

# Introduction

- Compared to persons in the general population, patients with kidney disease including those with end-stage renal disease (ESRD) undergoing dialysis, experience higher rates of death.<sup>1</sup> It has been previously demonstrated that patients who shorten their dialysis sessions have worse outcomes.<sup>2</sup> The actual reasons for this phenomenon are unknown. It is likely that longer dialysis treatments provide enhanced solute clearance beyond what is reflected by clearance of urea alone, which is used to define the adequacy of a dialysis session. It is also possible that prolonged dialysis sessions allow ultrafiltration to proceed slowly and in a manner that improves blood pressure control and allows for consistent achievement of dry weight.<sup>3</sup>
- Cardiovascular sequelae are likely a result of residual fluid experienced by patients who are not dialyzed to their optimal dry weight. Increased frequency of heart failure, myocardial infarction, and other cardiovascular events in patients may be due to excessive fluid accumulation.<sup>5</sup>
- Rapid ultrafiltration necessitated by shorter dialysis treatments may lead to episodic hypovolemia/hypotension with end-organ sequelae.
- Therefore, in the current analysis, we sought to examine the potential associations between dialysis session length and specific types of cardiovascular events and death.

# Objective

The primary goal of the current study was to estimate the association between duration of hemodialysis and rates of cardiovascular events and mortality.

# Methods

#### Patients

- The current study analyzed electronic medical records of US patients incident to in-center hemodialysis (01 Jan 2007–31 Dec 2008) who remained on this modality for  $\geq$  181 days and had Medicare or Medicaid as their primary insurer.
- Patients included in the analysis were treated at dialysis facilities located across the US within a large dialysis organization.

#### Analytics

- Dialysis session length was assessed over dialysis days 91-180 (to provide opportunity for initial equilibration to dialysis). This was referred to as the exposure assessment period (Figure 1).
- Cross-sectional association was estimated using contingency tables and chi-square testing. Outcomes were identified through US Renal Data System claims data, and were considered as those occurring on/after dialysis day 181 until death, care transfer, modality change, or end of study period (31 Dec 2009). Longitudinal associations were estimated using proportional hazards regression.

#### Exposure

- Dialysis session length was a patient-level distribution considered as mean value over the exposure assessment period. Dialysis session length was categorized this way:
- ≤179 minutes
- 180-194 minutes
- 195-209 minutes
- 210-224 minutes
- 225-239 minutes
- ≥240 minutes

#### Outcomes

- The patient outcomes studied during the at-risk period were:
- Atrial fibrillation
- Post-dialysis fluid-related hospitalization (hospitalization for fluid overload or hypotension immediately following dialysis)
- Composite endpoint for hospitalization from heart failure/fluid overload or cardiovascular mortality
- Hospitalization for heart failure and/or fluid overload
- Myocardial infarction
- Cardiovascular mortality (death attributed to myocardial infarction, atherosclerotic heart disease, cardiac arrhythmia, congestive heart failure, cardiomyopathy, cardiac arrest, valvular heart disease, pulmonary edema, cerebrovascular accident including intracranial hemorrhage, or ischemic brain damage/anoxic encephalopathy) – All-cause mortality

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# Shorter Hemodialysis Session Length Is Strongly Associated With Higher Rates of Mortality and Hospitalizations Steven Brunelli, MD, MSCE<sup>1</sup>; Emmanuel Anum, MBChB, PhD<sup>1</sup>; Karthik Ramakrishnan, MPH<sup>1</sup>; Jonna Jensen, PhD<sup>1</sup>; Gilbert Marlowe, BS<sup>1</sup>; Mahesh Krishnan, MD, MPH, MBA<sup>1</sup>; Allen Nissenson, MD<sup>2</sup>

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#### Model Adjustments

- All multivariate models were adjusted for the following variables:
- Age - Sex
- Race/ethnicity
- Etiology of ESRD
- Prior renal transplant
- Vascular access type
- Uncontrolled hypertension (mean sytolic blood pressure >140 mm Hg or mean diastolic blood pressure >90 mm Hg over exposure assessment period)
- Pre-existing diabetes, congestive heart failure, myocardial infarction, atrial fibrillation, cerebrovascular disease

