STUDY PROTOCOL

Cohort Study on A Following-up System of Native Arteriovenous Fistulae in Chinese Patients Treated by Maintenance Hemodialysis

（Ver. 1.1   2016/07/20）

Title: Cohort Study on A Following-up System of Native Arteriovenous Fistulae in Chinese Patients Treated by Maintenance Hemodialysis

Study design: Prospective cohort Study

Study Location: Blood Purification Center of Department of Nephrology, Peking University International Hospital,

Sponsor: Peking University International Hospital, Capital Medical University

Principal Investigator: Dongliang Zhang

NCT：02880761

Protocol status: Ver. 1.1   20/07/2016

TABLE OF CONTENTS

1. Introduction

At present, maintenance hemodialysis (MHD), globally, is the most common method of renal replacement treatment (RRT) for patients with end-stage renal diseases (ESRD). As a core technical problem of MHD, functional vascular access is the base of proceeding the treatment. It is well accepted as an important acknowledgment that native arterovenous fistulas (AVF) should be the first choice for vascular access. The construction of a functional AVF can be challenging, and high initial failure rates have been reported in many publications. Estimates of non-maturation rates vary from 10% to 33% in AVF. However, there are no well-established criteria that define fistula maturation. According to the vascular access guidelines of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI), mature permanent access has a flow of approximately 600 mL/min and a minimum diameter of 0.6 cm and is less than 0.6 cm below the surface of the skin. The arterialized veins of AVF should have a flow of more than 500 mL/min and a diameter larger than 0.5 cm, and be less than 0.6 cm deep according to the Chinese Expert Consensus of Vascular Accesses for Hemodialysis. Even when the Chinese standard was considered, there were 31.2% (101/324 patients) non-mature AVF in stable long-term (more than six months) MHD patients in eight hemodialysis centers in our previous cross-sectional study. However, their AVF could support enough flow to get an effective urine clearance ratio (Kt/V>1.2) during every hemodialysis session, which should be regarded as the functional accesses in our opinion. What are the differences between functional but non-mature AVF and function-and-maturation AVF? To the best of our knowledge, rarely there are reports on the functional access. Thus, in order to identify the characteristics of functional access in newly set-up AVF in MHD patients, we designed the prospective cohort study.

2. Aim of the study

To describe the ultrasound characteristics of newly set-up arteriovenous fistulas (AVF), also to identify predictors for maturation of AVF in the forearm.

To test the benefits of the ultrasound following-up protocol on AVF in MHD patients.

3. Methods

3.1 Patients

Patients beginning MHD treatment in Peking University International Hospital from July 2016 will be screened. If patients fit to the selection criteria, they might be enrolled into the present study. Enrolled patients were divided into intervention group and control group.

3.1.1 Entry criteria:

① Regular hemodialysis patients (4 hours per session and three times a week).

② Planning to construct a new radiocephalic AVF in forearm.

③ 18-70 years old.

3.1.2 Exclusion criteria:

① Predicted duration of MHD less than six months, such as transferring to peritoneal dialysis, planning to kidney transplantation, or short life expectancy, etc.

② Have the following complications: malignant tumors, active rheumatism, malnutrition and cachexia.

④ Acute renal dysfunction.

④ Having done any blood vessel operations on the same side of the arms that planned to create an AVF. But it was not been care in the present study whether there were vascular accesses or not in the contralateral arm.

⑤ Not accepted AVF personally.

⑥ Other kinds of vascular accesses, such as brachiocephalic AVF, upper limb AVF, graft accesses, and so on.

3.2 Detection and following up of the intervention group：

The basic information of the patients, including gender, age, dialysis length, hemodialysis access, and primary causes of renal failure, will be collected. The baseline data will be recorded, including height, weight, BMI, and blood pressure (BP). Ultrasonography detection on the forearm blood vessels would be conducted before the surgery of AVF creation (time 0, t0). The operations will be conducted by a certain nephrologist with more than ten years experience of doing AVF surgeries. Until the patients finish the AVF operation, they would be followed up at least six months.

