To cite this article: Budak AB, Saba T, Akalin N, Genctoy G, Haberal C. Prognostic factors for radiocephalic arteriovenous fistula maturation in patients with prior placement of a central venous catheter and relationship with inflammation.Turk J Clin Lab 2020; 11: 124-135.

Original Article

# Prognostic factors for radiocephalic arteriovenous fistula maturation in patients with prior placement of a central venous catheter and relationship with inflammation

## *Santral venöz katateri olan hastalarda radyosefalik arteriyovenöz fistül matürasyonunu için prognostik faktörler ve inflamasyonla ilişkisi*

Ali Baran BUDAK*[1], Tonguc SABA[1], Nalan AKALIN[2], Gultekin GENCTOY[3], Cevahir HABERAL[1]

[1]Başkent University Faculty of Medicine, Alanya Practice and Research Center, Department of Cardiovascular Surgery, Antalya/TURKEY
[2]Başkent University Faculty of Medicine, Alanya Practice and Research Center, Department of Biochemistry, Antalya/TURKEY
[3]Başkent University Faculty of Medicine, Alanya Practice and Research Center, Department of Nephrology, Antalya/TURKEY

## Abstract

**Aim:** A mature and functional arteriovenous fistula (AVF) is considered the best modality for vascular access(VA) for hemodialysis (HD) treatment but the incidence of early failure is high, especially in patients start their HD with a central venous catheter. The aim of this study was to evaluate the prognostic value and association of certain patient characteristics and specific inflammatory markers with early failure of AVF in patients who started their HD therapy with a CVC and a first autogenous radiocephalic AVF (RCAVF) was created after vascular consultation.

**Material and Methods:** A retrospective review of 168 patients with end-stage renal disease who underwent RCAVF creation by the same surgeon by using the same surgical technique and whose primary vascular access for HD treatment was obtained via CVC at the time of access consultation was performed. The patients enrolled into this study were categorized into two groups as Group 1: patients with early failure (n=46) and Group 2: patients with no failure (n=122). Demographic characteristics, medical comorbidities, preoperative doppler ultrasound mapping results, laboratory parameters, postoperative follow-up details of these patients were collected. Primary patency of all patients, early failure rate, maturation failure rate, duration of CVC was calculated.

**Results:** Female gender was found to be a significant risk factor in early failure of RCAVF (69.5% vs 36.1%; p=0.001). The number of patients whose diameter of cephalic vein< 2 mm were significantly higher in EF group (78.3% vs 22.1 ; p=0.028). The duration of CVC access of group 1 was significantly longer than group 2 (6.8 ± 3.6 months vs 2.3 ± 1.7 months, respectively; p<0.05). Overall maturation failure rate was 12.5% and primary patency at 1 year was 72.6%. Levels of C-Reactive protein (7.2 ± 9.6 vs 3.1 ± 3.3 mg/L, respectively; p=0.001) and neutrophil lymphocyte ratio (2.91± 0.30 vs 2.17 ± 0.22, respectively; p<0.05) was significantly lower at group 2 at one year.

**Conclusion:** In patients whose VA for HD treatment was provided by CVC, small cephalic vein diameter, female gender and systemic inflammation may play a role in early failure of RCAVF.

**Keywords:** autogenous radiocephalic arteriovenous fistula; early failure; cephalic vein; inflammation

Corresponding author*: Ali Baran BUDAK, Başkent University Faculty of Medicine, Alanya Practice and Research Center, Department of Cardiovascular Surgery, Antalya/TURKEY
E-mail: drbaranbudak@gmail.com
ORCID: 0000-0002-9772-1765
Recevied: 11.02.2020 accepted: 18.05.2020
Doi: 10.18663/tjcl.739377

Volume 11 Number 3 p: 124-135


## Öz

**Amaç:** Matüre ve fonksiyonel bir arteriovenöz fistül (AVF), hemodiyaliz (HD) tedavisi tedavisinde vasküler erişim için en iyi modalite olarak kabul edilir; ancak erken başarısızlık oranı HD tedavisine santral venöz kateter (SVK) ile başlayan hastalarda yüksektir. Bu çalışmanın amacı, HD tedavilerine SVK ile başlayan ve daha sonra ilk kez radiosefalik AVF (RSAVF) oluşturulan hastalarda belirli hasta özelliklerinin ve spesifik inflamatuar belirteçlerin AVF'nin erken başarısızlığı açısından prognostik değeri ve ilişkisini incelemekti.

**Gereç ve Yöntemler:** Aynı cerrah tarafından, aynı teknik kullanılarak RSAVF oluşturulan ve konsülte edildiği sırada HD tedavisi için damar erişimi SVK ile önceden sağlanmış son-dönem böbrek hastalığı bulunan 168 hasta retrospektif olarak tarandı. Bu çalışmaya alınan hastalar Grup 1: erken başarısızlık olan (n=46) ve Grup 2: erken başarısızlık olmayan (n=122) olarak iki gruba ayrıldı. Bu hastaların, demografik özellikleri, yandaş hastalıkları, preoperatif doppler ultrasomografi haritalama sonuçları, laboratuar parametreleri, postoperatif takip detayları toplandı. Tüm hastaların primer patens oranları, erken başarısızlık oranı, maturasyon başarısızlık oranı ve SVK süreleri hesaplandı.

**Bulgular:** Kadın cinsiyet RSAVF erken başarısızlığında anlamlı bir risk faktörü olarak bulunmuştur (%69.5 vs %36.1; p=0.001). Sefalik ven çapı< 2 mm olan hastaların sayısı Grup 1'de fazlaydı (%78.3 vs %22.1 ; p=0.028). Grup 1'de SVK erişim süresi Grup 2'den anlamlı olarak daha uzundu (6.8 ± 3.6 ay vs 2.3 ± 1.7 ay; p<0.05). Maturasyon yetersizlik oranı %12.5 ve 1-yıllık primer patensoranı%72.6 idi.Grup 2'de, Grup 1'e oranla 1.yılda C-Reaktif Proteindüzeyleri (7.2 ± 9.6 vs 3.1 ± 3.3 mg/L, respectively; p=0.001) ve nötrofil lenfosit oranı(2.91± 0.30 vs 2.17 ± 0.22, respectively; p<0.05) anlamlı derecede düşüktü.

**Sonuç:** Önceden HD tedavisi için damar erişimi SVK ile sağlanan hastalarda, küçük sefalik ven çapı, kadın cinsiyet ve sistemik inflamasyon, ilk defa açılan RSAVF'ün erken başarısızlığında rol oynayabilir.


**Anahtar kelimeler:** otojen radyosefalik arteriovenöz fistül; erken başarısızlık; sefalik ven; inflamasyon

## Introduction

An increase in the global incidence of end-stage renal disease (ESRD) has led to the increasing demand for hemodialysis[1,2], which is the most common method for treating ESRD. A mature and functional arteriovenous fistula (AVF) is considered the best modality for vascular access (VA) when compared to arteriovenous grafts (AVG), and central venous catheters (CVC) [3-5], and a radiocephalic AVF (RCAVF) at the level of the wrist is the first choice for VA creation; however recent studies have shown high failure rates of up to 46%, with one-year patencies range from 52% to 83% .[6] Surgeons often confront with smaller-caliber vessels, and construction of an AVF is more likely to result in early failure, leading to increased morbidities, related to reoperations, longer hospitalization, and increased costs.[7,8] Early failure of AVF also delay the establishment of permanent dialysis access. It is, therefore, important to identify patients who will have a high likelihood of early AVF failure. Early failure is defined as any fistula not used for dialysis due to loss patency (thrombosis, etc.) or lack of maturation.

