Kidney Medicine

Arteriovenous Fistula Histology, Hemodynamics, and Wall Mechanics: A Case Report of Successful and Failed Access in a Single Patient

Hannah Northrup, Yong He, Scott Berceli, Alfred K. Cheung, and Yan-Ting Shiu

The low 1-year patency rate of mature arteriovenous fistulas (AVFs) remains a significant clinical problem. Although vessel properties and biomechanics have been suggested to affect AVF function, understanding their roles in AVF patency failure is challenging owing to the heterogeneity within the patient population, including demographics and comorbid conditions. In this study, we present a case of a patient with 2 upper-arm AVFs with different 1-year patency outcomes and investigate whether they had different histologic features before the AVF creation surgery and biomechanics at 1 day and 6 weeks after the AVF creation surgery using magnetic resonance imaging–based fluid structure interaction simulations. Despite both AVFs being in the upper arm, created <1 year apart by the same surgeon, and having similar preoperative vessel diameters, the 1-year patent AVF had less preoperative intimal collagen and higher wall shear stress 1 day after AVF creation, when compared with the AVF that failed by 1 year. Thus, a low intimal collagen content before the AVF surgery and higher wall shear stress immediately after the AVF creation surgery may be important for long-term AVF patency and should be investigated with larger cohorts.

Complete author and article information provided before references.

Correspondence to Y.T. Shiu (y.shiu@hsc.utah.edu)

Kidney Med. 6(4):100801. Published online February 19, 2024.

doi: 10.1016/j.xkme.2024.100801

INTRODUCTION

The arteriovenous fistula (AVF) is the preferred vascular access for maintenance hemodialysis owing to its lower infection rates,[1] risk of thrombosis,[2] and overall decreased morbidity[1] compared with alternatives. However, many AVFs fail to mature,[3,4] and the 1-year failure rate for mature AVFs remains unacceptably high (up to 45%).[5]

A challenge for understanding the pathogenesis of AVF failure and for developing AVF therapies is the heterogeneous hemodialysis patient population. Patients referred for AVF creation often have multiple comorbid conditions in addition to advanced kidney disease.[6] In this study, we present a case in which a patient underwent 2 upper-arm AVF creation surgeries with opposing 1-year patency results, 1 failed and 1 successful. From both AVFs, we obtained operative vein samples for histology and postoperative magnetic resonance images at 1 day and 6 weeks for biomechanical simulation analysis (Fig 1A).

CASE REPORT

Before recruitment, a Hispanic man in his 50s with kidney failure and diabetes had been treated with dialysis through a brachiocephalic AVF in the left upper arm. One year after the first cannulation, this AVF failed owing to thrombosis, and the patient was switched to a catheter. This patient was recruited for this research study while waiting for a new AVF creation surgery and provided written consent for all procedures. The University of Utah institutional review board approved the study protocol. Detailed methods, including surgeries and simulations are provided in Item S1.

One month after being on dialysis through a catheter, the patient underwent a 1-stage brachiobasilic AVF creation surgery in the left upper arm. During the surgery, the basilic vein was completely mobilized and tunneled for transposition. Standard-of-care preoperative vascular ultrasound mapping of the left basilic vein showed a diameter range of 3.5-4.3 mm, and the left brachial artery diameter was 4 mm. A standard-of-care 6-week postoperative ultrasound showed that the AVF had an average flow volume of 1,157 mL/min. The AVF was first used for hemodialysis 3.5 months after its creation. Prompted by a decreased blood flow, a fistulogram was performed 5 months following the initial creation, identifying a stenosis at the transition between the fistula's mobilized and nonmobilized segments (swing zone). Angioplasty of this region was performed with a good anatomic result. At 7 months, a reduced AVF flow again prompted a fistulogram, demonstrating recurrent stenoses in the swing zone and a de novo stenosis in the AVF 1 cm downstream from the anastomosis. Angioplasty of these regions was again performed with an acceptable result. At 12 months, AVF dysfunction prompted a third fistulogram, revealing a significant stenosis in the vein downstream of the swing zone, which was treated with angioplasty. Two days following this intervention, the AVF thrombosed and was abandoned.

