



## A new method to determine anastomosis angle configuration for arteriovenous fistula maturation

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### Abstract

**Background:** The kidneys of patients with chronic kidney disease (CKD) do not function well enough and those in end-stage renal disease (ESRD) of CKD need hemodialysis (HD) as a common renal replacement therapy (RRT) procedure. HD requires a vascular access (VA), and arteriovenous fistula (AVF) is the common VA choice in the world due to its very few complications. Despite the widespread use of AVFs, some risk factors maximize AVF failure, which is accompanied by complications of the patient such as repeating VA surgeries and hospitalization. Therefore, finding effective factors in the success of surgery is highly important and, thus, this study aimed at measuring the effect of anastomosis angle on the success of AVF surgery.

**Methods:** This study evaluated the effect of conducted angle in an AVF anastomosis on AVF maturation. The images of 48 created AVFs for CKD patients was provided over a one-year period (from May 2016 to April 2017). Cross-tab analysis was used, and significance level was considered meaningful at  $p\text{-value} \leq 0.001$ . A centralized database was designed to integrate data. A method for image processing was developed and geometrical characteristics of the vessels (such as anastomosis angle) and also the diameter of artery and vein were measured via AutoCAD 2017 software and exported to the database along with other data.

**Results:** The rate of the AVF failure in the studied patients was 8.96%. The anastomosis angle  $\leq 30^\circ$  is preferable from the AVF status point of view because most AVF maturation (or least AVF failure) rates are detected at this range.

**Conclusion:** This study was performed based on a new approach without the need to measure hemodynamic parameters. Moreover, it signified the important role of anastomosis angle in the function of AVF, showing that the anastomosis angle  $\leq 30^\circ$  is a preferable intraoperative recommendation for AVF surgery.

**Keywords:** Vascular access surgery, Hemodialysis, Anastomosis angle, AVF failure, AVF maturation, Surgical process improvement

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### Introduction

End-stage renal disease (ESRD) is the final stage of chronic kidney disease (CKD) in which the kidneys no longer function well enough to meet the needs of daily life (1), and it has been estimated that almost 10% of the worldwide population is affected by CKD (2). Patients with

ESRD need renal replacement therapies (RRTs) such as hemodialysis (HD), peritoneal dialysis (PD), or kidney transplantation (3). Due to some conditions in the use of RRT (such as the shortage of available kidneys for transplantation), HD is the most common method used in

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#### ↑What is “already known” in this topic:

The anastomosis angle of AVF is of great importance for surgeons who are working in this field, as it helps increase the maturation of the fistula. However, most researchers have calculated hemodynamic conditions, specially “wall shear stress”, which need measuring the properties of blood flow and internal diameter of the vessel.

#### →What this article adds:

A new approach was provided to convert intraoperative images of fistulas into quantitative data. There was no need for additional specifications, and the analyses determined the optimal angle, which reduced the failure rate of the fistula operation. Moreover, the anastomosis angle had to be below or equal to 30 degrees ( $\leq 30^\circ$ ).

these patients (4).

HD requires an access for connecting the dialyzer machine to the patient's vascular system, and this connection is provided by a vascular access (VA). There are 3 main types of VA: (1) arteriovenous fistula (AVF), (2) arteriovenous graft (AVG), and (3) central venous catheter (CVC). AVF has the least association with morbidity and mortality, thus, different countries strongly recommend AVF (5). AVF remains the "first choice" for chronic HD (5) and the closest to the "ideal model" of VA (6). However, primary failure remains a common problem impeding arteriovenous fistula (AVF) maturation and increasing patients' morbidity and mortality (7). The major cause of AVF failure is either unsuccessful maturation or venous stenosis of a matured AVF (8). Moreover, the quality of the inflow artery and the outflow vein has consistently been associated with AV access success (9). Nevertheless, the rates of inadequate AVF maturation and functional failure are alarmingly high (10).

AVF is created by communication between artery and vein. Evaluating the effects of modifiable configurations on the results of VA surgery, such as the conducted angle between vessels, can reduce AVF failure rate and improve AVF maturation. Therefore, finding these factors is highly important for identifying complications of the patient, such as repeating VA surgeries and hospitalization. This study was conducted to provide an image processing method and measure the effect of anastomosis angle on the success of AVF surgery.