A fistula is considered mature when it is thought to be appropriate for cannulation with minimal complications, and to deliver the prescribed blood flow throughout the HD procedure. In other words, when a VA is cannulated successfully with two needles over a period of at least 6 HD sessions during 30 days, and delivering the prescribed blood flow throughout the HD procedure (at least 350 ml/ min), the VA is finally considered adequate for HD (functional and successfully used).[6,9]

In clinical practice, as many as 60%–80% of the incident, patients start their hemodialysis therapy with a CVC due to being unable to wait for the maturation of AVFs or having a condition in which AVF development is not feasible.[10,11] Among ESRD patients initiating hemodialysis with a CVC, the time at which they switch to a mature AVF is influenced by successful AVF maturation which depends on several factors including patient comorbidities and demographics; diameters of cephalic vein and radial artery; peri-operative and postoperative factors.[12-15] However, these studies are a mixed picture (i.e., not limited to RCAVFs) and included conflicting results and the evidence derived from these articles is not consistent Studies do not provide a solid platform for the planning of RCAVF formation, and does not assist in the process of informed consent (percentage likelihood of success

and/or failure). For example, many authors have agreed that duplex vein mapping increases utilization of AVF [16,17], but as vein diameter is dynamic (subject to constriction from changes in venous sympathetic tone), intraoperative measurements may differ from mapped vein diameters. Furthermore, Central Venous Pressure, positioning of the arm, hydration status, ambient room temperature, caffeine intake, and medications may contribute to misleading scans. As a result, though widely recommended, even duplex mapping may not improve functional AVF patency.[18]

Besides, several authors have noted the pivotal role of inflammation in neointimal hyperplasia, which is a foundation of AVF nonmaturation.[19-21] The relation between C-reactive protein (CRP) levels and the development of intimal hyperplasia[22]; thrombosis due to disproportionate intimal hyperplasia resulting in access thrombosis[23] has previously claimed. Likewise, neutrophile lymphocyte ratio (NLR) is a robust inflammatory indicator and associated with both coronary atherosclerosis and restenosis.[24] Given the undeniable role of inflammation in AVF stenosis as well as the histopathological similarity of AVF stenosis with atherosclerosis, a relationship between NLR and AVF stenosis/maturation was questioned.[25,26] Furthermore, previous studies have reported that CVC placement contributes to chronic inflammation independent of infection.[27,28]

The correlation of NLR with the AVF stenosis, as well as the role of NLR and CRP as a predictor of access failure and their pathogenic role in NIH is not clearly understood. Moreover, there are limited data about long-term serial changes in inflammatory marker levels and their relationship to access type in hemodialysis patients, and the contribution of access type to the inflammatory status of hemodialysis patients is not well described.[29,30]

The objective of this paper was to report our findings from the last 10 years in a university hospital located in Antalya. Since recent evidence has highlighted a failure of the literature to identify factors associated with maturation [31], we aimed to test the hypothesis that certain patients' characteristics (age, gender, vessel diameters, and medical comorbidities) affect the maturation of AVF. We also aimed to test the prognostic value and association of specific inflammatory markers (white cell count, neutrophil-lymphocyte ratio, C-reactive protein) with early failure of AVF in patients who started their HD therapy with a CVC and a first autogenous RCAVF was created after consultation to our department.

## Material and Methods

### Study Design, Setting and Patient Selection

We performed a retrospective chart review of all patients with ESRD who were referred to the department of vascular surgery service in Başkent University Faculty of Medicine, Alanya Practice and Research Center, Antalya-Turkey for creation of AVF for HD between 2010 and 2019. The study protocol was approved by Başkent University Institutional Review Board. Informed consent was obtained from all the patients participating in the study.

Between 2010-2019, we performed AVF construction in 468 patients with ESRD at our institution. Of them, 304 patients with first time autogenous AVF were included. Of the 304 patients, we selected 168 patients who had RCAVF created by the same surgeon by using the same surgical technique and whose VA for HD treatment was obtained via CVC at the time of access consultation and whose preoperative and intraoperative vessel diameters were recorded. Patients who had a life expectancy less than 12 months and to avoid factors influencing CRP levels, patients who had any sign of infection (fever, leukocytosis, cellulitis) or received PTA within 1 month before or after blood sampling, as well as those with rheumatic disease or cancer, were excluded in this study. We also excluded the AVFs that required 2-stage operations. The patients enrolled in this study were categorized into two groups as group 1: patients with early failure (n=46) and group 2: patients with no failure (n=122).

Each patient must be followed up at the vascular surgery and/or nephrology clinics for at least one year or until AVF failure. Data on the survival and prognostic predictors of AVF were extracted from the hospital's electronic database.

In our tertiary care university hospital, patients were regularly seen by the nephrologists, and the decision to start dialysis treatment was made based on the severity of the worsening of renal function. A detailed history and physical examination was undertaken from every patient, including age, gender, history, cause of chronic kidney disease, and the presence of comorbidities/risk factors and noted. The latter included diabetes mellitus (defined as the use of insulin or oral hypoglycemic agents), hypertension (systolic blood pressure >140 mmHg, diastolic blood pressure >90 mmHg, or use of anti-hypertensives), dyslipidemia (defined as the use of anti-lipidaemic agents, e.g., statins, ezetimibe, etc.), coronary artery disease (defined as the history of angina, myocardial

infarction, or coronary intervention, including angioplasty and/or bypass grafting), and peripheral arterial disease (PAD) (defined as the history of intermittent claudication, critical limb ischemia, or revascularization of the lower limbs).

The common causes of ESRD among the patients included in this study were diabetes mellitus, hypertension, and glomerulonephritis.

**Preoperative Vascular Evaluation**

Physical assessment always began by non-dominant arm blood vessels. The study environment was calm and had a pleasant temperature of 20ºC to prevent the underestimation of vessel size due to vasoconstriction. Patients were also in a supine position without angling the elbow joint to avoid vessel compression. The decision to create RCAVF was made through physical examination of arterial inflow by careful palpation of axillary, brachial, radial and ulnar arteries and negative Allen Test; where venous outflow was evaluated by clinical examination through visual enhancement of the cephalic vein which was provoked by placing a tourniquet on the upper arm while the patient clenches and releases the ipsilateral hand several times.

Radial artery inner diameters were routinely assessed at the level of intended anastomosis construction to exclude arterial stenosis, atherosclerotic plaques, and arterial calcification. AVF was not created in the presence of calcifications of the feeding artery wall [32], and anastomosis was not created distal to stenosis above 50% in the radial artery. We did not attempt to construct RCAVF with RA diameters below 1.5 mm. When the decision concerning RA suitability is doubtful, we look at venous mapping results and often decide for the RCAVF formation attempt when there is a large, distensible CV present with normal Doppler venous waveform, and well-established phenomena of respiratory filling

Criteria for venous size as a predictor of RCAVF outcome fluctuated even more than RA diameter cut-offs across published studies. Minimal CV internal diameters associated with RCAVF outcomes in the range of 1.6-2.6 mm were reported.[33-36] Similar to arterial preference, we did not use CV below 1.5 mm.[34] Venous outflow was assessed accurately to exclude venous outflow stenosis and accessory veins. Evaluation of vein compressibility and thrombus exclusion was performed before tourniquet placement.

