Original Article

# Role of color Doppler assessment in predicting outcomes of wrist Brescia-Cimino arteriovenous fistula creation: A single-center prospective study

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## ABSTRACT

**Introduction:** The most common reason for constructing an arteriovenous fistula (AVF) is chronic kidney disease. Various factors are associated with nonmaturation or failure of AVF, which can be evaluated using color Doppler/duplex ultrasound (DUS). We carried out this study to evaluate the role of pre- and postoperative DUS for the prediction of outcomes of wrist radiocephalic (RC) AVF.

**Methods:** In our prospective observational study, dialysis-dependent patients between 20 and 70 years of age undergoing primary RC-AVF from May 2019 to July 2020 were included. All patients underwent pre- and postoperative DUS examination after obtaining consent.

**Results:** Among 104 participants, 87 (83.7%) were male and 17 (16.3%) were female. Successful maturation was seen in 68 (65.4%) participants, whereas 90 (86.53%) had functional maturation. Radial artery diameter (RAD) ≥1.6 mm, cephalic vein diameter (CVD) ≥2.0 mm, vein distensibility (VD) ≥0.5 mm, and peak systolic velocity (PSV) RAD ≥30 cm/s were associated with higher successful maturation of AVF with statistically significant results ($P < 0.05$). RAD ≥1.6 mm, CVD ≥2.0 mm, VD ≥0.5 mm, and PSV RAD ≥30 cm/s were related to a greater probability of RC-AVF maturation. Among them, VD and PSV-RA were the most influencing factors predicting RC-AVF successful maturation.

**Conclusions:** If we consider the rule of six for AVF maturation, then the results will be much less than the actual fistulas which are dialyzable with adequate blood flow as per functional maturation criteria. Thus, more randomized studies are needed to define maturation criteria for the Indian population and to identify the effect of papaverine on successful AVF maturation.

## INTRODUCTION

The most prevalent reason for constructing an arteriovenous fistula (AVF) is chronic kidney disease (CKD). In India, according to the Global Burden of Disease 2017, CKD is the fifth most common reason for death.[1]

In end-stage renal disease (ESRD) patients, the ideal renal replacement modality is renal transplantation. Other management options are hemodialysis (HD) and peritoneal dialysis. However, the demand for transplants is much more than the availability of kidneys. It is estimated that the requirement for kidneys in India would range from 100,000 to 200,000 with only 5000 transplants being carried out annually. Thus, it has become very difficult for many ESRD patients to get transplants. Renal replacement therapy

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is found to be a mainstay in the treatment of patients who are waiting to receive a kidney transplant.[1]

For HD-dependent patients, vascular access has an important role. The most common method of vascular access is by creating AVF but the challenge is its construction and long-term patency rate.[2,3] In many patients, duplex ultrasound (DUS) was found to be beneficial over clinical examination in evaluating upper limb vasculature for example in obese patients, in patients with previous access surgeries in whom only clinical examination is not useful, and also in patients with arterial or venous diseases.[4-6] Functional patency is difficult to achieve due to complications like stenoses, which can contribute to thrombus formation or maturation failure and patency exists for 4–5 years in fistula accesses. Compared to other vascular accesses, native AVFs need the least intervention.

The role of DUS in routine surveillance of the condition is currently unclear.[7,8] Nonetheless, DUS is useful for assessing HD accesses such as grafts and AVFs in superficial structures. The DUS aids in the detection and localization of abnormalities that could hinder access function and patency. Previous studies have found that preoperative access – radial artery diameter (RAD) <1.6 mm and cephalic vein diameter (CVD) <2.0 mm and postoperative access – flow rate <500–600 ml/min or stenosis >50% found to correlate with increased failure in radiocephalic AV fistulas (RC-AVFs).[9,10] We, therefore, conducted the study to evaluate the role of pre- and postoperative DUS for the prediction of outcomes of wrist RC-AVF in North Karnataka.

## MATERIALS AND METHODS

We performed this prospective observational study from May 2019 to July 2020. 104 patients with age between 20 and 70 years were included who were HD-dependent and were undergoing primary RC-AVF formation in the nondominant upper limb. Ethical approval was obtained from the institutional ethical committee.

