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ORIGINAL ARTICLE

The Prevalence of Systolic Dysfunction in Patients on Hemodialysis with High Flow Arteriovenous Fistula

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ABSTRACT

Background: *Cardiovascular disease is the primary cause of mortality and morbidity in patients with chronic kidney disease. Arteriovenous fistulas have the uppermost long-term patency rate of all hemodialysis access options. Creation of a fistula may cause harmful effects on cardiac structure and function. The physiological effects could worsen until myocardial decompensation, which would cause the ejection fraction to drop and result in left ventricular hypertrophy and/or heart failure.*

Method: *This cross-sectional study was done at Imam Al-Hussein medical city and Imam Al-Hassan hospital in Karbala holy city starting from January to June 2022. One hundred fifty patients with end stage kidney disease were included in this study. All patients were assessed with color doppler ultrasonography for fistulas and transthoracic echocardiography for assessment of cardiac function.*

Results: *The prevalence of high flow fistulas was 41.3% (62 patients), 50% were of normal flow (75 patients), while 8.7% (13 patients) with low flow.*

Conclusion: *There`s a statistically significant association between the type of flow in the fistulas and the systolic function of the heart (P. value = 0.032). The patients with high flow velocity fistulas had a significantly higher prevalence of reduced systolic function. In addition, the patients with arm fistulas had more flow velocities than those with forearm fistulas.*

Keywords: Arteriovenous fistula, High Flow, Systolic Dysfunction, Hemodialysis

1. INTRODUCTION

Arteriovenous fistula (AVF) placement for hemodialysis (HD) might result in excessive cardiac output and, as a result, high-output heart failure (HOHF) (1). Due to decreased systemic vascular resistance, higher myocardial contractility, and an increase in preload, stroke volume, and heart rate, there is a simultaneous increase in cardiac output and a decrease in sub-endocardial perfusion (high myocardial demands) immediately after AVF development (2,3). After 4-6 weeks, arterialization—the thickening of the vascular wall—is brought on by increasing pressure that is passed from the artery to the vein through the fistula (4). The volume of blood in circulation grows over the next weeks along with an increase in atrial and brain natriuretic peptides (5,6). Atrial and ventricular chamber dimensions and function will change as the fistula grows in size and blood flow. This will also cause additional increases in left ventricular filling pressure (5,6,7,8). The physiological effects might worsen until myocardial decompensation, LV dilatability, and a fall in ejection fraction (EF), which could result in LVH or heart failure (5,9). All of these modifications come on top of the LVH, dilatation, and dysfunction that are already present due to the progressive uremic cardiomyopathy (8). Today, a high flow access has no established definition (HFA). Reference ranges for HFA were not produced for the National Kidney Foundation Kidney Dialysis Outcome Quality Initiative (NKF/KDOQI) or European Best Practice Guidelines sections on vascular access. Contrarily, the Vascular Access Society (VAS) defines a high-flow access as having a flow between 1 and 1.5 l/min or one where the flow is greater than 20% of cardiac output (7). Heart failure is typically more likely to develop in fistulas that flow more than 2 L/min and in those that are in the upper arm (7,10,11). If symptoms of heart failure appear, it is safe to assume that the AVF flow is too high. High-flow AVF, according to some specialists, occurs even in the absence of heart failure symptoms when flow surpasses 1500–2000 ml/min (12,13). Even months or years after the formation of the fistula, the flow velocity may increase as a result of remodeling, particularly of the feeding artery and arteriovenous anastomosis (14).

2. METHODOLOGY

A cross-sectional study was done at Imam Al-Hussein medical city and Imam Al-Hassan hospital in Karbala holy city starting from January to June 2022. One hundred fifty Iraqi patients were included in the study. All patients have AVF as a vascular access for HD and their fistulas examined to be patent by palpation of thrill. Patients with history of ischemic heart disease, valvular heart disease, heart failure or any symptoms related before fistula creation, also clinically failed AVF and patients with incomplete data were excluded. A pre-constructed data collection sheet was prepared. General Electric Healthcare Doppler ultrasound machines were used for assessment of AVF flow with linear array probe and frequencies (6-12 MHz). All patients underwent ultrasound just before their HD sessions. Doppler angle was set at ≤ 60° (16). The entire vascular diameter has measured to avoid neglecting low-speed blood flow along the vascular wall (16,17) (**Figure 1**).

