The Effects of Vascular Diameters on the Maturation and Patency of the Arteriovenous Fistulas for Hemodialysis

Damar Çaplarının Hemodiyaliz için Oluşturulan Arteriovenöz Fistüllerin Olgunlaşma ve Açıklıkları Üzerine Etkileri

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Abstract

Primary failure of arteriovenous fistula (AVF) is a serious problem. For decreasing the failure rates, pre-operative ultrasonographic evaluation of the target vessels is popular in recent years. However, in most clinics ultrasonographic evaluation is not routine. Operation is usually performed after physical examination. The aim of this study is to evaluate the primary failure reasons and the relation between vessel diameters and primary failure. 448 operations, including AVF creation, revisions and closures performed between 01.01.2012-31.12.2015 were evaluated retrospectively. Age, gender, race, site, side, operation, reason(s), used artery and vein, diameters, anastomosis type, thrill, patency and co-morbid diseases evaluated. Patencies were controlled on the 10th day, on the 1st, 6th months, 1st and 2nd years. Of the 448 operations, 86.38% was creation, 3.79% was closure and 9.82% were revision. Leading revision reason and performed procedure was thrombosis (56.81%) and thrombectomy. Leading reason of closures was ischemia (35.29%). Mean brachial artery diameter was 4.45±0.45 mm and mean radial artery diameter was 2.52±0.42 mm. Mean vein diameters were 3.31±0.60 mm for basilic vein and 2.47±0.64 mm for cephalic vein. In patients with less than diameter of 4.45 mm for brachial artery ($p<0.003$) and less than diameter of 2.15 mm for cephalic vein ($p<0.005$), dysmaturation or failure rates were significantly higher. Preoperative ultrasonographic evaluation of the vessels is a good choice even if the physical examination of the patient is good. We recommend min 4.45 mm brachial artery, min 2.15 mm cephalic vein and min 2.20 mm radial artery diameter. Presence of thrill at the end of the AVF creation is an important marker for an adequate, long lasting AVF.

Keywords: Arteriovenous Fistulas, Cardiovascular Surgical Procedure, Hemodialysis, Ultrasonography, Vascular Patency

Öz

Arteriovenöz fistülün (AVF) primer yetersizliği ciddi bir sorundur. Yetersizlik oranlarını azaltmak için, damarların preoperatif ultrasonografik değerlendirilmesi son yıllarda popülerdir. Ancak, çoğu klinikte ultrasonografik değerlendirme rutin değildir. Ameliyat genellikle fizik muayeneden sonra yapılmaktadır. Bu çalışmanın amacı primer yetersizlik nedenlerini, damar çapları ile primer yetersizlik arasındaki ilişkiyi değerlendirmektir. 01.01.2012-31.12.2015 arasında yapılan AVF oluşturma, revizyonlar ve kapatmalar dahil olmak üzere 448 operasyon retrospektif olarak değerlendirildi. Hastalar yaş, cinsiyet, ırk, operasyon yeri, tarafı, operasyon, nedeni, kullanılan arter, ven, çapları, anastomoz tipi, tril, açık kalım ve eşlik eden hastalıkları açısından değerlendirildi. Açık kalımlar 10. günde, 1. ve 6. aylarda, 1. ve 2. yılda kontrol edildi. 448 operasyonun %86.38'i oluşturma, %3.79'u kapatma ve %9.82'si revizyondu. En sık revizyon nedeni ve uygulanan prosedür tromboz (%56.81) ve trombektomiydi. Kapatmaların en sık nedeni iskemiydi (%35.29). Ortalama brakiyal arter çapı 4.45±0.45 mm ortalama radial arter çapı 2.52±0.42 mm idi. Ortalama bazilik ven çapı 3.31±0.60 mm ortalama cephalic ven çapı 2.47±0.64 mm idi. Brakiyal arter çapı 4.45 mm'den ($p<0.003$) ve cephalic ven çapı 2.15 mm'den ($p<0.005$) küçük olan hastalarda, dismatürasyon veya yetersizlik oranları anlamlı olarak yüksekti. Damarlarınn preoperatif ultrasonografik değerlendirilmesi, fizik muayene bulguları iyi bile olsa iyi bir seçenektir. Uzun ömürlü, yeterli bir AVF için minimum 4.45 mm'lik brakial arter, minimum 2.15 mm'lik cephalic ven ve minimum 2.20 mm'lik radial arter çapı olmasını öneririz. Ayrıca operasyon sonunda tril varlığı da uzun ömürlü, yeterli bir AVF için önemli bir işarettir.