Participants with veins with thrombosis, patients who need prosthetic grafts, patients with multiple punctures for venous access in the upper limb, and those <20 or >70 years of age were excluded. Demographic data, i.e., age, gender, and detailed medical history (associated medical illness if any, i.e., diabetes mellitus and hypertension [HTN]), were recorded and thorough physical and clinical examination was done.

All patients underwent pre- and postoperative DUS examination after obtaining written and informed consent. We used a standard DUS protocol for all the participants. BK Medical (ProFocus) ultrasound machine with high frequency (7–10 MHz) linear probe was used. The single registrar recorded all the findings and was trained by a radiologist, but to ensure some findings were randomly double-checked by a radiologist.

A preoperative color Doppler scan of nondominant upper limb vasculature was done to assess RAD [Figure 1a], CVD [Figure 1c], peak systolic velocity of radial artery (PSV-RA) [Figure 1b], cephalic vein distensibility (VD) [Figure 1d], and cephalic vein (CV) compressibility. Patients with noncompressible CV were excluded from the study. CVD is measured before and 2 min after the blood pressure (BP) measurement cuff at the arm inflated at 50–60 mmHg pressure, and the difference (VD) is calculated in millimeters.

### *Surgical steps*

All the patients in our study underwent RC-AVF creation in proximity to the wrist. A senior urologist or a senior registrar under supervision performed all the surgeries. The course of RA, CV, and tributaries was marked preoperatively using DUS [Figure 2a]. After identifying RA and CV, smaller tributaries of CV were ligated within proximity of 5–10 cm from the CV to RA anastomosis site [Figure 2b]. We performed all AVF surgeries under local anesthesia. We standardized our technique for all cases, i.e., 1 cm arteriotomy and 1.2 cm venotomy (unstretched length) [Figure 2c]. Veins were flushed with heparinized saline. CV to RA anastomosed in an end-to-side fashion with 6-0 polypropylene running sutures [Figure 2d]. In all the cases, soon after anastomosis, we instilled 1 ml papaverine around the anastomosis and along the outflow vein.

### *Postoperatively*

B-mode examination was done to look for thrombosis or stenotic area [Figure 3a]. Color Doppler scan was done at 2, 4, and 6 weeks postoperatively, and the following details were noted:

1. Blood flow across the AVF (AVF flow volume = 60 × area* × mean velocity*)
   *Area = The square of the radius × 3.14.[11]
   **Mean velocity is calculated using the color Doppler [Figure 3b]
2. Outflow vein diameter [Figure 3c]
3. Outflow vein depth (from skin) [Figure 3c].

Blood flow during the first cannulation for HD access was measured. Preoperative and postoperative findings were compared with the AVF creation outcomes, i.e., fistula matured or failed to mature (can develop thrombus or low flow rate).

### *Outcome definition*

Successful maturation of AVF has been considered if it fulfills all three following criteria after 6 weeks (Rule of six). "Postoperative blood flow of >600 ml/min, outflow vein diameter of ≥6 mm, and an outflow vein depth of ≤6 mm below the skin surface."[7]

Failure to mature (FTM) was considered when a thrombus formed immediately or later after AVF creation or those AVFs who did not fulfill the above criteria.

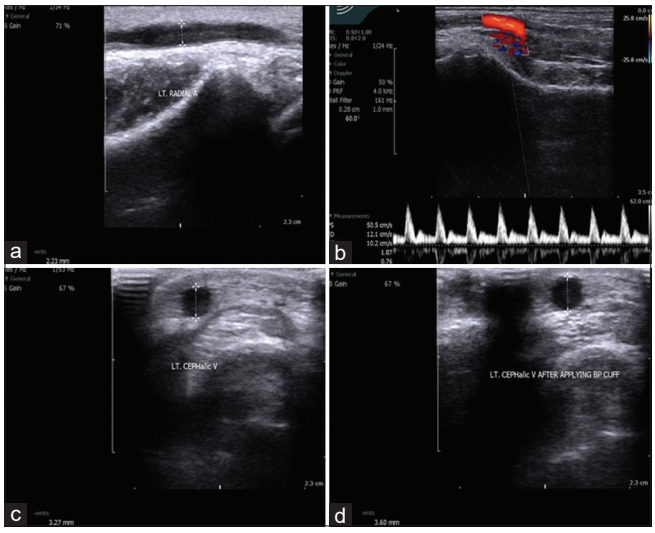


**Figure 1:** Preoperative assessment of vessels with duplex ultrasound. (a) Radial artery diameter measurement. (b) Radial artery peak systolic velocity measurement. (c) Cephalic vein diameter measurement. (d) Cephalic vein diameter after applying blood pressure cuff measurement