The patient underwent a right brachiocephalic AVF creation surgery 2 months following the abandonment of the left brachiobasilic AVF by the same surgeon. Preoperative vascular mapping showed that the cephalic vein diameter ranged from 2.4-4.5 mm, and the brachial artery diameter was 4.8 mm. A 6-week postoperative ultrasound showed that the AVF had an average flow rate of 1,233 mL/min. Dialysis using the AVF was initiated 3.5 months after creation. The AVF underwent

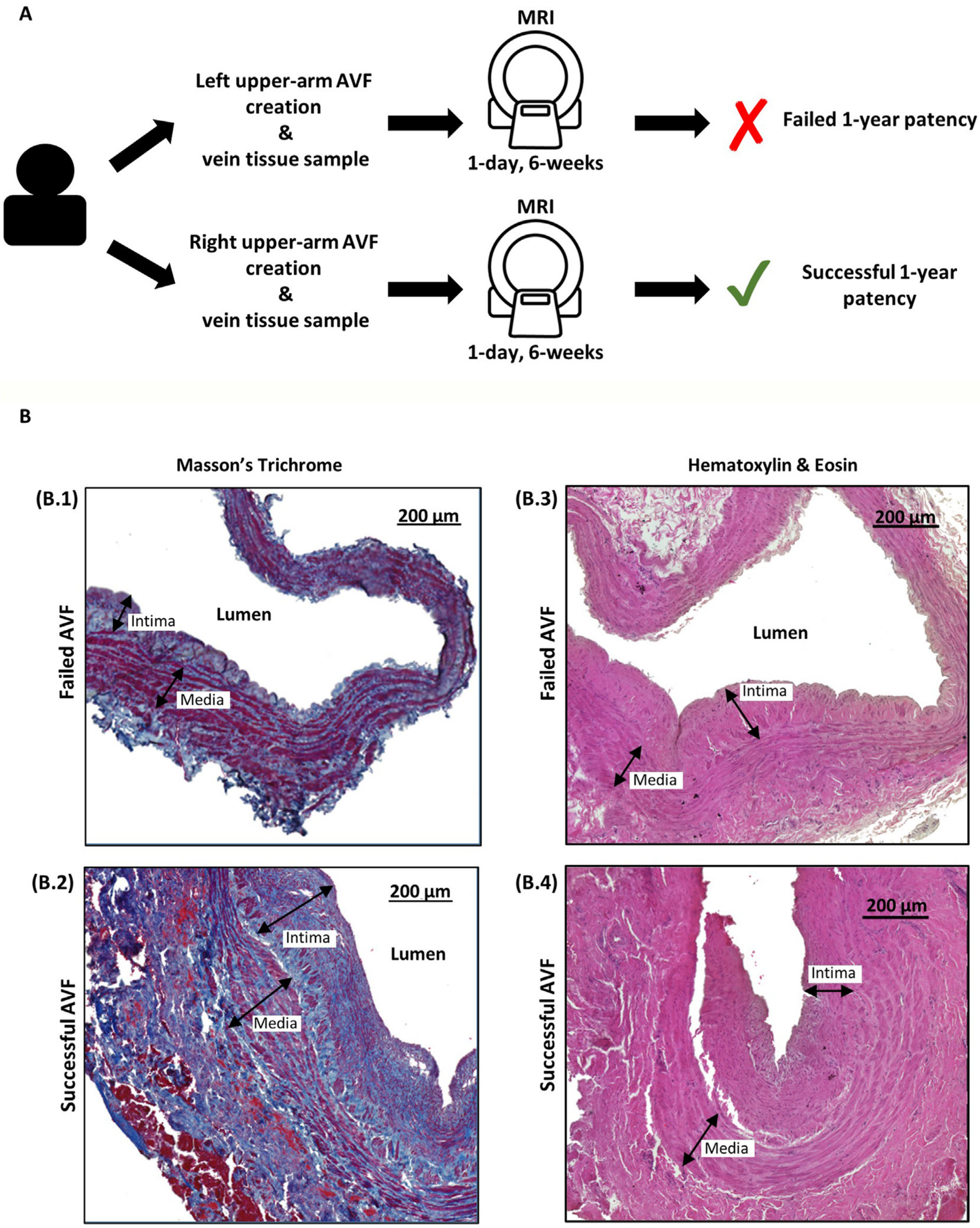

Figure 1. (A) Study design. (B) Preoperative vein samples of the failed and successful AVF showing (B.1 and B.2) Massons trichrome– and (B.3 and B.4) hematoxylin and eosin–stained images, with lumen, intimal, and medial layers labeled. Abbreviations: AVF, arteriovenous fistula; MRI, magnetic resonance image.

angioplasty 3.4 years after creation and continued to be the primary access until the patient's death 5 years after AVF creation.

