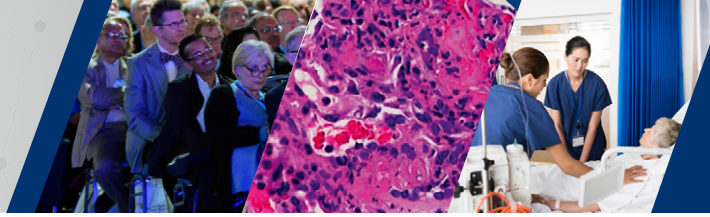

A Patient with Hemodialysis Access Problems

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Case History

A 55-year-old right-handed waitress with ESKD secondary to GN had been receiving hemodialysis for 4 years. She initiated dialysis urgently with a right internal jugular catheter. Because of her active ulcerative colitis, peritoneal dialysis is contraindicated. A left snuffbox arteriovenous fistula was created; however, it failed to mature and thrombosed shortly thereafter. An attempted thrombolysis was unsuccessful, as was a subsequent left wrist radio-cephalic fistula. A right radio-cephalic fistula was then created.

Question 1

After arteriovenous fistula creation, which of these statements is correct regarding successful maturation?

A. Ultrasound measurements at 2 weeks may help identify fistulas that are unlikely to mature.
B. Physical examination of the fistula may identify inflow stenosis but not outflow stenosis.
C. Infrared thermal imaging is unhelpful in predicting fistula maturation.

Discussion of Question 1

The correct answer is A. Although national guidelines recommend fistulas in all eligible patients, a major limitation is their high primary failure rate, with consequent prolonged catheter-dependence and potentially multiple intervention attempts to salvage them.

Dysfunctional fistulas caused by stenosis can be accurately detected and localized by physical examination, as evidenced by Asif *et al.* (1), with sensitivities and specificities for outflow stenosis (collapse) and inflow stenosis (augmentation) of 92% and 86%, and 85% and 71%, respectively. Thus, option B is incorrect.

A multicenter, prospective, observational study (2) performed ultrasounds in 602 fistulas preoperatively, and at 1 day, 2 weeks, and 6 weeks postcreation. Early 2-week postcreation ultrasound measurements of vessel flow and diameter may help identify fistulas that fail to mature: 77% forearm and 70% upper arm fistulas maintained >85% of their 2-week flows at 6 weeks postcreation. Specifically, 69%, 89%, and 97% with fistula blood flows (Qas) of 500–750, 750–1000, and ≥1000 ml/min at 2 weeks, respectively, maintained a fistula flow of ≥500 ml/min at 6 weeks. Additionally, 94% of upper arm veins with a diameter ≥0.4 cm at 2 weeks maintained it at 6 weeks. Thus, option A is correct.

Beyond standard physical examination and ultrasound, novel use of infrared thermal imaging has been shown to help predict fistula maturation in a prospective study of 100 consecutive patients (3), thus option C is incorrect. After fistula creation, hemodynamic reductions in blood flow and perfusion occur distal to the anastomosis before complete arterial remodeling. The accompanying skin temperature drop may predict subsequent fistula patency and maturation. Thermal images of both arms were captured by a portable thermal camera at baseline (preoperatively and within 30 minutes postoperatively) and at 6 weeks postcreation to evaluate primary patency and functional maturation. Infrared thermal imaging had an 88% positive predictive value and 86% negative predictive value in determining primary patency, and an 84% positive predictive value and 95% negative predictive value in determining functional maturation. Portable thermal imaging may be a complementary tool to help predict early fistula failure and warrants further evaluation.

Case Continued

The patient was asymptomatic and received adequate, complication-free dialysis through her fistula. On routine surveillance with ultrasound dilution (transonic flow measurement), her Qa decreased from 980 to 850 ml/min.

Question 2

What is the best next step in this patient?

A. Refer to a surgeon for a surgical revision.
B. Refer to an interventionalist for an angioplasty.
C. Do not intervene because there are no associated clinical abnormalities.
D. Check that the transonic machine was properly calibrated to determine Qa.

Discussion of Question 2

The correct answer is C. Access stenotic lesions undergo aggressive preemptive treatment to assist

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maturation, and to maintain patency. However, these repeated interventions may have deleterious effects on long-term access outcomes.

In a 3-year observational cohort study of 173 patients with new fistulas (4), those with two or more versus one versus no interventions for fistula maturation had cumulative survivals of 68%, 78%, and 92% at 1 year, and required 3.51, 1.37, and 0.76 interventions, respectively, to maintain patency. This suggests fistulas with intervention-assisted maturation have decreased cumulative survival and require more interventions to maintain patency than those without intervention-assisted maturation. Also, Harms *et al.* studied 289 fistulas and 310 grafts created over 5 years, to determine the effect of interventions before successful cannulation on access longevity (5). An intervention before successful cannulation was more frequently required in fistulas than grafts, and both accesses that required interventions had shorter secondary patency after successful cannulation.