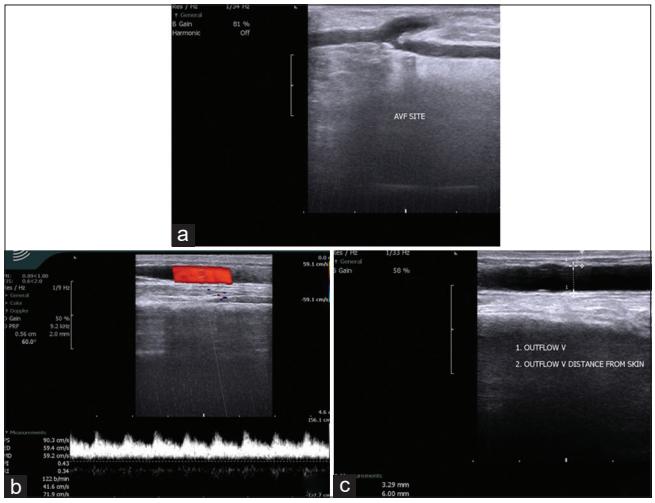


**Figure 3:** Postoperative assessment with duplex ultrasound. (a) B-mode scan showing AV fistula site. (b) Measurement of blood flow through AV fistula. (c) Measurement of outflow vein diameter and its distance from the skin. AV = Arteriovenous

Functional maturation: successful two-needle cannulations for HD after 4 weeks of AVF creation with a flow rate of >250 ml/min for a minimum of six consecutive HD sessions.

### *Statistical analysis*

Data were analyzed using SPSS version 20.0 (Armonk, Chicago, USA). Categorical data were expressed in terms of rates, ratio, and proportions, and continuous data were expressed as mean and standard deviation (SD). The Chi-square and/or Fisher's exact test was used for categorical data comparison, whereas the Wilcoxon signed-rank test was used for continuous data. The discrimination of RAD, CVD, and PSV-RA in predicting successful maturation was determined by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy. The significance of the *P* value is considered when $P < 0.05$.

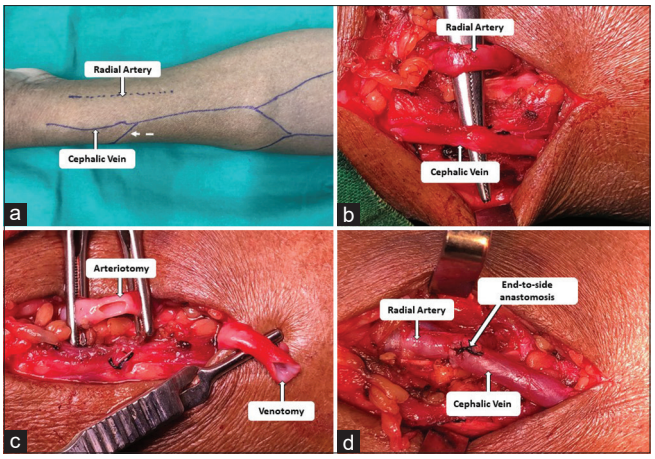


**Figure 2:** (a) Preoperative vascular marking with duplex ultrasound guidance. (b) Skeletonized radial artery and cephalic vein. (c) Arteriotomy and venotomy. (d) Cephalic vein to radial artery end-to-side anastomosis

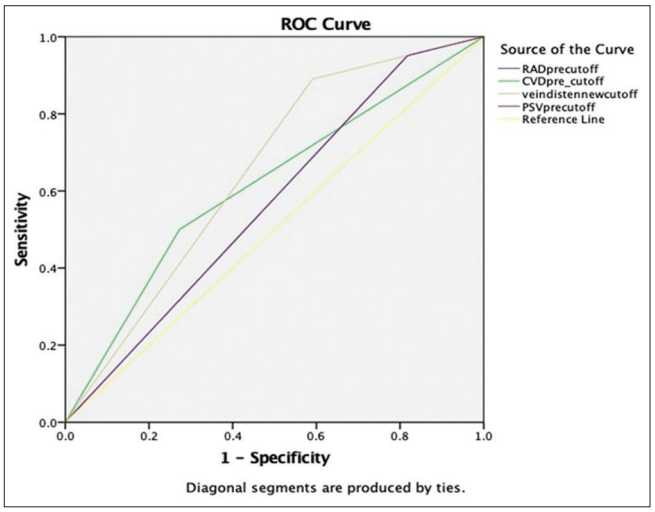


**Figure 4:** ROC curve analysis of preoperative parameters in assessing successful maturation of arteriovenous fistula ($n$ = 104). ROC = Receiver-operator-curve, RAD = Radial artery diameter, CVD = Cephalic vein diameter, PSV = Peak systolic velocity