## Methods

This study was implemented based on images of AVF surgeries and it calculated the measures of angles between the involved vessels in any AVF. Then, the status of each patient's AVF was followed and the relationship between the angle and AVF maturation / failure was found.

Statistical method was crosstab analysis, and significant level was considered meaningful at  $p\text{-value} \leq 0.001$ . A centralized database was designed for integrating variety data. A method for image processing was developed and geometrical characteristics of the vessels, such as anastomosis angle, and the diameter of artery and vein were measured via AutoCAD 2017 software and exported to database along with other data.

## Study variables

To achieve the goals of the study, the data of 48 ESRD patients were collected in 3 stages: (1) preoperative (age, gender, marital status, weight, height, smoking, diabetes mellitus (DM), hypertensive, heart disease, drugs, CKD duration), (2) intraoperative (AVF hand (right/left), AVF site (radial/radial up), anastomosis type (end-to-side (ETS) /side-to-side (STS)), image processing and vessels characteristics measuring), and (3) postoperative (AVF status (failure/ maturation)). One of the AVF images is shown in Fig. 1; the vessel is the vein connected to artery (the below vessel):

## Inclusion criteria were as follow

- (i) ESRD patients who referred by a nephrologist for

AVF creation from May 2016 to April 2017;

- (ii) Range of each patient's BP had to be more than 100/60 and less than 145/90 in day of operation.

## Exclusion criteria were as follow

- (i) BP under 100/60;
- (ii) Veins with diameter  $< 2$  mm because they have no suitable vein continuity;
- (iii) Artery with atherosclerosis or one that was not suitable due to having diameters  $< 2$  mm;
- (iv) Patients who have used anti-coagulation drugs;
- (v) Or those whose vascular system was prepared only for brachiocephalic VA, but not for radio-cephalic VA.

In this study, similar to many other studies (11,12), to examine the effects of gathered parameters on thrombosis, the role of this variable was considered as the dependent (label) variable.

The final material was constructed from merging 3 stages of data: (i) demographic data of patients, (ii) images of their created AVF, and (iii) status of their AVF after surgery.

## Ethical approval of the research

All participants gave informed consent before participation. The patients were admitted and underwent native AVF operation by the same surgeon to receive HD. The patients were informed about the study and their written consent was obtained.

## Methodology

The images were imported into AutoCAD 2017 software and the geometrical characteristics of the vessels, such as anastomosis angle creating AVF, and also the diameter of

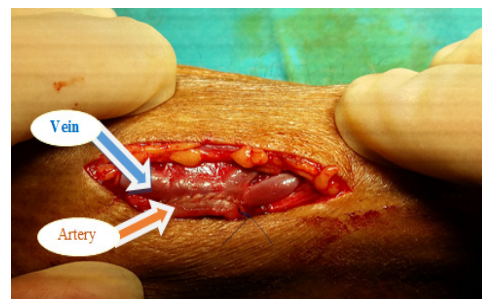


Fig. 1. The vessels in an AVF created via VA surgery

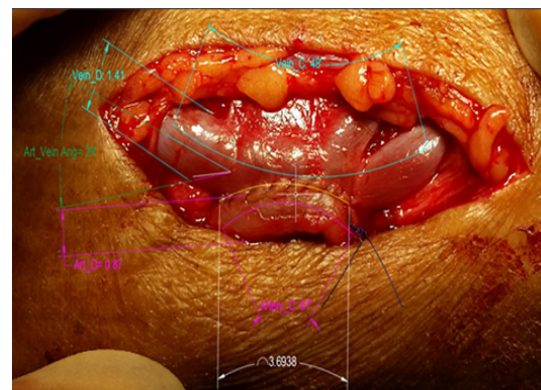


Fig. 2. Calculating measures of AVF parts: The green and yellow colors show the anastomosis angle and length of AVF, respectively. Also, the pink and cyan colors show the vessels diameter and their curve, respectively.

