, with the standard deviation calculated from pooling matched 3xIHD and DHHD patients.

Differences <10% suggest similarity between matched 3xIHD and DHHD patients.

***Kaplan-Meier estimates of survival following DHHD initiation in DHHD patients and the corresponding index date in matched 3xIHD patients***

*Left panel:* intention-to-treat analysis; *Right panel:* as-treated analysis, with censoring at modality change.

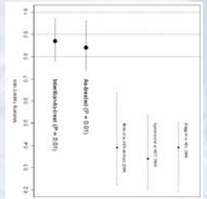




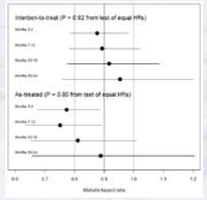


***Mortality hazard ratios for DHHD vs. matched 3xIHD, from Cox regression***

Hazard ratios in study cohort and standardized mortality ratios in published studies.



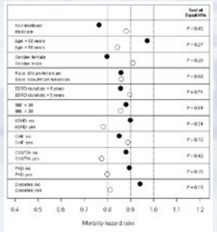

***Interval hazard ratios for DHHD vs. matched 3xIHD, from Cox regression***




***Mortality hazard ratios for DHHD vs. matched 3xIHD in selected strata of study cohort, from Cox regression***

All hazards ratios were derived from intention-to-treat analysis.

*P*-values were derived from Wald tests of equal hazard ratios in each pair of strata.




## Conclusions

- Over a relatively brief follow-up interval, DHHD was associated with lower risk of death, compared to 3xIHD.
- The estimated effect was smaller than previously reported, likely owing to superior control of confounding.
- However, the estimated effect is largely congruent with recent findings from the Frequent Hemodialysis Network (FHN) trial, in which hemodialysis six times per week resulted in significant improvement in the composite endpoint of death or increase in left ventricular mass (*NEJM*, 2010).
- The estimated effect was insensitive to the definition of the follow-up interval, and there was no credible evidence of heterogeneity in the effect across strata defined by patient characteristics.
- Continued follow-up of DHHD patients is needed to more precisely estimate the effects of DHHD on mortality.
- Further studies are needed to assess the effects of DHHD on morbidity, including cardiovascular disease and infection.

**www.cdrg.org**

funded in part by a grant from __ ____