Since the threshold diameters for both RA and CV diameters for a suitable RCAVF were 2.0 mm, and diameters between 1.6-1.9 were defined as "grey zone", so we decided to compare the groups taking 2.0 mm as a threshold.[34-37]

Evaluation of the dominant arm was performed solely when the non-dominant arm evaluation was unsatisfactory.[38]

**Laboratory Tests**

All laboratory studies were performed by Başkent University Laboratories (Alanya, Antalya-TR) using automated methods. The laboratory parameters of the patients in the study are the median of the variables in one-year, starting from the preoperative evaluation to postoperative 12th month. In the author's institution, an automated hematology analyzer model (Cell Dyn, Ruby LH 780, Abbott, Abbott Park, IL, USA) was used to measure all CBC specimens, including WBC, hemoglobin, platelet counts and WBC differential percentages. The machine was calibrated three times daily for quality control. CRP and biochemical parameters were measured by an automated clinical chemistry analyzer using the spectrophotometric method (Architect c8000, Abbott, Abbott Park, IL, USA). iPTH value was measured by an automated analyzer using chemiflex technology (Architect i2000SR immunoassay analyzer, Abbott, Abbott Park, IL, USA).

**Surgical Technique**

All patients were scheduled for a primary AVF creation between the radial artery and cephalic vein (Figure 1).

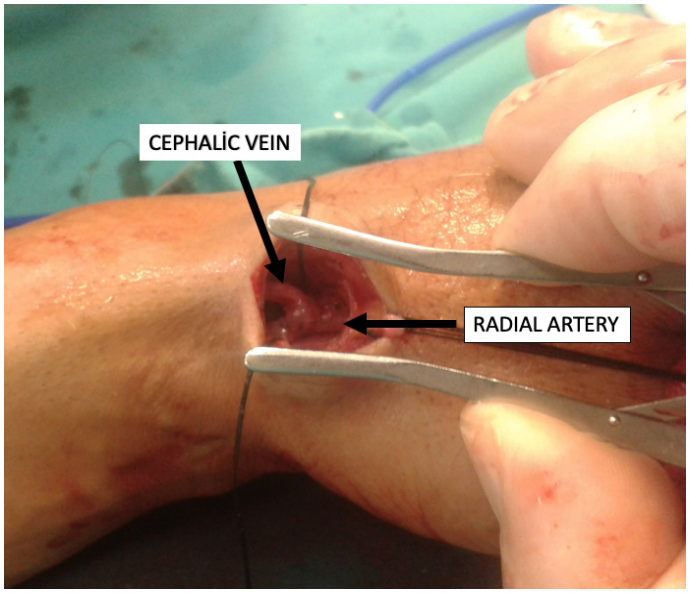



Figure 1: Autogenous radio-cephalic arteriovenous fistula

All the patients gave their informed consent before surgery.

The creation of AVF was performed under local anesthesia (2% Lidocaine-Xylocaine). A longitudinal 3-4 cm skin incision was used, as this was found to give good access to both vein and artery. While evaluated during preoperative planning, a vein diameter of less than 2.5 mm on the preoperative ultrasound duplex did not preclude the surgeon from exploring the vessel in the operating room. Intraoperatively, hydrodilatation maneuver was routinely done with a 4-fr infant feeding catheter for a vein with a diameter <2 mm. During the hydrodilatation, the continuity of the cephalic vein and any recognizable resistance changes were followed closely. If the surgeon felt that it responded adequately, the vein was then used for an AV fistula. If it did not, the patient received a prosthetic graft or another type of autogenous fistula, which is out of the scope for this study. Following clamping, for the standard arteriotomy, the radial artery was incised 6 mm. An end-to-side anastomosis was created between the cephalic vein and the radial artery using continuous polypropylene sutures (7/0 Prolene) with the aid of 2.5x magnifying loupes. A palpable date thrill was taken as an indicator of successful AVF creation.

**Anticoagulation**

Following exploration of the arteries and veins and before placing the clamp, 5,000 IE heparin was routinely administered intravenously to all patients during AVF creation.

**Follow-up**

Antibiotherapy and antiaggregant treatment were not used routinely during the postoperative term.

Postoperative surveillance was scheduled at two weeks and then every month for an additional three to six months to monitor the AVF outcomes and possible complications. All AVFs were assessed clinically 6-8 weeks postoperatively for the presence of a strong thrill over a sufficiently dilated (e.g., 8-10 cm length and >5- 6 mm diameter) vein with a superficial course. Clinical criteria were used for the detection of nonfunctioning AVFs. The inability to cannulate the AVF or to obtain sufficient dialysis blood flow within 6 weeks with three sessions per week after fistula creation was classified as maturation failure, regardless of whether it is patent. If the AVF was considered mature, CVC was removed from the patient; otherwise, CVC was continued to be the route of VA for HD and an additional surgical, or endovascular intervention would be performed to promote fistula maturation or patency. US was performed for all patients with nonmaturating AVFs.

**Outcome Measure Definition, Primary And Secondary End-Points**

The primary endpoint was fistula maturation and functioning AVF, which was defined by the determination of both vascular surgeon and nephrologist. We aimed to evaluate our patients' characteristics that have been reported to be associated with AVF non-maturation and loss of patency in the literature. Primary patency, success rate, assisted primary patency, and primary failure rates were also primary endpoints. We examined the relationship between demographic characteristics including age, gender, diabetes, hypertension, peripheral vascular disease, coronary artery disease, body-mass index, smoking, the type and duration of CVC used; preoperative and intraoperative physical examination and measurements of vessels diameters were also used.

Secondary endpoints were included preoperative (after CVC access)- perioperative and postoperative (max 12-months) blood work studies including CRP, neutrophil, leukocyte, hemoglobin, platelet, albumin, low-density lipoprotein, triglyceride, parathyroid hormone, calcium, phosphorus values and examination of the relationship between maturation process and inflammation.

Reporting Standards for Arterio-Venous Accesses of the Society for Vascular Surgery and the American Association for Vascular Surgery were used to define access functionality and patency.[39] Primary patency was defined as the interval from the time of access creation to any intervention designed to maintain or reestablish patency or to access thrombosis or the time of measurement of patency. Early failure status was assigned to patients with loss of primary patency of the AVF within three months as recorded in the three-month follow-up. Early failure is defined as any fistula that was not used for dialysis either due to loss patency or lack of maturation. This included AVFs that may have required balloon angioplasty to assist with maturation. Early thrombosis of AVF was defined as an immediate failure due to thrombosis of the fistula within 24 hours of creation. Maturation failure is defined as insufficient access flow to maintain dialysis or the inability to cannulate an AVF, within 6 weeks with three sessions per week after fistula creation.[40] Generally, the physical examination conducted

by an experienced dialysis nurse is sufficiently reliable for determining whether the fistula is mature and, therefore, ready for the puncture.[32,41] However, in cases of slow-maturing fistulae, obesity or non-maturation, an ultrasound examination and assessment of hemodynamic parameters (AVF blood flow,) could help to determine whether an AVF is suitable for cannulation or instead failed to mature and is therefore likely to undergo thrombosis as well as having a low flow volume. AVF maturation was defined as the clinical use of the AVF with two needles for 75% of dialysis sessions over a continuous 4 week period, including either a mean dialysis machine blood pump speed of >300 ml/min over four consecutive sessions or a measured Kt/V.1.4 or a urea reduction ratio (URR) >70%(BB).

