



Intensive Hemodialysis, Left Ventricular Hypertrophy, and Cardiovascular Disease

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The prevalence of cardiovascular disease, including cardiac arrhythmia, coronary artery disease, cardiomyopathy, and valvular heart disease, is higher in hemodialysis (HD) patients than in the US resident population. Cardiovascular disease is the leading cause of death in HD patients and the principal discharge diagnosis accompanying 1 in 4 hospital admissions. Furthermore, the rate of hospital admissions for either heart failure or fluid overload is persistently high despite widespread use of β -blockers and renin-angiotensin system inhibitors and attempts to manage fluid overload with ultrafiltration. An important predictor of cardiovascular mortality and morbidity in dialysis patients is left ventricular hypertrophy (LVH). LVH is an adaptive response to increased cardiac work, typically caused by combined pressure and volume overload, resulting in cardiomyocyte hypertrophy and increased intercellular matrix. In new dialysis patients, the prevalence of LVH is 75%. Regression of LVH may reduce cardiovascular risk, including the incidence of heart failure, complications after myocardial infarction, and sudden arrhythmic death. Multiple randomized clinical trials show that intensive HD reduces left ventricular mass, a measure of LVH. Short daily and nocturnal schedules in the Frequent Hemodialysis Network trial reduced left ventricular mass by 14 (10%) and 11 (8%) g, respectively, relative to 3 sessions per week. Comparable efficacy was observed in an earlier trial of nocturnal HD. Intensive HD also improves cardiac rhythm. Clinical benefits have been reported only in observational studies. Daily home HD is associated with 17% and 16% lower risks for cardiovascular death and hospitalization, respectively; admissions for cerebrovascular disease, heart failure, and hypertensive disease, which collectively constitute around half of cardiovascular hospitalizations, were less likely with daily home HD. Relative to peritoneal dialysis, daily home HD is likewise associated with lower risk for cardiovascular hospitalization. In conclusion, intensive HD likely reduces left ventricular mass and may lead to lower risks for adverse cardiac events.

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Cardiovascular disease is a major cause of morbidity and mortality in dialysis patients. In particular, cardiovascular disease is the leading primary cause of death in both hemodialysis (HD) and peritoneal dialysis (PD) patients. In contemporary HD patients, the unadjusted cardiovascular-related death rate is nearly 30 times higher than in the US resident population.^{1,2} Thus, although both hospital admission and death rates have recently declined in dialysis patients, there is ongoing need for novel interventions to reduce the risk for cardiovascular disease in dialysis patients.

The vast majority of in-center HD patients undergo treatment 3 times per week, for an average of 3 hours and 37 minutes per session.³ This schedule introduces 2 challenges. First, the limited duration of each session and the need to remove excess fluid may together necessitate aggressive ultrafiltration. Second, the schedule includes an approximately 72-hour interval between consecutive sessions on Friday and Monday or Saturday and Tuesday. Multiple studies have suggested that this interval is associated with increased risks for mortality and morbidity. In a study of more than 32,000 patients, Foley et al⁴ found that the death

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rate on the day following the long interval was 23% higher than on other days and that the cardiovascular-related hospital admission rate was 124% higher (Fig 1). These findings have been corroborated by cardiovascular-related death patterns in the DOPPS (Dialysis Outcomes and Practice Patterns Study),⁵ the United Kingdom Renal Registry,⁶ and The Australia and New Zealand Dialysis and Transplant Registry.⁷ Long interdialytic intervals and aggressive ultrafiltration in response to interdialytic weight gain collectively engender large and potentially rapid changes in fluid and solutes, thereby placing stress on the heart and peripheral vasculature. Such stress might be classified as iatrogenic because HD session frequency and duration are modifiable. Intensive HD, including short daily and nocturnal treatment, lessens the “unphysiology” of the usual schedule and may substantially improve cardiovascular outcomes.⁸

Here, we briefly describe the epidemiology of cardiovascular disease in dialysis patients; discuss the pathophysiology and clinical significance of left ventricular hypertrophy (LVH), as reflected by measures of left ventricular mass in grams or indexed to body surface area; assess the effects of intensive HD

on LVH; and assess population studies regarding associations of intensive HD with cardiovascular outcomes. The body of evidence supports positive effects of intensive HD on subclinical cardiovascular measures and suggests that these effects logically translate to improved cardiovascular health.