In the histology analysis of the native (preoperative) veins, the failed and successful AVFs had an intimal area of 0.18 mm^2 and 3.08 mm^2, respectively. Masson's trichrome staining showed that the failed AVF vein had more collagen in the intima than the successful AVF (72% vs 55%), whereas collagen in the medial layer was similar between the 2 vessels (42% vs 47%) (Fig 1B.1 and B.2). Hematoxylin and eosin staining showed cellularized intimal hyperplasia in both vessels (Fig 1B.3 and B.4).

The average cross-sectional area at 1 day was 21.03 and 28.80 mm^2 for the failed (left) and successful (right) AVF, respectively. From 1 day to 6 weeks, the cross-sectional area in the failed AVF increased by 42% to 29.96 mm^2, and the cross-sectional area in the successful AVF increased by 60% to 45.95 mm^2 (Fig 2A). In terms of blood flow parameters, when values were averaged over the length of the AVF vein, the failed AVF had smaller values than the successful AVF at

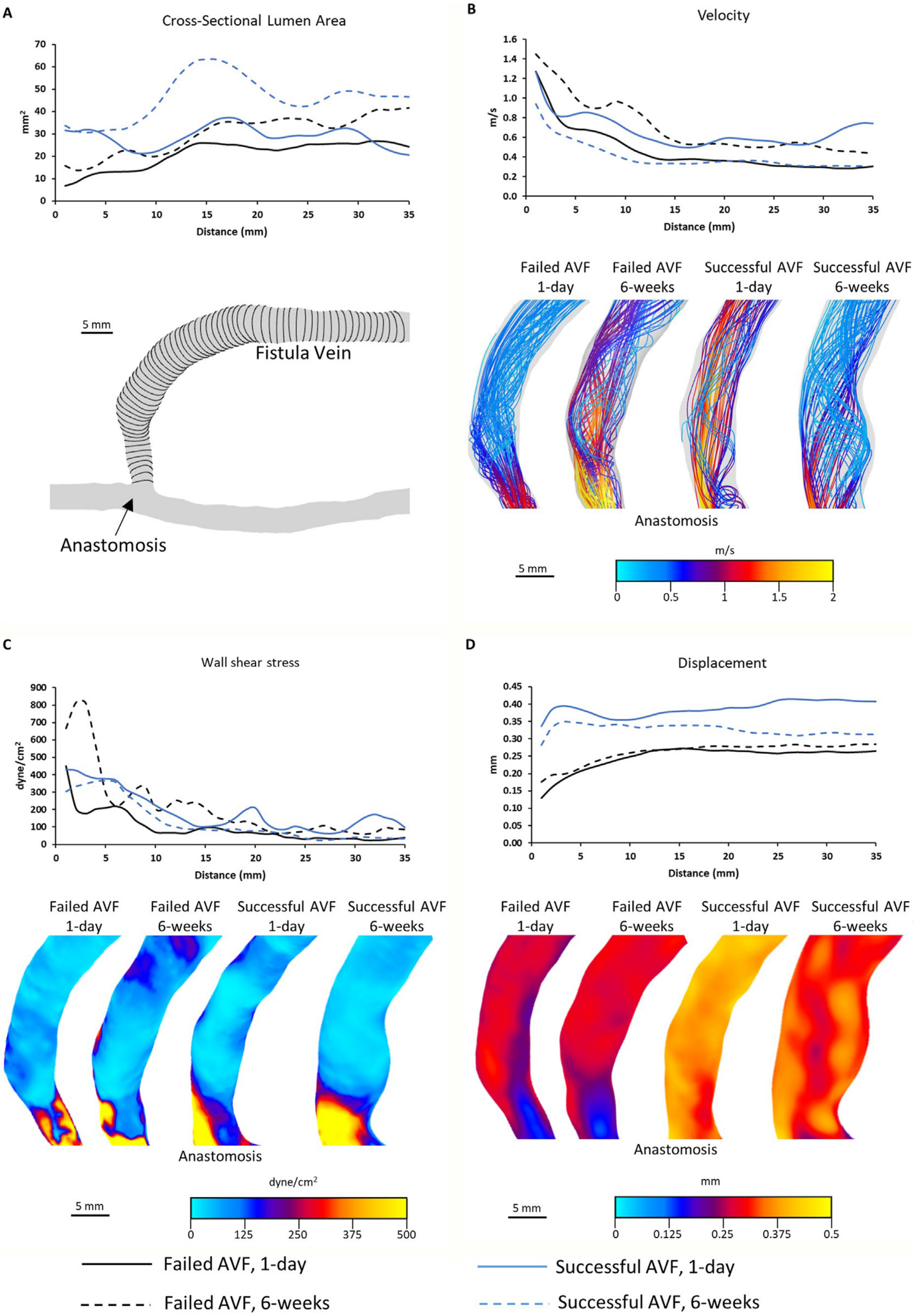

Figure 2. Hemodynamic and wall mechanics of the failed AVF and the successful AVF at 1 day and 6 weeks after the AVF creation surgery. (A) Cross-sectional area based on the distance away from anastomosis. The image below shows the slice location from which data were extracted for panels A-D. (B) Velocity magnitude, (C) wall shear stress, and (D) wall displacement based on the distance away from anastomosis and respective color maps of the fistula vein. Data and color maps are averaged over a cardiac cycle. Abbreviation: AVF, arteriovenous fistula.

1 day for velocity (0.46 vs 0.67 m/s) and wall shear stress (93.2 vs 187.0 dyne/cm^2) (Fig 2B-D). From 1 day to 6 weeks, however, these values increased in the failed AVF (percent change in velocity: 51%; wall shear stress: 128%) and decreased in the successful AVF (percent change in velocity: −39%; wall shear stress: −32%). By 6 weeks, the values of velocity and wall shear stress were larger for the failed than the successful AVF (velocity: 0.70 vs 0.40 m/s; wall shear stress: 212.9 vs 127.9 dyne/cm^2). Velocity and wall shear stress values were the highest near anastomosis in both AVFs (Fig 2B-D; Fig S1A and B).

For biomechanical parameters, wall displacement was higher for the successful than the failed AVF at both 1 day and 6 weeks throughout the AVF, with average values of 0.39 and 0.25 mm at 1 day and of 0.33 and 0.26 mm at 6 weeks for the successful and failed AVF, respectively. From 1 day to 6 weeks, the successful AVF decreased by 16%, whereas the failed AVF increased by 6%. As shown in the contour plots, the successful AVF at 1 day had the most uniform displacement throughout the AVF (Fig 2D; Fig S2).