## Statistical Analysis

Data are given as percentages and means ± SD. Rates were calculated for each patient by dividing the number of events/procedures by the duration of follow-up in years. Survival on dialysis was calculated by the Kaplan-Meier method. Group differences were analyzed by the Student's t test and Mann Whitney-U test. The Chi square analysis was used to compare occurrence rates of adverse events and categorical variables. All tests were two sided, and differences were considered significant at P<0.05. Data were collected, tabulated, and statistically analyzed using an IBM personal computer with statistical package of the social sciences, version 25.0 (SPSS, Inc., Chicago, IL, USA).

## Results

A total of 168 patients were recruited in the study. The demographics and preoperative vessel diameter measurements of all patients included in the study are listed in Table 1.

Of the total 168 patients, 76 (45.2%) were female, and female gender was found to be a significant risk factor in EF of RCAVF (69.5% vs 36.1%; p=0.001). The most common comorbidity was HT (n=123, 73.2%), followed by DM (n=91, 54.2%). There were no significant differences between the groups in terms of age, BMI, DM, HT, KAH, PVD and smoking habits, as shown in Table 1. Even there was a tendency, the radial artery diameters were not significantly higher in NF group than in EF group (p=0.074). The number of patients whose CV diameter < 2 mm were significantly higher in EF group (78.3% vs 22.1 ; p=0.028) (Table 1).

**Table 1:** Baseline demographic characteristics and preoperative vessel measurements

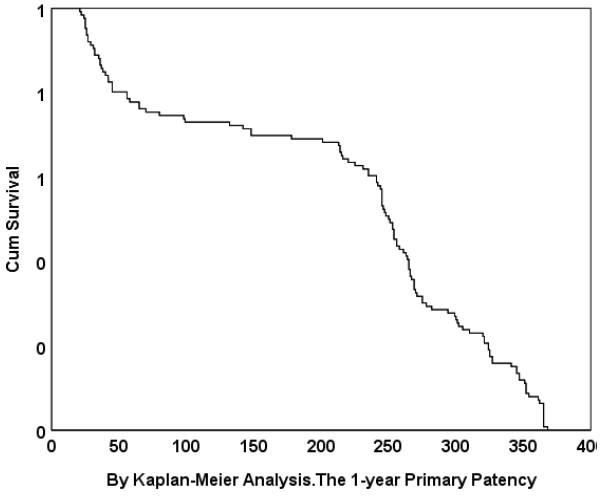
| | Group:1 Early Failure (n=46) | | Group:2 No Failure (n=122) | | |
|---|---|---|---|---|---|
| Demographics | N or median | | N or median | | P |
| Age | 63.1±7.8 | | 61.6 ± 8.7 | | 0.654 |
| BMI | 25.2 ± 4.8 | | 25.7±5.1 | | 0.694 |
| Gender | | | | | |
| Female | 32 | 69.5% | 44 | 36.1% | 0.001 |
| Male | 14 | 30.5% | 78 | 63.9% | |
| Diabetes Mellitus | | | | | |
| No Diabetes Mellitus | 20 | 43.5% | 57 | 46.7% | 0.626 |
| Diabetes Mellitus | 26 | 56.5% | 65 | 53.3% | |
| Hypertension | | | | | |
| No Hypertension | 12 | 26.1% | 33 | 27.1% | 0.485 |
| Hypertension | 34 | 73.9% | 89 | 72.9% | |
| CAD | | | | | |
| No CAD | 37 | 80.4% | 96 | 78.7% | 0.485 |
| CAD | 9 | 19.6% | 26 | 21,3% | |
| PVD | | | | | |
| No PVD | 42 | 91.3% | 112 | 91.8% | 0.694 |
| PVD | 4 | 8.7% | 10 | 8.2% | |
| Smoking | | | | | |
| No Smoking | 32 | 69.6% | 93 | 76.2% | 0.745 |
| Smoking | 14 | 30.4% | 29 | 23.8% | |
| Cephalic vein diameter (mm) | | | | | |
| 1,5-1.9 | 36 | 78.3% | 27 | 22.1% | 0.028 |
| >2.0 | 10 | 21.7% | 95 | 77.9% | |
| Radial artery diameter (mm) | | | | | |
| 1.5-1.9 | 16 | 34.8% | 32 | 26.3% | 0.074 |
| >2.0 | 30 | 65.2% | 90 | 73.7% | |

Abbreviations: BMI: Body-mass index; CAD: Coronary artery disease; PVD: peripheral vascular disease.

Abbreviations: BMI: Body-mass index; CAD: Coronary artery disease; PVD: peripheral vascular disease.

In group 1, of the 46 patients which was classified as early failure, an early thrombosis of AVF was diagnosed in 25 patients (54.3%) and a maturation failure was diagnosed in 6-8 weeks follow-up control in 21 patients (45.7%). In group 2, 39 patients (84.7%) were succesfully treated with thrombectomy ± balloon angioplasty; whereas a new creation of brachiocephalic AVF was required in 7 patients (15.3%). Considering group 1, their duration of CVC access was significantly longer than group 2 (6.8 ± 3.6 months vs 2.3 ± 1.7 months, respectively; p<0.05).

Considering the all study group, the overall maturation failure rate was calculated as 12.5%. Primary patency at 1 year was 72.6%. Kaplan-Meier survival analysis of RCAVF primary patency is shown in figure 2.




| | Median ± SE (Estimate) | %95 Confidence Interval Std. Error |
|---|---|---|
| Primary Failure | 29 ± 2.43 | 24.237 - 33.763 |
| Primary Patency | 250 ±3.96 | 242.235 - 257.765 |

**Figure 2:** Kaplan–Meier survival analysis of arteriovenous fistula(AVF) primary patency. AVF primary patency rate was 72.6 %.

Regarding outcomes for the secondary endpoints, no statistically significant difference among the groups was found in levels of albumin, calcium, intact PTH, serum TG, LDL, blood hemoglobin, WBC and PLT count depicted in table 2. CRP level was higher than the normal range (normal range <3.0 mg/l) at the first 30-days and did not differ between the groups. CRP levels of group 2 were significantly lower than group 1(7.2 ± 9.6 vs. 3.1 ± 3.3 mg/L, respectively; p=0.001) at 1-year. Likewise, the same pattern was followed by the NLR. Median NLR was high in postoperative 30 days in both groups (3.44 ± 0.49 vs. 3.21 ± 0.64, respectively; p=0.342). NLR at 1-year was significantly lower in group 2 when vompared to the NLR of group 1 (2.91± 0.30 vs. 2.17 ± 0.22, respectively; p<0.05).

**Table 2:** Laboratory parameters of the patients

| Parameter | Group 1 (N=46) | Group 2 (N=122) | |
|---|---|---|---|
| | mean ± sd | mean ± sd | p |
| Serum CRP (mg/L) First 30 days | 9.3±11.8 | 8.7±10.7 | 0,059 |
| Serum CRP (mg/L) One year | 7.2 ± 9.6 | 3.1 ± 3.3 | <0.05 |
| Serum Albumin (gr/dl) | 3,3(±0,6) | 3,5(±0,5) | 0,123 |
| Serum Calcium (mg/dl) | 8,4(±1,7) | 8,5(±1,0) | 0,810 |
| Intact PTH (pg/ml) | 264(±183) | 258(±194) | 0,878 |
| Serum TGL (mg/dl) | 150(±72) | 163(±94) | 0,497 |
| Serum LDL (mg/dl) | 90,8(±45) | 95,7(±33) | 0,371 |
| Blood Hemoglobin (g/dl) | 9,9(±1,6) | 10,0(±1,2) | 0,620 |
| White blood cells (109 cell/l) | 7.1 ± 2.2 | 7.3 ± 2.1 | 0.290 |
| PLT (K/mm3) | 230,9(±80) | 220,6(±63) | 0,535 |
| NLR (first 30 days) | 3.44 ± 0.49 | 3.21 ± 0.64 | 0.342 |
| NLR (one year) | 2.91± 0.30 | 2.17 ± 0.22 | <0.05 |

