Tackling the Achilles’ Heel of Hemodialysis

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More than 375,000 patients undergo long-term hemodialysis treatment in the United States, but the outcomes have remained abysmal, with the rate of death during the first year of hemodialysis therapy exceeding 20%. Although the development half a century ago of techniques for sustainable vascular access rendered long-term extracorporeal treatment feasible, vascular access remains the Achilles’ heel of hemodialysis. The current options include arteriovenous fistulas, synthetic grafts, and central venous catheters, with a clear hierarchy among these options. Native arteriovenous fistulas — simple anastomoses of forearm arteries and veins — yield the best outcomes. Among otherwise similar patients, those with functioning dialysis fistulas live the longest and have the fewest infectious complications. Such fistulas, however, need to mature for several weeks or months until they can accommodate the blood flow necessary for dialysis, and many fistulas never mature sufficiently for adequate use. Synthetic vascular grafts can be used in patients whose native vessels may not support a fistula. These grafts can be used sooner than fistulas but carry higher risks of infection. Least desirable of all the options is the implantation of a permanent, usually cuffed, central venous hemodialysis catheter. Although central hemodialysis catheters can be inserted quickly and are available for use immediately, they are associated with particularly high rates of infection, hospitalization, and death. These catheters are prone to partial or total occlusion, which may lead to inadequate dialysis and missed dialysis sessions. As a result, maintaining central venous catheters is costly and burdensome to the patient. All in all, most clinicians agree that the use of central venous hemodialysis catheters should be avoided whenever possible.

There have been several initiatives aimed at increasing the number of patients in whom fistulas are used for hemodialysis. As a result, the use of fistulas has increased in recent years, predominantly replacing the use of synthetic grafts; in 2007, fistulas were used 55% of the time, and synthetic grafts 27% of the time. Unfortunately, 18% of patients still use central venous catheters, either because they start dialysis without a functioning peripheral vascular access or because all suitable peripheral vessels have been exhausted over the course of years of hemodialysis treatment and frequent vascular-access failures. In 2008, a central venous catheter was used in 74% of the patients in the United States who were undergoing hemodialysis for the first time as outpatients. Only 16% of patients had a maturing arteriovenous fistula or graft in place, strongly suggesting that more than half the patients initiating hemodialysis had to rely on cuffed central venous catheters for several months until a peripheral venous access could be established and would be available for use. The rates of associated serious infections during the first months of hemodialysis treatment have been exceedingly high — more than 200 hospitalizations for (systemic) vascular-access–related infections per 1000 patient-years in the first 6 months.

For patients who must rely on a central venous catheter for hemodialysis treatment, the findings by Hemmelgarn et al. in this issue of the Journal provide important new evidence. A simple regimen in which recombinant tissue plasminogen activator (rt-PA) was used for sealing the two lumina of the dialysis catheter once a week (with heparin used for the other two treatments each week) was superior to a regimen in which heparin seals were used after all the treatments; the rate of access failure was halved,
and access-related infection was reduced by two thirds. Certainly, rt-PA is substantially more expensive than heparin, but the authors suggest that using this clinically superior strategy may also be cost-effective because of the complications it prevents. One caveat is that because of the small study size, the hard end points of access removal, access-related hospitalization including infectious complications, and death from any cause or from an infectious cause could not be conclusively assessed. However, the study outcomes were carefully selected and were as close a surrogate for a hard end point as we can find in this setting. Furthermore, the sample size was certainly too small to observe potential rare, but catastrophic, adverse events such as massive bleeding, though both heparin and rt-PA should be aspirated from the catheter lumen and discarded immediately before the catheter is used so that little to none of the anticoagulant substances left in the catheter when it was sealed after the previous hemodialysis treatment should reach the systemic circulation.

The evidence from this trial is exciting because the use of rt-PA is among the first strategies to show efficacy with respect to the end point of access failure. There are, however, several studies that have shown the superior efficacy of other strategies for sealing catheters, as compared with the use of heparin alone, with respect to vascular-access–related infectious outcomes; such strategies include the use of antibiotics (e.g., gentamicin) and citrate solutions. It would be interesting to directly compare the rt-PA strategy used in the present study with some of the other approaches. The protocol by Hemmelgarn et al., however, is appealing in that it seems to kill two birds with one stone—namely, access failure and infection.