The following formula on which flow velocity measurement based:

Qa (ml/min) = TAMEAN (cm/s) x section area [π r2 (cm2)] x 60

Where:

Qa: flow velocity, TAMEAN: time averaged mean velocity, r: inner diameter, π = 3.14.

Echocardiograms obtained using Doppler echocardiography machine (Philips Healthcare) with a S5-1-MHz transducer. On 2D-guided M-mode images, LV internal dimensions are measured at each of end-diastole and end-systole from the tissue-blood border (white-black transition) (**Figure 2**). The following formula on which ejection fraction measurements based:

EF = (EDV - ESV / EDV) *100% (18).

Where:

EF: Ejection fraction, EDV: End diastolic volume, ESV: End systolic volume.

LV volume is estimated by Teichholz formula:

Volume = 7/(2.4 + D) × D3

Where: D: linear LV diameter (19).

Data analysis performed using international business machines statistical package for social sciences (IBM SPSS) software for Microsoft windows version 26. Chi-square test, ANOVA test were used, and P. value was considered significant at level ≤ 0.05.

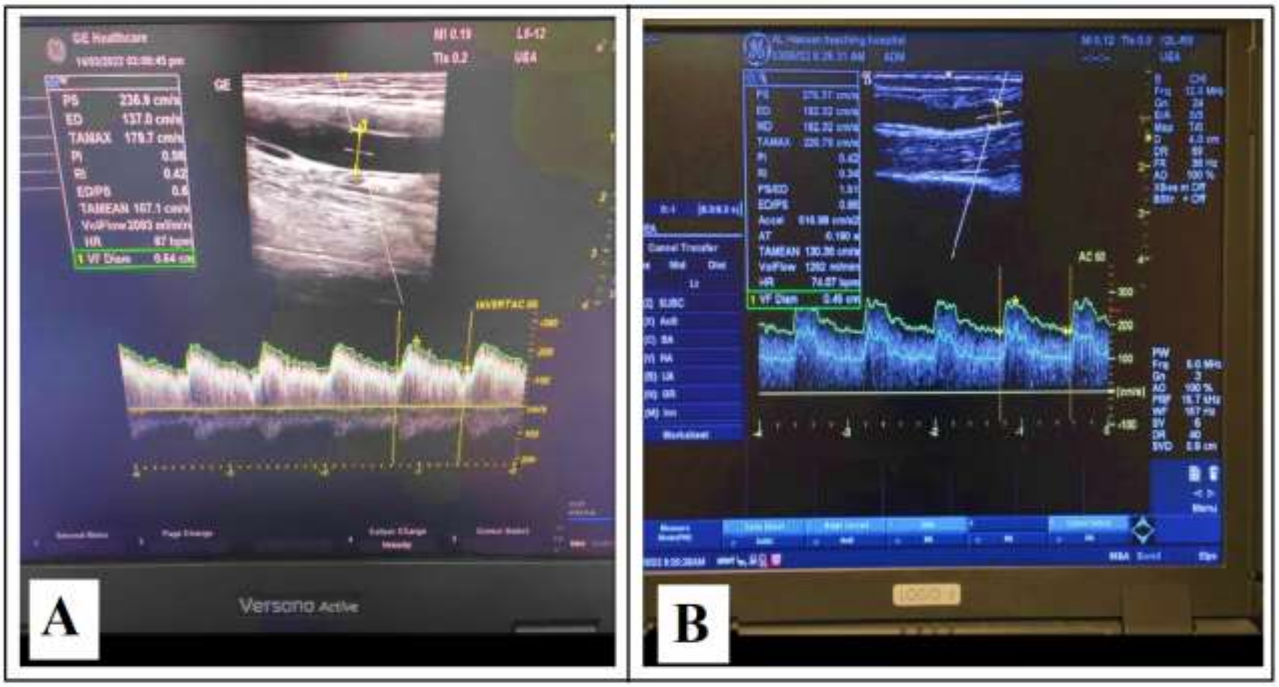

Figure 1. Ultra-sonographic flow velocity measurements of native arteriovenous fistula
A- an example of high flow velocity AVF (GE Healthcare versana active machine)
B- an example of normal flow velocity AVF (GE Healthcare LOGIC e machine)

