The Sisyphean Task of Getting the Arteriovenous Fistula to Mature

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Dialysis access literature is full of allegories borrowed from Greek mythology—names of Achilles, Hercules, and Pandora have been used to describe many challenges encountered by nephrologists. Following this tradition, we add the study by Diep et al. to the list of publications dedicated to the disentanglement of factors hindering our efforts to create a perfect vascular access for dialysis—a truly Sisyphean task.

Dialysis access failure remains a significant barrier to providing adequate RRT. Autologous arteriovenous fistula (AVF) placement is the preferred access modality for most patients when developing an “ESKD Life Plan,” given the well-documented benefits compared with tunneled vascular catheters (TVC), including lower bloodstream infections, decreased morbidity and mortality, and higher dialysis blood flow rates (1). In the United States, 80% of patients on incident hemodialysis rely on TVC use, with almost half of patients dependent on AVF at 6 months (1). Reasons for the lower use of AVF as access for dialysis include difficulty in predicting kidney failure trajectories, and delays in referral to nephrology and vascular specialists, compounded by patient acceptance and personal experiences. In patients who do receive an AVF, 60% have primary failure and additional 20% have secondary failure within the first 12 months of use (2,3).

In large retrospective studies, central venous catheter use, including TVCs, is associated with increased primary failure and delayed AVF maturation (4). These outcomes are thought to result from the direct injurious effects of a vascular catheter on the adjacent blood vessel. A number of important characteristics of the vascular catheter affect the risk of endothelial damage, which may increase the risk of either delayed maturation or primary failure of an AVF (Table 1). One limitation of the previously mentioned studies is the lack of granularity—they frequently do not identify the location of the TVC and have high risk for confounding bias, given that TVC are also associated with increased mortality in the context of severity of illness, frailty, poor access to medical care, and more (4,8).

In this issue, Diep et al. report their single-center retrospective analysis to determine the effects of TVC laterality on an upper-limb AVF functionality at 6 and 12 months (9). As expected, the No TVC group had higher AVF function compared with TVC at both time points. Within the TVC group, performance of AVF placed contralateral to TVC was superior to ipsilateral AVF placement, but this effect lost statistical significance by 12 months. Their data suggest that ipsilateral TVC placement is associated with delayed AVF maturation, a divergent finding from previous studies, which showed similar 6-month primary failure rates in these patient groups (10–12). An important consideration in explaining these differences is the heterogeneity in definitions used when describing successful AVF cannulation or AVF maturation, with Diep et al. using the closest definition to the Kidney Health Initiatives’ recommendations (Table 2). Additionally, in contrast to previous papers, the authors did not separately classify nonmaturation and primary failure rate, because of the small number of patients (3%) with secondary AVF failure, which is considerably lower compared with other studies (2). Strengths of this study include a well-distributed and representative patient population in terms of demographics, comorbidities, and etiology of ESKD, and a low drop-out rate in the TVC group at 6 months.

Diep et al. make note of their sample-size limitations, a problem shared by similar studies cited in their paper and here, which may account for some of the discrepancy noted in their primary analysis. All relevant studies (10–12) are retrospective, with heterogeneous populations with regard to known risk factors of AVF failure, including race, age, and sex representation, along with country of origin (6). Kim et al. mention a sample size of 166 patients needed to detect a 15% decrease in maturation rate with 90% power, suggesting 83 patients (assuming equal ipsilateral and contralateral division) would be needed in the ipsilateral TVC group, a number not achieved by any study (11). A much larger sample size would be beneficial in deducing if the inferiority of ipsilateral TVC is, in fact, related to the unfavorable left-sided positioning of the internal jugular (IJ) TVC. The need to place a left IJ TVC would suggest the patient has remained catheter dependent and has required multiple catheters, while waiting for AVF surgery, and possibly even had a catheter-related bloodstream infection. Left IJ TVC make up a larger percent of the ipsilateral TVC group compared with contralateral in the study, where left TVC have a longer catheter...
In summary, Diep et al. present data that highlight the interesting association of ipsilateral TVC and increased likelihood of AVF failure at 6 months, this time in the Australian region. They offer a more global outlook on what the practicing nephrologist can expect at 6 and 12 months after AVF creation, which can aid in patient counseling. Additionally, the authors were able to document the association of increased TVC duration with lower AVF function. Finally, this study highlights the need for prospective analysis of large sample sizes of TVC presence with AVF using standardized definitions to better help patients delineate an accurate ESKD Life Plan. However, the challenges of conducting a pragmatic study in this heterogenous population may remain a Herculean task.