Anahtar Kelimeler: Arteriyovenöz Fistül, Damar Açık Kalımı, Hemodiyaliz, Kardiyovasküler Cerrahi Prosedür, Ultrasonografi

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Introduction

The leading treatment modality in the end-stage renal disease (ESRD) is the hemodialysis (HD) far from the renal transplantation or peritoneal dialysis (1). Arteriovenous fistulas (AVF), grafts (AVG) or central venous catheters (CVC) can be used for HD. In many studies, it was shown that AVF or AVG meets the lower morbidity and mortality rates (2-6). Autogenous AVF (surgically created communications between vein and artery, usually in the upper extremities) are the most used options, because of allowing effective and long lasting vascular access (7). Despite their lower morbidity and mortality rates, the main problems about the AVF are maturation and failure. "Maturation" can be described as the condition of allowing minimum 350-450 ml/min blood flow for a 3-4 hours HD session and allowing to be cannulated by two dialysis needles with increased blood flow, increased vein diameter and increased visibility of the vein (8). The common reasons for the dysmaturation or failure of an AVF can be listed as small diameters of the artery or vein, faults in the surgical technique, enforcement during entry of the dialysis needles, hypotension, hypertension in long term, atherosclerosis, diabetes and also disordered metabolisms of minerals (8,9). If we look at the issue from this perspective, the patients that we create AVF are mostly elderly patients with co-morbid diseases and maturation or maintenance of a created AVF remains as a serious problem in front of us. As one of these reasons, small diameters of the arteries and veins are those that we can`t change and depend on the patient. However, as a non-invasive and simple procedure, ultrasonography (USG) gives us

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the chance of evaluating the diameters, lumen pathologies and the wall structure of the vessels before the surgery (10). Flow measurements can also be made with the Color Doppler mode before or after the surgery. There are studies which state the pre-operative imaging of the vessels reduces the dysmaturation or failure rates of the AVF (11). Also, evaluating the vessels with USG before the surgery has become a recommended rule in some of the guidelines by the time (National Kidney Foundation Kidney Disease Outcomes Quality Initiative 2006; American College of Cardiology Foundation Appropriate Use Criteria Task Force et al. 2013). Despite of the recommendations and studies, in most of the clinics which the AVF were created, preoperative use of USG has not become routine and remained for only for patients who have predictable arterial or venous problems.

The aim of this study is to evaluate the relationship between the diameters of the vascular structures, surgical technique, co-morbid diseases of the patients and patency time. We also evaluated the other interventions (revisions and closures) that we performed to AVF in our clinic. We reported our results in the light of the literature.

Material and Method

448 operations performed to AVF, including new AVF creation, revisions and closures in our cardiovascular surgery clinic between 01.01.2012-31.12.2015 were evaluated retrospectively. Age, sex, race, operation site, side, applied operation, reason(s) for the operation, used artery and diameter, used vein and diameter, anastomosis type, presence and intensity of thrill, patency of the AVF and co-morbid diseases of the patients were collected from the patients' hospitalization files and electronic data. Diameters of the arteries and veins were measured under light tourniquet via sphygmomanometer sleeve of 40 mmHg. before the operation. Mindray Digital Ultrasonic Diagnostic Imaging System, Model: DP-10 (Shenzhen Mindray Bio-Medical Electronics Co. Ltd, Shangai International Holding Corp. GmbH (Europe), Hamburg/Germany) was used for the measurement of the diameters. All anastomoses were performed with the same brand of 7/0, 8 mm., round, double needle, blue monofilament prolene sutures under the local anesthesia (Prilocaine HCl) by only 2 surgeons who are also the authors. The presence and intensity of the thrill was measured according to the scale that we create in our clinic by the same two surgeons (0= no thrill, 1= Light thrill, 2= Strong thrill). All patients' systolic blood pressures were between 90-140 mmHg. during the thrill measurements. Unless contraindicated, 100 mg. acetylsalicylic acid and appropriate antibioteraphy were given to all the patients who AVF had been created. The patencies of the AVF were controlled firstly on the 10th day, after the operation at the same session with getting sutures. Then, at the end of the 1st month, just before the use of AVF, at the end of the 6th month, at the end of the 1st and at the end of the 2nd year, in cooperation with the nephrology clinic and dialysis center of our hospital. Summary statistics were expressed as mean ± standard deviation or percentage (%). Logistic regression was used to determine whether there is any statistically significant association between artery and vein diameters, and dysmaturation or failure of AVF. ROC analyses were used to determine the cut-off values for artery and vein diameters. Chi-square test was used to evaluate an association between risk groups and AVF dysmaturation or failure. Log-rank test and Kaplan-Meire estimation were used to assess the differences between high and low-risk groups in terms of patency rates. Finally, Log-rank test was used to determine the potential effect of co-morbid diseases on the dysmaturation of AVF. All statistical analyses were performed using the software R. A p-value of <0.05 was considered statistically significant.