A systematic review and meta-analysis compared access surveillance and preemptive correction of stenosis to routine clinical monitoring and deferred salvage (6) and found preemptive intervention did not improve access longevity. One explanation is that endovascular interventions induce endothelial injury and aggressive neointimal hyperplasia, notable by increased, progressive cellular proliferation activity in restenotic fistula lesions compared with nonintervened upon primary stenotic lesion (7). Alternatively, fistulas requiring intervention may have been created from inadequate vessels, leading to poor outcomes. These associations require further study to determine the risk/benefit of such procedures on access longevity. Until such time, arteriovenous access should not be intervened upon without associated clinical abnormalities.

A patient should be referred for further access evaluation and possible intervention only in the presence of abnormal physical examination or dialysis clinical indicators such as extremity swelling, abnormal access thrill/bruit, prolonged bleeding after decannulation, inadequate dialysis with no other cause, *etc.* In other words, findings on clinical monitoring are primary indicators whereas those found on surveillance are supportive; supportive surveillance findings in a fistula are an absolute Qa$\leq$450 ml/min or a 25% decrease from baseline. Thus, given that this patient was asymptomatic, referring to a surgeon (option A) or interventionalist (option B) is incorrect. Equipment used on patients should be checked and calibrated before use, not after; thus option D is incorrect.

Case Continued

She remained asymptomatic for another year, but progressively required longer time to achieve hemostasis after dialysis, and her clearance decreased. Her nephrologist referred her to an interventionalist for further evaluation and her symptoms resolved after angioplasty of a tight outflow stenosis. However, her symptoms recurred repeatedly and each successive intervention was within a shorter time period. Over the next 2 years, she required multiple procedures before the fistula thrombosed and was abandoned. She became increasingly frustrated with her poor access experience and suffered "surgical fatigue." She refused long-term catheter use because she was aware of the increased infection risk. She asks whether there are other options for vascular access without the need for further open surgery.

Question 3

Which is the correct response for this patient who refuses open surgery?

A. There are no other options to create an arteriovenous access, open surgery is required.
B. There is another option to create a fistula without open surgery.
C. There is another option to create a graft without open surgery.
D. Bioengineered vessels provide another conduit for vascular access without open surgery.
E. Options B and C are correct.

Discussion of Question 3

The correct answer is E. New technology, and the ability to manipulate local factors that may affect maturation and creation of an arteriovenous access have advanced its management and creation possibilities beyond open surgery, supporting option E and invalidating option A. For example, a pilot study of nine patients evaluated the 6-month procedure success, patency, and safety of endovascularly implanted connector systems that allowed for minimally invasive creation of arteriovenous grafts (8). Three patients dropped out for device-unrelated reasons. The remaining six patients had patent grafts: two with assisted and four with unassisted patency, with flow rates $>$1 L/min. There were no device-related major adverse events. A larger study is ongoing.

In terms of arteriovenous fistulas, a prospective, multicenter, single-arm trial enrolled 107 patients in whom 102 proximal radial artery to perforating vein fistula were created under ultrasound guidance using a thermal resistance anastomosis device (9). Cumulative patency was 86.7% and functional patency was 92.3% at 360 days, although a large number of secondary maturation procedures were required, including anastomotic balloon dilation (72%), brachial vein embolization (32%), cubital vein ligation (31%), and surgical transposition (26%).

Using different technology, another trial enrolled 60 patients in whom endovascular arteriovenous fistula between the ulnar artery and ulnar vein were created with magnetic catheters using radiofrequency energy (10). Cumulative patency was 84% at 1 year, and functional patency was 64% in those patients who received dialysis. These endovascular arteriovenous fistula required substantially fewer interventions to facilitate and maintain patency compared with fistulas created with open surgery. Serious procedure- or device-related adverse events (8.3%) are now mitigated by updated technology.

Lastly, option D is incorrect as bioengineered human acellular vessels require surgical implantation, as demonstrated in a phase two, single-arm trial (n=60) (11). Human vascular smooth muscle cells, cultured on a biodegradable polymer, were decellularized, although extracellular

matrix proteins and the mechanical properties of the access were retained. The initial results suggest that the human acellular vessels were safe, durable as a hemodialysis conduit, well tolerated, and had no significant immunogenic potential. Primary patency at 12 months was 28% and secondary patency 89%. Phase three trials are ongoing.