## RESULTS

Baseline patient data are shown in Table 1. Among 104 participants with ESRD in the study, 87 (83.7%) were male and 17 (16.3%) were female. The age range of participants was from 20 to 70 years with a mean (±SD) age was 51 (±13.5) years. The nondominant limb was left in 98 (94.2%) study participants.

### *Preoperative color Doppler scan*

Mean (SD) of preoperative color Doppler RAD, PSV-RAD, CVD, CVD after applying BP cuff, and VD was 2.07 mm (±0.36), 33 cm/s (±8.78),

**Table 1: Baseline characteristics**

| Baseline characteristics | *n* (%) |
|---|---|
| Gender | |
| Male | 87 (83.7) |
| Female | 17 (16.3) |
| Age group | |
| 20-35 | 16 (15.4) |
| 36-60 | 58 (55.8) |
| 61-70 | 30 (28.8) |
| History of hypertension | 88 (84.6) |
| History of diabetes | 27 (26) |
| Nondominant limb | |
| Left | 98 (94.2) |
| Right | 6 (5.8) |

**Table 2: Preoperative color Doppler scan measurements of study participants (*n*=104)**

| Preoperative color Doppler scan | Mean (±SD) | Minimum | Maximum |
|---|---|---|---|
| Radial artery diameter (mm) | 2.07 (±0.36) | 1.34 | 3.12 |
| Peak systolic velocity at radial artery (cm/s) | 33 (±8.78) | 12 | 55 |
| Cephalic vein diameter (mm) | 1.97 (±0.45) | 1.2 | 4.11 |
| Cephalic vein diameter after applying BP cuff (mm) | 2.81 (±0.55) | 1.54 | 4.70 |
| Vein distensibility (mm) | 0.83 (±0.55) | 0.08 | 2.03 |

SD=Standard deviation, BP=Blood pressure

1.97 mm (±0.45), 2.81 mm (±0.55), and 0.83 mm (±0.55), respectively [Table 2].

### *Postoperative color Doppler scan*

Mean (SD) of postoperative color Doppler at 2 weeks for the diameter of outflow vein, outflow vein distance from the skin, Time-averaged mean velocity (TAM) at AV fistula, and blood flow through AV fistula was 5.13 mm (±0.70), 3.9 mm (±0.78), 42 cm/s (±8.4), and 558 ml/min (±204), respectively.

Mean (SD) of postoperative color Doppler at 4 weeks for the diameter of outflow vein, outflow vein distance from the skin, TAM at AV fistula, and blood flow through AV fistula was 5.7 mm (±0.51), 3.7 mm (±0.76),47 cm/s (±8.1), and 756 ml/min (±199), respectively.

Mean (SD) of postoperative color Doppler at 6 weeks for the diameter of outflow vein, outflow vein distance from the skin, TAM at AV fistula, and blood flow through AV fistula was 6.06 mm (±0.46), 3.4 mm (±0.73), 50 cm/s (±7.68), and 893 ml/min (±199), respectively.

Successful maturation, as per rule of six, was noted in 68 (65.4%) participants. Ninety (86.53%) patients had primary patency in our study as they were fulfilling functional maturation criteria.

The Chi-square test was applied to look for any association preoperative parameters such as RAD, CVD, VD, and PSV-RA with the maturation of an AV fistula. It was found from the analysis that RAD ≥1.6 mm, CVD ≥2.0 mm, VD ≥0.5 mm, and PSV-RA ≥30 cm/s were associated with a higher proportion of successful outcomes, which were statistically significant [Table 3].

Among all the preoperative parameters, VD (area under the curve [AUC] = 0.650) and PSV-RA (AUC = 0.567) were found to be a fair predictor of successful maturation of AVF [Table 4 and Figure 4]. VD has PPV of 84.88% and NPV of 50%. PSV-RA has PPV of 81.25% and NPV of 50%.