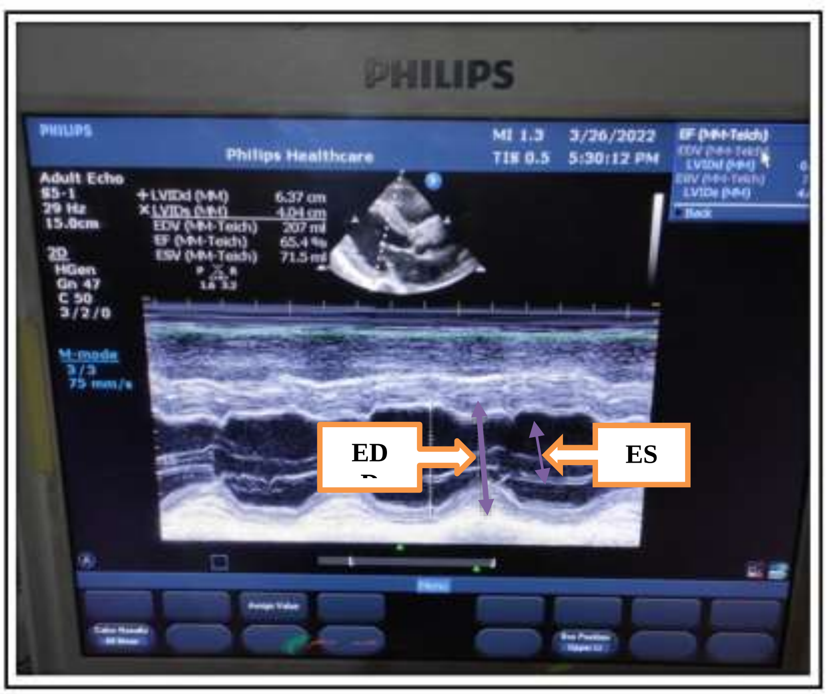

Figure (2) Left ventricular M-mode measurements: parasternal long axis view.

ESD: End-systolic dimension, EDD: End-diastolic dimension.

Definitions:

Left ventricular systolic function classified according to the American College of Cardiology (ACC): Hyper dynamic: LVEF < 70%, Normal: LVEF 50% - 70%, Mild dysfunction: LVEF 40% - 49%, Moderate dysfunction: LVEF 30% - 39%, Severe dysfunction: LVEF > 30% (20).

AVF flow velocity classified according to NKF/KDOQI criteria for the definition of AVF flow velocity: Low flow > 600 ml/min, Normal flow (600 ml/min to 1500 ml/min), High flow AVF ≤ 1500 ml/min (7,21).

3. RESULTS

This study includes one hundred fifty patients with chronic kidney disease on HD with AVF as their vascular access. Of the total 150 patients, 87 patients were males (58%) and 63 were females (42%) as shown in (**Table 1**). The mean age of the patients included in this study was 50.39 ± 13.9, table 3-4. The prevalence of high flow velocity AVF was 41.3% (62 patients), 50% of the patients have normal velocity AVF (75 patients) while 8.7% (13 patients) with low velocity AVF, (**Table 2**). The variables of the patients were studied using chi-square and ANOVA tests. There`s a statistically significant adverse impact for the chronic diseases (diabetes mellitus, hypertension), and site of AVF on the flow velocity of the AVF (P. value > 0.05 by using Chi-square test) while there is no statistically significant association between gender, BMI, family history of CKD, number of HD sessions per week, number of AVF created, with the flow velocity of the AVF (P. value < 0.05 by using Chi-square test), (**Table 3**). There is no statistically significant association between the age of the patients, the duration of CKD and the duration of the AVF (time since creation) with the flow velocity in the AVF (P. value < 0.05 by using ANOVA test), (**Table 4**). There`s a statistically significant association between the flow velocity of the AVF and the systolic function of the heart (P. value 0.032) , (**Table 5**).

