putative kidney function–associated genes and loci. Importantly, the kidney regulatory annotation maps and eQTL maps seem to be converging. For example, Sieber et al.,9 identified an open chromatin area at the DAB2 locus in the human kidney. They also identified important long-range interactions in this region, where the variant was associated with DAB2 expression. This region in the genome is one that previously had been identified in GWAS and eQTL studies (Figure 1) indicating that the nucleotide variants are associated with with kidney disease and regulate the expression of DAB2 in the kidney. Furthermore the role of DAB2 as kidney disease gene was confirmed in mouse genetic models.

In summary, the study by Sieber et al.9 is a major step forward in generating open chromatin and chromatin interaction maps for samples of human kidney glomeruli and tubules. This type of information will be important for understanding gene regulation in the kidney and annotation of human genetic studies. Future research will focus on defining the cell type-specific epigenome and chromatin accessibility and interaction. Furthermore, integration of data from different sources—such as larger GWAS datasets, studies with better phenotyping information, larger and improved eQTL studies, and improved regulatory annotation via epigenome and chromatin mapping—will be essential to identify high-confidence causal genes. Finally, experimental validation via animal models will be needed to confirm that these “high-confidence” causal genes actually define “true” disease-causing genes.

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DISCLOSURES

None.

REFERENCES


Cardiopulmonary Resuscitation in Outpatient Dialysis Clinics: Perception of Futility?

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Cardiac arrest (CA) accounts for approximately 25% of deaths in the hemodialysis (HD) population. Moreover, patients on HD have increased mortality with CA in comparison with the general population. Finally, for those patients who survive, there may be a higher rate of discharge to nursing homes and lower functional status. Improving outcomes after CA requires a multipronged approach, including education to provide timely cardiopulmonary resuscitation (CPR) and defibrillation when appropriate and secondary preventative strategies for survivors. Intuitively, it is expected that all outpatient dialysis staff are competent to provide CPR and that they are capable of using automated external defibrillators (AEDs) as indicated. Sadly, retrospective studies thus far suggest that resuscitation efforts and deployment rates of AEDs are generally low.

In this issue of the Journal of the American Society of Nephrology, Pun et al.5 aimed to provide a contemporary examination using the Cardiac Arrest Registry to Enhance Survival to describe the rate of CPR and outcomes in ambulatory patients having a CA in outpatient dialysis facilities. They included adult patients in

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Taken together, these results substantiate the urgency of rapid CPR and AED use at the time of the arrest. Most (66%) of the arrests presented with a nonshockable rhythm, but there was a greater proportion of shockable first rhythms (41% versus 25%) when dialysis staff were the first to install the AED. However, there was a greater proportion of shockable first rhythms (41% versus 25%) when dialysis staff were the first to install the AED. Predictors of dialysis staff–initiated CPR included patients who were men (odds ratio [OR], 1.80; 95% confidence interval [95% CI], 1.00 to 3.23), witnessed OHCA (OR, 3.33; 95% CI, 1.59 to 6.98), and large dialysis clinics (OR, 1.04; 95% CI, 1.01 to 1.08 per increase in number of dialysis stations). The only predictor of dialysis staff–initiated AED use was larger dialysis clinics. Overall, 48% survived to hospital admission, 54% of these patients survived to discharge, and of these patients, 82% had favorable neurologic status. Although this study describes the current practice pattern, it also poses multiple difficult questions.

From an electrophysiologic point of view, Pun et al.5 found a predominance of nonventricular arrhythmias in their cohort (33% initial shockable rhythm). Similar findings were noted by Roy-Chaudhury et al.6 using data from implantable loop recorders. These investigators showed that the majority of clinically significant arrhythmias in patients on conventional HD are bradycardia and asystole, peaking particularly during the first dialysis session of the week and the last 12 hours before dialysis. In contrast, older retrospective studies suggested that the most common arrhythmias leading to CA are, in fact, ventricular in origin followed by asystole. In a Canadian cohort, the most common cause of CA was ventricular arrhythmias (32%) followed by bradycardia (26%).7 Taken together, these results substantiate the urgency for clinical researchers to understand the pathogenesis of CA in the HD population, especially given that modifications of traditional cardiovascular risks (including coronary revascularization) have not altered the rates of sudden cardiac death in this vulnerable population.

Equally concerning, one must question why one in five patients experiencing CA in the dialysis unit did not receive CPR. Furthermore, the notion of sex disparity in CPR has also been consistently observed in this publication as well as bystander CPR studies in the general population.8 The lack of staff participation in performing CPR suggests inadequate training and/or lack of comfort in delivering resuscitation in an outpatient clinic. It is also plausible that the staff may feel an element of social awkwardness for them to apply CPR or AED to patients who are women. Moreover, it is tempting to speculate that the perception of futility given the overall poor outcomes of the patient population on HD may explain the suboptimal staff participation rates of CPR. We are unable to ascertain the severity of frailty and/or overall functional status of the patient cohort that may also represent possible confounders.

The data from this study are both encouraging and concerning. Indeed, it seems that rapid initiation of CPR and use of an AED are associated with better patient outcomes after OHCA. Moving forward, identification of barriers to dialysis staff–initiated CPR and AED may be done through a mixed-methods study by debriefing dialysis clinic staff. Arguably, however, the most important interventions to improve outcomes are in the prevention of CA. Simplistically, modifications to the dialysis prescription (e.g., changes in dialysate composition, alteration of HD frequency and duration, and adjustment of ultrafiltration rate) are potential interventions that may affect sudden cardiac death. There is also a paucity of evidence in medical or device interventional studies on the primary or secondary prevention of CA. The difficulty in recruiting to the now terminated Wearable Cardioverter Defibrillator in Hemodialysis Patients trial (ClinicalTrials.gov Identifier: NCT02481206) is an example of challenges facing this type of interventional study.

In sum, the study by Pun et al.5 confirms that rapid initiation of CPR and AED use are associated with improved clinical outcomes. However, in reflecting on the present state of available evidence in the field, it is not surprising that one may perceive a sense of futility. We hope that our call to action will serve as a reminder to motivate awareness and future research to address this important aspect of dialysis care.

DISCLOSURES
None.

REFERENCES