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Access-related hand ischemia and the Hemodialysis Fistula Maturation Study

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Objective: **Access-related hand ischemia (ARHI) is a major complication after hemodialysis access construction. This study was designed to prospectively describe its incidence, predictors, interventions, and associated access maturation.**

Methods: **The Hemodialysis Fistula Maturation Study is a multicenter prospective cohort study designed to identify predictors of autogenous arteriovenous access (arteriovenous fistula [AVF]) maturation. Symptoms and interventions for ARHI were documented, and participants who received interventions for ARHI were compared with other participants using a nested case-control design. Associations of ARHI with clinical, ultrasound, vascular function, and vein histologic variables were each individually evaluated using conditional logistic regression; the association with maturation was assessed by relative risk, Pearson χ^2 test, and multiple logistic regression.**

Results: **The study cohort included 602 participants with median follow-up of 2.1 years (10th-90th percentiles, 0.7-3.5 years). Mean age was 55.1 ± 13.4 (standard deviation) years; the majority were male (70%), white (47%), diabetic (59%), smokers (55%), and on dialysis (64%) and underwent an upper arm AVF (76%). Symptoms of ARHI occurred in 45 (7%) participants, and intervention was required in 26 (4%). Interventions included distal revascularization with interval ligation (13), ligation (7), banding (4), revision using distal inflow (1), and proximalization of arterial inflow (1). Interventions were performed ≤7 days after AVF creation in 4 participants (15%), between 8 and 30 days in 6 (23%), and >30 days in 16 (63%). Female gender (odds ratio, 3.17; 95% confidence interval, 1.27-7.91; $P = .013$), diabetes (13.62 [1.81-102.4]; $P = .011$), coronary artery disease (2.60 [1.03-6.58]; $P = .044$), higher preoperative venous capacitance (per %/10 mm Hg, 2.76 [1.07-6.52]; $P = .021$), and maximum venous outflow slope (per [mL/100 mL/min]/10 mm Hg, 1.13 [1.03-1.25]; $P = .011$) were significantly associated with interventions; a lower carotid-femoral pulse wave velocity and the outflow vein diameter in the early postoperative period (days 0-3) approached significance ($P < .10$). Intervention for ARHI was not associated with AVF maturation failure (unadjusted risk ratio, 1.18 [0.69-2.04], $P = .56$; adjusted odds ratio, 0.97 [0.41-2.31], $P = .95$).**

Conclusions: **Remedial intervention for ARHI after AVF construction is uncommon. Diabetes, female gender, capacitant outflow veins, and coronary artery disease are all associated with an increased risk of intervention. These higher risk patients should be counseled preoperatively, their operative plans should be designed to reduce the risk of hand ischemia, and they should be observed closely. (J Vasc Surg 2016;■:1-9.)**

The hemodynamic changes associated with the construction of an autogenous (arteriovenous fistula [AVF]) or prosthetic (arteriovenous graft [AVG]) arteriovenous hemodialysis access in the upper extremity can lead to hand ischemia. This phenomenon, termed the steal syndrome or access-related hand ischemia (ARHI), can lead to significant disability. Symptoms of either acute or chronic ischemia have been reported in up to 20% of brachial artery-based procedures[2-9] and 2% of radial artery-based procedures,[10-12] with up to half of the patients in the brachial artery group requiring some type of remedial intervention. The true incidence of ARHI associated with AVFs and AVGs is uncertain, given the retrospective nature of the various studies, reported predominantly from referral centers. Multiple risk factors for ARHI have been identified and include female gender, advanced age, diabetes, peripheral artery disease, coronary artery disease, multiple previous access procedures, prior episodes of hand ischemia,

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anastomotic configuration, and large outflow veins.[5,8,13-16] The predictive value of these various risk factors has been insufficient to identify patients at such a high risk that the index access procedure should be avoided. A variety of remedial treatments have been reported, including those designed not only to reverse the symptoms but also to salvage the access. Unfortunately, there is no consensus about the optimal remedial treatment.

This study was designed to prospectively define the incidence, predictors, and remedial treatments of ARHI along with its impact on the maturation rate within the Hemodialysis Fistula Maturation (HFM) Study.