#### Figure 1. Study Design



# Results

#### Table 1. Cohort Characteristics and Cardiovascular Comorbidities at Study Baseline

Categorical Variables N = 39,864		Ν		Proportion (%)			
Female sex		17,493		43.9			
Race/Ethnicity							
White		18,381		46.1			
Black		12,623		31.7			
Hispanic		5,832		14.6			
Asian		1,274		3.2			
Other		1,735			4.4		
Etiology of ESRD							
Diabetes		18,735		47.0			
Hypertension		12,110		30.4			
Glomerular disease		2,880		7.2			
Other		6,139		15.4			
CV Comorbidities							
Prior renal transplant <sup>a</sup>		704		1.8			
Prevalent diabetes <sup>a</sup>		27,152		68.1			
Prevalent heart failure <sup>a</sup>		15,903			39.9		
Prevalent myocardial infarction <sup>a</sup>		10,067		25.3			
Prevalent atrial fibrillation <sup>a</sup>		2,381		6.0			
Prevalent ischemic stroke <sup>b</sup>		344		0.9			
Prevalent hemorrhagic stroke <sup>b</sup>		65		0.2			
Prevalent cerebrovascular disease <sup>c</sup>		3,464		8.71			
Uncontrolled hypertension <sup>d</sup>		37,829		94.9			
Continuous Variables	Ν	Mean	SD	Median	Lower quartile	Upper quartile	
Age, years (at dialysis initiation)	39,864	62.2	15.3	63	52	74	

Abbreviations: CMS, Centers for Medicare and Medicaid Services; CV, cardiovascular; ESRD, end-stage renal disease; EHR, electronic health record; SD, standard deviation.

<sup>a</sup>Defined based on CMS Medical Evidence Form 2728 data, or claims (1 inpatient, or 2 outpatient), or DaVita EHR prior to dialysis day 180. <sup>b</sup>Defined based on claims (1 inpatient, or 2 outpatient) or DaVita EHR prior to dialvsis day 180. Data from CMS Medical Evidence Form 2728 not included because they do not distinguish among ischemic stroke, hemorrhagic stroke, or transient ischemic attack. <sup>c</sup>Defined based on CMS Medical Evidence Form 2728. claims (1 inpatient. or 2 outpatient). DaVita EHR prior to dialysis day 180. Includes ischemic stroke, hemorrhagic stroke, and transcient ischemic attack. <sup>d</sup>Defined as mean pre-dialysis blood pressure >140/90 mm Hg or post-dialysis blood pressure >130/85 mm Hg during the exposure assessment period (dialysis days 91-180).

#### Table 2. Incidence Rates and Cumulative Incidence of Outcomes

Variable N = 39,782	Number patients affected	% patients affected	Incidence rate per 100 patient-years (95% CI)
Hospitalization for HF/volume overload	8,896	22.4	24.4 (23.9-24.9)
Composite hospitalization for HF/volume overload/CV mortality	10,805	27.2	27.8 (27.3-28.4)
Cardiovascular mortality	2,976	7.5	5.6 (5.4-5.8)
All-cause mortality	7,646	19.2	14.2 (13.8-14.6)
Myocardial infarction	2,396	6.0	6.0 (5.7-6.2)
Post-dialysis fluid-related hospitalization	751	1.9	1.9 (1.8-2.0)
Atrial fibrillation	2,789	7.0	7.0 (6.7-7.2)

Abbreviations: CI, confidence interval; CV, cardiovascular; HF, heart failure. At-risk period began on dialysis day 181 and continued until death or censoring

#### Figure 2. Session Length and Outcomes Measured



#### Figure 3. Session Length and Risk for Mortality



≥240 minutes used as reference = 1.0

• In total, 39,864 patients qualified for the analysis. Of the 7,185 patients who had mean dialysis session length of  $\geq$ 240 minutes, 77% had mean session lengths between 240 and 255, while 92% had mean sessions lengths between 240 and 270 minutes.

### Discussion

- These study results demonstrate a dose response association between incrementally shorter session length and risk of heart failure/fluid overload hospitalization, myocardial infarction, post-dialysis fluid related hospitalization, cardiovascular mortality, and allcause mortality. Atrial fibrillation was not associated with dialysis session length.
- These findings also add potential mechanistic links that may underlie the repeated observation that shorter dialysis session is related to increased mortality.
- It is possible that the mechanisms that trigger cardiovascular events share biochemical pathways with fluid retention in patients undergoing hemodialysis.

#### Conclusions

- These findings represent additional evidence that in the context of thrice-weekly in-center hemodialysis, longer treatments are associated with improved patient health and survival.
- Randomized trials are needed to test causality.

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