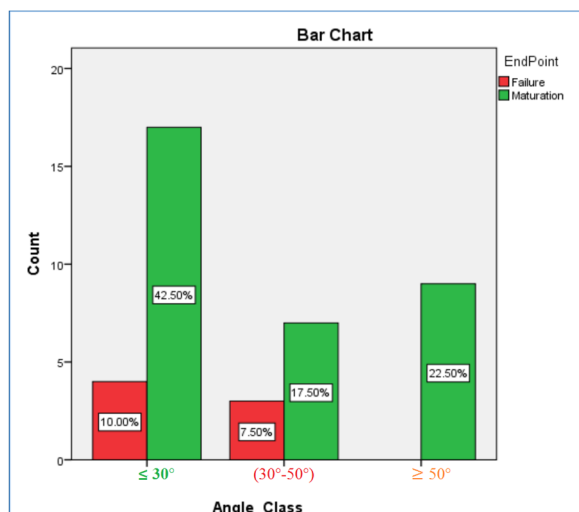


Fig 3. The crosstab analysis revealed that the least difference of AVF maturation and AVF failure rate occurred for anastomosis Angles  $\leq 30^\circ$ .

artery and vein were measured using this software. One of these images, which consists of measures of AVF, is shown in Fig. 2.

## Results

Considering the interpretability of the classified categories and according to the calculated measures of created angles, all categories were classified into 3 parts: (1) less than or equal to  $30^\circ$ , (2)  $30^\circ$ - $50^\circ$ , and (3)  $\geq 50^\circ$ .

The results of crosstab analysis confirmed that the anastomosis angle is a major determinant of the hemodynamics factor and that the lowest difference between AVF maturation rate and AVF failure rate exists in degrees  $\leq 30^\circ$  of anastomosis angle (Figure 3).

Despite the lower rate of AVF failure in the second bar in Figure 3 (17.5% in  $(30^\circ$ - $50^\circ)$  and in the third angle range ( $\geq 50^\circ$ ), there was no AVF failure. However, the difference of AVF maturation rate and AVF failure rates in them were

10% and 22.5%, respectively. Therefore, the most meaningful difference existed in the first angle range ( $\leq 30^\circ$ ) (maturation rate – failure rate = 32.5%). Thus, it can be concluded the anastomosis angle  $\leq 30^\circ$  is a preferable intraoperative recommendation for AVF surgery, and selecting this angle range during operation is as an effective factor in the success of the surgery.

## Discussion

### AVF Failure and Patency Rates

The rate of AVF failure varies significantly in the literature, leading to heterogeneity in the published primary patency rates (12).

In a 2014 study, of 338 autologous AVFs, 326 patients had obvious AVFs for dialysis (96.4% surgical success rate, or 3.6% AVF failure rate) (13). Sari et al. detected AVF failure in 81 patients out of 831 studied cases (rate = 10%) (14), and Monroy-Cuadros et al. reported 15.3% for incidence rates of primary AVF failure and never using AVF after operation (15).

Predictably, in a meta-analysis on 46 articles (7,393 AVFs), the overall risk of primary failure was 23%, but it increased to 37% in the elderly (12,16), and primary fistula function was achieved in 26 of 43 patients (60%), meaning that AVF failure rate was equal to 40% (17). In the past years, a worse situation has been reported indicating that from 101 fistulas only 47 fistulas (46.5%) developed sufficiently to be used for dialysis, representing the AVF failure rate of 53.5% (18).

The rate of AVF failure in this study (8.96%) was not very high compared to the average reported AVF failure rates in other parts of the world. We published similar results in 2008 (7) and found the failure rates of 8.05% at that time; and in an article in 2013 (19), we observed the failure rates of 7.45% from Dec 2010 to Nov 2010. These reports show that the AVF failure rate did not have any significant changes.