Outcomes were compared with selected baseline characteristics and their association was assessed between sex, age group, history of diabetes, and HTN with successful maturation. It was found that there was no association between any of the factors and outcomes of the AV fistula.

### *Adverse outcomes*

Adverse outcomes during or after surgery were noted in 16 (15.38%) study participants. Two patients had episodes of hypotension, four had thrombus, three had stenosis, six had postoperative limb edema, and one had a large hematoma.

## DISCUSSION

We did this study to evaluate the outcome of wrist RC AVF by preoperative and postoperative color Doppler scan. Many studies currently focus on the role of gender in the outcome of AVF. Some discovered female gender as a risk factor for a favorable AVF outcome.[2,7,10] However, we did not find any statistically significant difference in the maturation of AVFs between males and females. The age range of participants was from 20 to 70 years with a mean (±SD) age was 51 (±13.5) years. A study done by Dasari *et al*.[12] reported a mean age of 50.2 ± 12.01 years. A study was done by Pieutura *et al*.[13] reported a 19–79 years of age (with a mean age of 46.7 years).

### *Arterial diameter*

Wong *et al*.[11] concluded that a diameter <1.6 mm was correlated with fistula failure. Malovrh[14] found a diameter <1.5 mm had a low success rate (around 45%). Lemson *et al*.[15] found that ineffective forearm AVFs had significantly smaller mean preoperative RAD than patients with working fistulas. Silva *et al*.[4] suggested and many researchers followed a minimum diameter of 2 mm. The feeding artery definitely leads to a favorable result of AVF surgery. However, results from various studies concluded differently. The results obtained in this study showed successful AVF maturation when RAD is >1.6 mm with an odds ratio (OR) of 2.55 (95% confidence interval [CI]) (1.08–6.07) which is statistically significant ($P = 0.001$).

### *Peak systolic velocity*

Adequate arterial inflow is important for AVF maturation. However, due to the small diameter of the RA, precise preoperative flow rate calculation is difficult. Yerdel

**Table 3: Association between preoperative parameters and arteriovenous fistula maturation (*n*=104)**

| Preoperative parameters | AVF maturation | | OR (95% CI) | *P* |
|---|---|---|---|---|
| | Successful, *n* (%) | Unsuccessful, *n* (%) | | |
| Radial artery diameter (mm) | | | | |
| <1.6 | 1 (1.5) | 7 (19.4) | 16.17 (1.9-37.4) | 0.001 |
| ≥1.6 | 67 (98.5) | 29 (80.6) | | |
| Cephalic vein diameter (mm) | | | | |
| <2.0 | 32 (47.1) | 25 (69.4) | 2.55 (1.08-6.07) | 0.029 |
| ≥2.0 | 36 (52.9) | 11 (30.6) | | |
| Vein distensibility (mm) | | | | |
| ≥0.5 | 63 (92.6) | 27 (75) | 8.12 (2.17-13.6) | 0.011 |
| <0.5 | 5 (7.3) | 9 (25) | | |
| Peak systolic velocity (cm/s) | | | | |
| <30 | 30 (44.1) | 5 (13.9) | 2.3 (1.2-4.98) | 0.022 |
| ≥30 | 38 (55.9) | 31 (86.1) | | |

Chi-square test applied, Fisher's exact test, $P<0.05$ is significant. OR=Odds ratio, CI=Confidence interval, AVF=Arteriovenous fistula

**Table 4: Receiver operator curve analysis of preoperative parameters in assessing successful maturation of arteriovenous fistula (*n*=104)**

| Parameter | AUC | 95% CI | *P* |
|---|---|---|---|
| Radial artery diameter | 0.567 | 0.423-0.710 | 0.340 |
| Cephalic vein diameter | 0.614 | 0.485-0.742 | 0.103 |
| Vein distensibility | 0.650 | 0.508-0.791 | 0.073 |
| Peak systolic volume | 0.567 | 0.423-0.791 | 0.073 |

AUC=Area under the curve, CI=Confidence interval

*et al*.[16] found a preoperative arterial flow of <40 ml/min was associated with a higher rate of immediate failure, although the result was not statistically significant. Malovrh[17] also concluded a mean preoperative flow of 54.5 ml/min in effective AVF and a mean flow rate of 24.1 ml/min in failed AVF. In our study, PSV-RA higher than 30 cm/s is associated with better AVF outcomes, with an OR of 2.3 (1.2–4.98) with a 95% CI that is statistically significant ($P$ = 0.022). A receiver operator curve analysis revealed that a minimum PSV-RA cutoff point of 30 cm/s had the highest predictive value of RC-AVF failure.

