

Sudden Cardiac Death in Dialysis Patients

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In 2002, the annual mortality rate for prevalent dialysis patients in the United States was 230 deaths per 1000 patient-years.(1) Cardiac disease, the single most common cause, accounted for 43% of all-cause mortality.(1) In the United States Renal Data System (USRDS) database, 62% of cardiac deaths (27% of all-cause mortality) are attributable to arrhythmic mechanisms. Clinical trial data are concordant; the HEMO and 4D trials reported 25-26% of dialysis patient deaths due to sudden cardiac death.(2;3) The Cardiovascular Special Studies Center (CVSSC) of the USRDS estimated the sudden cardiac death rate for period prevalent US dialysis patients in 2002 at approximately 7% per year.(1)

Heightened vulnerability to sudden cardiac death is likely attributable to risk factors common to end-stage renal disease (ESRD) patients. Obstructive coronary artery disease is an important contributor to sudden cardiac death, but as 4D surprisingly showed no difference in sudden death between patients receiving atorvastatin or placebo, it may not be the pre-eminent cause for dialysis patients. Clinical trials on statins in the non-ESRD population showed reduction in coronary heart disease, including sudden death. The null result for 4D suggests that our conception of coronary heart disease death in the general population may not apply to dialysis patients.

A recent USRDS CVSSC publication focuses on high dialysis patient mortality after coronary revascularization.(4) Survival is best for patients receiving surgical coronary revascularization using the internal mammary graft; the 2-year all-cause mortality rate was 43% even for these patients. Approximately one-quarter of all deaths were ascribed to arrhythmic mechanisms. The persistence of a significant residual hazard of arrhythmically-mediated death after coronary revascularization implies that

mechanisms other than ischemic heart disease are important contributors. Left ventricular hypertrophy (present in at least 75% of dialysis patients); rapid electrolyte shifts and hyperkalemia in patients receiving conventional thrice-weekly hemodialysis; autonomic dysfunction (including sleep apnea); and abnormalities in myocardial ultrastructure and function, including endothelial dysfunction, interstitial fibrosis, and decreased myocardial perfusion reserve with resultant diminished tolerance of myocardial ischemia, are potential causes of dialysis patients' special vulnerability to sudden cardiac death.(5-10)

The non-physiologic nature of thrice-weekly hemodialysis (and the attendant large electrolyte shifts) contributes to the hazard of sudden cardiac death. In a classic observational study,(11) Bleyer et al reported a 50% increase in cardiac deaths on Mondays for patients dialyzing Monday, Wednesday, and Friday, and similar findings on Tuesdays for patients dialyzing on Tuesday, Thursday, and Saturday. On Mondays, for patients dialyzing Monday, Wednesday, and Friday, risk of sudden death in the 12 hours before dialysis was increased threefold, and by 1.7 for 12 hours after starting the dialysis session.(12) If the major problem were rapid electrolyte shifts, peritoneal dialysis patients should have a markedly lower risk of sudden death than hemodialysis patients.

Surprisingly, although the rate of cardiac arrest is indeed about 50% higher for hemodialysis than peritoneal dialysis patients 3 months after dialysis initiation, the rates are similar 2 years after initiation, and are higher for peritoneal dialysis patients 3 years after initiation (Figure 1).(1) More intriguing for improving cardiac survival in ESRD patients is the potential benefit of long-duration quotidian dialysis. Culleton et al(13) found left ventricular mass (determined by cardiac magnetic resonance imaging) reduced

in patients receiving nocturnal dialysis 6 times a week compared to those receiving thrice-weekly hemodialysis.

Data are limited on prevention of sudden cardiac death in dialysis patients. However, in a retrospective analysis of cardiac arrests occurring during hemodialysis sessions, Karnik et al(14) reported that use of 0 or 1.0 mEq/L potassium dialysate was associated with a twofold increased risk of cardiac arrest, suggesting that routine very low potassium dialysate should be avoided. In the general population, beta-blockers and angiotensin converting enzyme inhibitors (ACEIs) are proven therapies for reducing mortality in patients with congestive heart failure. Cice et al(15) conducted a small prospective randomized trial of carvedilol in 114 Neapolitan dialysis patients with dilated cardiomyopathy. Compared to placebo, they found a significant reduction in cardiovascular mortality and a trend toward reduction in sudden death, a finding concordant with large clinical trials of beta-blockers in the general population and supporting carvedilol use in dialysis patients with dilated cardiomyopathy. The largest prospective trial of ACEIs in dialysis patients, FOSIDIAL,(16) found no reduction in cardiovascular events for fosinopril compared to placebo, but this trial was underpowered. A small randomized trial of candesartan (an angiotensin receptor blocker [ARB])(17) surprisingly demonstrated a nearly threefold reduction in cardiovascular events, but this finding needs replication in a larger study. Based on current, limited, data, using carvedilol and ACEIs or ARBs to improve long-term outcomes in dialysis patients with dilated cardiomyopathy seems reasonable.

The reported cardiac arrest rate in hemodialysis centers ranges from 4.5-7 per 100,000 hemodialysis sessions.(14;18) On-site capability for external defibrillation

(preferably with automatic external defibrillators [AEDs]) was recommended in 2005(19) Lehrich et al(18) challenged this recommendation, as they reported 19% 30-day and 9.5% 1-year survival after cardiac arrest occurring in dialysis centers with on-site AEDs and 15% and 7.8% in centers without AEDs.

Most sudden deaths, however, occur outside of medical settings; the benefit from AEDs in dialysis centers is not unexpectedly modest. A more aggressive approach is use of implantable cardioverter defibrillators (ICDs) for primary or secondary prevention of sudden cardiac death. No dialysis patients were entered into any published randomized ICD trial. Observational data, however, suggest that for cardiac arrest survivors on dialysis, the benefit of ICD implantation is not attenuated by ESRD; we found a 42% reduction in all-cause mortality for patients receiving ICDs, even after adjustment for comorbid illness.(20) The role of ICDs for primary prevention of sudden cardiac death in dialysis patients remains uncertain, and should be tested in a prospective, randomized clinical trial adequately powered for the primary endpoint of all-cause mortality.

Dialysis patients are at significant risk for sudden cardiac death. Aggressive efforts to improve their cardiovascular outcomes are warranted.

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Legend

Figure 1. Cardiac arrest event rates and event-free probabilities, incident dialysis patients on Medicare, aged ≥ 20 years, 2000-2002 combined. Monthly event rates months 1-6 after dialysis initiation, mean monthly event rates in each following 6-month interval. Adjusted for age, sex, race, and diabetic status.¹