These novel devices and vessels, although not currently approved for use in the United States, may eventually lead to a paradigm shift in vascular access creation. Having a range of vascular access creation and management options is necessary to individualize vascular access care to achieve positive outcomes for patients on dialysis.

Acknowledgments

For most American Society of Nephrology (ASN) Kidney Week attendees, case-based clinical nephrology talks are one of the most exciting venues. The Nephrology Quiz and Questionnaire (NQ&Q) is the essence of clinical nephrology and represents what drew all of us into the field of nephrology. This year's NQ&Q in "The Big Easy" (city of New Orleans), with full-house attendance, was no exception. The expert discussants prepared vignettes of puzzling cases, which illustrated some topical, challenging, or controversial aspect of the diagnosis or management of key clinical areas of nephrology. These eight interesting cases were presented and eloquently discussed by our four expert ASN faculty. Subsequently, each discussant prepared a manuscript summarizing his or her case discussions, which serves as the main text of this article (Mark A. Perazella and Michael Choi, Comoderators).

Disclosures

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References

1. Asif A, Leon C, Orozco-Vargas LC, Krishnamurthy G, Choi KL, Mercado C, Merrill D, Thomas I, Salman L, Artikov S, Bourgoignie JJ: Accuracy of physical examination in the detection of arteriovenous fistula stenosis. *Clin J Am Soc Nephrol* 2: 1191–1194, 2017
2. Robbin ML, Greene T, Cheung AK, Allon M, Berceli SA, Kaufman JS, Allen M, Imrey PB, Radeva MK, Shiu YT, Umphrey HR, Young CJ; Hemodialysis Fistula Maturation Study Group: Arteriovenous fistula development in the first 6 weeks after creation. *Radiology* 279: 620–629, 2016
3. Al Shakarchi J, Hodson J, Field M, Inston N: Novel use of infrared thermal imaging to predict arteriovenous fistula patency and maturation. *J Vasc Access* 18: 313–318, 2017
4. Lee T, Ullah A, Allon M, Succop P, El-Khatib M, Munda R, Roy-Chaudhury P: Decreased cumulative access survival in arteriovenous fistulas requiring interventions to promote maturation. *Clin J Am Soc Nephrol* 6: 575–581, 2011
5. Harms JC, Rangarajan S, Young CJ, Barker-Finkel J, Allon M: Outcomes of arteriovenous fistulas and grafts with or without intervention before successful use. *J Vasc Surg* 64: 155–162, 2016
6. Ravani P, Quinn RR, Oliver MJ, Karsanji DJ, James MT, MacRae JM, Palmer SC, Strippoli GF: Preemptive correction of arteriovenous access stenosis: A systematic review and meta-analysis of randomized controlled trials. *Am J Kidney Dis* 67: 446–460, 2016
7. Chang CJ, Ko PJ, Hsu LA, Ko YS, Ko YL, Chen CF, Huang CC, Hsu TS, Lee YS, Pang JH: Highly increased cell proliferation activity in the restenotic hemodialysis vascular access after percutaneous transluminal angioplasty: Implication in prevention of restenosis. *Am J Kidney Dis* 43: 74–84, 2004
8. Ebner A, Ross JR, Setum CM, Kallok MJ, Yevzlin AS: Transcatheter anastomosis connector system for vascular access graft placement: Results from a first-in-human pilot study. *J Vasc Access* 17: 111–117, 2016
9. Hull JE, Jennings WC, Cooper RI, Waheed U, Schaefer ME, Narayan R: The pivotal multicenter trial of ultrasound-guided percutaneous arteriovenous fistula creation for hemodialysis access. *J Vasc Interv Radiol* 29: 149–158.e5, 2018
10. Lok CE, Rajan DK, Clement J, Kiaii M, Sidhu R, Thomson K, Buldo G, Dipchand C, Moist L, Sasal J; NEAT Investigators: Endovascular proximal forearm arteriovenous fistula for hemodialysis access: Results of the prospective, multicenter Novel Endovascular Access Trial (NEAT). *Am J Kidney Dis* 70: 486–497, 2017
11. Lawson JH, Glickman MH, Ilzecki M, Jakimowicz T, Jaroszynski A, Peden EK, Pilgrim AJ, Prichard HL, Guziewicz M, Przywara S, Szmidt J, Turek J, Witkiewicz W, Zapotoczny N, Zubilewicz T, Niklason LE: Bioengineered human acellular vessels for dialysis access in patients with end-stage renal disease: Two phase 2 single-arm trials. *Lancet* 387: 2026–2034, 2016

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