METHODS

HFM Study design

The HFM Study was a multicenter, National Institutes of Health-funded, prospective study conducted at seven academic centers in the United States with a target enrollment of 600 participants and follow-up extending up to 4 years.[1] It was designed to identify predictors of AVF maturation within four domains: (1) anatomy, (2) biology, (3) clinical attributes, and (4) processes of care. The study was observational in that the clinical decisions regarding the AVF were dictated by the clinical team, with the exception that no interventions to facilitate maturation were to be performed within the first 6 weeks after construction. Enrollment criteria included (1) current or anticipated hemodialysis within 3 months, (2) life expectancy >9 months, (3) age exceeding consent minimum (ie, 18-21 years) and <80 years unless on dialysis, and (4) single-stage upper extremity AVF. The primary outcome measure was unassisted clinical maturation, defined as use of the AVF for dialysis over 4 weeks with specific, predefined criteria.[1] Preoperative measurements included ultrasound mapping of the upper extremity arteries and veins, flow-mediated dilation (FMD) and nitroglycerin-mediated dilation (NMD) of the brachial artery, arterial pulse wave velocity (PWV), and venous plethysmography. Postoperative measurements included ultrasound examinations within 3 days of the access procedure and at 2 weeks, at 6 weeks, and before intervention or initial cannulation.

ARHI

ARHI was included as a secondary outcome measure.[1] All symptoms (ie, pain, paresthesia, motor dysfunction, tissue loss) and interventions for ARHI were documented throughout the perioperative and follow-up periods.

Participants

Medical history and medications were defined at the time of enrollment. Peripheral artery disease was defined as prior amputation, carotid endarterectomy, carotid angioplasty, claudication, or lower extremity revascularization. Coronary artery disease was defined as prior angina, myocardial infarction, coronary artery bypass, or percutaneous revascularization.

Ultrasound

Preoperative mapping of the arteries and veins was performed along with the measurement of the blood flow in the brachial artery.[17-19] Internal diameter measurements of the artery and veins were performed in the anteroposterior dimension on a transverse image with a linear transducer (9 MHz or higher). Measurements included the internal diameter of the brachial artery 2 cm cranial to the antecubital fossa and the radial artery 2 cm cranial to the wrist. The cephalic and basilic veins in the upper arm were measured at the antecubital fossa and mid and cranial upper arm; the cephalic vein in the forearm was measured at the wrist and mid and cranial forearm. Arterial calcification was graded as absent, mild to moderate, or severe (circumferential). Postoperative AVF evaluation was performed using a standardized protocol.[20] The brachial or radial artery internal diameter measurements were obtained 2 cm cranial to the anastomosis. The AVF draining vein internal diameter measurements and blood flow were obtained 2, 5, 10, and 15 cm cranial to the anastomosis. The tests were performed by personnel trained by the ultrasound core laboratory and the studies were read at the core laboratory.

Vascular function tests

The tests were performed to characterize endothelial-dependent (FMD) and endothelial-independent (NMD) arterial vasodilation, arterial stiffness (carotid-radial PWV—extremity, carotid-femoral PWV—central), and venous capacitance (venous occlusion plethysmography). They were performed within 45 days before the AVF procedure on the arm for the planned surgical procedure unless there was already a functional, ipsilateral access. The tests were performed by personnel trained by the vascular function core laboratory and the studies were read at the core laboratory.

Venous occlusion plethysmography. The Hokanson EC5 strain-gauge plethysmography device with NIVP3 software was used for waveform acquisition and analysis (D.E. Hokanson, Inc, Bellevue, Wash). A strain gauge of appropriate size was placed around the forearm at its greatest diameter. A straight segmental arm cuff (SC10D, Hokanson, Inc) was placed on the upper arm and inflated for 3 minutes to a designated pressure and deflated. Waveforms were acquired while the cuff was inflated and for 5 seconds after deflation. The procedure was successively performed at cuff inflations to 20, 30, 40, 50, and 60 mm Hg, with maximum venous outflow and fractional change in forearm volume measured. Estimated slopes from their respective linear regressions on cuff pressure were used as measures of venous outflow and capacitance.

PWV. PWV was measured using the SphygmoCor system (AtCor Medical, Itasca, Ill). Carotid-radial and carotid-femoral distances were taken as the lengths by which the distance from the sternal notch to the radial or femoral pulse, respectively, exceeded that from the sternal notch to the carotid pulse. Pulse waveforms were recorded