Results

A total of 448 operations were evaluated retrospectively. Of the 448 operations, 86.38% (n=387) were AVF creation, 3.79% (n=17) were closure and 9.82% (n=44) were revisions. The leading reason for the revisions was thrombosis with 56.81% (n=25) and thrombectomy was the most performed procedure in revisions (Table 1). The leading reason of closures was ischemia of the upper extremity with 35.29% (n=6), aneurysms were in the second place with 23.52% (n=5), cardiac failure and infection were sharing the third place with 17.64% (n=3). Only one AVF was closed because of a successful renal transplantation. Of the 387 AVF created patients who were referred to our cardiovascular surgery clinic for the creation of AVF by the nephrology clinic of our hospital, 36.4% (n=141) were female, 63.6% (n=246) were male. All patients were white race. Mean age was 66.82±13.33, mean patency time was 16.35±14.88 months (min=0, median=12, max=64). 28.9% (n=112) of the created AVF were at the elbow level, 71.1% (n=275) were at the wrist level. 81.1% (n=337) were on the left side, 12.9% (n=50) were on the right side. In 387 AVF creation operations; 60.6% (n=274) radial artery, 39.4% (n=113) brachial artery, 94.6% (n=366) cephalic vein and 5.4% (n=21) basilic vein were used. At the end of the AVF creation operations; in 88.6% (n=343) patient strong trill, in 10.3 % (n=40) patient light trill and in 1.0 % (n=4) patient no trill was obtained. In 91.2% (n=349) of the patients' pulsation was present simultaneously with trill and in 9.8% (n=38) no pulsation was present (Table 2). Mean values of the used vascular structures for AVF creation and patency time were given in Table 3. Number and percentage of closed

AVF at the 10th day, 1st month, 6th month, 1st year and 2nd year of the follow-up were given in Table 4. Cephalic vein diameter was statistically useful in predicting whether the AVF would be dysmatured or failed on the 10th day, 1st and 6th month of follow-up (in order; OR=0.19, p=0.012; OR=0.35, p=0.020; OR=0.56, p=0.003; Univariate Logistic Regression). Brachial artery diameter was also statistically useful for the 6th month (OR=0.22, p=0.006, Logistic Regression). In the ROC analysis of these parameters; based on the 6th month, cut-off values to be used to define patient's groups as high and low AVF dysmaturation and/or failure risk were determined as 4.45 mm for brachial artery (AUROC=0.674, sensitivity=0.74, specificity=0.59) and 2.15 mm for cephalic vein (AUROC=0.731, sensitivity=0.80, specificity=0.57 for 10th day; AUROC=0.677, sensitivity=0.78, specificity=0.58 for 1st month; and AUROC=0.619, sensitivity=0.57, specificity=0.61 for 6th month). AVF dysmaturation or failure rates were significantly higher in patients whose brachial artery diameter were less than 4.45 mm at the 6th month (36.4% vs. 12.2%, p=0.003, Chi-square test) and at the 1st year (%54.5 vs. %34.5, p=0.032, Chi-square test) of follow-up. AVF dysmaturation or failure rates were also significantly higher in patients whose cephalic vein diameter were less than 2.15 mm on the 10th day, 1st month and 6th months (7.4% vs. 1.5%, 11% vs. 2.5%, 41.1% vs. 24.6% respectively, all p<0.005, Chi-square test). In the survival analysis; estimation of patency rates for all patients were given in Table 5 and Figure 1. According to the cut-off value 2.15 mm that we determined for cephalic vein, we obtained significant difference about patency rates at the 6th month and 12th month of follow-up between the high and low risk groups (p=0.011 and p=0.0047, Log-rank test, Kaplan-Meier Analysis) (Figure 2). According to the cut-off value 4.45 mm that we determined for brachial artery, we obtained significant difference about patency times at the 24th month of follow up between the high and low risk groups (p=0.009, Log-rank test, Kaplan-Meier Analysis) (Figure 3). Mean radial artery diameter was 2.52±0.42 mm. Mean radial artery diameter of the non-patent AVF was 2.21 ± 0.39 mm. The difference was not statistically significant. Only 8.01% (n=31) of the patients had no co-morbid diseases. However, in the rest of them, hypertension, diabetes and atherosclerotic heart diseases were the top 3 co-morbid diseases with the 70.03% (n=272), 45.2% (n=175) and 21.2% (n=82) respectively. None of the co-morbid diseases had potential effect alone on the dysmaturation of the AVF (p>0.05, Log-rank test) (Table 6). In the evaluation of thrill and patency, of the 387 AVF created patients, 1.03% (n=4) had no thrill, 9.30% (n=36) had light thrill and 89.66% (n=347) had strong thrill. The AVF of the "no thrill" patients were not matured already at the 10th day control. AVF of the all "light thrill" patients were failed until the end of 1st year. At the end of the 2nd year 18.87% of "strong thrill" patients' AVF were also not patent.

