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In Practice

Sudden Cardiac Death Among Hemodialysis Patients

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Hemodialysis patients carry a large burden of cardiovascular disease; most onerous is the high risk for sudden cardiac death. Defining sudden cardiac death among hemodialysis patients and understanding its pathogenesis are challenging, but inferences from the existing literature reveal differences between sudden cardiac death among hemodialysis patients and the general population. Vascular calcifications and left ventricular hypertrophy may play a role in the pathophysiology of sudden cardiac death, whereas traditional cardiovascular risk factors seem to have a more muted effect. Arrhythmic triggers also differ in this group as compared to the general population, with some arising uniquely from the hemodialysis procedure. Combined, these factors may alter the types of terminal arrhythmias that lead to sudden cardiac death among hemodialysis patients, having important implications for prevention strategies. This review highlights current knowledge on the epidemiology, pathophysiology, and risk factors for sudden cardiac death among hemodialysis patients. We then examine strategies for prevention, including the use of specific cardiac medications and device-based therapies such as implantable defibrillators. We also discuss dialysis-specific prevention strategies, including minimizing exposure to low potassium and calcium dialysate concentrations, extending dialysis treatment times or adding sessions to avoid rapid ultrafiltration, and lowering dialysate temperature.
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CASE PRESENTATION

A 26-year-old African American man was brought to the hospital following a sudden cardiac arrest during hemodialysis (HD) at his outpatient dialysis center. He was being dialyzed on a 2-mEq/L potassium bath and 2-mEq/L calcium bath with dialysate temperature of 37°C and ultrafiltration goal of 3.9 L. He was 1.5 hours into his 4-hour 45-minute HD treatment when he suddenly became unresponsive. Cardiopulmonary resuscitation (CPR) was started while an automated external defibrillator (AED) was attached and subsequently delivered a shock for ventricular fibrillation.

The patient had a history of obesity-related glomerulopathy and was on HD therapy for 10 months prior to his cardiac arrest. His other medical problems included paroxysmal atrial fibrillation, left- and right-sided systolic dysfunction with left-sided diastolic dysfunction, and aortic valve infective endocarditis requiring replacement 5 months prior to the cardiac arrest. He frequently presented with large interdialytic weight gain, leading to large ultrafiltration goals and intradialytic hypotension.

This case offers the opportunity to explore several aspects of sudden cardiac arrest and sudden cardiac death (SCD) among dialysis patients. What are the epidemiology and pathophysiology of SCD in dialysis patients? What are the modifiable dialysis-specific risk factors? What primary and secondary SCD prevention strategies are effective in this population? This article reviews the epidemic of SCD in the HD population with a focus on prevention.

DEFINITION OF SCD

SCD is the largest contributor to mortality among HD patients. Cardiac arrest accounts for a quarter of HD patient deaths[1] (Fig 1). International data from the Dialysis Outcomes and Practice Patterns registry show that SCD among HD patients is more common in the United States (33% of all deaths) than in other countries, including Japan (23%), Australia/New Zealand (19%), and Canada (18%). It is unknown whether these findings are from different reporting schemes, dialysis practices, or baseline patient characteristics.[2]

It is important to acknowledge that these SCD epidemiology data are derived from large population registries that lack a systemic adjudication process and may be prone to misclassification. There is no universally accepted and precise definition of SCD. First identified as a specific cause of death by Hinkle and Thaler,[3] SCD has been defined broadly as a natural, rapid, and unexpected cardiac death within an hour of symptom onset.[4] Other definitions include death without an obvious noncardiac cause in patients well within the last 24 hours.[5] Paramount to the classification of death as SCD is the ability to determine: (1) the clinical circumstances surrounding death, and (2) the timing of progression from symptoms to cardiac arrest. This poses several difficulties when applied to the HD population. First,