Table 1. Reported rates of AVF failure in researches during 1999 and 2017

Reference.	Publishing Year	Region	No. Patients	AVF Failure rate
Miller et al.	1999	Birmingham, US	101	53.5%
Tordoir et al.	2003	Netherlands	43	40%
Khavanin Zadeh et al.	2008	Iran	100	8.05%
Monroy-Cuadros et al.	2010	Canada	831	10%
Rezapour et al.	2013	Iran	193	7.45%
MacRae et al.; Al-Jaishi, et al.	2014	London	7,393	23-37%
Yoo et al.	2014	Busan	338	3.6%
Sari et al.	2016	Turkey	36	15.3%
Rezapour et al.	2018	Iran	48	8.96%

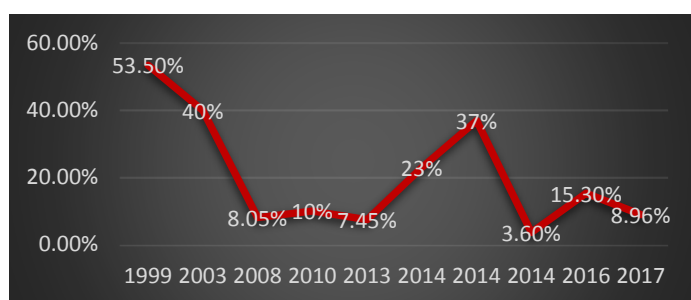


Fig. 4. The descending trend of AVF failure rates in recent decades in the world



Table 1 summarizes the discussed range of AVF failure rates, sorted according to year of publication.

Figure 4 illustrates the mentioned AVF failure rates, showing a descending trend of AVF failure rates in recent decades

#### **Risk factors that cause AVF failure**

Fistula failure factors are studied using various methods. Parts of studies have focused on discovering influential rules between biomechanical, geometrical, and thermodynamical parameters, such as the effect of similar diameters of vein and artery vessels on the AVF maturation (20). Some other researchers have tried to emphasize the associations between characteristics of ESRD patients (such as positive history of hypertension and/or diabetes mellitus (DM)) with the AVF failure result (19,21-22), which overall can be useful in predicting surgical complications, specially reasons of nonmaturation in AVF after VA operation. Also, when data mining techniques are applied, some "inverse effects" of these characteristics on the AVF are revealed, such as the unusual effect of hemoglobin (HB) level in smoking HD patients (23) or proper behavior of non-hypertensive ESRD patients towards their AVF maturation versus risk of positive history of Blood Pressure (BP) (24-25). Moreover, these studies provide insight that helps constructing a system for VA surgeons (26) to provide them with hints about adjusting preoperative factors of ESRD patients, such as HB level (7,11), DM (19,27-28), triglyceride and phosphate (29), and BP (30), to increase the likelihood of AVF maturation.

From another perspective, performing a meta-analysis on published researches concludes many inscrutable points in different studying conditions; for example, there are conflicts on risk of BP toward AVF failure. While a study in 2016 on 36 HD patients did not find any relationship between BP and thrombosis formation ( $p>0.05$ ) (14), in 2 more detailed reviews on 87 HD patients, a significant relationship was found between the systolic blood pressure (SBP) and the delay of AVF maturation (30). Moreover, under publishing research in Nature journal, which was done on 480 HD patients, indicated that the patients with a positive history of hypertension have more matured AVF (31).

Therefore, there are relatively contradictory views about the mentioned non-geometric factors. However, more geometric studies should be conducted to achieve a more accurate and realistic low-risk AVF failure model. In this study, we examined the association between potentially modifiable VA factors, particularly the effect of angle of artery and venous vessels, on the AVF maturation. The results can play a consultative role in practical decision-making for surgeons and can also provide an intraoperative model for vascular access surgery (VAS).

#### **Effects of anastomosis angle on AVF**

The effects of hemodynamics factors on AVF maturation have been studied in some researches in recent years (24). In a 2016 published study, it was found that "maturation time", the time after VA operation and starting HD, decreases when diameters of the vein and artery are close to

one another (19). In accordance with Poiseuille's law (32), the radius of a stenosis is much more significant than its length (33-36).

Anastomotic model for AVF operation is studied by other researchers using different methods. Ene-Iordache et al. have employed Wall Shear Stress (WSS) analysis and found that in AVF for HD, the anastomosis angle does affect the local disturbed flow patterns and that acute angles would lead to less intima formation, either on the vein or arterial side. They recommended that clinicians consider this at the time of AVF creation because anastomosis angle is in part amenable to surgical manipulation. Also, they concluded that an acute angle ( $30^\circ$ - $40^\circ$ ) is the preferred choice (37).