Table 1. Reasons for revisions and performed procedures

Reasons For Revisions And Performed Procedures	n	%
Thrombosis / Thrombectomy	25	56.81
Bleeding / Pimary vessel repair	8	18.18
Aneurysm / Aneurysmectomy	5	11.36
Infection / Debridement	4	9.09
Vein Stenosis / Resection and reanastomosis	2	4.54

(n: count, %: percentage)

Table 2. Demographic data of the 387 patient who were created AVF.

Sex	63.6% (n:246) Male 36.4% (n:141) Female
Mean Age	66.82±13.33
Race	100% (n: 387) White race
Mean Patency Time	16.35±14.88 Months
Localizations of the Created AVF	28.9% (n:112) Elbow level 71.1% (n:275) Wrist level
Side	81.1% (n:337) Left 12.9% (n:50) Right
Used Arteries	39.4% (n:113) Brachial artery 60.6% (n:274) Radial artery
Used Veins	5.4% (n:21) Basilic vein 94.6% (n:366) Cephalic vein
Thrill	1.00% (n:4) No thrill (0) 10.3% (n: 40) Light thrill (1) 88.6% (n:343) Strong thrill (2)
Pulsation	9.8% (n:38) No pulsation (0) 91.2% (n:349) Pulsation (1)

Table 3: Summary statistics of vessel diameters and patency time.

	Diameter (mm) Mean±SD Median (Min, Max)	Patency (month) Mean±SD Median (Min, Max)
BrachialArtery (n=113)	4.45±0.45 4.5 (3.3, 5.5)	17.57±15.24 14 (0, 62)
Radial Artery (n=274)	2.52±0.42 2.6 (1.3, 3.5)	15.85±14.72 11.5 (0, 64)
Basilic Vein (n=21)	3.31±0.60 3.5 (2.1, 4.2)	21.77±16.02 18 (0, 48)
Cephalic Vein (n=366)	2.47±0.64 2.3 (1.5, 4.7)	16.04±14.77 12 (0, 64)

Discussion

Accessing hemodialysis through an AVF is the preferred and recommended way by the international guidelines for long-term hemodialysis (12).

Table 4. Number and percentage of closed AVF at the 10th day, 1st month, 6th month, 1st year and 2ndof the year follow-up.

	Number of AFV at the10th day		Number of AFV At the 1st month		Number of AFV At the 6th month		Number of AFV At the 1st year		Number of AFV At the 2nd year	
	M*	F**	M*	F**	M*	F**	M*	F**	M*	F**
Brachial Artery	111	2 (1.8%)	109	4 (3.6%)	86	27 (23.9%)	63	50 (44.2%)	33	80 (70.8%)
Radial Artery	259	15 (5.5%)	253	21 (7.7%)	180	94 (34.3%)	137	137 (50.0%)	79	195 (71.2%)
Basilic Vein	19	2 (9.5%)	19	2 (9.5%)	17	4 (19.0%)	14	7 (33.3%)	10	11 (52.4%)
Cephalic Vein	351	15 (4.1%)	343	23 (6.3%)	249	117 (32%)	186	180 (49.2%)	102	264 (72.1%)

*M: Matured **F: Failed

Table 5. AVF patency rates based on Kaplan-Meier estimation.

Follow up Time	Probability Of patency	95% CI for patency rate
0	99.2%	98.4 – 100
10th day	94.3%	92.0 – 96.7
1st month	87.8%	84.6 – 91.1
6th month	68.0%	63.4 – 72.8
12th month	53.2%	48.4 – 58.6
24th month	30.9%	26.4 – 36.0

Table 6. The co-morbid diseases of the patients.