## Discussion

The process of AVF maturation is complex and remains poorly understood, despite numerous studies describing the pathophysiology of the process and biomechanical factors associated. High failure rates for arteriovenous fistula (AVF) are a persistent problem, and Cook et al claimed that failure of maturation may occur in up to 53% of AVF in their invited commentary.[42] Our single-center study of incident hemodialysis patients with enrolled 168 patient-12 month follow-up has demonstrated the cumulative AVF patency rate of 72,6% at 1 year. Previous studies reported AVF cumulative survival rates ranging from 44 to 87%, but the comparison could be misleading as the rates were reported in different definitions.[43] Bashar et al., reported 52 functionally matured fistula from a total of 97 fistulae (53.60%).[44] Al-Jaishi et al analyzing pool of 12,383 patients from 62 unique cohorts reported primary and cumulative AVF patency rates of 60% and 71% respectively.[45] The low to moderate primary patency rate warrants the search for critical factors that affect vascular access outcomes.

Certain clinical factors including female gender, age ≥65 years and forearm AVF placement remain as significant risk factors for AVF failure despite the use of routine vein mapping (46). Bashar et al. found female gender to be associated with a poor maturation rate (26). Miller et al found that fistula adequacy is worse in women, with higher risk of technical failures and early thrombosis.[47] Wasse et al.reported that females were 36% less likely than males to use an AVF at dialysis initiation. [48] The exact mechanism of different AVF outcomes between genders is unclear, but it has been suggested that difference in vascular diameter, reactivity and impaired ability of venous dilatation to arterial pressure being the possible explanations. [47] We did not find age as a prognostic factor for early failure. There has been conflicting results in literature about age. Some studies identified old age as a poor prognostic indicator[49,50], whereas others did not.[51,52] DM is one of the most common causes of ESRD (53), the second most common cause in our study, but it was not associated with adverse outcome of fistula maturation during the first three months of its creation, namely resulting in early failure[54], but it may have a negative impact on late AVF survival [55] since DM promotes platelet aggregation [56] and vascular calcification.[57]

We perform a detailed preoperative vascular evaluation as well as a detailed careful physical examination. We believe that physical examination plays a pivotal role in making a proper decision to create RCAVF. When the decision concerning RA suitability is doubtful, we look at venous mapping results and

often decide for the RCAVF formation attempt when there is a large, distensible CV present with normal Doppler venous waveform and well established phenomena of respiratory filling. In a study by Wells et al, US was considered unnecessary in majority of patients who fulfilled the clinical criteria for AVF creation.[58] Two subsequent randomized controlled trials also did not find additional advantage of vein mapping over clinical assessment in patients with favourable anatomy, in terms of early AVF failure and cumulative AVF survival rate.[59,60] Wong et al admitted that preoperative vein mapping may improve AVF maturation rates but the difference did not reach statistical significance and suggested that larger clinical trial is needed to confirm the clinical benefit .[18] On the other hand, Hossain et al. reported that the primary failure rate in the ultrasound group was 18% compared with 47% ($P < 0.001$) in the group of patients who did not undergo ultrasound examination. In patients without preoperative ultrasound, there were higher rates of new access creation (31% vs 9%; $P< .001$) and fistula abandonment (66% vs 39%; $P < .001$).[61]

There is also an ongoing debate about the threshold of vessel diameters. Wong et al reported that cephalic vein diameter less than 1.6 mm was associated with early radiocephalic AVF failure.[62] Mendes et al found low AVF success rate of 16% in vein diameter of 2 mm or less, as compared to 76% of those >2 mm in a cohort of 44 patients.[36] On the other hand, Lee etal., did not find vein size to be statistically significant in predicting fistula maturation, and AVF can be successfully created in mean vein diameter of <2 mm in more than 70% of patients.[63] Eslami MH et al, a larger target vein diameter was the most predictive variables predicting early failure.[64] The conflict about the use of US is because of veins dynamic status: subject to constriction from changes in venous sympathetic tone, intraoperative measurements may differ from mapped vein diameter and postoperative ultrasound protocols do not take dynamic enlargement with access augmentation (occlusion of the outflow) into account. The use of vein diameter and to a lesser degree, arterial diameter has been tested as a predictor for fistula maturation with reasonable success. There is an increasing agreement that a minimal arterial diameter >2 mm and venous >2 mm should be considered as a cut-off point, as anything less than that is likely to be associated with nonmaturation.[65,66] In our study, not the radial artery diameter but the CV vein diameter found to play a significant role in early failure. A diameter of CV< 2mm was found to be important in early failure.

It is well known that the low resistance circuit, resulting from the creation of the anastomosis between the artery and the vein, triggers an immediate increase in blood flow and elevation of blood pressure in the veins. Elevation of blood flow rate is responsible for a rapid increase in wall shear stress (WSS) and venous tensile stress induced by the velocity gradient on the luminal vessel surface.[67] On the other hand, WSS changes are the major determinants of vessel dilatation and remodeling. In rodent models of venous thrombosis created by ligation of inferior vena cava to induce venous hypertension and altered WSS, thrombus initiation is associated with a rapid vein wall inflammatory reaction involving early endothelial activation and neutrophil infiltration, similarly to observations conducted in the arterial side.[68] In studies studying local hemodynamic conditions in AVF using computational fluid Dynamics, Ene-Lordache and Ramuzzi suggested that despite the significant increase in flow rate, in selected locations, the WSS is oscillating and in average it is low in magnitude.[69] The same team also showed that, while the flow is almost laminar in the proximal arterial limb, in the venous segment leading the velocity field is highly unstable and multidirectional [70] leading a transitional laminar to turbulent-like flow developing in areas of the juxta-anastomotic vein. The presence of disturbed WSS patterns (unstable in direction and magnitude) may induce different physical stimuli in endothelial cells that actually lead to the proliferation of neointimal cells and to induction of a proinflammatory state preventing vessel wall dilatation and outward remodeling of arterial and venous vessels that take place when endothelial cells are exposed to unidirectional WSS directed along vessel axis.

The relationship between high levels of CRP and HD was previously described.[21] CRP serum concentration increases in cases of inflammation, infection and tissue damage. Kaygin et al. found a threefold increase in serum CRP levels in unsuccessful AVF cases and a positive correlation.[21] Wali et al.[71] have stated that AVF insufficiency appears as a result of platelet activation and intimal hyperplasia which is caused by the secretion of mediators because of primary and/or secondary defects in vascular endothelium due to mucoid or myxoid degeneration, mural calcification, inflammatory reaction or erythrocyte/macrophage infiltration on the vascular wall. Chou et al[22] identified CRP level as an independent risk factor for fistula thrombosis. These investigators suggested that CRP level strongly predicts access thrombosis events in maintenance hemodialysis patients, possibly because CRP is a marker of intimal hyperplasia in AVFs.

Morena et al.[72] have stated that due to mineral metabolism deterioration in HD patients and due to inflammation, thrombosis risk increases in the group where CRP, Calcium, PTH increases. In addition, some studies have identified CRP

level as a risk factor for the development of access thrombosis. [73,74] In our study, we did not find a difference in terms of calcium and pth.