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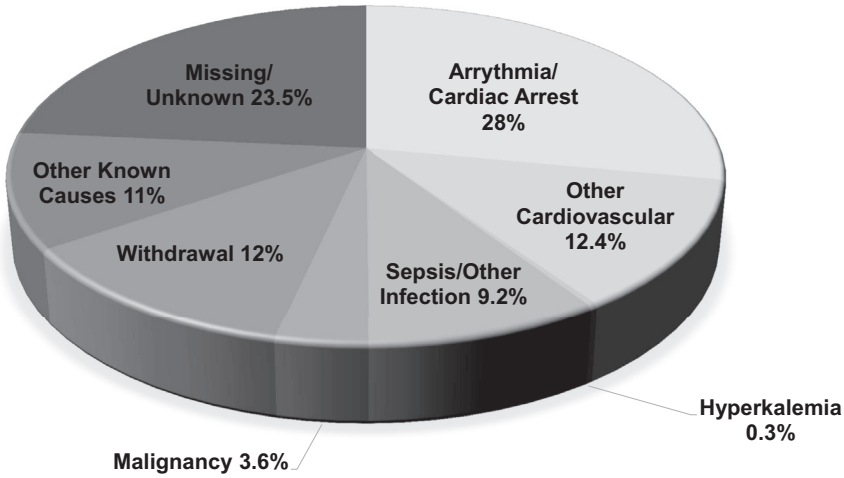

Figure 1. Causes of death among dialysis patients 2011 to 2013. Other cardiovascular causes include acute myocardial infarction, atherosclerotic heart disease, congestive heart failure, cerebrovascular accident, and other cardiac events.[1] Adapted from the US Renal Data System, 2015 Annual Data Report, Fig 9.1b.

many deaths are unwitnessed and limited information is available about the circumstances of death, making the exclusion of a noncardiac cause challenging.[6] Patients with end-stage renal disease (ESRD) may be susceptible to other causes of sudden unexpected death, such as cerebral hemorrhage, pulmonary or air embolism, or aortic dissection, which may be mistaken for SCD if there are no clinical or autopsy data available to confirm a primary cardiac cause. The potential for misclassification of SCD was seen in an autopsy series of 93 Japanese dialysis patients who were apparent victims of SCD. Stroke was found as the most frequent cause (25.8%), followed by cardiac disease (19.4%) and infections (17.2%).[7] Second, the timing and unexpected nature of death can also be difficult to ascertain because patients with ESRD are chronically ill with numerous comorbid conditions and are frequently hospitalized. What qualifies a death as an "unexpected death" in this population can be subject to interpretation. Cardiac arrests in the setting of withdrawal from dialysis therapy or after missing dialysis treatment have been included in SCD definitions in some studies, but consensus is that these circumstances should be excluded because cardiac arrest is not unexpected in these situations.[2,8,9]

Due to the difficulty determining the circumstances and timing of sudden death, SCD definitions used in studies of the ESRD population have been variable, leading to wide variations in reported SCD rates. A recent systematic review evaluated 42 cohort studies and randomized controlled trials (RCTs) reporting on SCD rates in patients with ESRD.[10] Only 25 studies provided a specific definition for SCD, and of those, only 17 included a measure of time in their SCD definition. Reported SCD rates varied widely from 0.4% to 10.4% annually. Despite the troubling variability in SCD definitions across studies,[11] clinical trials such as the Hemodialysis (HEMO) Study, Die Deutsche Diabetes Dialyse Studie (4D), and Evaluation of Cinacalcet HCl Therapy to Lower Cardiovascular Events (EVOLVE) Trial, in which cause of death was carefully adjudicated, all reported a consistent proportion of 22% to 26% of all trial deaths attributed to SCD.[12-14] This is similar to what has been consistently reported by large population registries such as the US Renal Data System (USRDS), and 2 studies comparing causes of death reported by the USRDS with adjudicated sources have shown reasonable sensitivity and specificity for cardiac causes of death.[11,15] However, improved harmonization of SCD definitions across studies is needed in order to accurately track SCD rates and test interventions to reduce its incidence. Such a definition should exclude in-hospital and hospice patients, as well as death following withdrawal of HD therapy or after missing an HD treatment.

Although patients with ESRD receiving long-term dialysis are at the highest risk for SCD, it is important to note that patients with moderate kidney disease are also at elevated risk. The absolute number of individuals affected by SCD is much higher among patients with chronic kidney disease (CKD) given the higher prevalence of CKD compared to ESRD in the general population (Fig 2). This highlights the opportunity for early SCD risk modification and the role of slowing CKD progression to reduce the impact of SCD overall.

PATHOPHYSIOLOGY OF SCD

The pathophysiology of SCD is thought to result from the combination of a vulnerable myocardium and an acute proarrhythmic trigger that leads to a terminal arrhythmia.[16] In the general population, this manifests as ischemic cardiomyopathy with reduced left ventricular ejection fraction (LVEF) that is prone