STUDY PROTOCOL

Title: Understanding the Patient-Centered Outcomes for One-Stage and Two-Sage Brachial Basilic Arteriovenous fistulas: A Pilot Trial

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Objective:

We are proposing a randomized pilot trial, comparing the effectiveness of one stage to two-stage surgical approach for the creation of an upper arm brachial-basilic arteriovenous fistula (BBAVF). The target population are patients on renal replacement therapy who are receiving hemodialysis (HD) with central venous catheters (CVCs) at the time of the surgery and are candidates for a new BBAVF.

Design:

A BBAVF is a reliable autogenous hemodialysis access in patients without suitable cephalic vein.[1, 2] It can be created in either one or two stages.[3] The advantage of the one-stage approach is a shorter time between access creation and the cannulation for HD. The disadvantage is the potential for a longer upper arm incision if the AVF fails to mature. Although the two-stage approach can circumvent a more extensive procedure if the AVF fails, the need for two separate operations usually leads to more extended CVC dependency and a higher risk of CVC-related bacteremia (CRB). While literature confirms good results for BBAVFs, comparative studies of one-stage and two-stage methods are limited.[1] They rest on small case series and few have reported relevant clinical outcomes, including functional patency, duration of CVC dependency, and postoperative complications. In addition, an insufficient number of studies have used intention-to-treat analysis to account for the risk of primary fistula failure. The majority of these studies have concentrated on the fistula-related outcomes rather than patient centric and patient-reported outcomes (PROs), including the quality of life (QOL) measure.[3] There is a clinical equipoise in the surgical approach for the creation of a BBAVF and it is unclear whether patients prefer a one-stage or two-stage procedure.[1] Currently, the decision to use one-stage or two-stage approach varies widely among access surgeons and is based on factors such as the size of basilic vein and surgeon's bias or preference. A patient-centered approach, incorporating a balance between population-based evidence and individual patient perspectives might be preferred. This pilot study will allow us to understand patient-centered outcomes and QOL measures regarding the respective BBAVF techniques. We will use the valuable results to design a Patient-Centered Outcomes Research Institute (PCORI)-sponsored pragmatic clinical trial to determine the optimal surgical procedure for a BBAVF and to understand the perspective of patients receiving a complex AVF.

The plan is to enroll 10 patients (n=5 in each group) with ESRD receiving hemodialysis with a CVC from the Banner University Medical Center. Within each cohort, the subjects will be randomized in a 1:1 ratio to one. Within each cohort, the subjects will be randomized in a 1:1 ratio to one stage and two-stage surgical approaches. The randomization scheme is as follow:

Methods:

The target population are patients on renal replacement therapy who are receiving hemodialysis (HD) with central venous catheters (CVCs) at the time of the surgery and are candidates for a new BBAVF. The surgery is a standard of care procedure that is being done whether the potential subject is enrolled in the study. Upon enrollment the study subject will fill out the PROMIS/CAT questionnaires. The study team will follow a randomized protocol so the study subject will be randomized to the one or two stage approach. The subjects will then be seen at the standard of care intervals for follow-up. At the 6 month and 12-month standard of care follow-p visits the subjects will be asked to fill out the PROMIS/CAT questionnaires again. The subjects medical record will be followed for AE and SAE study related problems during the 12 months post surgical procedure.

Primary endpoint is Primary Clinical Functional Patency, defined as the successful use of the index fistula with two dialysis needles for at least 75% of dialysis sessions within a 4-week period to achieve the prescribed dialysis. The primary endpoint will be compared between two techniques during available follow-up up to 12-months (from the index procedure in the one-stage approach and the first procedure for the two-stage approach). Secondary endpoints will include: 1) Fistula-related outcome: stenosis and thrombosis, wound infection, arm swelling, hand ischemia, and surgery or intervention; 2) CVC-related outcome: duration of catheter-dependency, infection, bacteremia, and additional CVC procedure (exchange, placement of new catheter); and 3) Composite outcomes of Primary Clinical Functional Patency or CVC-related bacteremia or death. We will compare the PROs using the Patient-Reported Outcome Measurement Information System (PROMIS) Computerized Adaptive Testing (CAT) in the randomized patients.

Hypothesis: Primary Clinical Functional Patency will be superior following two-stage approach compared with the one-stage BBBAVF approach. Patients who underwent the two-stage procedure will have higher risks of infectious complications due to a more extended CVC dependency. The PROs will be affected by the number of procedures (one vs. two), postoperative fistula-related or CVC-related complications, and the duration of CVC dependency.

Statistical Analysis Plan:

The primary analysis of the primary endpoint will be a comparison of the primary clinical functional patency by treatment approach, where the distributions are based on available follow up to 12 months. A log-rank test will be used to evaluate the null. The secondary analytic method of the secondary endpoints will utilize a Cox regression model to adjust for the subject factors to adjust for baseline imbalance such as vein size. Based on a recent publication utilizing primary patency rate as the main outcome, the reported rates of primary functional patency of one-stage BBAVF was 56% at 12-month follow-up and was 72% for the two-stage procedure.[12] Based on a two-sided Fisher's exact test at significance level of 5%, a sample size of 153 per group is required to achieve a power of 80% to detect the percentage patency difference of 16% (56% vs. 72%). A sample size of 336 participants (168 per arm), with an estimated loss to follow-up rate of 10%, will be required to achieve a 5% significance level. With the restraint of the time and resources of this ASDIN research grant, the pilot trial will be exploratory and will be used to demonstrate the feasibility of the research plan in a high-risk ESRD population and the recruitment target.

The changes in the individuals' PROMIS domain scores and overall scores from the baseline will be compared between the patients who underwent a one-stage procedure and those who had a two-stage procedure. The analysis will be performed after excluding those who do not complete the two-stage procedure (only first procedure for two-stage approach). The impact of clinical events including infection and catheter-related complication on PROMIS domain scores will be evaluated using the student T-test.