DISCUSSION

In this analysis of 2 fistulas from a single patient, we found that although both AVFs were in the upper arm, created only 1 year apart with similar preoperative ultrasound vein diameters, the failed AVF was more fibrotic perioperatively in the venous intimal layer and had lower wall shear stress and wall displacement at 1 day after the AVF creation surgery compared with the successful AVF.

At baseline, the successful AVF had a larger intimal hyperplasic lesion than the failed AVF. However, preexisting venous hyperplasia was not associated with AVF maturation failure in a large multicentered cohort study.[7] Indeed, magnetic resonance image–derived 3-dimensional reconstructions showed that the successful AVF had a larger lumen area than the failed AVF at both 1 day and 6 weeks. Thus, neither preoperative vein lumen diameters nor the magnitude of hyperplasia was predictive of fistula lumen enlargement.

In AVF literature, preoperative venous medial fibrosis was not associated with AVF nonmaturation,[8,9] but postoperative venous medial fibrosis in 2-stage AVFs was associated with nonmaturation.[8] This patient showed similar results with collagen content in the media of the failed and the successful AVF. However, the intima collagen percentage in the failed AVF was larger than that in the successful AVF. Previous studies did not investigate the association between intimal fibrosis and 1-year AVF patency. Therefore, our finding suggests a need to consider intimal fibrosis in AVF patency.

Initial high levels of wall shear stress may promote outward remodeling of the AVF,[10] whereas a long-term increase may indicate poor remodeling.[11] The failed AVF had lower wall shear stress than the successful AVF at 1 day, and wall shear stress in the failed AVF increased from 1 day to 6 weeks, indicating poor remodeling. In contrast, wall shear stress in the successful AVF was higher at 1 day and then decreased by 6 weeks. These trends agree with an ancillary study of Hemodialysis Fistula Maturation Consortium that showed that large wall shear stress at early time points was beneficial for AVF lumen expansion, and wall shear stress decreased with time.[12] However, this prior study[12] did not investigate 1-year patency or wall biomechanics. Should additional large cohort studies solidify the association between postoperative simulation–derived wall shear stress (or wall displacement) and long-term patency, simulations may be useful as a diagnostic tool to help predict the long-term clinical utility of the AVF.