Comorbid Diseases	n	%	p-value (Log-rank test)
No comorbid diseases	31	8.01	
Hypertension	272	70.03	0.27
Diabetes	175	45.2	0.65
Atherosclerotic heart disease	82	21.2	0.64
Chronic obstructive pulmonary disease	49	12.7	0.75
Congestive heart failure	37	9.6	0.63
Atrial fibrillation	16	4.1	0.33
Asthma	16	4.1	0.72
Polycystic renal disease	14	3.61	0.45
Malignancies	13	3.4	0.87
Hypercholesterolemia	13	3.4	0.68
Cerebrovascular event	10	2.58	0.97
Parkinson`s disease	8	2.06	019
Peripheral arterial disease	8	2.06	0.38
Urinary calculus	7	1.80	0.55
Epilepsy	7	1.80	0.53

(n: count, %: percentage)

However, primary AVF failure, which means the inadequacy status for the hemodialysis after creation, is a major problem particularly for patients those are advanced aged, have diabetes mellitus and/or vascular diseases (13,14). As a result of their study, Nakata et al. found that patency rates of the advanced aged patients and diabetic patients AVF were significantly lower (10). Kazemzadeh et al. reported that patency rate of the female patients AVF were also significantly lower (15). Diehm et al. reported female sex and diabetes mellitus as risk factors for patency of venous access (16). On the other hand, Wand et al. reported that the co-morbid diseases of the patients have not a significant influence over primary failure and their success rate was 64% at the end of the 2nd year (17). In our study, mean age was 66.82±13.33, unfortunately only 8.01% of the patients have no co-morbid diseases and the patency rate was 72.55% at the end of the 2nd year. In the light of these findings we think that preoperative physical examination of the artery and vein those are planned to be used for AVF creation is not sufficient alone too, as it mentioned in the previous studies (18). As a part of the improving

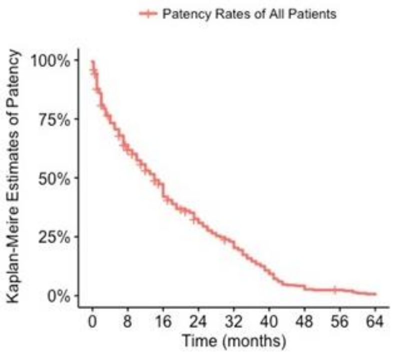

Figure 1. Survival plot of patency rates for all patients.

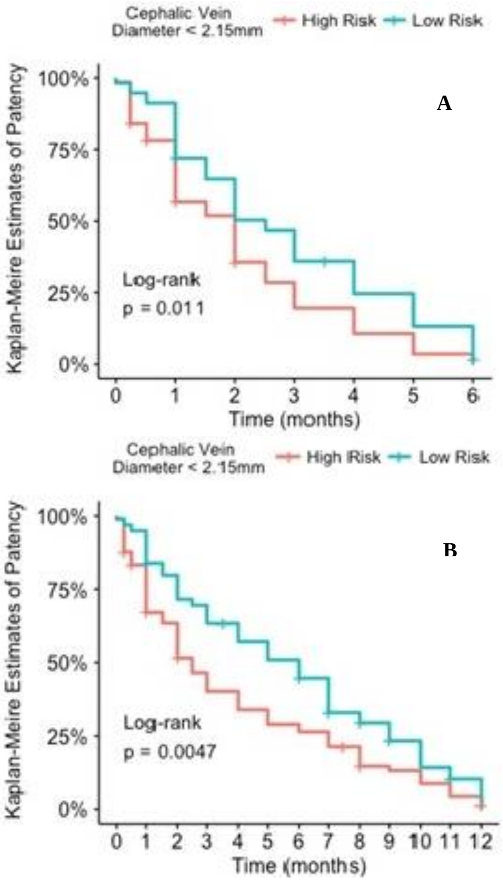

Figure 2. A: Kaplan-Meier plots of high-risk **B:** low-risk groups based on cephalic vein diameter for 6 and 12 month follow up.

efforts, Lok et al. have prepeared a scoring system to group the risk factors for dysmaturation or failure, which the advanced age, peripheral vascular disease, coronary artery disease and white race were the top clinical predictors. However, they could not able to predict the AVF maturation (19). Already, the current guidelines recommend the evaluation of the vessels with the ultrasonography beside the physical examination for improving the dysmaturation rates (20). As a simple, non-invasive technique ultrasonography gives information about both anatomic and physiologic status the vessels by using the Color Doppler mode and/or B-mode of the device (10). A blood flow of 20-40 ml/min in the radial artery might provide better results for the AVF