During following up, vascular ultrasound examinations for assessment of AVF are proceed at the end of two weeks (t1), two months (t2), three months (t3), and six months after operation (t6), regularly. When patients are detected by ultrasound, they lie down and expose the arm completely. The distal segment of brachial artery (a1), proximal segment of radial artery (a2) and ulnar artery (a3), distal segment of radial artery (a4) and ulnar artery (a5), cephalic vein draining segment nearly 0.5 cm far from the anastomosis (a6), and cephalic vein downstream segment nearly 0.5cm far from a6 (a7) should be examined by linear transducer with higher-frequency (3-12 MHz) using Philips Ultrasound equipment （HD11XE，CX50，IU22，Philips Ultrasound, USA.）

(Figure 1) .The sonographic evaluation parameters including lumen diameter (D), resistance index (RI), blood flow volume (BFV) of every vascular segment above will be measured and recorded. These evaluations are performed by two experienced radiologists in ultrasound, respectively, and all results would be averaged. The procedure of ultrasound examination follows the suggestion of America Institute of Ultrasound in Medicine (AIUM).
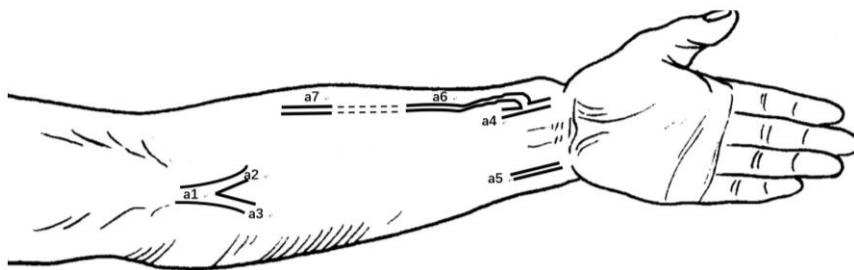
Figure 1　　Ultrasound examination sites of arteriovenous fistula in forearm

The sign of a1 is the distal segment of brachial artery, a2 is the proximal segment of radial artery, a3 is the proximal segment of ulnar artery, a4 is the distal segment of radial artery, a5 is the ulnar artery, a6 is the cephalic vein draining segment nearly 5 cm far from the anastomosis, and a7 is the cephalic vein downstream segment more than 5 cm far from a6.

Physical examination would be performed by experienced nurses to decide if the AVF could be punctured for MHD at the end of third month after operation. The urine clearance index of Kt/V is calculated once per month by simple single pool module, which using pre- and post-dialysis blood urine concentrations in one midweek hemodialysis session when the AVF punctuation begin. The first testing of Kt/V was performed after three times successful cannulations of the new AVF during hemodialysis treatments. If there were several values of Kt/V, mean value of Kt/V would be calculated and been used in statistic analysis.

All AVF give a dialysis session of mean Kt/V>1.2 would be defined as a functional access. If the Kt/V≤1.2 and uncapable cannulation repeatedly, the AVF is certified as dysfunctional. The enrolled patients with functional AVF will be divided into Maturation group (Group M) and Non-maturation group (Group N). Mature AVF is defined as both BFV(t3)>500ml/mL and D(t3)>0.5cm, otherwise, the AVF would be stated as non-maturation. Because the distance from skin to AVF veins in forearm is seldom larger than 0.6 cm in Chinese MHD patients, we ignored this parameter in this study.

All adverse events of dialysis accesses will be recorded in enrolled patients, including secondary AVF operation, thrombosis of AVF, stenosis, puncture failure, bleeding at puncture point after dialysis, and so on.

3.3 Statistical analysis

Metrological data is expressed as mean ± standard deviation (SD). The baseline variables are compared by independent t-test for measurement data and by χ^2 test for count data between Group M and Group N. The means of Kt/V are calculated for every patient and they are compared between two groups. Whether the AVF could be mature or not, predict factors are detected by Logistic Regression among these parameters on basement. The differences of the parameters between two groups are compared using General Linear Model Repeated Measures (GLM-RM) for continuous variables during following up. The results of GLM-RM can also identify the parameters' changes along with the timeline. The outcome events were compared between intervention group and control group. $P<0.05$ is considered to indicate a significant difference. All of the analyses are performed using SPSS software (version 13.0 for Windows; SPSS Inc., Chicago, IL, USA).