The patients enrolled in our study started their HD therapy with a CVC due to being unable to wait for the maturation of AVF. A history of CVC placement or prolonged use of CVC was a poor prognostic predictor of AVF survival[75,76], but the mechanisms by which preexisting CVCs affect AVF maturation remain elusive. Systemic inflammation, a common condition occurring in the setting of CVC placement [27,77], has been proposed as a pathogenetic mechanism underlying neointimal hyperplasia [78], which is a foundation of AVF failure.

Available evidence suggests that CRP is an objective measure of a patient's inflammatory state and that it accurately reflects the generation of proinflammatory cytokines, such as IL-6 and tumor necrosis factor-alpha.[29, 30] There are limited data about long-term serial changes in inflammatory marker levels and their relationship to access type in hemodialysis patients, and the contribution of access type to the inflammatory status of hemodialysis patients is not well described.[29,30] Our study corroborated the findings of previous studies [77] that CVCs in comparison to fistulas have a greater state of inflammation defined by CRP levels in incident hemodialysis patients.Banerjee et al [79], reported that CRP levels decreased over time in cases of an AVF, with the highest inflammatory state 30 days after access placement, and found a significant decrease in CRP levels when there was a change from a CVC to an AVF was associated with decreased CRP levels compared with patients who used CVCs at both times. As also consistent with our study, Goldstein et al. [77], who investigated the levels of inflammatory markers at the time of dialysis initiation and again 6 months later, found that patients with persistent CVC use from dialysis initiation through 6 months had consistently high inflammatory levels over the period, whereas the levels of inflammatory markers were attenuated in patients who changed from a catheter to an AVF. Their findings are consistent with our study as we also obtained a significant decrease in CRP levels after changing the VA from CVC to AVF- not in 30 days but in 1 year-. This finding was strengthened further by our findings on the association of the inflammatory state reflected by NLR.

NLR level increased with CVC and stay high when a mature functioning AVF was obtained. In patients whose CVC was removed, a dramatic decrement in NLR was observed in one year. The clinical trials showed that IL-6, pentraxin and complement system had roles in AVF dysfunction [80,81]. Yilmaz et al. [25] reported that in chronic HD patients with established AVF access, patients who developed late stenosis were found to have higher level of NLR. An increased level of NLR reflects inflammation .[24,80-83] Spark et al. Evaluated NLR to predict mortality in patients with chronic critical limb ischemia. They found that an elevated NLR along with a high troponin level (>0.1) was the only independent predictor of mortality in those patient.[84] In a study of 83 patients who underwent infrapopliteal percutaneous interventions for critical limb ischemia, Chan et al.[85] reported that those with NLR > 5.25 had an increased risk of death.

This finding that change in CRP levels and NLR are associated with change in access type adds additional support to the body of the observational evidence, suggesting that the catheter itself contributes to an increase in inflammatory marker levels in hemodialysis patients.

## Study Limitation

Nevertheless, this study was limited by being a retrospective study. Hence, some data might have been unavailable, such as blood flow measurements and the results of other inflammatory marker blood tests. This study was conducted with a homogeneous cohort of ESRD patients from a single institution. Hence, the results might not be the same in other settings where people have different reference ranges for WBC counts or dissimilar material types of CVC are used.

## Conclusion

As a conclusion, early failure of RCAVF is an obstacle we have to overcome. Certain clinical factors including female gender, anatomical factors including a diameter of CV < 2mm was found significant in early failure. A history of CVC placement or prolonged use of CVC is a poor prognostic predictor of AVF survival in which systemic inflammation plays an important role. A significant decrease in CRP levels was observed after changing the VA from CVC to AVF- not in 30 days but in 1 year-. This finding was strengthened further by our findings on the association of the inflammatory state reflected by NLR.

## Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

## References

1. Fila B, Ibeas J, Tey RR, et al. Arteriovenous fistula for haemodialysis: the role of surgical experience and vascular ac- cess education. Nefrologia 2016; 36: 89-94.
2. Takemoto Y, Naganuma T. Economic issues of chronic kidney disease and end-stage renal disease. Contrib Nephrol 2019; 198: 87-93.
3. Bashar K, Healy D, Browne LD, Kheirelseid EA, Walsh MT, Moloney MC, et al. Role of far infrared therapy in dialysis arterio-venous fistula maturation and survival: systematic review and meta-

analysis. PLoS One. (2014); 9: e104931.

4. Chand DH, Valentini RP, Kamil ES. Hemodialysis vascular access options in pediatrics: considerations for patients and practitioners. Pediatr Nephrol. (2009); 24: 1121–1128.
5. Santoro A, Canova C, Freyrie A, Mancini E. Vascular access for hemodialysis. J Nephrol. (2006); 19: 259–264.
6. Schmidli J, Widmer MK, Basile C, Donato G, Gallieni M, et al. Editor's Choice - Vascular Access: 2018 Clinical Practice Guidelines of the European Society for Vascular Surgery (ESVS). Eur J Vasc Endovasc Surg 2018 Jun;55(6):757-818.
7. Feldman HI, Kobrin S, Wasserstein A. Hemodialysis vascular access morbidity. J Am Soc Nephrol 1996;7:523-35.
8. National Kidney Foundation-Dialysis Outcomes Quality Initiative. National Kidney Foundation. NKF-DOQI clinical practice guidelines for vascular access. Am J Kidney Dis 1997;30(suppl):S150-91.
9. Miller PE, Tolwani A, Luscy CP, Deierhoi MH, Bailey R, Redden DT, et al. Predictors of adequacy of arteriovenous fistulas in hemodialysis patients. Kidney Int 1999;56:275e80.
10. R.L.Pisoni, E.W.Young, D.M.Dykstra, etal.,Vascular access use in Europe and the United States: results from the DOPPS, Kidney Int. 61 (1) (2002) 305–316.
11. A.J. Collins, R.N. Foley, D.T. Gilbertson, S.C. Chen, The state of chronic kidney disease, ESRD, and morbidity and mortality in the first year of dialysis, Clin. J. Am. Soc. Nephrol. 4 (Suppl 1) (2009) S5–S11.
12. Lauvao LS, Ihnat DM, Goshima KR, Chavez L, Gruessner AC, Mills Sr JL. Vein diameter is the major predictor of fistula maturation. J Vasc Surg 2009; 49 (6) :1499-504.
13. Maya ID, O'Neal JC, Young CJ, Barker-Finkel J, Allon M. Outcomes of brachiocephalic fistulas, transposed brachiobasilic fistulas, and upper arm grafts. Clin J Am Soc Nephrol 2009;4(1): 86e92.
14. Dageforde LA, Harms KA, Feurer ID, et al. Increased mini- mum vein diameter on preoperative mapping with duplex ultrasound is associated with arteriovenous fistula maturation and secondary patency. J Vasc Surg 2015;61:170-6.
15. Robbin ML, Chamberlain NE, Lockhart ME, et al. Hemodial- ysis arteriovenous fistula maturity: US evaluation. Radiology 2002; 225: 59-64.
16. National Kidney Foundation's KDOQI 2006 Vascular Access Guidelines. Am J Kidney Dis 2006;48: S177-322.
17. Sidawy AN, Spergel LM, Besarab A, Allon M, Jennings WC, Padberg Jr FT, et al. The Society for Vascular Surgery: clinical practice guidelines for the surgical placement and maintenance of arteriovenous hemodialysis access. J Vasc Surg 2008; 48:2Se 25S.
18. Wong CS, McNicholas N, Healy D, Clarke-Moloney M, Coffey JC, Grace PA, Walsh SR. A systematic review of preoperative duplex ultrasonography and arteriovenous fistula formation. J Vasc Surg 2013; 57:1129e33.
19. A. Brahmbhatt, A. Remuzzi, M. Franzoni, S. Misra, The molecular mechanisms of hemodialysis vascular access failure, Kidney Int. 89 (2) (2016) 303–316.
20. H. Hu, S. Patel, J.J. Hanisch, et al., Future research directions to improve fistula maturation and reduce access failure, Semin. Vasc. Surg. 29 (4) (2016) 153–171.
21. M.A. Kaygin, U. Halici, A. Aydin, et al., The relationship between arteriovenous fistula success and inflammation, Ren, Fail 35 (8) (2013) 1085–1088.
22. Chou CY, Kuo HL, Yung YF, Liu YL, Huang CC. C-reactive Protein Predicts Vascular Access Thrombosis in Hemodialysis Patients. Blood Purif 2006;24(4):342-6.
23. de Graaf R, Dammers R, Vainas T, Hoeks AP, Tordoir JH. Detection of cell-cycle regulators in failed arteriovenous fistulas for hemodialysis. Nephrol Dial Transplant. 2003;18:814-818.
24. Muhammed Suliman MA, Bahnacy Juma AA, Ali Almadhani AA, Pathare AV, Alkindi SS, Uwe Werner F. Predictive value of neutrophil to lymphocyte ratio in outcomes of patients with acute coronary syndrome. Arch Med Res. 2010;41(8):618–622.
25. Yilmaz H, Alper Bozkurt A, Cakmak M, Celik HT, et al. Relationship Between Late Arteriovenous Fistula (AVF) Stenosis and Neutrophil-Lymphocyte Ratio (NLR) in Chronic Hemodialysis Patients. Ren Fail 2014 Oct;36(9):1390-4.
26. Bashar K, Zafar A , Ahmed K, Kheirelseid EAH, Healy D et al. Can a Neutrophil-Lymphocyte Ratio Derived From Preoperative Blood Tests Predict Arteriovenous Fistula Maturation? Ann Vasc Surg 2016 Aug;35:60-7.
27. Dukkipati JR, Molnar MZ, Park J ,etal., Association of vascular access type with inflammatory marker levels in maintenance hemodialysis patients, Semin. Dial. 27 (4) (2014) 415–423.
28. Wongmahisorn Y. Maturation of arteriovenous fistulas in patients with and without preexisting hemodialysis catheters. Annals of Medicine and Surgery 2019;48:11-16.
29. Sachdeva M, Kovalchuk O, Bitzer M, Mokrzycki MH. Vascular access type and changes in inflammatory markers in incident dialysis patients: a pilot study. J Vasc Access. 2009;10:174-179.
30. Coli L, Donati G, Cappucilli ML, et al. Role of the he- modialysis vascular access type in inflammation status and monocyte activation. Int J Artif Organs. 2011;34:481-488.
31. McGrogan DG, Maxwell AP, Khawaja AZ, Inston NG. Current tools for prediction of arteriovenous fistula outcomes. Clin Kidney J 2015;8:282e9.