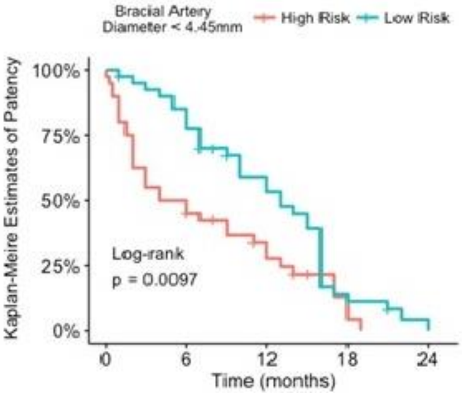

Figure 3. Kaplan-Meier plots of high-risk and low-risk groups based on brachial artery diameter for 24 month follow up.

maturation has been stated by Sato et al. as a physiological marker (21). As anatomical marker, while a diameter of less than 2.0 mm for the radial artery was stated as a risk factor for the dysmaturation (22,23), no certain diameter was recommeded for the brachial artery. In our study, we defined the cut-off value of 4.45 mm for brachial artery and obtained statistically significant result about the patency rates between less or greater diameters. So, we recommend a min 4.45 mm brachial artery diameter for a long lasting, matured AVF at the elbow level. On the other hand, the vein diameter had been stated as the main predictor for AVF maturation by a group of authors (23,24) and a diameter of 1.6-2.5 mm for cephalic vein under light tourniquet was recommended (23,25). However, there are also some studies that any relation between the patency and vein diameter could not determine (10). In our study, we also defined the cut-off value of 2.15 mm for cephalic vein and obtained statistically significant result about the patency rates between less or greater diameters. So, we recommend a min 2.15 mm cephalic vein diameter for a long lasting, matured AVF at the wrist level. At the same level, mean radial artery diameter was 2.52±0.42 mm. Mean radial artery diameter of the non-patent AVF was 2.21±0.39 mm. However, the difference was not statistically significant. As one of the results of their study, Sahasrabudhe et al. established direct relation between the thrill at the end of the surgery and AVF maturation. They got thrill from 88.91% (449 of 505) of the patients at the end of the surgery. They also stated that they began anticoagulants and early handball exercises to these patients (26). In our study, we ordered 100 mg of acetylsalicylic acid to all the patients that we created AVF. At the end of the surgery, we could not get trill only in 1.03% of the patients. We used a scale which we created in our clinic for the evaluation of the thrill and according to this scale, we got "light trill" in 9.30% of the patients. We observed that the status of "no trill" and "light trill" were incompatible with the AVF maturation. Moreover, we observed that 18.87% of the AVF which we got "strong thrill" at the end of the surgery were failed at the end of the

2nd year of the follow-up. Also, in our literature review, we have met some studies which indicate the surgical skill of the surgeon might also be the reason of dysmaturation or failure. In their study, Saran et al. stated that in their training period, surgeons who created more than 25 AVF, had lower primary failure rates than the ones who did not (27). This study was performed by only 2 cardiovascular surgeons. Both surgeons had performed much more than 25 AVF creations. So, we think that besides the presence of these much factors those can be the reason of dysmaturation or failure, surgeon`s skill should be weak or ineffective factor.

Conclusions

Today, AVF is the gold standard venous access for long-term hemodialysis and primary failure or dysmaturation is a serious problem that we have to take care. Ultrasonographic evaluation of the vessels those planned to be used is a good choice even if the physical examination of the patient is good. Arterial and venous diameters at the anastomosis site may provide us insight to create an adequate, long lasting AVF. We recommend >4.45 mm of brachial artery diameter at the elbow level >2.2 mm of radial artery and >2.15 mm of cephalic vein diameter at the wrist level. However, we could not obtain statistically significant result for radial artery diameter. Studies with larger patient population may give significant results. We also think that presence of strong thrill at the end of the AVF creation is an important marker for an adequate, long lasting AVF.

Limitations

This study is a single center performed study and gives the results of only our clinic. Structures and diameters of the target vessels were evaluated in this study. However, blood flow in the target vessels are also important parameters for the primary failure and/or dysmaturation. Performing a multi-center study including the blood flows in the target vessels may give more significant results about the issue.

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