EPIDEMIOLOGY OF CARDIOVASCULAR DISEASE

Prevalence of Comorbid Conditions at Dialysis Initiation

Cardiovascular comorbid conditions at dialysis therapy initiation are recorded on the End-Stage Renal Disease (ESRD) Medical Evidence Report (CMS [Centers for Medicare & Medicaid Services] form 2728). In incident patients with ESRD from 2011 to 2013, the prevalence (ie, either presence or history) of congestive heart failure was 30%; atherosclerotic heart disease, 18%; other cardiac disease (not defined by form instructions), 18%; cerebrovascular accident or transient ischemic attack, 9%; and peripheral vascular disease, 12%.² Analyses of both Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Study participants and elderly patients with Medicare

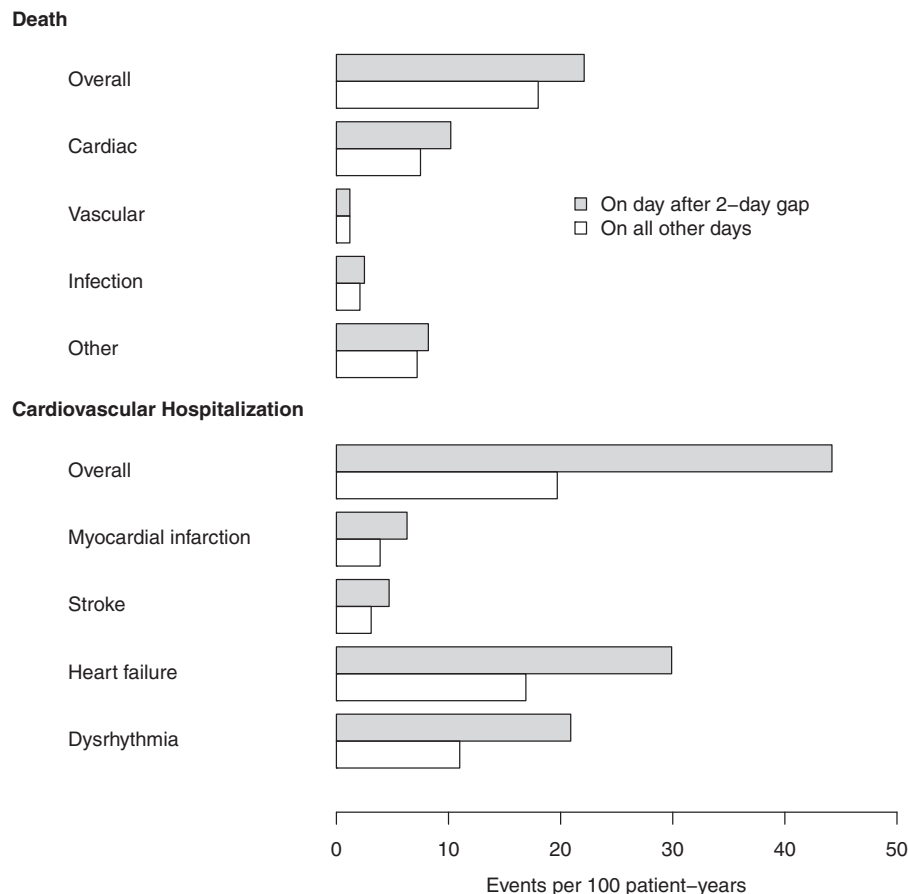


Figure 1. Rates of death and cardiovascular hospitalization on the day after the 2-day gap in dialysis treatment and on all other days.⁴

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