Table 1. Gender distribution of the patients

Gender	No.	%
Male	87	58
Female	63	42
Total	150	100

Table 2. Distribution according to AVF flow velocity

AVF flow velocity	No.	%	Mean ± SD (ml/min.)
Low	13	8.7	460.7 ± 101.1
Normal	75	50	963.3 ± 275.9
High	62	41.3	2269.4 ± 683.7
Total	150	100	1459.2 ± 436.6

AVF= Arteriovenous fistula, SD: Standard deviation

Table 3. Association between variables and AVF flow velocity

Variable		Flow velocity			Total	P. value
		Low	Normal	High		
Gender	Male	9	38	40	87	0.182
	Female	4	37	22	63	
Body mass index	Normal	10	39	27	76	0.225
	Overweight	1	24	24	49	
	Obese	2	12	11	25	
Chronic diseases	Negative	1	7	6	14	<0.001
	DM	0	2	0	2	
	HTN	5	31	50	86	
	DM + HTN	7	35	6	48	
Family history of CKD	Positive	1	11	11	23	0.642
	Negative	12	64	51	127	
Number of hemodialysis sessions per week	1	0	5	2	7	0.739
	2	6	34	32	72	
	3	7	36	27	70	
	4	0	0	1	1	
AVF site	Arm	6	60	57	123	<0.001
	Forearm	7	15	5	27	
AVF number	1	12	63	57	132	0.497
	2	1	10	4	15	
	3	0	2	0	2	
	4	0	0	1	1	
Total		13	75	62	150	

Chi-square test used in comparison. DM : diabetes mellitus, HTN : hypertension, CKD : chronic kidney disease.

Table 4. Association between variables and AVF flow velocity

Variable	Flow velocity	No.	Mean ± SD	P. value
Age of patients (years)	Low	13	50.54 ± 13.10	0.134
	Normal	75	52.55 ± 13.60	
	High	62	47.74 ± 14.20	
Total		150	50.39 ± 13.90	
Duration of CKD (years)	Low	13	2.65 ± 1.90	0.574
	Normal	75	3.82 ± 4.20	
	High	62	3.67 ± 3.10	
Total		150	3.66 ± 3.60	
AVF duration (years)	Low	13	1.76 ± 1.60	0.130
	Normal	75	1.89 ± 1.50	
	High	62	2.52 ± 2.30	
Total		150	2.14 ± 1.90	

ANOVA test used in all comparisons. AVF : arteriovenous fistula, SD: Standard deviation

Table 5. Association between AVF flow velocity and systolic function of the heart

Systolic function of the heart	AVF flow velocity						Total		P. value
	Low		Normal		High				
	No.	%	No.	%	No.	%	No.	%	
Mild dysfunction	3	2	2	1.3	8	5.3	13	8.6	0.032
Normal	7	4.7	60	40	48	32	115	76.7	
Hyper- dynamic	3	2	13	8.7	6	4	22	14.7	
Total	13	8.7	75	50	62	41.3	150	100	
EF (Mean ± SD)	63 % ± 8.3 %				60 % ± 8.9 %		61.7 % ± 8.1		

P. value estimated by using Chi-square test, SD: Standard deviation

4. DISCUSSION

The association between AVF flow velocity and cardiovascular complications such as heart failure has been reported previously. The current study is directed to estimate the prevalence of high flow velocity AVF in our population and to assess the relationship between AVF flow velocity and cardiac systolic function. Our data established that the prevalence of high flow velocity AVF was 41.3% using 1500 ml/min as cut off point with a mean velocity flow of 2269.4 ± 683.7 for high flow AVF, 963.3 ± 275.9 for the normal flow AVF and 460.7 ± 101.1 for the low flow AVF. With a mean flow of 3430.13 1256.28 ml/min for the HFA group as opposed to a mean flow of 958.63 487.35 ml/min for the non-HFA group, Saleh et al. (22) showed that the prevalence of HFA was 24% in 2018 using 2000 ml/min as a cutoff point. Study conducted by Schier et al (23) 2013 evaluated the prevalence of AVF closure brought on by HOHF in recipients of renal transplants. 29 out of 113 patients (or 25.7%) needed an AVF closure as a result of HF symptoms, according to the authors' study. In comparison to the non-closure group, the mean Qa in the AVF closure group was 2197.2 ml/min as opposed to 850.9 ml/min. Heart failure may be predisposed to by specific AVF or patient features. In our study, high flow velocity AVF patients have lower EF than normal and low flow AVF patients combined, with a mean value of 60 8.9% versus 63 ± 8.3%. (table 5). Saleh et al. reported that in 2018, the HFA group of patients had a considerably reduced EF with a mean value of 57.32% as opposed to the non-HFA group's 62.90%. With a statistically significant correlation between HFA and compromised LV function, 12% (8 patients) of patients exhibited LV systolic dysfunction (EF 55%). (22). Another study at 2013 in China when fifty HD patients who had used AVF as the vascular access were included. Cardiac output, cardiac index and peripheral vascular resistance (PVR) measured using the ultrasound dilution technique. The results showed that CO, CI were significantly increased, and PVR was reduced when the Qa of AVF was more than 2 l/min. Echocardiography showed when Qa increased the EF reduced (24). Depending on all of these results, this study depends on EF estimation by M-mode echocardiography as assessment of cardiac systolic function in HD patients with AVF. It is easily measured and nearly the same results were produced.