The difference in patency between the 2 AVFs might also be because of the difference in the vein type. The failed AVF used the basilic vein, whereas the successful AVF used the cephalic vein. Although the 2 vessels have different lumen sizes, a 2009 study found no significant difference between the 2 AVF types in either primary or secondary patency.[13] Consequently, brachiocephalic and brachiobasilic AVFs are often studied as upper-arm AVF collectively. However, the angiograms of the failed AVF showed that the initial stenosis was located at the transition between the mobilized and nonmobilized segments of the fistula, a common site of stenosis in brachiobasilic AVFs.[14] With the basilic vein being deeper, it requires transposition with complete mobilization, whereas the more superficial cephalic vein does not.[13] The inherent differences in the native vein characters and surgical techniques may lead to varying hemodynamics and remodeling. Thus, the anatomy of the basilic vein and transposition required for AVF creation may be a precursor to juxta-anastomotic stenosis and be associated with the differences seen in the other parameters studied in this research. Additional research is needed to answer this question.

High 1-year AVF patency failure remains a significant clinical problem that is poorly understood with no effective treatments. By studying a single patient with a failed and a successful AVF, we uncovered potential associations that lay the groundwork for future larger cohort studies on specifically preoperative intimal fibrosis, surgical techniques, and postoperative vascular biomechanics in relation to AVF maturation and patency for improved clinical practices.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Figure S1: (A) Average velocity magnitude and (B) average wall shear stress color maps of the failed AVF at 1 day and 6 weeks, and successful AVF at 1 day and 6 weeks.

Figure S2: Displacement color maps of the failed AVF at 1 day and 6 weeks, and successful AVF at 1 day and 6 weeks.

Item S1: Detailed methods.

ARTICLE INFORMATION

Authors' Full Names and Academic Degrees: Hannah Northrup, PhD, Yong He, PhD, Scott Berceli, MD, PhD, Alfred K. Cheung, MD, and Yan-Ting Shiu, PhD.

Authors' Affiliations: Division of Nephrology and Hypertension, Department of Internal Medicine (HN, AKC, YTS), University of Utah, Salt Lake City, UT; Division of Vascular Surgery and Endovascular Therapy (YH, SB), University of Florida, Gainesville, FL; Malcom Randall Veterans Affairs Medical Center (SB), Gainesville, FL; and George E. Wahlen Veterans Affairs Medical Center (YTS), Salt Lake City, UT.

Address for Correspondence: Yan-Ting Shiu, PhD, Professor of Internal Medicine, Division of Nephrology and Hypertension, University of Utah, 30 N Mario Capecchi Driver, 3rd floor south, Salt Lake City, UT 84112. Email: y.shiu@hsc.utah.edu

Support: Dr Berceli has been supported by the following grants: NIH R01DK0887 and NIH R01DK119274. Dr Cheung has been supported by the following grants: NIH R01DK0887 and NIH R01HL06764. Dr Shiu has been supported by the following grants: VA 101BX004133, NIH R01DK100505, NIH R01DK129299, NIH R01DK121227, and NIH R01HL153244.

Financial Disclosure: The authors declare that they have no relevant financial interests.

Acknowledgments: The authors thank Timmy Lee for his advice; and Amani Oumar, Brayden Fairbourn, and Yuxia He for their work on histology.

Prior Presentation: This work has been published in part by The University of Utah ProQuest Dissertations Publishing as part of the first author Hannah Northrup's dissertation, "Effects of treatments on the geometry and vascular biomechanics of arteriovenous fistulas in rodents and patients" per PhD graduation requirements.

Patient Protections: The authors declare that they have obtained consent from the patient reported in this article for publication of the information about him/her that appears within this case report and any associated supplementary material.

Data Sharing: Requests to access the data sets should be directed to YTS, y.shiu@hsc.utah.edu.

Peer Review: Received May 15, 2023. Evaluated by 1 external peer reviewer, with direct editorial input from the Editor-in-Chief. Accepted in revised form November 12, 2023.

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