Given this new evidence, one can expect that dialysis providers will swiftly adopt the strategy of using rt-PA once a week. The once-weekly rt-PA strategy has the additional value of accessibility. Dialysis units already use rt-PA, although the use is based more on experience than on evidence, and can incorporate this proven treatment regimen in their standard-of-care protocols immediately. It is important to note, however, that rt-PA may invalidate certain laboratory measurements (e.g., parathyroid hormone and phosphate levels) when the blood used for those measurements is drawn through the central venous catheter, and so routine laboratory blood drawings should be scheduled accordingly.

The study by Hemmelgarn et al. and some other recent findings allow tempered optimism that we are now making some progress in providing quality evidence to improve the care of the vascular access in patients with chronic kidney disease who currently require dialysis. For others, increased screening for chronic kidney disease, routine reporting of estimated glomerular filtration rate, greater awareness of the possible presence of chronic kidney disease and of its complications among providers and affected patients, decreased use of the nondominant arm for blood drawings, and timely referral of appropriate patients to nephrologists may also improve the chances that arteriovenous fistulas can be created early enough to be available for hemodialysis when needed. But there is still a long and treacherous journey ahead until the day we might be able to say that vascular access used to be the Achilles’ heel of hemodialysis.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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A Critic’s Assessment of Our Approach to Cardiac Arrest

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In this issue of the Journal, Weisfeldt et al. report that ventricular fibrillation is identified less frequently during sudden cardiac arrest in the home than in public places, even when the arrest is witnessed. The authors surmise that age and coexisting illnesses are responsible and that the location of sudden cardiac arrest may be a surrogate for underlying disease severity. In addition, poorer outcomes were observed with use of the automated external defibrillator (AED) in the home, as compared with public AED use. The authors conclude that perhaps AEDs should be reserved for public locations and cardiopulmonary resuscitation (CPR) should be taught more broadly, as the better path to improving survival from sudden cardiac arrest. This research is controversial in several respects.

Does this study really show that ventricular fibrillation in sudden cardiac arrest occurs less often in the home than in public? Without electrocardiographic (ECG) data regarding the onset of the event, we cannot know for certain. What we do know is that untreated ventricular fibrillation will deteriorate to asystole over a period of minutes, and probably more rapidly in patients with more advanced cardiac disease; after 25 minutes, nearly all patients are in asystole. Although primary bradyarrhythmias as the cause of sudden cardiac arrest are becoming more common, most instances of bradycardia — specifically asystole — follow ventricular fibrillation. These considerations alter the interpretation of the findings that Weisfeldt et al. report. If the home rescuer takes just 60 seconds longer to call 911, as compared with the public witness, then the findings could be explained simply as a matter of response speed. The Home Use of Automated External Defibrillators for Sudden Cardiac Arrest trial (NCT00047411) showed that spouses confronted with the sudden collapse of a loved one commonly exhibit emotional distress and confusion, thus delaying an effective response.

How much time actually elapses between witnessing and assessing the collapse and dialing 911? Does this interval differ between the home and the public setting? Does it differ between those who have CPR training and those who do not? Knowing the answers to these questions has broad implications. The greater number of bystanders who witness sudden cardiac arrest in public makes calling 911 more likely to occur closer to the time of collapse. Moreover, those who have completed CPR courses know that they should call 911 promptly. Because seconds matter, even a modest delay in the 911 call could lead to differences in outcome. Consequently, the lone rescuer at home, who is probably less aware of the critical importance of speed, would lose the race to a public bystander.

What about AED use in the home? Certainly, at present, no grounds exist to broadly promote publicly financed home AEDs. However, this policy assessment should not dissuade persons from purchasing their own AEDs. The dismissal of home AEDs is premature, and other than the personal expense, there is no known downside from such a purchase. Moreover, some home rescuers do indeed act quickly and can save a life. Perhaps the presence of ECG monitoring technologies in the home would prompt a more rapid response and shave off valuable seconds to minutes, improving outcomes of arrests at home.

As an alternative to a home AED, the increased use of CPR does not make sense to me. At best, CPR represents a placeholder. Overall survival rates remain poor, and 300,000 sudden cardiac deaths still occur annually in spite of national CPR awareness. One simple reason for such gloomy results may be the logistic impossibility of responding to a broadly disseminated, quasirandom event that causes death within minutes. Yet there may be another, more subtle reason for this bleak lack of progress. If CPR were a drug or a surgical procedure, its value would be tested prospectively, but it has not


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