32. Davidson I, Chan D, Dolmatch B, et al. Duplex Ultrasound evaluation for dialysis access selection and maintenance: a practical guide. J Vasc Access 2008;9(1):1-9.
33. Malovrh M. Native arteriovenous fistula: preoperative evaluation. Am J Kidney Dis. 2002;39(6):1218-1225.
34. Pajek J, Malovrth M. Preoperative ultrasound still valuable for radio-cephalic arteriovenous fistula creation? J Vasc Access 2017; 18 (Suppl 1): S5-S9
35. Brimble KS, Rabbat ChG, Treleaven DJ, Ingram AJ. Utility of ultrasonographic venous assessment prior to forearm arteriovenous fistula creation. Clin Nephrol. 2002;58(2):122-127.
36. Mendes RR, Farber MA, Marston WA, Dinwiddie LC, Keagy BA, Burnham SJ. Prediction of wrist arteriovenous fistula maturation with preoperative vein mapping with ultrasonography. J Vasc Surg. 2002;36(3):460-463.
37. Kordzadeh A, Chung J, Panayiotopoulos YP. Cephalic vein and radial artery diameter in formation of radiocephalic arteriovenous fistula: a systematic review. J Vasc Access. 2015;16(6): 506-511.
38. Silva MB Jr, Hobson RWII, Pappas PJ, et al. A strategy for increasing use of autogenous hemodialysis access procedures: impact of preoperative noninvasive evaluation. J Vasc Surg. 1998;27(2):302-307.
39. Sidawy AN, Gray R, Besarab A, Henry M, Ascher E, et al. Recommended standards for reports dealing with arteriovenous hemodialysis accesses. J Vasc Surg 2002;35(3):603e10.
40. Barreto P, Almeida P, Matos N, Queirós JA, J Pinheiro J et al. Preoperative Vessel Mapping in Chronic Kidney Disease Patients - A Center Experience. J Vasc Access 2016 Jul 12;17(4):320-7.
41. Malovrh M. The role of sonography in the planning of arteriovenous fistulas for hemodialysis. Semin Dial. 2003; 16:299- 303.
42. Cook KM, Padberg Jr FT. Is There an Accurate Pre-operative Criterion for Dialysis Access Artery or Vein Diameter? Eur J Vasc Endovasc Surg 2017 Jun;53(6):879.
43. Allon M, Robbin ML. Increasing arteriovenous fistulas in hemodialysis patients: problems and solutions. Kidney Int 2002; 62:1109-24.
44. Bashar K, Zafar A, Elsheikh S, Healy DA, Clarke-Moloney M, Casserly L, Burke PE, Kavanagh EG, Walsh SR. Predictive Parameters of Arteriovenous Fistula Functional Maturation in a Population of Patients with End-Stage Renal Disease. PLoS One. 2015; 10(3):e0119958.
45. Al-Jaishi AA, Oliver M, Thomas SM et al. Patency rates of the arteriovenous fistula for hemodialysis: a systematic review and meta-analysis. Am J Kidney Dis 2014; 63:464-78.
46. Peterson WJ, Barker J, Allon M. Disparities in fistula maturation persist despite preoperative vascular mapping. Clin J Am Soc Nephrol 2008; 3:437-41.
47. Miller CD, Robbin ML, Allon M. Gender differences in outcomes of arteriovenous fistulas in hemodialysis patients. Kidney Int 2003; 63:346-52.
48. Wasse H, Hopson DS, McClellan W. Racial and Gender Differences in Arteriovenous Fistula Use among Incident Hemodialysis Patients. Am J Nephrol. 2010; 32(3):234-241.
49. Lee T, Thamer M, Zhang Q, et al. Vascular access type and clinical outcomes among elderly patients on hemodialysis. Clin J Am Soc Nephrol 2017; 12: 1823-30.
50. Richardson AI 2nd, Leake A, Schmieder GC, et al. Should fistulas really be first in the elderly patient? J Vasc Access 2009; 10: 199-202.
51. Lok CE, Oliver MJ, Su J, et al. Arteriovenous fistula out- comes in the era of the elderly dialysis population. Kidney Int 2005; 67: 2462-9.
52. Schinstock CA, Albright RC, Williams AW, et al. Outcomes of arteriovenous fistula creation after the Fistula First Initiative. Clin J Am Soc Nephrol 2011; 6: 1996-2002.
53. Polenakovic M, Sikole A, Nikolov IG, Georgiev D, Selim G, et al. Diabetics on dialysis in the Republic of Macedonia: A nationwide epidemiological study. Prilozi. 2010; 31(1):261-77.
54. Gjorgjievski N, Vidimliski PD, Gerasimovska V, Kuzmanovska SP et al. Primary Failure of the Arteriovenous Fistula in Patients With Chronic Kidney Disease Stage 4/5. Open Access Maced J Med Sci 2019 Jun 15;7(11):1782-1787.
55. Wongmahisorn Y. Survival and Prognostic Predictors of Primary Arteriovenous Fistula for Hemodialysis. Ann Vasc Dis 2019 Dec 25;12(4):493-499.
56. Paneni F, Beckman JA, Creager MA, et al. Diabetes and vas- cular disease: pathophysiology, clinical consequences, and medical therapy: part I. Eur Heart J 2013; 34: 2436-43.
57. Liabeuf S, Olivier B, Vemeer C, et al. Vascular calcification in patients with type 2 diabetes: the involvement of matrix Gla protein. Cardiovasc Diabetol 2014; 13: 85.
58. Wells AC, Fernando, Butler A, Huguet E, Bardley JA, Pettigrew GJ. Selective use of ultrasonographic vascular mapping in the assessment of patients before hemodialysis access surgery. Br J Surg 2005; 92:1439-43.
59. Nursal TZ, Oguzkurt L, Tercan F et al. Is routine preoperative ultrasonographic mapping for arteriovenous fistula creation necessary in patients with favourable physical examination findings? Results of a randomized controlled trial. World J Surg 2006; 30:1100-07.