Table 1. Catheter characteristics associated with higher rates of vascular damage or fistula nonmaturation (4–7)

| Catheter Attribute | Vascular Association |
|--------------------|----------------------|
| Location           | • Higher rate of vein stenosis with subclavian compared with IJ location<br>• Left IJ with more angulated course to atrium and more contact to lateral wall of superior vena cava promoting endothelial injury |
| Length             | • Right IJ catheter length shorter than left IJ catheter<br>• PICC placement with increase in thrombosis and central venous stenosis rates<br>• Femoral TVC are longer, potentially increasing the risk of endothelial injury |
| Luminal size       | • Larger TVC crowd the central vein lumen leading to endothelial injury and thrombosis<br>• Endovascular cardiac devices and PICC increase central venous stenosis and thrombosis |
| Duration           | • Longer duration of catheter associated with lower AVF maturation |
| Infection risk     | • Nontunneled central venous catheters have high rates of infection, which increase sclerosis and thrombosis<br>• Antimicrobial-coated catheters do not consistently lower infection rates despite increased cost |
| Imaging device     | • Ultrasound and fluoroscopy use during placement reduces the number of cannulation attempts and reduce malposition of catheter or its tip |
| Number of catheters| • Risk of central venous stenosis increases with total number of central catheters placed during a lifetime |

IJ, internal jugular; PICC, peripherally inserted central catheter; TVC, tunneled vascular catheter; AVF, arteriovenous fistula.

Table 2. Heterogeneity in definitions used for successful cannulation and maturation of arteriovenous fistulas in literature

| Reference | Definition |
|-----------|------------|
| AVF maturation | Duplex ultrasound showing ≥4 mm minimum access-vessel internal diameter and access blood flow ≥5000 ml/min (Rule of 6s): At 6 weeks after surgery, blood flow 600 ml/min, location 6 mm from skin surface with a diameter ≥6 mm and palpable thrill in fistula vein |
| KHI (13) | Hemodialysis with two needles for ≥75% of dialysis sessions within 4-week period |
| Kim et al., 2019 (11) | Two needles for ≥50% of hemodialysis over 2-week period |
| Functional cannulation | Three consecutive hemodialysis sessions (two needles, dialysis blood flow ≥250 ml/min) |
| KHI (13) | One successful hemodialysis with both cannula |
| Diep et al., 2021 (9) | Four consecutive dialysis sessions |
| Shingarev et al., 2012 (10) | |
| Kim et al., 2019 (11) | |
| Ozpak and Yilmaz, 2019 (12) | |

AVF, arteriovenous fistula; KHI, Kidney Health Initiative.

Disclosures

T. J. Vachharajani reports being a scientific advisor or member of the Editorial Boards of the Indian Journal of Nephrology, Journal of Vascular Access, Kidney International Reports, and Seminars in Dialysis, an Associate Editor of Frontiers in Nephrology (Blood Purification Section), Member of the North American Regional Boards of International Society of Nephrology, and Editor-in-Chief of The Open Urology and Nephrology Journal; and reports other interests/relationships with the International Board of Directors AVATAR Foundation, India. All remaining authors have nothing to disclose.

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K. Bartolomeo was responsible for the visualization and wrote the original draft; R. Shingarev and T. Vachharajani were responsible for the conceptualization and provided supervision; all authors reviewed and edited the manuscript.

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