More precisely, in chapter 3 of Ene-Iordache's book (38), which is based on his previous studies and those of his colleagues (39), he stated, "We have found that in side-to-end radial-cephalic AVF for HD, the anastomosis angle does impact on the local disturbed flow patterns. Among the 4 geometries ( $30^\circ$ ,  $45^\circ$ ,  $60^\circ$  and  $90^\circ$ ), the smaller angle ( $30^\circ$ ) would be the preferred choice that minimizes the development of neointima. Clinicians should consider this at the time of AVF creation because anastomosis angle is in part amenable to surgical manipulation."

Silva J.A et al. have analyzed the blood flow through computational modeling in AVF used in HD (40). They obtained the possibility of stenosis formation caused by hyperplasia by computing the results for WSS, oscillatory shear index (OSI), velocity, and local circulation fields, and they found that higher angles present more secondary flows and larger extensions of stagnation regions near the critical areas of the junctions. According to their mentioned results, "a range around  $25^\circ$  was identified to be the most suitable choice for clinical applications, minimizing the possibility of diseases."

Similarly, Grus et al. calculated the parameters of the flow field, such as WSS and OSI, and showed that the maximum of spatial gradient of WSS decreased and OSI increased with wider bypass and more acute angle (41). Then, they concluded that more acute anastomosis angle promotes hemodynamics known to reduce formation of intimal hyperplasia.

On the other hand, in a 2012 study on radio cephalic arteriovenous fistula (RCAVF) at wrist, Hassan et al. investigated 18 three-dimensional models of RCAVF and they concluded that for an average flowrate, anastomosis angle should be maintained between  $45^\circ$  and  $60^\circ$  to minimize adverse effects (42). Also, a mathematical study on an end-to-side (ETS) AVF has investigated the hemodynamic impact of anastomosis size and angle on pressure drop and flow distribution (43). They concluded that pressure drop decreased with a larger anastomosis cross-sectional area and an angle wider than  $43^\circ$ , while it was almost stable for smaller angles. In a 2013 study (44), Jeffery et al. found that venous outflow, which is associated with AVF aneurysm (AVFA) (45), is the lowest by configurations angle of  $45^\circ$  in ETS anastomosis.

Table 2. Recommended degrees for anastomosis Angle in AVF operation

Reference.	Publishing Year	No. Patients / Models	Analysis Method	preferable Angle in AVFs
Ene-Iordache et al.	2015-2013	4	Computational Fluid Dynamic (CFD)	30°
Van Canneyt et al.	2010	1	Mathematical	43°
Ene-Iordache et al.	2012	4	WSS	30°- 40°
Hassan et al.	2012	18	CFD	45°- 60°
Hull et al.	2013	17	CFD	45°
Silva et al.	2015	6	WSS and OSI	25°
Grus et al.	2016	3	WSS	Acute angle
Rezapour et al.	2018	48	Image processing and Cross-tab analysis	≤ 30°

Table 2 presents the recommended degrees for anastomosis angle in AVF operation

Calculating hemodynamic conditions, such as WSS, requires measuring the properties of blood flow and internal diameter of the vessel; for instance, Gnasso et al. have calculated WSS according to the following formula (46):

Wall shear stress = blood viscosity  $\times$  blood velocity / internal diameter of vessel.

Which needs measuring the properties of the blood flow and the internal diameter of the vessel. However, the presented method does not need these specifications to reach the desired angle.

### Conclusion

Summing up the rates of this study and other published rates of AVF failure in the world shows that the trend of AVF failure rates has been descending in the recent decades, which is a promising outcome for the treatment of ESRD patients by this VA method.

Vessels analyses showed that the best angle between artery and vein, which has the lowest rate of AVF failure, should be maintained around 30° during operation. The finding can become an intraoperative pattern to configure angle among AVF surgical vessels.

Although the present study uses a new method for measuring VAS components, the results of other researches support our conclusion. Therefore, our invented methodology can be used by other researchers.

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### Conflict of Interests

The authors declare that they have no competing interests.

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