60. Smith GE, Barnes R, Chetter IC. Randomized clinical trial of selective versus routine preoperative duplex ultrasound imaging before arteriovenous fistula surger. Br J Surg 2014; 101:469-74.
61. Hossain S, Sharma A, Dubois L, DeRose G, Duncan A, Power AH. Preoperative point-of-care ultrasound and its impact on arteriovenous fistula maturation outcomes. J Vasc Surg. 2018; 68(4):1157-1165.
62. Wong V, Ward R, Taylor J, Selvakumar S, How TV, Bakran A. Factors associated with early failure of arteriovenous fistulae for haemodialysis access. Eur J Vasc Endovasc Surg 1996; 12:207-13.
63. Lee KG, Chong TT, Goh N, Achudan S, Tan YL, et al. Outcomes of Arteriovenous Fistula Creation, Effect of Preoperative Vein Mapping and Predictors of Fistula Success in Incident Haemodialysis Patients: A Single-Centre Experience. Nephrology (Carlton) 2017 May;22(5):382-387.
64. Eslami MH, Zhu CK, Rybin D, Doros G, Siracuse JJ, Farber A. Simple Predictive Model of Early Failure Among Patients Undergoing First-Time Arteriovenous Fistula Creation. Ann Vasc Surg 2016 Aug;35:46-52.
65. Leblanc M, Saint-Sauveur E, Pichette V. Native arteriovenous fistula for hemodialysis: what to expect early after creation? J Vasc Access 2003;4:39-44.
66. 2006 Updates Clinical Practice Guidelines and Recommendations [Internet]. Available at: http://www.kidney.org/professionals/kdoqi/pdf/12-50-0210_JAG_DCP_Guidelines- VA_Oct06_SectionC_ofC.pdf; 2006. Accessed November 18, 2015.
67. Remuzzi A, Bozzetto M. Biological and Physical Factors Involved in the Maturation of Arteriovenous Fistula for Hemodialysis. Cardiovasc Eng Technol 2017 Sep;8(3):273-279.
68. Bergan, J. J., L. Pascarella, and G. W. Schmid-Schonbein. Pathogenesis of primary chronic venous disease: insights from animal models of venous hypertension. J. Vasc. Surg. 47:183–192, 2008.
69. Ene-Iordache, B., and A. Remuzzi. Disturbed flow in radial-cephalic arteriovenous fistulae for haemodialysis: low and oscillating shear stress locates the sites of stenosis. Nephrol. Dial. Transplant. 27:358–368, 2012.
70. Ene-Iordache, B., C. Semperboni, G. Dubini, and A. Remuzzi. Disturbed flow in a patient-specific arteriovenous fistula for hemodialysis: multidirectional and reciprocating near-wall flow patterns. J. Biomech. 48:2195–2200, 2015.
71. Wali MA, Eid RA, Dewan M, Al-Homrany AM. Pre-existing histopathological changes in the cephalic vein of renal failure patients before arterio-venous fistula (AVF) construction. Ann Thorac Cardiovasc Surg. 2006;12:341–348.
72. Morena M, Bosc JY, Jaussent I, et al. The role of mineral metabolism and inflammation on dialysis vascular access failure. Vasc Access. 2006;7:77–82.
73. Schillinger M, Exner M, Sabeti S, et al. Excessive carotid in-stent neointimal formation predicts late cardiovascular events. J Endovasc Ther. 2004;11:229-239.
74. Hashimoto H, Kitagawa K, Hougaku H, Etani H, Hori M. Realtionship between C-reactive protein and progression of early carotid atherosclerosis in hypertensive subjects. Stroke. 2004;35: 1625-1630.
75. Erkut B, Ünlü Y, Ceviz M, et al. Primary arteriovenous fistulas in the forearm for hemodialysis: effect of miscellaneous factors in fistula patency. Ren Fail 2006; 28: 275-81.
76. Radoui A, Lyoussfi Z, Haddiya I, et al. Survival of the first arteriovenous fistula in 96 patients on chronic hemodialysis. Ann Vasc Surg 2011; 25: 630-3.
77. Goldstein SL, Ikizler TA, Zappitelli M, Silverstein DM, Ayus JC. Non-infected hemodialysis catheters are associated with increased inflammation compared to arteriovenous fistulas. Kidney Int. 2009;76:1063-1069.
78. J.C. Duque, L. Martinez, M. Tabbara, et al., Arteriovenous fistula maturation in patients with permanent access created prior to or after hemodialysis initiation, J. Vasc. Access 18 (3) (2017) 185–191.
79. Banerjee T, Kim SJ, Astor B, Shafi T, et al. Vascular Access Type, Inflammatory Markers, and Mortality in Incident Hemodialysis Patients: The Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. Am J Kidney Dis 2014 Dec;64(6):954-61.
80. Marrone D, Pertosa G, Simone S, et al. Local activation of interleukin 6 signaling is associated with arteriovenous fistula stenosis in hemodialysis patients. Am J Kidney Dis. 2007; 49(5):664–673.
81. Castellano G, Di Vittorio A, Dalfino G, et al. Pentraxin 3 and complement cascade activatio{Bibliography}n in the failure of arteriovenous fistula. Atherosclerosis. 2010;209(1):241–247.
82. Arbel Y, Finkelstein A, Halkin A, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis. 2012;225(2):456–460.
83. Dogan M, Akyel A, Cimen T, et al. Relationship between neutrophil-to-lymphocyte ratio and saphenous vein graft disease in patients with coronary bypass. Clin Appl Thromb Hemost. 2013.
84. Spark JI, Sarveswaran J, Blest N, et al. An elevated neutrophil-lymphocyte ratio independently predicts mortal- ity in chronic critical limb ischemia. J Vasc Surg 2010;52: 632-6.
85. Chan C, Puckridge P, Ullah S, et al. Neutrophil-lymphocyte ratio as a prognostic marker of outcome in infrapopliteal percutaneous interventions for critical limb ischemia. J Vasc Surg 2014;60:661e8.