In this study, patients with both arm and forearm AVFs were included. The brachial artery used to measure Qa in the arm AVFs and this is consistent with Lomonte et.al study (25) who did the measurements in the brachial artery too, where there is a proven correlation with AVF flow velocity. On the other hand, measurements using the radial artery in the forearm AVFs can be under-estimated, given that in a great number of cases, the AVF receives part of the blood flow from the ulnar artery through the palmar arch. When the fistula is created, the brachial artery's normal blood flow, which is close to 50 ml/min, rapidly increases by 10- to 20-fold (25). As access flow has been shown to be up to twice as high in arms compared with forearm fistulas, arm AVFs typically have the highest Qa. (7,26). In our study, 46.3% of patients who have arm AVFs with Qa exceed 1500 ml/min compared to 18.5% those who have forearm AVFs with high Qa. According to Basile et alobservational .'s cross-sectional study from 2016, which included 56 patients with lower arm AVFs and 30 with upper arm AVFs, upper arm AVFs statistically significantly increased Qa and decreased SVR compared to lower arm AVFs (27). In 2018, 100 chronic ESRD patients undergoing HD sessions at the dialysis center of Ain Shams University were a part of a study in Egypt (22). 34 females and 66 males, with a mean age of 48.48 13.75 years, made up the study population. Both age and gender show no statistical significant relationships with flow velocity in AVF as shown also in this study where of total 150 patients enrolled in the study 58% are males and 42% are females with mean age 50.39 ± 13.9. These random sampling results means that there is no specific gender or age preference to be affected by high flow velocity AVF, however high Qa fistula patients have slightly lower mean age group than non-high flow (table 4). In our study the relationship between BMI and Qa was not statistically significant (P. value <0.05). These results may due to increment in the prevalence of obesity among population in Iraq in last years. A study done at 2015 in Iraq (28) shows 30.8% of the study sample were normal weight (BMI 18.5–24.9 kg/m2), 31.8% were overweight (25.0–29.9 kg/m2), 33.9% were obese and the rest 3.5% were underweight (BMI <18.5 kg/m2). The relationship between BMI and Qa in our study is different from that study in Egypt that shows significant relationship between these two variables (22).

As hypertension is strongly associated with CKD both as a cause and as a complication, most of the patients included in our study had hypertension (134 patients) (89.3%) and one third were diabetic (50 patients) (33.3%) (table 3). In our study, the relationship between chronic diseases (hypertension, diabetes mellitus or both) and Qa value was statistically significant as a whole (table 3) but in 2018 Saleh et al. study (22) when the relationship between the flow velocity and same chronic diseases studied separately both were statistically not significant. The number of HD sessions per week, the duration of CKD and the duration of AVF since creation, all showed no statistically significant relationship with Qa. These relationships were also studied in Egypt and showed the same results (22).

5. CONCLUSIONS

The patients with high flow velocity AVFs have higher prevalence of reduced systolic function (ejection fraction). In addition, the patients with arm AVFs develop higher flow velocities than those with forearm AVFs.

Ethical Approval:

All ethical issues were approved by the author. Data collection and patients enrollment were in accordance with Declaration of Helsinki of World Medical Association , 2013 for the ethical principles of researches involving human. Signed informed consent was obtained from each participant and data were kept confidentially.

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