### *Venous diameter*

Silva *et al*. when taking RAD >2 mm and CVD >2.5 mm as criteria found a failure rate of only 8.3% of primary AVF.[4] Lockhart *et al*. observed a significantly low success rate AVF (approximately 36%) using the same criteria.[18] Some studies revealed greater AVF success with >2 mm diameter veins,[19] whereas others found a marginal diameter of 2.6 mm, but only in women.[20] Although the vein's internal diameter is not always taken as a factor influencing the outcome of AVF, another study showed all AVFs with vein diameter <1.6 mm were unsuccessful.[21] In our study, participants with CVD >2 mm had better successful maturation with an OR of 2.55 (1.08–6.07) (95% CI) which is also statistically significant ($P$ = 0.001).

These differences imply that vessel diameters are a crucial, but not the only factor in determining how successfully an AVF matures. It seems that the maturation of the AVF is also influenced by the functional characteristics of blood vessels.[6,22]

### *Venous distensibility*

In addition, it appears that a crucial factor influencing the success of AVF is VDWhen a vein and an artery are anastomosed, the flow through the vein increases, which causes dilation. The properties of a vein's wall, which are impacted by prior inflammatory processes and punctures, determine how wide a vein will expand. Venography was used by Kim *et al*. to measure the change in CVD while wearing and without a tourniquet. They discovered that when the diameter grew by >0.35 mm, there was a 7.4 times higher likelihood of effective AVF maturation.[23] VD was identified by our study's findings as a crucial variable in the successful prediction of AVF development.

In our study, VD of >0.5 mm is associated with an increased success rate of AVF surgery (sensitivity 89.02% and specificity 40.2%). The likelihood of a favorable outcome was roughly eight times higher for patients with VD of >0.5 mm (OR 6.98, $P$ = 0.004).

The outcomes are in line with previous studies that highlighted the significance of VD as a functional parameter influencing the success of AVF.[24] While previous studies have presented VD as a percentage or as mL/mmHg, this study expresses VD in millimeters.

In addition, more than twice as many individuals were investigated (50 vs. 104) and similar results were found (0.35 vs. 0.5 mm).

A study done by Srivastava *et al*.[25] found that in more than 90% of cases, the RAD, CVD, and PSV were all >2 mm, 2.2 mm, and 32.8 cm/s, respectively.

A study done by Dasari *et al*.[26] reported an overall success rate of 68.3%, with a 31.7% failure rate. In addition, they stated that CVD, RAD, PSV, RA flow rate preoperatively, and increase in flow rate at Post-operative day (POD) 1 and POD 8 as well as the increase in CVD was the predominant factors influencing the RC-AVF success.

In this study, 68 (65.4%) study participants attained maturation criteria (as per the rule of six) after 6 weeks. In our study, FTM and thrombosis were the primary reasons for the loss of AVF.

If we consider these functional maturation criteria as defined in various studies,[27] then 90 (86.53%) patients had functional maturation in our study.

A significant proportion of AVFs fails due to poor flow, which can lead to thrombus development when there is intimal damage. Inadequate fistula flow can indeed be caused by arterial or juxta-anastomotic stenosis, but it is believed that venous spasm at the dissection's edge is the main culprit. Intimal damage may easily lead to thrombosis as the vein near the anastomosis is full of blood and the flow is very slow. Applying a local anesthetic may cause venous dilatation over time; papaverine hydrochloride is utilized for quick results,[28] which in turn aid in avoiding the development of thrombus. There are a few studies in the literature that demonstrate the use of papaverine for favorable AVF outcomes.

## CONCLUSIONS

RAD ≥1.6 mm, CVD ≥2.0 mm, VD ≥0.5 mm, and PSV-RA ≥30 cm/s were associated with a higher proportion of successful maturation of AV fistula. Among them, VD and PSV-RA were the most influencing factors in assessing whether RC-AVF will be successful. If we consider the rule of six for AVF maturation criteria, then the success is lower than the actual dialyzable fistulas as per functional maturation criteria.

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