Why Aren't There More Effective Therapies for Dialysis Vascular Access Dysfunction?

Collaboration and a precision medicine approach could be the keys to improving dialysis vascular access care.

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Dialysis is the lifeline for patients with end-stage renal disease, and vascular access dysfunction is its "Achilles heel." Although arteriovenous fistulas (AVFs) are the preferred mode of permanent dialysis vascular access, AVF maturation failure (ie, the inability of the AVF to develop adequate blood flow or sufficient diameter to support hemodialysis) is a significant problem, as more than 50% of AVFs fail to mature.[1]

In many instances, AVF maturation failure is characterized by a perianastomotic venous stenosis. This often necessitates multiple endovascular and surgical procedures that increase both patient morbidity and cost. More importantly, AVF maturation failure often results in prolonged use of tunneled dialysis catheters with all of their attendant risks of infection, thrombosis, and central vein obstruction. In marked contrast, arteriovenous grafts (AVGs) often function well initially, but are plagued by late development of a fairly reproducible stenosis at the graft-vein anastomosis, which also requires multiple interventions, resulting in an unassisted primary patency rate of only 23% at 1 year.[2] In both instances, AVF and AVG stenoses are thought to be due to aggressive neointimal hyperplasia in combination with a lack of outward remodeling or potentially some inward/negative remodeling.[3]

Despite the magnitude of the clinical problem and the fact that we have a reasonable understanding of the biology of dialysis access stenosis, effective therapies for this important clinical problem are lacking. Indeed, our current standard of care for dialysis access stenosis is balloon angioplasty, which may in fact be partly responsible for the aggressive restenosis that we see in hemodialysis patients, as angioplasty causes endothelial and smooth muscle cell injury and therefore could exacerbate neointimal hyperplasia.

The following sections examine the reasons for the unacceptable current state of affairs.

A MULTIDISCIPLINARY PROBLEM IN SEARCH OF A MULTIDISCIPLINARY SOLUTION

By definition, dialysis vascular access is a multidisciplinary issue that can likely only be addressed through a multidisciplinary approach. Thus, the different stakeholder groups involved in dialysis vascular access care include surgeons (general, transplant, and vascular), interventional radiologists, nephrologists, nurses, technicians, and dialysis administrators. In addition to this broad swathe of individuals, I would argue that the patient's preferences, input from industry partners, and consensus with federal agencies (US Food and Drug Administration and Centers for Medicare & Medicaid Services) are also critical to the development of novel therapies and improved process of care pathways so that we can take better care of our patients with dialysis vascular access dysfunction.

LACK OF CONSENSUS ON CLINICAL TRIAL ENDPOINTS

An important reason for the current lack of targeted therapies for dialysis vascular access stenosis is that there is no consensus among the different specialties about

the appropriate clinical trial endpoints. From the radiologist's perspective, the demonstration of flow and a lack of postintervention residual stenosis are most important. However, from a surgeon's point of view, a lack of thrombosis is often the critical issue. For a nephrologist, the ability to dialyze patients through the access is essential. Moreover, it is almost certain that no one has asked patients about which aspects of their dialysis vascular access they consider most important. In an attempt to address this important gap, the Kidney Health Initiative[4] has instituted a project with the goal of bringing together all of the stakeholders in this issue in order to develop a set of consensus clinical trial endpoints for new therapies to enhance AVF, AVG, and tunneled dialysis catheter placement and maintenance.

THE URGENT NEED FOR PRECISION MEDICINE

We currently employ a one-size-fits-all approach in dialysis vascular access, particularly with regard to the fistula-first concept, as well as the use of angioplasty for dialysis access stenosis. I believe that as we move toward the future, we will need to embrace the concept of individualization of care, with patients receiving the types of vascular access that are best suited for them. This decision should be based on clinical, demographic, and biological criteria. With regard to the latter, we are confident that the rapid advances in genomics, metabolomics, and proteomics will allow us to develop predictors for AVF success or failure, for example.

CONCLUSION

In summary, I strongly believe that a collaborative, interactive, and consensus-building approach that embraces precision medicine concepts is the only way to improve dialysis vascular access care. Moreover, it is likely that the current transition from a volume-based health care system to one that recognizes added value above all else will be a powerful trigger for the rapid adoption of such a diagnostic and therapeutic paradigm. ■

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